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Asymmetric organocatalyzed reaction sequence to construct bridged bicyclic acetals via multicatalytic process involving iminium catalysis and anion-binding catalysis

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Supporting Information

Content

A. General information

The ^{1}H and ^{13}C NMR spectra were recorded at 500 MHz or 600 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). Coupling constants are given in Hz. The following abbreviations are used to indicate the multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. High-resolution mass spectra (HRMS) were obtained from the Waters Q-Tof Ultima Global. X-ray data were obtained from Zhongke chemical technology service center. Optical rotations are reported as follows: $[\alpha]_D^{20}$ (c in g per 100 mL, solvent: $CHCl_3$).

Note: NMR signals containing common solvent contaminants were list. H_2O in $CDCl_3$ at 1.56 ppm ^{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; Grease in $CDCl_3$ at 0.86 (m), 1.26 (br, s) ppm ^{1}H NMR; *n*-hexane in $CDCl_3$ at 0.88 (t), 1.26 (m) 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 a Hitachi Chromaste. Daicel Chiralpak IA, IC, ID, or AD 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*) catalysts.

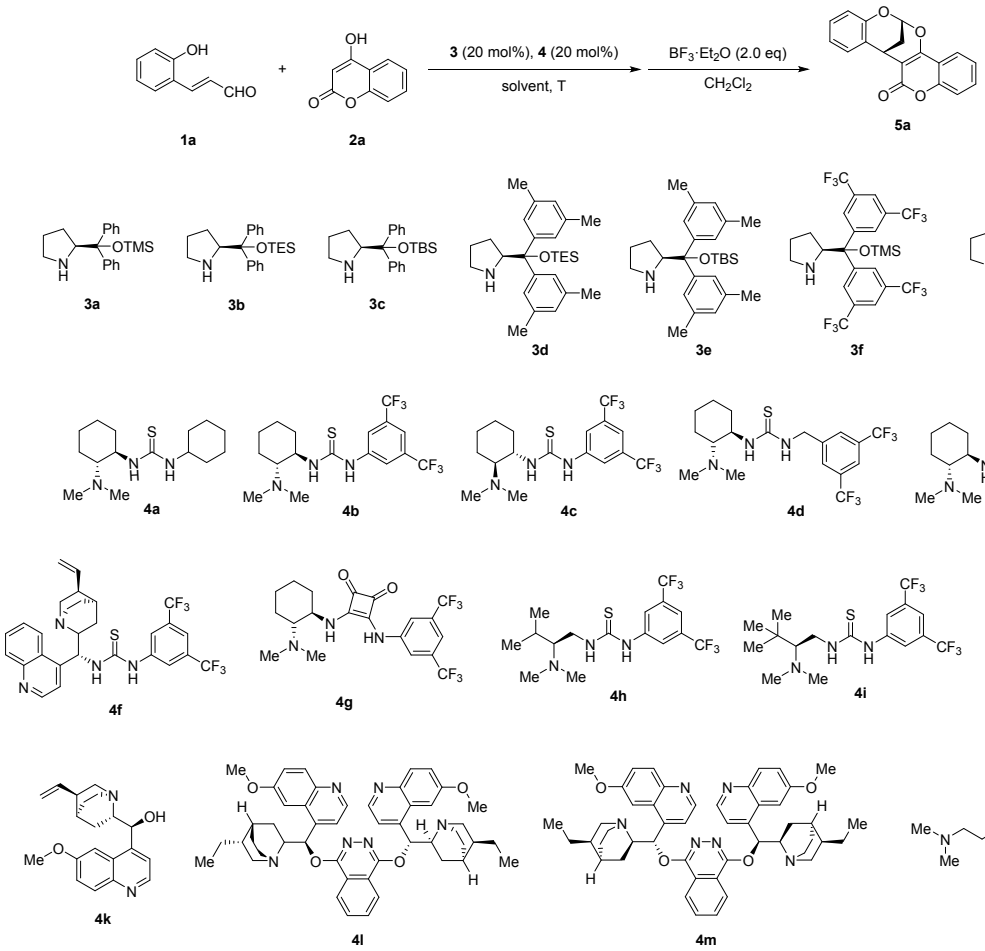
Commercial reagents and solvents were purchased from Sigma Aldrich, Fluka, and Alfa Aesar used as received, without further purification. The 2-hydroxy cinnamaldehydes **1** were prepared according to literature procedures.[1] 4-

[1] Chen, Y.-H.; Sun, X.-L.; Guan, H.-S.; Liu, Y.-K. *J. Org. Chem.* **2017**, *82*, 4774.

Hydroxycoumarins **2** were prepared according to literature procedures.[2]

[2] Nolan, K. A.; Doncaster, J. R.; Dunstan, M. S.; Scott, K. A.; Frenkel, A. D.; Siegel, D.; Ross, D.; Barnes, J.; Levy, C.; Leys, D.; Whitehead, R. C.; Stratford, I. J.; Bryce, R. A., *J. Med. Chem*. **2009**, *52*, 7142.

B. Optimization of the reaction conditions



entry [b]	3	4	solvent	T(°C)	t (h) [c]	yield (%) [d]	ee (%) [e]
1	**3a**	-	CH_2Cl_2	25	24	45	28
2	**3b**	-	CH_2Cl_2	25	24	19	23
3	**3c**	-	CH_2Cl_2	25	24	17	30
4	**3d**	-	CH_2Cl_2	25	24	23	3
5	**3e**	-	CH_2Cl_2	25	24	18	5
6	**3f**	-	CH_2Cl_2	25	5	41	77
7	**3g**	-	CH_2Cl_2	25	12	27	86
8 [f]	**3f**	-	CH_2Cl_2	25	5	39	71

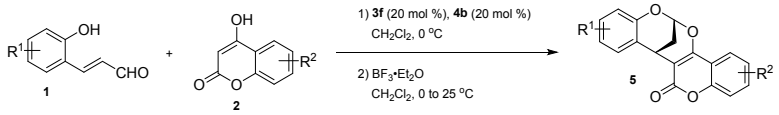
9[g]	**3f**	-	CH_2Cl_2	25	5	64	77
10	**3f**	-	CH_2Cl_2	25	5	51	79
11	**3f**	-	CH_2Cl_2	0	72	64	95
12[g]	**3f**	-	CH_2Cl_2	0	20	85	90
13[f]	**3f**	**4a**	CH_2Cl_2	0	18	73	89
14	**3f**	**4a**	CH_2Cl_2	0	18	70	93
15	**3f**	**4b**	CH_2Cl_2	0	18	75	97
16	**3f**	**4c**	CH_2Cl_2	0	18	62	96
17	**3f**	**4d**	CH_2Cl_2	0	18	55	96
18	**3f**	**4e**	CH_2Cl_2	0	18	65	97
19	**3f**	**4f**	CH_2Cl_2	0	30	75	95
20	**3f**	**4g**	CH_2Cl_2	0	30	80	92
21	**3f**	**4h**	CH_2Cl_2	0	18	62	96
22	**3f**	**4i**	CH_2Cl_2	0	24	68	94
23	**3f**	**4j**	CH_2Cl_2	0	24	43	94
24	**3f**	**4k**	CH_2Cl_2	0	24	46	95
25	**3f**	**4l**	CH_2Cl_2	0	24	68	90
26	**3f**	**4m**	CH_2Cl_2	0	24	31	80
27	**3f**	**4b**	DCE	0	36	76	96
28	**3f**	**4b**	$CHCl_3$	0	48	73	96
29	**3f**	**4b**	toluene	0	48	28	77
30	**3f**	**4b**	xylene	0	48	25	80
31[h]	**3f**	**4b**	CH_2Cl_2	0	25	73	98
32[i]	**3f**	**4b**	CH_2Cl_2	0	48	68	99
33[f][h]	**3f**	**4b**	CH_2Cl_2	0	24	68	73

34[h]	**3f**	**4n**	CH_2Cl_2	0	22	68	95
35[h] [j]	**3f**	**4b**	CH_2Cl_2	0	>120	68	86

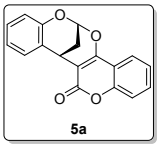
[*a*] Unless otherwise specified, all reactions were carried out using **1a** (0.10 mmol, 1.0 equiv), **2a** (0.12 mmol, 1.2 equiv) in solvent (0.2 mL) with cat. **3** (20 mol %) and co-cat. **4** (20 mol %) at 0 °C. After full conversion of **1a** ,0.3 mL solvent was added to the solution, then BF_3•Et_2O (2.0 eq) was added in one pot. After workup, the mixture was purified by flash chromatography on silica gel to afford **5a**. [*b*] Entry 1-9 were performed by two steps After full conversion of **1a**, the crude product was obtained by flash chromatography on silica gel. Then the crude product was dissolved in 0.5 mL CH_2Cl_2, 1.0 eq BF_3•Et_2O was added to the solution and allowed to stir at 25 °C. [*c*] For the first step. [*d*] Isolated yield of **5a**. [*e*] Determined by HPLC analyses of isolated compound **5a** on chiral stationary phases. [*f*] Use BA (0.2 eq) as additive. [*g*] Use DIPEA (0.2 eq) as additive. [*h*] Reaction in solvent (0.5 mL). [*i*] Reaction in solvent (1.0 mL). [*j*] Use **3f** (10 mmol %) and **4b** (10 mmol %).

TMS = trimethylsilyl
TES = triethylsilyl
TBS = (1,1-dimethylethyl)dimethylsilyl
DCE = 1,2-dichloroethane
BA = benzoic acid
DIPEA = N,N-diisopropylethylamine

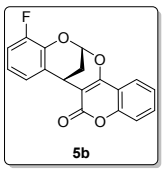
C. Scope of the reaction



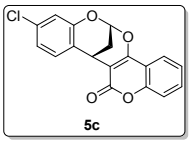
General procedure: A glass vial equipped with a magnetic stirring bar was charged with **1** (0.10 mmol, 1.0 equiv), catalyst **3f** (0.02 mmol, 0.2 equiv) and catalyst **4b** (0.02 mmol, 0.2 equiv) in CH_2Cl_2 (0.5 mL) and the resulting solution was stirred for about 10 min at 0 °C. Then **2** (0.12 mmol, 1.2 equiv) was added. After full conversion of first step, BF_3•Et_2O (2.0 eq) was added to the reaction mixture in situ and the reaction mixture was allowed to stir at 25 °C. After completion of the reaction, the reaction mixture was purified by flash chromatography on silica gel to give product **5** for NMR and HPLC analysis. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



5a was obtained as a white solid 21.2 mg in 73% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 8/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.81 (d, J = 7.8 Hz, 1H), 7.52-7.46 (m, 2H), 7.30-7.23 (m, 2H), 7.18 – 7.11 (m, 1H), 6.94 (t, J = 8.0 Hz, 2H), 6.40 (d, J = 1.6 Hz, 1H), 4.29 (s, 1H), 2.38 – 2.31 (m, 1H), 2.28 – 2.22 (m, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 161.7, 157.8, 152.5, 150.5, 132.1, 128.6, 128.5, 125.5, 124.2, 123.0, 122.1, 116.8, 116.4, 115.1, 106.5, 93.2, 25.5, 24.6 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{18}H_{13}O_4^+$ 293.0808; found: 293.0809. **$[\alpha]_D^{20}$** -67.13 (c = 0.32 in $CHCl_3$).The enantiomeric excess was determined by HPLC using Chiralpak IC column [*n*-hexane/*i*-PrOH= 80/20, 1 mL/min], λ = 210 nm, t_{major} = 16.01 min, t_{minor} = 18.69 min, **ee = 98%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1.**

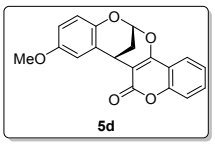


5b was obtained as a white solid 15 mg in 48% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 8/1).**^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.84-7.78 (m, 1H), 7.57 – 7.47 (m, 1H), 7.31-7.24 (m, 3H), 6.99 – 6.91 (m, 1H), 6.91-6.83 (m, 1H), 6.48 (d, J = 1.8 Hz, 1H), 4.33 (s, 1H), 2.39 – 2.33 (m, 1H), 2.32 – 2.25 (m, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 161.3, 157.5, 152.3, 151.9, 149.9, 138.6(d, J_{CF} = 11.0 Hz), 132.1, 127.9, 124.1 (d, J_{CF} = 163.0 Hz), 123.3(d, J_{CF} = 3.5 Hz), 121.8(d, J_{CF} = 7.0 Hz), 116.6, 115.2(d, J_{CF} = 17.8 Hz), 114.7, 105.8, 92.6, 25.0, 24.0 (d, J_{CF} = 2.7 Hz) ppm. **^{19}F NMR** (400 MHz, $CDCl_3$) δ -135.7 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{18}H_{12}FO_4^+$ 311.0714; found:311.0711. **$[\alpha]_D^{20}$** -35.45 (c = 0.67 in $CHCl_3$). The enantiomeric excess was determined by HPLC using Chiralpak IC column [*n*-hexane/*i*-PrOH= 80/20, 1 mL/min], λ = 210 nm, t_{major} = 15.95 min, t_{minor} = 15.05 min, **ee = 99%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1.**



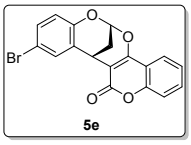
5c was obtained as a white solid 20 mg in 61% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 8/1).**^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.81 (d, J = 7.5 Hz, 1H), 7.55 – 7.47 (m, 1H), 7.41 (d, J = 8.1 Hz, 1H), 7.28 (d, J = 7.9 Hz, 2H), 6.97 – 6.88 (m, 2H), 6.38 (d, J = 1.5 Hz, 1H), 4.27 (s, 1H), 2.31 (d, J = 13.4 Hz, 1H), 2.26 (d, J = 13.4 Hz, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 161.6, 157.7, 152.5, 151.2, 133.7, 132.3, 129.3, 124.3, 124.1, 123.0, 122.4, 116.9, 116.9, 115.0, 106.2, 93.0, 25.3, 24.2 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{18}H_{12}ClO_4^+$ 327.0419; found:327.0420. **$[\alpha]_D^{20}$** -34.06 (c = 1.67 in $CHCl_3$). The enantiomeric excess was determined by HPLC using Chiralpak IC column [*n*-hexane/*i*-PrOH= 80/20, 1 mL/min], λ = 210 nm, t_{major} = 12.61 min, t_{minor} = 11.75 min, **ee = 99%**. The diastereomeric ratio was determined by ^{1}H NMR,

***dr* >20:1.**



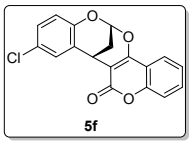
5d

5d was obtained as a white solid 15.4 mg in 48% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 8/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.8 Hz, 1H), 7.54 – 7.43 (m, 1H), 7.30-7.22 (m, 2H), 7.11 (d, *J* = 7.7 Hz, 1H), 6.90 (t, *J* = 7.9 Hz, 1H), 6.77 (d, *J* = 8.1 Hz, 1H), 6.51 (d, *J* = 1.4 Hz, 1H), 4.31 (s, 1H), 3.87 (s, 3H), 2.36 (d, *J* = 13.4 Hz, 1H), 2.24 (d, *J* = 13.4 Hz, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 161.5, 157.7, 152.3, 147.8, 139.5, 131.9, 126.3, 124.0, 122.9, 121.9, 120.3, 116.6, 114.9, 110.5, 106.2, 92.8, 55.9, 25.0, 24.2 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{19}H_{15}O_5^+$ 323.0914; found: 323.0915. **$[\alpha]_D^{20}$** -30.94 (c = 1.25 in $CHCl_3$). The enantiomeric excess was determined by HPLC using Chiralpak IC column [*n*-hexane/*i*-PrOH= 80/20, 1 mL/min], λ = 210 nm, t_{major} = 34.49 min, t_{minor} = 31.84 min, **ee = 97%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1.**



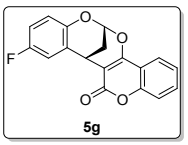
5e

5e was obtained as a white solid 25.6 mg in 69% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 8/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.9 Hz, 1H), 7.61 (d, *J* = 1.8 Hz, 1H), 7.51 (dd, *J* = 8.2, 7.4 Hz, 1H), 7.32 – 7.20 (m, 3H), 6.80 (d, *J* = 8.6 Hz, 1H), 6.38 (s, 1H), 4.24 (s, 1H), 2.30 (d, *J* = 13.5 Hz, 1H), 2.24 (d, *J* = 13.5 Hz, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 161.3, 157.6, 152.3, 149.5, 132.1, 131.2, 130.8, 127.3, 124.1, 122.8, 118.0, 116.7, 114.7, 114.1, 105.7, 92.8, 24.9, 24.2 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{18}H_{12}BrO_4^+$ 370.9913; found: 370.9918. **$[\alpha]_D^{20}$** 66.15 (c = 1.67 in $CHCl_3$). The enantiomeric excess was determined by HPLC using Chiralpak IC column [*n*-hexane/*i*-PrOH= 80/20, 1 mL/min], λ = 210 nm, t_{major} = 19.55 min, t_{minor} = 17.85 min, **ee = 86%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1.**



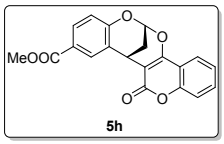
5f

5f was obtained as a white solid 18.1 mg in 55% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 8/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.81 (d, J = 7.9 Hz, 1H), 7.51 (t, J = 7.8 Hz, 1H), 7.47 (d, J = 1.9 Hz, 1H), 7.34 – 7.23 (m, 2H), 7.10 (dd, J = 8.7, 1.8 Hz, 1H), 6.86 (d, J = 8.6 Hz, 1H), 6.38 (s, 1H), 4.25 (s, 1H), 2.31 (d, J = 13.5 Hz, 1H), 2.25 (d, J = 13.5 Hz, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 161.5, 157.8, 152.6, 149.2, 132.4, 128.5, 128.2, 127.0, 127.0, 124.3, 123.0, 117.7, 116.9, 115.0, 105.9, 93.1, 25.2, 24.5 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{18}H_{12}ClO_4^+$ 327.0419; found: 327.0415. **$[\alpha]_D^{20}$** 32.33 (c = 1.5 in $CHCl_3$). The enantiomeric excess was determined by HPLC using Chiralpak IC column [*n*-hexane/*i*-PrOH= 80/20, 1 mL/min], λ = 210 nm, t_{major} = 18.48 min, t_{minor} = 16.16 min, **ee = 91%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1.**



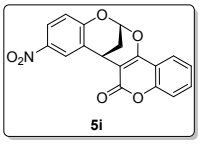
5g

5g was obtained as a white solid 19.6 mg in 63% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 8/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.83 – 7.74 (m, 1H), 7.54 – 7.45 (m, 1H), 7.30-7.23 (m, 2H), 7.20 (dd, J = 8.2, 2.7 Hz, 1H), 6.37 (d, J = 1.7 Hz, 1H), 4.24 (d, J = 1.6 Hz, 1H), 2.31 (dt, J = 13.4, 2.2 Hz, 1H), 2.24 (dt, J = 13.5, 2.5 Hz, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 161.6, 158.5, 157.9, 156.6, 152.5, 146.5, 132.3, 126.7(d, J_{CF}= 7.8 Hz), 124.3, 123.0, 117.3(d, J_{CF} = 8.1 Hz), 116.9, 115.2(d, J_{CF} = 47.6 Hz), 115.0, 105.9, 93.2, 25.2, 24.7 ppm. **^{19}F NMR** (400 MHz, $CDCl_3$) δ -121.6 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{18}H_{12}FO_4^+$ 311.0714; found: 311.0716. **$[\alpha]_D^{20}$** -39.76 (c = 1.58 in $CHCl_3$). The enantiomeric excess was determined by HPLC using Chiralpak IC column [*n*-hexane/*i*-PrOH= 80/20, 1 mL/min], λ = 210 nm, t_{major} = 16.72 min, t_{minor} = 15.53 min, **ee = 97%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1.**



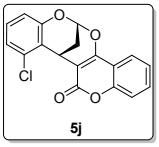
5h

5h was obtained as a white solid 21.6 mg in 59% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.16 (d, J = 2.1 Hz, 1H), 7.86 (dd, J = 8.5, 2.1 Hz, 1H), 7.81 (dd, J = 8.2, 1.5 Hz, 1H), 7.53 – 7.49 (m, 1H), 7.32 – 7.26 (m, 2H), 6.96 (d, J = 8.5 Hz, 1H), 6.43 (q, J = 1.9 Hz, 1H), 4.34 (d, J = 1.8 Hz, 1H), 3.88 (s, 3H), 2.37 – 2.25 (m, 2H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.5, 161.3, 157.3, 154.3, 152.4, 132.2, 130.3, 130.0, 125.3, 124.1, 124.1, 122.8, 116.7, 116.4, 114.7, 105.9, 92.9, 52.0, 25.1, 24.4 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{20}H_{15}O_6^+$ 351.0863; found: 351.0861. **$[\alpha]_D^{20}$** 5.76 (c = 1.67 in $CHCl_3$) The enantiomeric excess was determined by HPLC using Chiralpak IA column [*n*-hexane/*i*-PrOH= 70/30, 1 mL/min], λ = 210 nm, t_{major} = 25.15 min, t_{minor} = 11.96 min, **ee = 97%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1.**



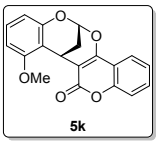
5i

5i was obtained as a white solid 12 mg in 36% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.41 (d, J = 2.7 Hz, 1H), 8.06 (dd, J = 9.0, 2.7 Hz, 1H), 7.82 (dd, J = 8.2, 1.5 Hz, 1H), 7.59 – 7.50 (m, 1H), 7.30 (dd, J = 7.7, 6.0 Hz, 2H), 7.03 (d, J = 9.0 Hz, 1H), 6.47 (d, J = 1.9 Hz, 1H), 4.40 (d, J = 1.8 Hz, 1H), 2.40 – 2.29 (m, 2H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 157.3, 155.7, 152.4, 142.3, 132.5, 126.2, 124.4, 124.3, 124.2, 122.8, 116.9, 116.9, 114.5, 105.3, 92.9, 24.8, 24.4 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{18}H_{12}NO_6^+$ 338.0659; found: 338.0656. **$[\alpha]_D^{20}$ -**45.55 (c = 0.75 in $CHCl_3$). The enantiomeric excess was determined by HPLC using Chiralpak IA column [*n*-hexane/*i*-PrOH= 65/35, 1 mL/min], λ = 210 nm, t_{major} = 14.11 min, t_{minor} = 12.17 min, **ee = 99%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1.**



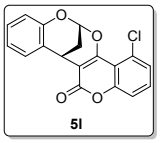
5j

5j was obtained as a white solid 20 mg in 61% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 8/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.82 (dd, J = 7.9, 1.4 Hz, 1H), 7.54 – 7.47 (m, 1H), 7.31 – 7.23 (m, 2H), 7.11 – 7.01 (m, 2H), 6.85 (dd, J = 7.7, 1.5 Hz, 1H), 6.36 (dd, J = 3.7, 1.8 Hz, 1H), 4.86 (d, J = 1.6 Hz, 1H), 2.26 (dd, J = 5.0, 2.3 Hz, 2H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 160.8, 158.1, 152.5, 151.9, 133.2, 132.2, 128.5, 123.9, 123.7, 123.4, 122.8, 116.6, 115.1, 114.7, 105.0, 92.3, 25.5, 21.9 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{18}H_{12}ClO_4^+$ 327.0419; found: 327.0416. The enantiomeric excess was determined by HPLC using Chiralpak IC column [*n*-hexane/*i*-PrOH= 80/20, 1 mL/min], λ = 210 nm, t_{major} = 36.76 min, t_{minor} = 31.54 min, **ee = 6%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1.**

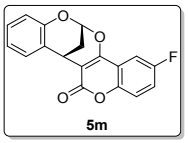


5k

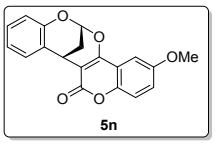
5k was obtained as a white solid 18 mg in 56% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 5/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.86 – 7.76 (m, 1H), 7.55 – 7.41 (m, 1H), 7.26 – 7.20 (m, 2H), 7.09 (t, J = 8.2 Hz, 1H), 6.55 (dd, J = 18.6, 8.2 Hz, 2H), 6.35 (d, J = 1.8 Hz, 1H), 4.79 (d, J = 1.7 Hz, 1H), 3.90 (s, 3H), 2.29 – 2.14 (m, 2H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 160.9, 158.2, 157.0, 152.4, 151.2, 131.8, 128.2, 123.8, 122.7, 116.5, 115.0, 114.2, 109.0, 106.4, 104.4, 92.5, 56.1, 25.4, 18.1 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{19}H_{15}O_5^+$ 323.0914; found: 323.0917. The enantiomeric excess was determined by HPLC using Chiralpak IC column [*n*-hexane/*i*-PrOH= 75/25, 1 mL/min], λ = 210 nm, t_{major} = 26.28 min, t_{minor} = 18.99 min, **ee = 23%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1.**



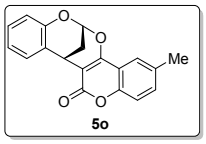
5l was obtained as a white solid 16.7 mg in 50% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 8/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.52 – 7.44 (m, 1H), 7.34 (t, J = 8.1 Hz, 1H), 7.30 – 7.24 (m, 1H), 7.22 – 7.12 (m, 2H), 6.94 (dd, J = 11.5, 4.3 Hz, 2H), 6.43 (dd, J = 3.9, 1.9 Hz, 1H), 4.32 (dd, J = 4.7, 2.7 Hz, 1H), 2.32 (ddd, J = 13.4, 2.7, 2.1 Hz, 1H), 2.25 – 2.19 (m, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 160.4, 158.0, 153.8, 150.3, 131.2, 130.8, 128.4, 128.4, 127.7, 125.0, 122.0, 116.3, 116.0, 113.2, 107.2, 92.6, 24.5, 24.5 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{18}H_{12}ClO_4^+$ 327.0419; found:327.0422. **$[\alpha]_D^{20}$** 50.98 (c = 1.25 in $CHCl_3$). The enantiomeric excess was determined by HPLC using Chiralpak IC column [*n*-hexane/*i*-PrOH= 80/20, 1 mL/min], λ = 210 nm, t_{major} = 14.89 min, t_{minor} = 17.69 min, **ee = 95%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



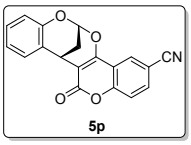
5m was obtained as a white solid 21 mg in 68% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 8/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.52 – 7.43 (m, 2H), 7.29 – 7.10 (m, 3H), 6.94 (t, J = 7.9 Hz, 2H), 6.39 (d, J = 1.6 Hz, 1H), 4.28 (d, J = 1.4 Hz, 1H), 2.38 – 2.32 (m, 1H), 2.28 – 2.21 (m, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 161.3, 159.8, 157.9, 157.0, 150.5, 148.6(d, J_{CF} = 2.1 Hz), 128.6(d, J_{CF} = 2.3 Hz), 125.2, 122.3, 119.7(d, J_{CF} = 24.6 Hz), 118.5(d, J_{CF} = 8.3 Hz), 116.5, 116.1(d, J_{CF} = 9.0 Hz), 108.9(d, J_{CF} = 25.5 Hz), 107.3, 93.3, 25.4, 24.6 ppm. **^{19}F NMR** (400 MHz, $CDCl_3$) δ -117.0 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{18}H_{12}FO_4^+$ 311.0714; found: 311.0718. **$[\alpha]_D^{20}$** -33.54 (c = 1.75 in $CHCl_3$). The enantiomeric excess was determined by HPLC using Chiralpak IC column [*n*-hexane/*i*-PrOH= 80/20, 1 mL/min], λ = 210 nm, t_{major} = 13.83 min, t_{minor} = 16.99 min, **ee = 92%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



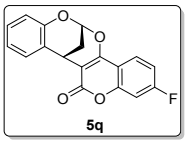
5n was obtained as a white solid 21 mg in 68% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 8/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.5 Hz, 1H), 7.23 (d, *J* = 2.9 Hz, 1H), 7.20 (d, *J* = 9.0 Hz, 1H), 7.17-7.12 (m,1H), 7.07 (dd, *J* = 9.0, 3.0 Hz, 1H), 6.94 (t, *J* = 7.7 Hz, 2H), 6.40 (d, *J* = 1.8 Hz, 1H), 4.29 (d, *J* = 1.6 Hz, 1H), 3.85 (s, 3H), 2.38 – 2.31 (m, 1H), 2.27 – 2.21 (m, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 161.6, 157.3, 155.9, 150.3, 146.8, 128.4, 128.3, 125.3, 122.0, 120.4, 117.8, 116.2, 115.2, 106.5, 104.2, 93.0, 55.8, 25.2, 24.4 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{19}H_{15}O_5^+$ 323.0914; found: 323.0912. **$[\alpha]_D^{20}$** 16.49 (c = 1.83 in $CHCl_3$).The enantiomeric excess was determined by HPLC using Chiralpak IC column [*n*-hexane/*i*-PrOH= 80/20, 1 mL/min], λ = 210 nm, t_{major} = 23.89 min, t_{minor} = 30.70 min, **ee = 91%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



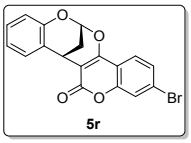
5o was obtained as a white solid 17.4 mg in 56% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 8/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.61 (s, 1H), 7.48 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.29 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.19 – 7.11 (m, 2H), 6.93 (t, *J* = 8.2 Hz, 2H), 6.38 (d, *J* = 1.9 Hz, 1H), 4.28 (d, *J* = 1.7 Hz, 1H), 2.39 (s, 3H), 2.36 – 2.31 (m, 1H), 2.26 – 2.21 (m, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 161.7, 157.5, 150.4, 150.3, 133.7, 132.9, 128.4, 128.2, 125.4, 122.4, 121.9, 116.4, 116.2, 114.6, 106.2, 93.0, 25.3, 24.4, 20.9 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{19}H_{15}O_4^+$ 307.0965; found: 307.0969. **$[\alpha]_D^{20}$** -7.33 (c = 1.42 in $CHCl_3$). The enantiomeric excess was determined by HPLC using Chiralpak IC column [*n*-hexane/*i*-PrOH= 80/20, 1 mL/min], λ = 210 nm, t_{major} = 18.69 min, t_{minor} = 22.43 min, **ee = 97%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



5p was obtained as a white solid 15.2 mg in 48% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 5/1). **^{1}H NMR** (400 MHz, $CDCl_3$). δ 8.16 (d, J = 1.9 Hz, 1H), 7.75 (dd, J = 8.6, 2.0 Hz, 1H), 7.45 (d, J = 7.4 Hz, 1H), 7.36 (d, J = 8.6 Hz, 1H), 7.17 (td, J = 7.8, 1.6 Hz, 1H), 6.96 (t, J = 7.5 Hz, 2H), 6.43 (d, J = 1.8 Hz, 1H), 4.28 (d, J = 1.7 Hz, 1H), 2.49 – 2.30 (m, 1H), 2.33 – 2.20 (m, 1H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 160.1, 156.2, 154.4, 150.2, 134.8, 128.7, 128.4, 127.9, 124.6, 122.2, 118.0, 117.7, 116.5, 115.9, 108.2, 107.9, 93.3, 25.1, 24.4 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{19}H_{12}NO_4^+$ 318.0761; found: 318.0763. **$[\alpha]_D^{20}$** 60.17 (c = 0.75 in $CHCl_3$). The enantiomeric excess was determined by HPLC using Chiralpak IA column [*n*-hexane/*i*-PrOH= 75/25, 1 mL/min], λ = 210 nm, t_{major} = 15.87 min, t_{minor} = 21.07 min, **ee = 97%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.

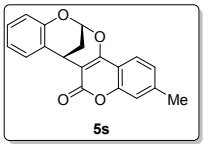


5q was obtained as a white solid 21.6 mg in 69% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 8/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.85 – 7.76 (m, 1H), 7.47 (d, J = 7.5 Hz, 1H), 7.15 (t, J = 7.7 Hz, 1H), 7.05-6.89 (m, 4H), 6.39 (s, 1H), 4.26 (s, 1H), 2.34 (d, J = 13.4 Hz, 1H), 2.24 (d, J = 13.4 Hz, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 165.8, 163.8, 161.5, 157.5, 153.7, 150.5, 128.6(d, J_{CF} = 3.6 Hz), 125.4, 124.9(d, J_{CF} = 10.3 Hz), 122.3, 116.5, 112.5(d, J_{CF} = 22.8 Hz), 111.8, 105.5, 104.4(d, J_{CF} = 25.7 Hz), 93.3, 25.5, 24.5 ppm. **^{19}F NMR** (400 MHz, $CDCl_3$) δ -105.1 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{18}H_{12}FO_4^+$ 311.0714; found:311.0717. **$[\alpha]_D^{20}$** -50.03 (c = 2.08 in $CHCl_3$).The enantiomeric excess was determined by HPLC using Chiralpak IC column [*n*-hexane/*i*-PrOH= 80/20, 1 mL/min], λ = 210 nm, t_{major} = 13.09 min, t_{minor} = 16.88 min, **ee = 82%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



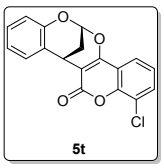
5r

5r was obtained as a white solid 31 mg in 82% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 8/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.66 (dd, J = 8.2, 5.2 Hz, 1H), 7.50 – 7.42 (m, 2H), 7.38 (dd, J = 8.4, 1.3 Hz, 1H), 7.19 – 7.12 (m, 1H), 6.99 – 6.89 (m, 2H), 6.38 (d, J = 1.6 Hz, 1H), 4.26 (d, J = 1.4 Hz, 1H), 2.37 – 2.30 (m, 1H), 2.24 (dt, J = 13.4, 2.3 Hz, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 161.0, 157.4, 152.6, 150.4, 128.6, 127.7, 126.0, 125.2, 124.1, 122.3, 120.0, 116.5, 114.2, 110.2, 106.7, 93.3, 25.4, 24.6 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{18}H_{12}BrO_4^+$ 370.9913; found: 370.9916. **$[\alpha]_D^{20}$** -86.13 (c = 0.41 in $CHCl_3$).The enantiomeric excess was determined by HPLC using Chiralpak IC column [*n*-hexane/*i*-PrOH= 80/20, 1 mL/min], λ = 210 nm, t_{major} = 15.51 min, t_{minor} = 20.97 min, **ee = 82%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



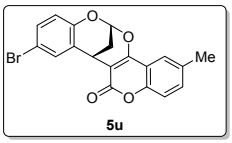
5s

5s was obtained as a white solid 16.1 mg in 51% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 8/1).**^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.67 (d, J = 8.4 Hz, 1H), 7.48 (d, J = 7.5 Hz, 1H), 7.18-7.11 (m, 1H), 7.10-7.03 (m, 2H), 6.94 (t, J = 8.0 Hz, 2H), 6.37 (d, J = 1.8 Hz, 1H), 4.27 (d, J = 1.5 Hz, 1H), 2.41 (s, 3H), 2.33 (dt, J = 13.3, 2.3 Hz, 1H), 2.27 – 2.20 (m, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 161.9, 157.9, 152.6, 150.5, 143.3, 128.6, 128.4, 125.7, 125.4, 122.6, 122.1, 116.9, 116.4, 112.6, 105.5, 93.2, 25.5, 24.6, 21.9 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{19}H_{15}O_4^+$ 307.0965; found: 307.0966. **$[\alpha]_D^{20}$** -64.90 (c = 1.25 in $CHCl_3$). The enantiomeric excess was determined by HPLC using Chiralpak IC column [*n*-hexane/*i*-PrOH= 80/20, 1 mL/min], λ = 210 nm, t_{major} = 20.90 min, t_{minor} = 29.97 min, **ee = 89%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



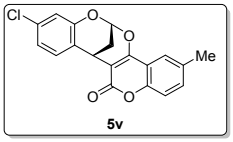
5t

5t was obtained as a white solid 14.3 mg in 44% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 8/1).**^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.71 (dd, J = 8.0, 1.2 Hz, 1H), 7.54 (dd, J = 7.9, 1.2 Hz, 1H), 7.48 (dd, J = 7.5, 1.1 Hz, 1H), 7.22 – 7.11 (m, 2H), 6.98 – 6.90 (m, 2H), 6.40 (d, J = 1.7 Hz, 1H), 4.30 (d, J = 1.6 Hz, 1H), 2.41 – 2.32 (m, 1H), 2.25 (dt, J = 13.4, 2.5 Hz, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 160.3, 157.2, 150.2, 148.0, 132.2, 128.4, 128.4, 125.0, 124.1, 122.1, 121.6, 121.3, 116.4, 116.3, 106.8, 93.1, 25.1, 24.4 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{18}H_{12}ClO_4^+$ 327.0419; found:327.0416. **$[\alpha]_D^{20}$** -104.00 (c = 1.17 in $CHCl_3$).The enantiomeric excess was determined by HPLC using Chiralpak IC column [*n*-hexane/*i*-PrOH= 80/20, 1 mL/min], λ = 210 nm, t_{major} = 20.60 min, t_{minor} = 23.01 min, **ee = 82%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.

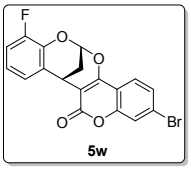


5u

5u was obtained as a white solid 14 mg in 36% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 8/1).**^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.61 (dd, J = 5.0, 1.7 Hz, 2H), 7.31 (dd, J = 8.5, 1.6 Hz, 1H), 7.23 (dd, J = 8.6, 2.4 Hz, 1H), 7.18 (d, J = 8.4 Hz, 1H), 6.80 (d, J = 8.6 Hz, 1H), 6.37 (d, J = 1.8 Hz, 1H), 4.24 (d, J = 1.7 Hz, 1H), 2.40 (s, 3H), 2.33 – 2.26 (m, 1H), 2.26 – 2.20 (m, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 161.7, 157.8, 150.7, 149.8, 134.1, 133.4, 131.4, 131.1, 127.6, 122.7, 118.2, 116.7, 114.6, 114.4, 105.8, 93.0, 25.2, 24.5, 21.1 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{19}H_{14}BrO_4^+$ 385.0070; found: 385.0072. **$[\alpha]_D^{20}$** 42.69 (c = 1.00 in $CHCl_3$). The enantiomeric excess was determined by HPLC using Chiralpak IC column [*n*-hexane/*i*-PrOH= 90/10, 1 mL/min], λ = 210 nm, t_{major} = 43.09 min, t_{minor} = 37.95 min, **ee = 85%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.

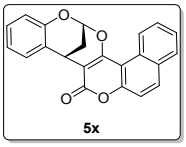


5v was obtained as a white solid 20 mg in 59% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 8/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.60 (s, 1H), 7.40 (d, J = 8.1 Hz, 1H), 7.31 (dd, J = 8.4, 1.5 Hz, 1H), 7.17 (d, J = 8.4 Hz, 1H), 6.98 – 6.88 (m, 2H), 6.37 (d, J = 1.8 Hz, 1H), 4.25 (d, J = 1.5 Hz, 1H), 2.40 (s, 3H), 2.34 – 2.27 (m, 1H), 2.27 – 2.21 (m, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 161.8, 157.6, 151.2, 150.7, 134.1, 133.6, 133.3, 129.3, 124.2, 122.6, 122.3, 116.8, 116.7, 114.6, 106.1, 93.0, 25.3, 24.2, 21.1 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{19}H_{14}ClO_4^+$ 341.0575; found: 341.0572. **$[\alpha]_D^{20}$** -26.69 (c = 1.5 in $CHCl_3$). The enantiomeric excess was determined by HPLC using Chiralpak IC column [*n*-hexane/*i*-PrOH= 90/10, 1 mL/min], λ = 210 nm, t_{major} = 25.91 min, t_{minor} = 24.59 min, **ee = 99%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.

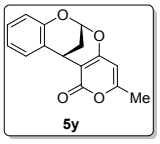


5w was obtained as a white solid 18 mg in 46% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 8/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.67 (d, J = 8.5 Hz, 1H), 7.46 (d, J = 1.7 Hz, 1H), 7.41 (dd, J = 8.5, 1.8 Hz, 1H), 7.25 (d, J = 7.7 Hz, 1H), 7.00 – 6.92 (m, 1H), 6.92-6.84 (m, 1H), 6.47 (dd, J = 3.7, 1.9 Hz, 1H), 4.31 (s, 1H), 2.39 – 2.33 (m, 1H), 2.27 (ddd, J = 13.6, 3.0, 2.2 Hz, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 160.7, 157.2, 152.5, 127.6, 127.6, 126.1, 124.0, 123.3(d, J_{CF} = 3.7 Hz), 121.9(d, J_{CF} = 6.9 Hz), 119.9, 115.3(d, J_{CF} = 17.8 Hz), 113.7, 110.0, 106.1, 92.6, 24.9, 24.1 ppm. **^{19}F NMR** (400 MHz, $CDCl_3$) δ -135.6 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{18}H_{11}BrFO_4^+$ 388.9819; found: 388.9820. **$[\alpha]_D^{20}$** -38.12 (c = 1.33 in $CHCl_3$). The enantiomeric excess was determined by HPLC using Chiralpak IA column [*n*-hexane/*i*-PrOH= 90/10, 1 mL/min], λ = 210 nm, t_{major} = 19.73 min, t_{minor} = 14.82 min, **ee = 96%**. The

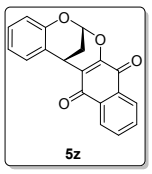
diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



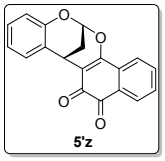
5x was obtained as a white solid 20 mg in 58% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 10/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.26 (d, J = 8.8 Hz, 1H), 7.92 (d, J = 9.0 Hz, 1H), 7.84 (t, J = 8.7 Hz, 1H), 7.65 (t, J = 7.8 Hz, 1H), 7.58 – 7.49 (m, 2H), 7.40 (d, J = 8.9 Hz, 1H), 7.16 (t, J = 7.7 Hz, 1H), 6.96 (t, J = 8.7 Hz, 2H), 6.60 (s, 1H), 4.41 (s, 1H), 2.40 (d, J = 13.3 Hz, 1H), 2.31 (d, J = 13.3 Hz, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 161.3, 161.1, 153.1, 150.2, 133.7, 130.8, 128.9, 128.8, 128.5, 128.3, 128.3, 126.5, 125.8, 125.4, 122.0, 117.1, 116.2, 108.6, 106.4, 92.9, 24.7, 24.5 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{22}H_{15}O_4^+$ 343.0965; found: 343.0961. **$[\alpha]_D^{20}$** 68.06 (c = 1.33 in $CHCl_3$). The enantiomeric excess was determined by HPLC using Chiralpak IC column [*n*-hexane/*i*-PrOH= 80/20, 1 mL/min], λ = 210 nm, t_{major} = 31.32 min, t_{minor} = 41.45 min, **ee = 95%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



5y was obtained as a white solid 13 mg in 51% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 8/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.52 – 7.32 (m, 1H), 7.19 – 7.08 (m, 1H), 7.00 – 6.83 (m, 2H), 6.17 (d, J = 1.8 Hz, 1H), 5.83 (s, 1H), 4.11 (s, 1H), 2.23 (dt, J = 13.2, 2.3 Hz, 1H), 2.16 (s, 3H), 2.14 – 2.08 (m, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 163.4, 162.3, 161.0, 150.5, 128.5, 128.3, 125.9, 122.1, 116.4, 103.8, 99.9, 93.0, 25.4, 24.0, 20.1 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{15}H_{13}O_4^+$ 257.0808; found: 257.0804. **$[\alpha]_D^{20}$** -140.09 (c = 0.67 in $CHCl_3$).The enantiomeric excess was determined by HPLC using Chiralpak IC column [*n*-hexane/*i*-PrOH= 80/20, 1 mL/min], λ = 210 nm, t_{major} = 15.41 min, t_{minor} = 18.39 min, **ee = 72%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



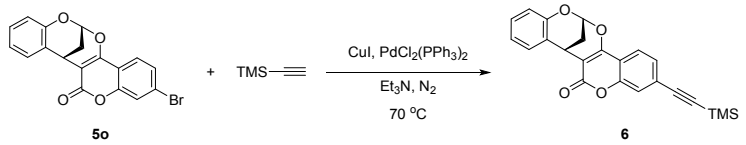
5z was obtained as a yellow solid 6.7 mg in 22% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 8/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.07 (t, *J* = 6.7 Hz, 2H), 7.74 – 7.63 (m, 2H), 7.40 (d, *J* = 7.6 Hz, 1H), 7.14 (t, *J* = 7.7 Hz, 1H), 6.92 (dd, *J* = 14.8, 7.6 Hz, 2H), 6.38 (s, 1H), 4.45 (s, 1H), 2.35 - 2.25 (m, 1H), 2.17 – 2.10 (m, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 182. 6, 179.1, 152.5, 150.7, 134.1, 133.4, 131.6, 130.8, 128.7, 128.4, 126.5, 126.2, 125.0, 124.2, 121.8, 116.5, 92.9, 24.4, 23.3 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{19}H_{13}O_4^+$ 305.0808; found: 305.0809. **$[\alpha]_D^{20}$** -192.8 (c = 0.50 in $CHCl_3$).The enantiomeric excess was determined by HPLC using Chiralpak IC column [*n*-hexane/*i*-PrOH= 80/20, 1 mL/min], λ = 210 nm, t_{major} = 45.30 min, t_{minor} = 22.72 min, **ee = 86%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



5'z was obtained as an orange solid 20 mg in 65% yield for two steps after column chromatography on silica gel (petroleum ether/ethyl acetate = 7/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.4 Hz, 1H), 7.84 (d, *J* = 7.6 Hz, 1H), 7.63 (t, *J* = 7.3 Hz, 1H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.41 (d, *J* = 7.3 Hz, 1H), 7.14 (t, *J* = 7.5 Hz, 1H), 6.93 (d, *J* = 6.6 Hz, 2H), 6.42 (s, 1H), 4.34 (d, *J* = 31.2 Hz, 1H), 2.31 (d, *J* = 13.2 Hz, 1H), 2.22 (d, *J* = 13.2 Hz, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 179.1, 176.8, 160.5, 150.1, 135.0, 131.2, 131.1, 129.8, 129.1, 128.6, 128.3, 125.2, 124.6, 122.0, 118.4, 116.2, 93.5, 25.0, 23.0 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{19}H_{13}O_4^+$ 305.0808; found: 305.0806. **$[\alpha]_D^{20}$** -138.74 (c = 0.83 in $CHCl_3$).The enantiomeric excess was determined by HPLC using Chiralpak IC column [*n*-hexane/*i*-PrOH/dichloromethane = 75/20/5, 1 mL/min], λ = 210 nm, t_{major} = 22.81 min, t_{minor} = 24.36 min, **ee = 87%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.

D. Synthetic transformations

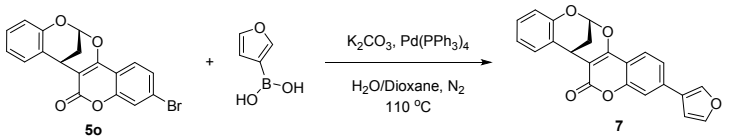
(8*R*,14*S*)-4-((trimethylsilyl)ethynyl)-1*H*,14*H*-8,14-methanobenzo[7,8][1,3]dioxocino [5,4-*c*]chromen-1-one (6)



5o 6

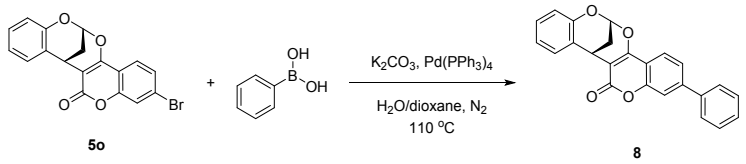
A round Schlenk flask equipped with a stirring bar was charged with **5o** (25 mg, 0.07 mmol), trimethylsilyl acetylene (15 µL, 0.11 mmol) and 1 mL of freshly distilled dry triethylamine. A mixture of $[(PPh_3)_2PdCl_2]$ (1.5 mg, 0.002 mmol), and CuI (0.5 mg , 0.003 mmol) was added under N_2. Then the suspension was allowed to stir at 70 °C. After completion of the reaction, it was allowed to cool down to room temperature and then was diluted with ethyl acetate, washed with saturated aqueous NH_4Cl solution and brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) to give the desired product **8**.(17 mg, 65%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.76 – 7.68 (m, 1H), 7.47 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.36-7.29 (m, 2H), 7.19-7.12 (m, 1H), 6.99 – 6.90 (m, 2H), 6.43 – 6.33 (m, 1H), 4.28 (d, *J* = 1.7 Hz, 1H), 2.37 – 2.30 (m, 1H), 2.28 – 2.19 (m, 1H), 0.33 – 0.20 (m, 9H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 161.4, 157.3, 152.1, 150.5, 128.7, 128.6, 127.8, 127.0, 125.3, 122.8, 122.2, 119.9, 116.5, 115.1, 106.9, 103.5, 98.5, 93.3, 25.4, 24.6, 0.0 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{23}H_{21}O_4Si^+$ 389.1204; found: 389.1207. **$[\alpha]_D^{20}$** -0.25 (c = 1.08 in $CHCl_3$). The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.

(8*R*,14*S*)-4-(furan-3-yl)-1*H*,14*H*-8,14-methanobenzo[7,8][1,3]dioxocino[5,4-*c*]chromen-1-one (7)



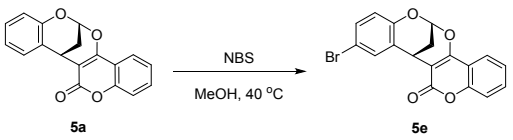
A round Schlenk flask equipped with a stirring bar was charged with **5o** (25 mg, 0.07 mmol), phenylboronic acid (9 mg, 0.08 mmol), $Pd(PPh_3)_4$ (3.1 mg, 0.003 mmol), and K_2CO_3 (20 mg, 0.15 mmol). The component solvent of dioxane and H_2O (1 mL, 1:1 v/v) was added under N_2 at room temperature. Then the reaction mixture was moved to stir at 110 °C. After the reaction was completed, it was allowed to cool down to room temperature and was concentrated under reduced pressure. Then the residue was diluted with ethyl acetate, washed with saturated aqueous NH_4Cl solution and brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 8:1) to give the desired product **7.** (13 mg, 54%).**^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.84 – 7.75 (m, 2H), 7.53 – 7.46 (m, 2H), 7.42 – 7.34 (m, 2H), 7.20-7.10 (m, 1H), 7.00-6.90 (m, 2H), 6.74 – 6.68 (m, 1H), 6.40 (d, *J* = 1.8 Hz, 1H), 4.29 (d, *J* = 1.7 Hz, 1H), 2.38 – 2.31 (m, 1H), 2.29 – 2.22 (m, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 161.5, 157.5, 152.8, 150.3, 144.2, 139.8, 136.5, 128.4, 128.3, 125.3, 125.2, 123.2, 122.0, 121.6, 116.2, 113.5, 113.2, 108.5, 105.8, 93.0, 25.3, 24.4 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{22}H_{15}O_5^+$ 359.0914; found: 359.0916. **$[\alpha]_D^{20}$** -0.54 (c = 1.08 in $CHCl_3$). The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.

(8*R*,14*S*)-4-phenyl-1*H*,14*H*-8,14-methanobenzo[7,8][1,3]dioxocino[5,4-*c*]chromen-1-one (8)



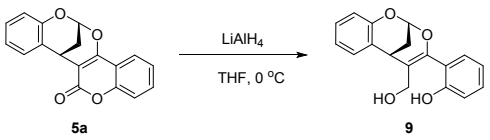
A round Schlenk flask equipped with a stirring bar was charged with **5o** (23 mg, 0.06 mmol), phenylboronic acid (9.2 mg, 0.07 mmol), $Pd(PPh_3)_4$ (2.9 mg, 0.002 mmol), and K_2CO_3 (19 mg, 0.14 mmol). The component solvent of dioxane and H_2O (1 mL, 1:1 v/v) was added under N_2 at room temperature. Then the reaction mixture was moved to stir at 110 °C. After the reaction was completed, it was allowed to cool down to room temperature and was concentrated under reduced pressure. The residue was diluted with ethyl acetate, washed with saturated aqueous NH_4Cl solution and brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Then the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 8:1) to give the desired product **6.** (18.4 mg, 81%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.86 (d, J = 8.2 Hz, 1H), 7.60 (d, J = 7.4 Hz, 2H), 7.55 – 7.43 (m, 5H), 7.40 (t, J = 7.3 Hz, 1H), 7.16 (t, J = 7.2 Hz, 1H), 6.95 (t, J = 7.5 Hz, 2H), 6.41 (d, J = 1.4 Hz, 1H), 4.31 (s, 1H), 2.36 (d, J = 13.4 Hz, 1H), 2.26 (d, J = 13.4 Hz, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 161.8, 157.7, 152.9, 150.5, 145.3, 139.4, 129.3, 128.7, 128.6, 128.5, 127.4, 125.6, 123.3, 123.1, 122.2, 116.4, 115.0, 114.0, 106.3, 93.2, 25.5, 24.6 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{24}H_{17}O_4^+$ 369.1121; found: 369.1125. **$[\alpha]_D^{20}$** -3.70 (c = 1.50 in $CHCl_3$). The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.

(8*R*,14*S*)-12-bromo-1*H*,14*H*-8,14-methanobenzo[7,8][1,3]dioxocino[5,4-*c*]chromen-1-one (5e)



To a solution of **5a** (20 mg, 0.068 mmol) in CH_3OH (1 mL) was added N-bromosuccinimide (1.2 equiv.), then the reaction mixture was allowed to stir at 40 °C. Until the starting material **5a** was consumed completely, the solvent was removed under vacuum and the crude product was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 8:1) to obtain **5e** as a white solid. (18 mg, 71%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.80 (dd, J = 7.9, 1.2 Hz, 1H), 7.61 (d, J = 2.3 Hz, 1H), 7.55 – 7.48 (m, 1H), 7.32 – 7.20 (m, 3H), 6.81 (d, J = 8.6 Hz, 1H), 6.38 (d, J = 1.8 Hz, 1H), 4.24 (d, J = 1.7 Hz, 1H), 2.33 – 2.27 (m, 1H), 2.24 (ddd, J = 13.5, 2.9, 2.3 Hz, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 161.5, 157.8, 152.5, 149.7, 132.4, 131.4, 131.0, 127.5, 124.3, 123.0, 118.2, 116.9, 114.9, 114.4, 105.9, 93.1, 25.2, 24.5 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{18}H_{12}BrO_4^+$ 370.9913; found: 370.9910. **$[\alpha]_D^{20}$** 79.49 (c = 1.50 in $CHCl_3$).The enantiomeric excess was determined by HPLC using Chiralpak IC column [*n*-hexane/*i*-PrOH= 80/20, 1 mL/min], λ = 210 nm, t_{major} = 19.89 min, t_{minor} = 18.21 min, **ee = 97%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.

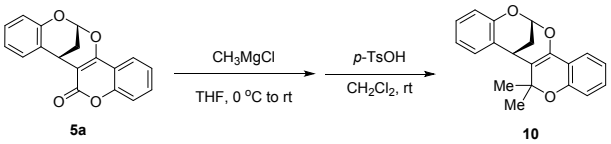
2-((2*R*,6*S*)-5-(hydroxymethyl)-6*H*-2,6-methanobenzo[*d*][1,3]dioxocin-4-yl)phenol (9)



5a 9

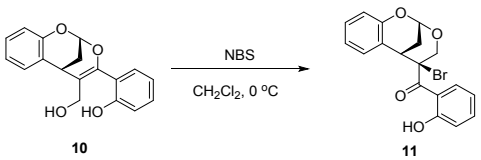
To a magnetically stirred suspension of $LiAlH_4$ (20 mg, 0.52 mmol) in 0.5 mL of anhydrous tetrahydrofuran (THF), was added dropwise a solution of **5a** (30 mg, 0.10 mmol) in anhydrous tetrahydrofuran (0.5 mL) at 0 °C. After the reaction was completed , the mixture was added dropwise a small amount of 15 % KOH solution. Then the white suspension was filtered, the filtrate was evaporated and the crude product was purified by column chromatography on a silica gel (petroleum ether/ethyl acetate = 2/1) to get the desired product **9** .(20 mg, 66%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.26 – 7.22 (m, 2H), 7.21-7.14 (m, 2H), 6.98 (d, *J* = 8.0 Hz, 1H), 6.94-6.84 (m, 3H), 6.60 (s, 1H), 6.12 (d, *J* = 1.7 Hz, 1H), 4.04 (s, 2H), 3.73 (s, 1H), 2.29 (ddd, *J* = 13.0, 3.1, 1.9 Hz, 1H), 2.13 (dt, *J* = 13.1, 2.2 Hz, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 154.4, 151.9, 145.6, 131.0, 130.6, 128.2, 127.5, 126.9, 121.3, 120.3, 120.1, 117.0, 116.4, 116.2, 92.5, 61.9, 28.3, 26.1 ppm. **HRMS:** $[M-H]^-$ *calcd*. For $C_{18}H_{15}O_4^-$ 295.0976; found: 295.0978. **$[\alpha]_D^{20}$** -27.06 (c = 1.08 in $CHCl_3$). The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.

(8*R*,14*S*)-1,1-dimethyl-1*H*,14*H*-8,14-methanobenzo[7,8][1,3]dioxocino[5,4-*c*]chromene (10)



To a stirred solution of **5a** (18 mg, 0.062 mmol) in 0.5 mL anhydrous of tetrahydrofuran (THF),a solution of methyl magnesium chloride (3 M in tetrahydrofuran, 206 μL, 0.62 mmol) was added at 0 °C under N_2. Then the reaction mixture was allowed to stir at room temperature .After stirring for about 30 min (TLC monitoring), the reaction mixture was poured into water. The organic phase was separated and the aqueous phase was extracted with ethyl acetate. The combined organic phases were washed with water and brine, dried with Na_2SO_4, and concentrated in vacuo. The residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate = 3/1). The obtained product was dissolved in CH_2Cl_2 (0.5 mL), then *p*-TsOH (11 mg, 0.062 mmol) was added to the solution. The reaction mixture was allowed to stir at 25 °C until the reaction was completed. The product was purified by chromatography on silica gel (petroleum ether/ethyl acetate = 50/1) to afford the desired product **10**. (11 mg, 60% for two steps). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.42 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.19 – 7.09 (m, 3H), 6.95 (d, *J* = 7.9 Hz, 1H), 6.92-6.85 (m, 2H), 6.76 (d, *J* = 8.0 Hz, 1H), 6.15 (d, *J* = 1.7 Hz, 1H), 3.51 (s, 1H) 2.18 (ddd, *J* = 12.9, 3.1, 2.0 Hz, 1H), 2.06 (dt, *J* = 12.9, 2.5 Hz, 1H), 1.65 (s, 3H), 1.26 (s, 3H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 152.7, 151.6, 139.2, 129.5, 127.9, 127.2, 126.4, 121.7, 120.7, 120.7, 118.4, 116.5, 116.1, 112.8, 91.4, 79.1, 27.1, 26.8, 26.7, 26.6 ppm. **HRMS:** $[M+H]^+$ *calcd*. For $C_{20}H_{19}O_3^+$ 307.1329; found: 307.1325. **$[\alpha]_D^{20}$** -37.52 (c = 0.92 in $CHCl_3$). The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.

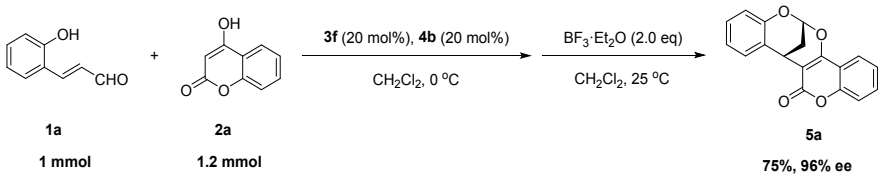
(5-bromo-5,6-dihydro-4*H*-2,6-methanobenzo[d][1,3]dioxocin-5-yl)(2-hydroxyphenyl)methanone (11)



10 **11**

To a stirred solution of **10** (38 mg, 0.13 mmol) in 1.0 mL CH_2Cl_2, was added bromosuccinimide (27.4 mg, 0.15 mmol) at 0 °C. After the full conversion of **10**, The product was purified by chromatography on silica gel (petroleum ether/ethyl acetate = 25/1) to afford the desired product **11** (42 mg, 86%).**^{1}H NMR** (600 MHz, $CDCl_3$) δ 11.65 (s, 1H), 8.47 (d, *J* = 8.3 Hz, 1H), 7.56 – 7.49 (m, 1H), 7.37 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.33 – 7.28 (m, 1H), 7.14 – 7.07 (m, 1H), 7.04 - 6.99 (m, 1H), 6.99 – 6.93 (m, 2H), 5.60 (s, 1H), 4.51 (dd, *J* = 12.2, 1.0 Hz, 1H), 4.12 (s, 1H), 3.81 (d, *J* = 12.1 Hz, 1H), 2.11 (d, *J* = 13.8 Hz, 1H), 2.00 (ddd, *J* = 13.9, 4.1, 1.7 Hz, 1H) ppm. **^{13}C NMR** (125 MHz, CDCl3) δ 198.2, 163.6, 154.9, 136.7, 132.0, 131.2, 129.8, 120.5, 120.2, 119.8, 118.4, 116.1, 115.7, 91.6, 64.3, 63.7, 37.2, 28.4 ppm. **HRMS:** $[M+Na]^+$ *calcd*. For $C_{18}H_{15}BrNaO_4^+$ 397.0046; found: 397.0048. **$[\alpha]_D^{20}$** -90.51 (c = 0.67 in $CHCl_3$). The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.

E. 1 mmol scale

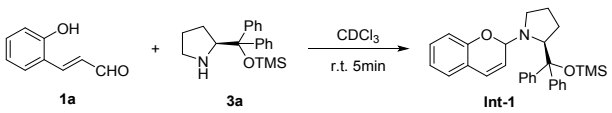


A glass vial equipped with a magnetic stirring bar was charged with **1a** (1.0 mmol, 1.0 equiv), catalyst **3f** (0.2 mmol, 0.2 equiv) and catalyst **4b** (0.2 mmol, 0.2 equiv) in CH_2Cl_2 (5.0 mL) and the resulting solution was stirred for about 10 min at 0 °C. Then **2a** (1.2 mmol, 1.2 equiv) was added. After full conversion of first step, BF_3•Et_2O (2.0 eq) was added to the reaction mixture in situ and the reaction mixture was allowed to stir at 25 °C. After completion of the reaction, the reaction mixture was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 8/1) to give product **5a** 220 mg with 75% yield and 96% ee.

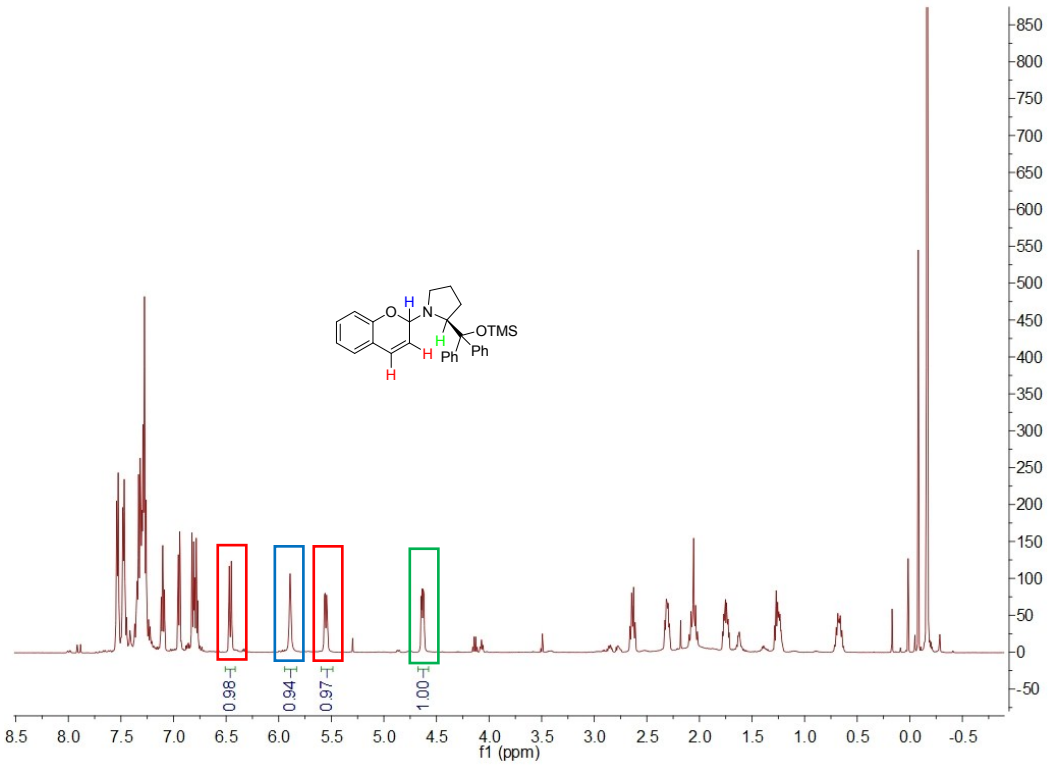
F. NMR and Control Experiments

NMR experiments

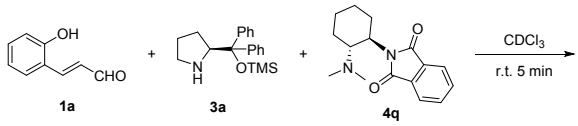
1)



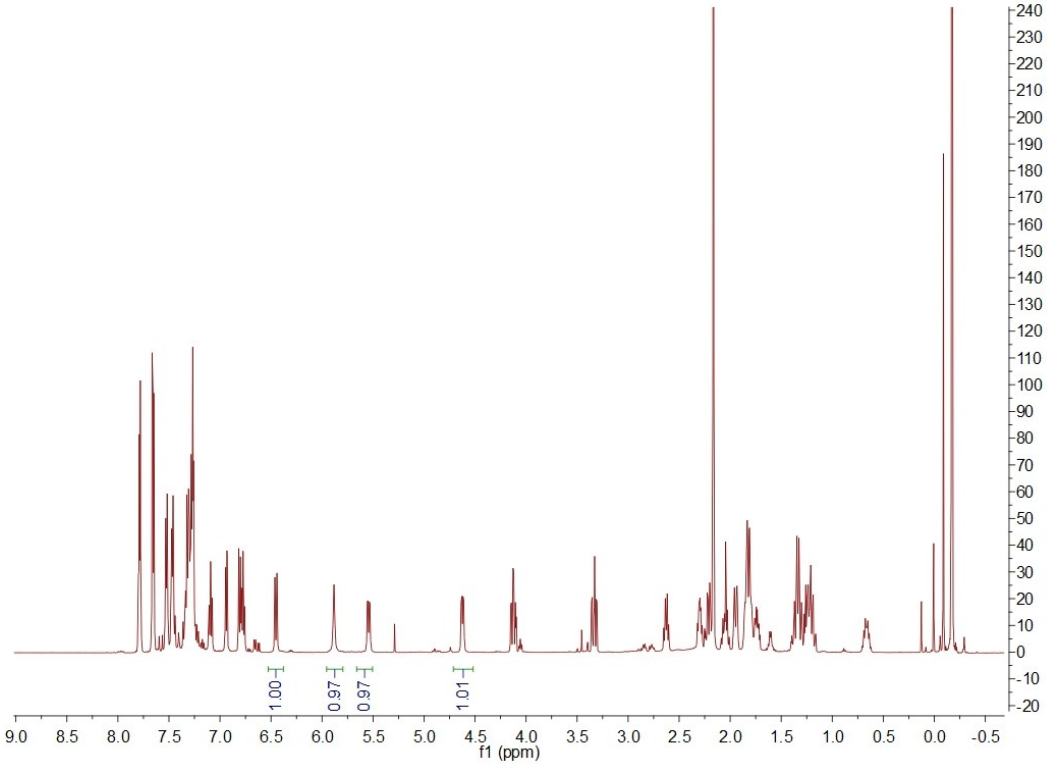
General procedure: To a solution of catalyst **3a** (0.05 mmol) in $CDCl_3$ (0.4 ml) was added **1a** (0.05 mmol), and the mixture was allowed at room temperature for about 5 min. Then the system was monitored by ^1H NMR (500 MHz). The result showed that a high concentration of aminal **Int-1** was generated quickly.



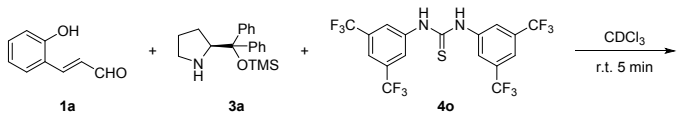
2)



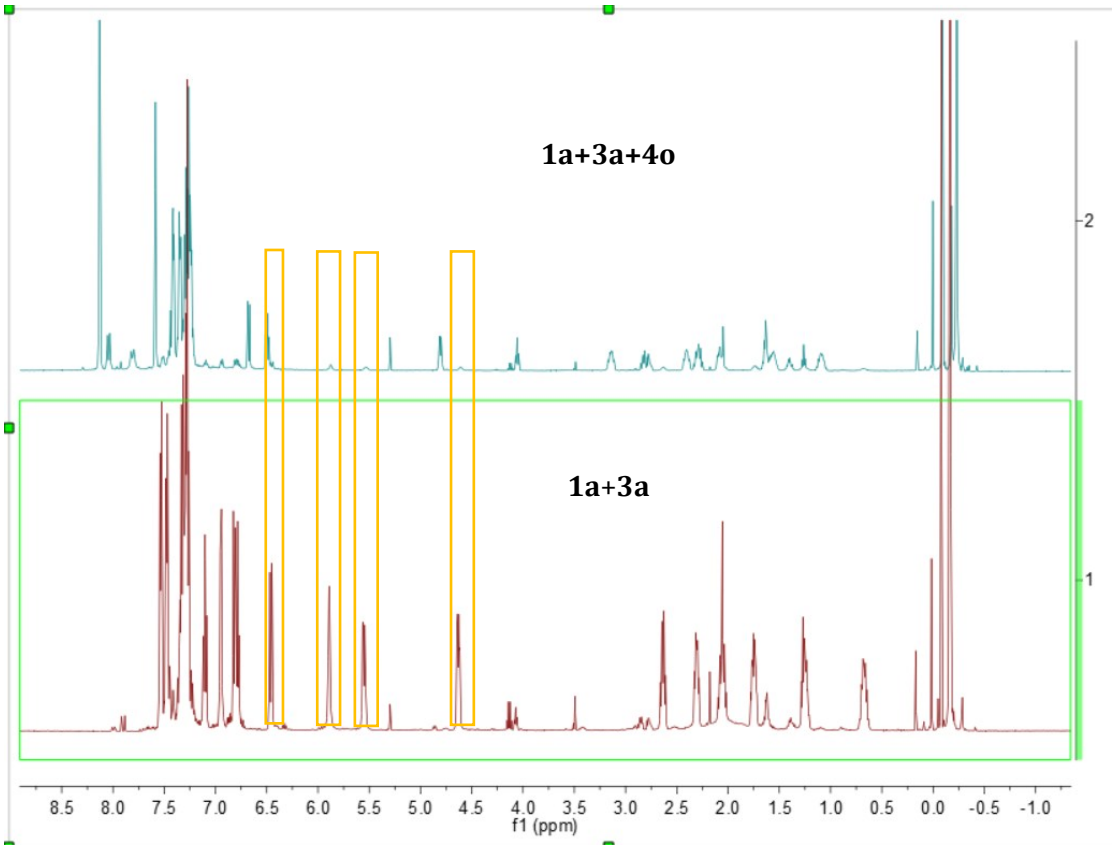
General procedure: To a solution of catalyst **3a** (0.05 mmol) and **4q** (0.05 mmol) in $CDCl_3$ (0.4 ml) was added **1a** (0.05 mmol), and the mixture was allowed at room temperature for about 5 min. Then the system was monitored by ^1H NMR (500 MHz).The result showed that tertiary amine has little effect on **Int-1**.



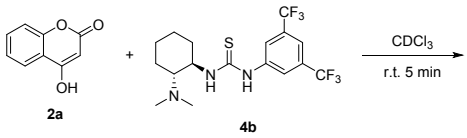
3)



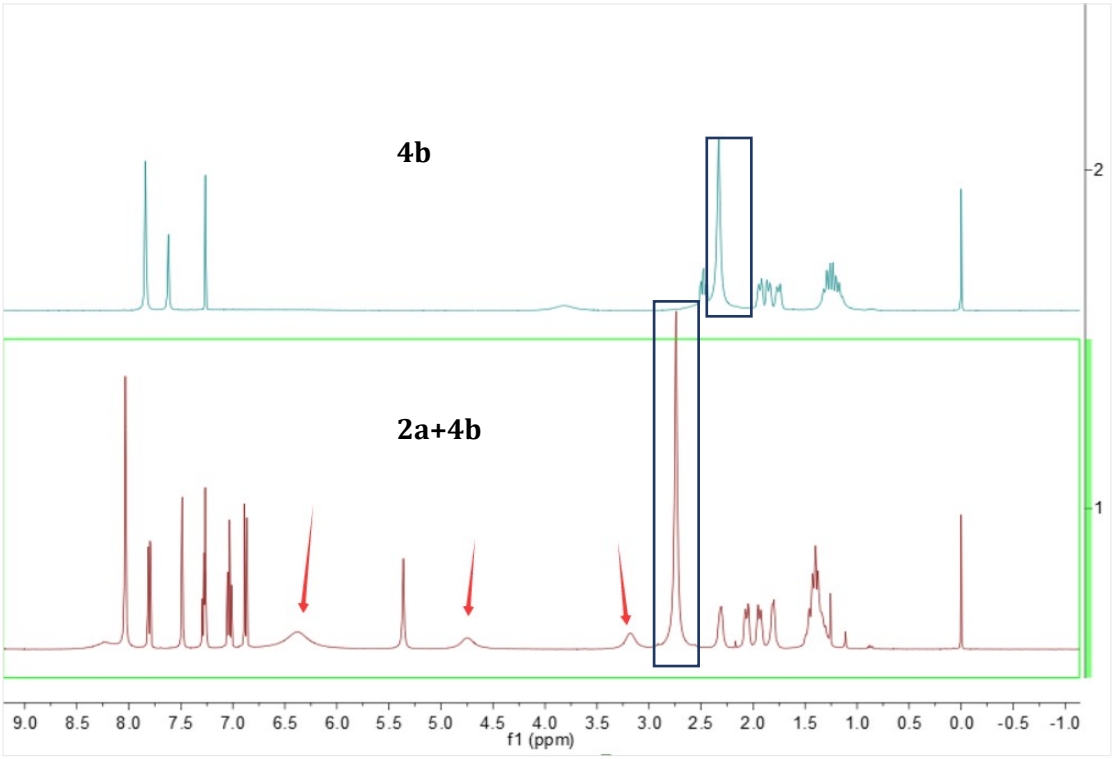
General procedure: To a solution of catalyst **3a** (0.05 mmol) and **4o** (0.05 mmol) in $CDCl_3$ (0.4 ml) was added **1a** (0.05 mmol), and the mixture was allowed at room temperature for about 5 min. Then the system was monitored by ^1H NMR (500 MHz). The result showed that thiourea has significant effect on **Int-1**. Addition of thiourea results in disappearance of **Int-1**.



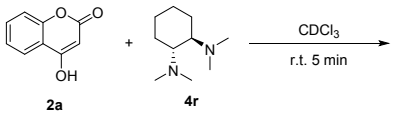
4)



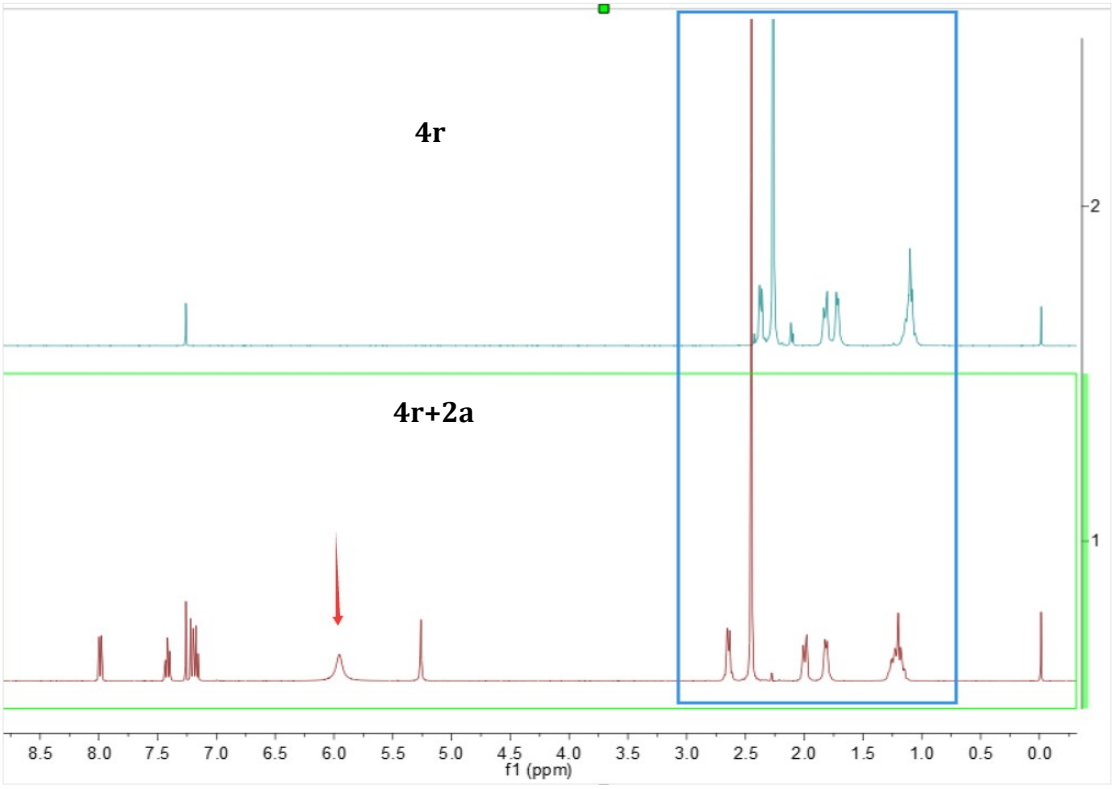
General procedure: To a solution of **2a** (0.05 mmol) in $CDCl_3$ (0.5 ml) was added catalyst **4b** (0.05 mmol), the solution was changed immediately from turbidity to clarification Then the system was monitored by ^1H NMR (400 MHz). A dramatic proton shift of catalyst **4b** showed that **4b** has great interaction with **2a**.



5)

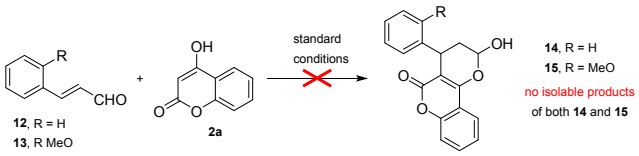


General procedure: To a solution of **2a** (0.05 mmol) in $CDCl_3$ (0.5 ml) was added catalyst **4r** (0.05 mmol), the solution was also changed immediately from turbidity to clarification Then the system was monitored by ^1H NMR (400 MHz). A similar dramatic proton shift of catalyst **4r** showed that amine has significant effect on **2a**.



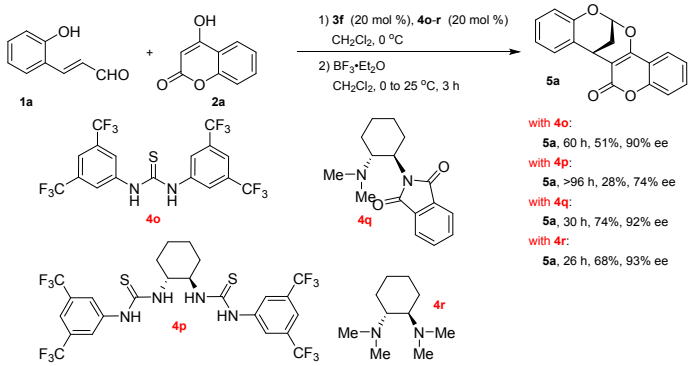
Control experiments:

1)



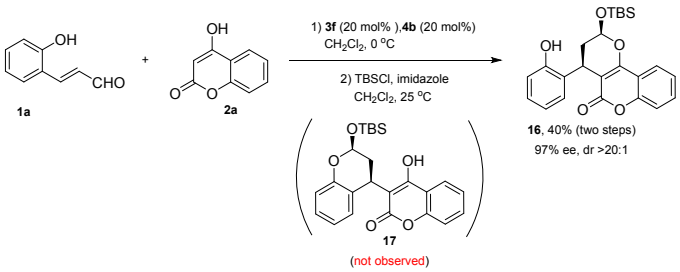
These results clearly indicated the important role of the phenolic hydroxyl group of substrates **1** in the developed multicatalytic system.

2)



These results emphasized the crucial role of bifunctional thiourea-tertiary amine catalysts for the superior efficiency of this multicatalytic system. It should be noted that base cocatalysts should be beneficial for stereochemical induction in this multicatalytic. system.

3)



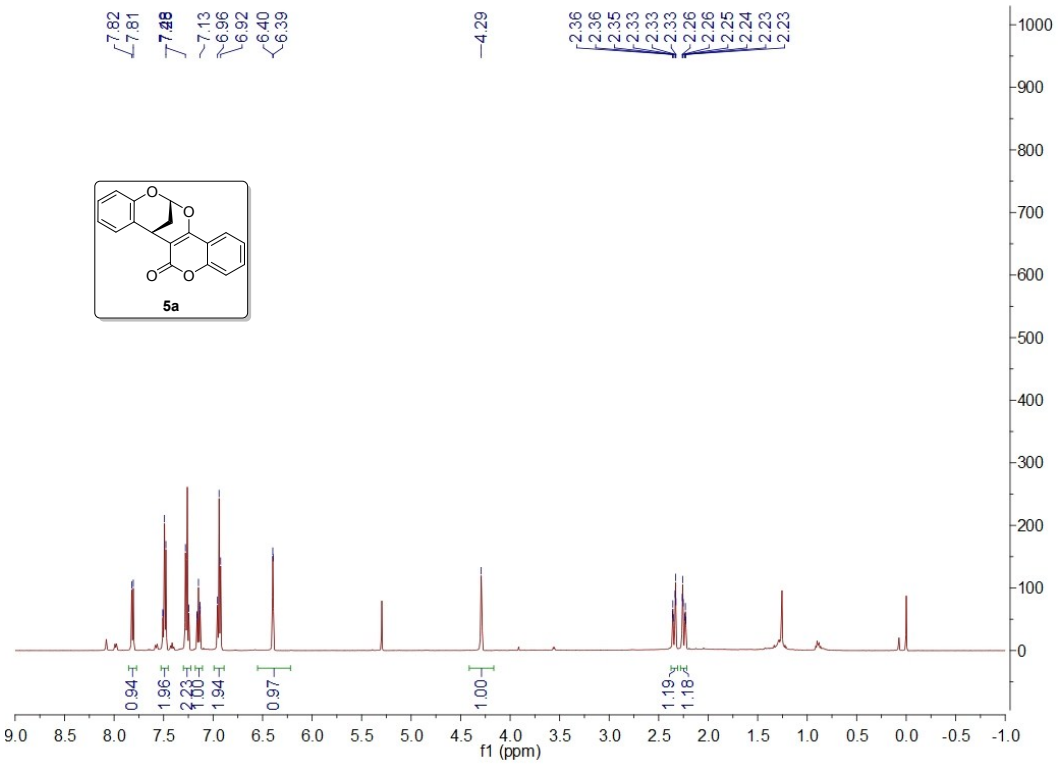
The results demonstrated the reaction intermediate of the Michael addition step.

Experiment procedure of **16** :

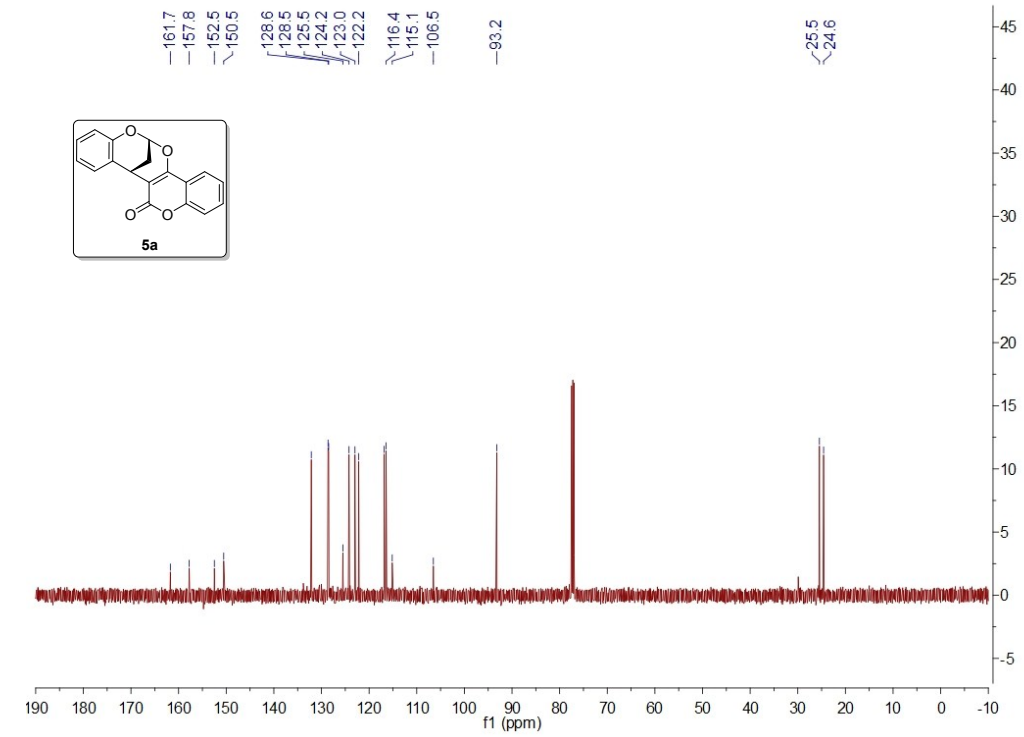
A glass vial equipped with a magnetic stirring bar was charged with **1** (0.10 mmol, 1.0 equiv), catalyst **3e** (0.02 mmol, 0.2 equiv) and catalyst **4b** (0.02 mmol, 0.2 equiv) in CH_2Cl_2 (0.5 mL) and the resulting solution was stirred for about 10 min at 0 °C. Then **2** (0.12 mmol, 1.2 equiv) was added. After full conversion of **1**, the crude product was purified by chromatography on silica gel (dichloromethane/ methanol = 20/1). The crude product was dissolved with CH_2Cl_2, then imidazole (0.3 mmol, 3.0 eq) and *tert*-butyldimethylchlorosilane (0.03 mmol, 3.0 eq) was added to the solution. The reaction mixture was allowed to stir at 25 °C until the reaction was completed. Then water was dropped to the mixture. The organic phase was separated and the aqueous phase was extracted with ethyl acetate. The combined organic phases were washed with water and brine, dried with Na_2SO_4, and concentrated in vacuo. The residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate = 20/1) to afford compound **12** (17 mg, 40% for two steps). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.73 (s, 1H), 7.74 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.56 – 7.47 (m, 1H), 7.33 (d, *J* = 8.3 Hz, 1H), 7.22 (dd, *J* = 16.6, 8.4 Hz, 2H), 7.08 (d, *J* = 7.8 Hz, 1H), 6.93 (dd, *J* = 7.5, 4.8 Hz, 2H), 5.71 (t, *J* = 2.4 Hz, 1H), 4.80 (d, *J* = 10.2 Hz, 1H), 2.72 (ddd, *J* = 13.6, 10.5, 2.7 Hz, 1H), 2.16 (d, *J* = 14.7 Hz, 1H), 0.85 (s, 12H), 0.21 (s, 3H), 0.12 (s, 3H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 164.5, 160.4, 152.5, 151.0, 131.8, 129.4, 128.6, 123.8, 123.5, 122.5, 121.7, 118.5, 116.8, 116.2, 108.9, 90.7, 34.9, 26.2, 25.5, 18.3, -4.9, -5.5 ppm. **HRMS:** $[M+Na]^+$ *calcd*. For $C_{24}H_{28}NaO_5Si^+$ 447.1598; found: 447.1596. **$[\alpha]_D^{20}$** -39.91 (c = 1.33 in $CHCl_3$). The enantiomeric excess was determined by HPLC using Chiralpak IC column [*n*-hexane/*i*-PrOH= 80/20, 1 mL/min], λ = 210 nm, t_{major} = 10.44 min, t_{minor} = 9.55 min, **ee = 97%**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.

G. NMR spectra and HPLC traces

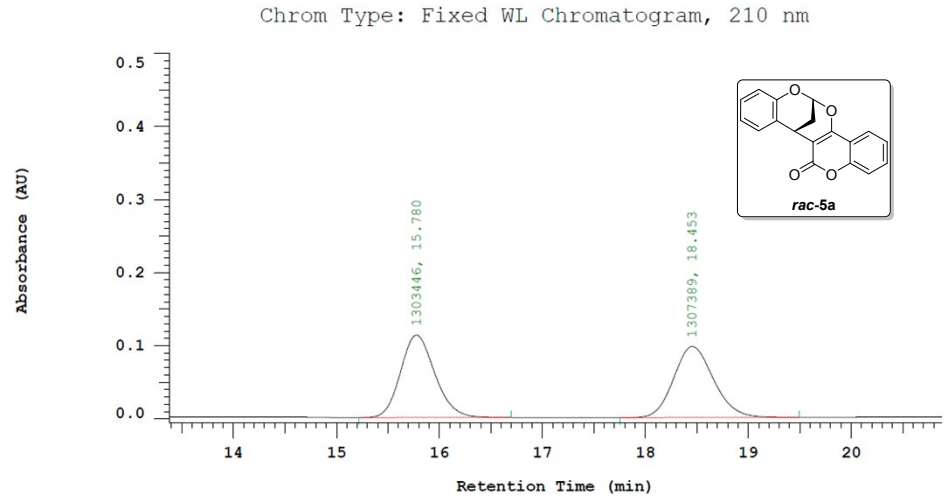
The ^{1}H NMR spectrum of 5a (500 MHz, $CDCl_3$)



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
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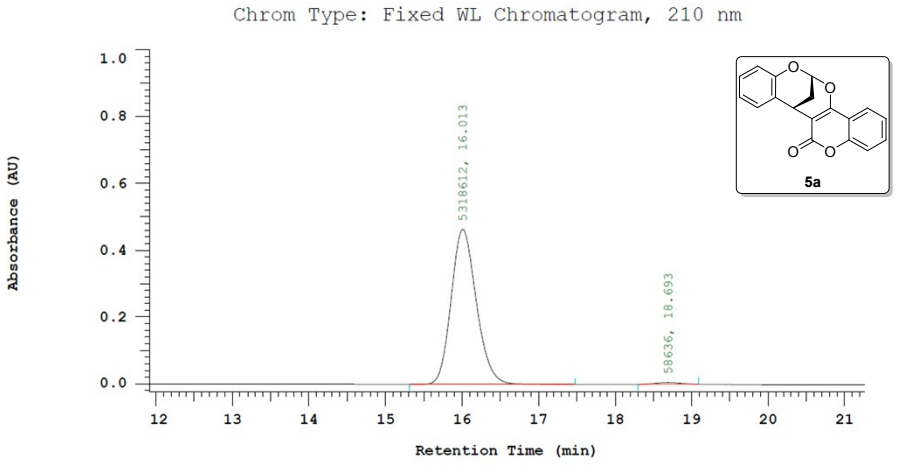
2	18.453	1307389	50.076	BB
		2610835	100.000	

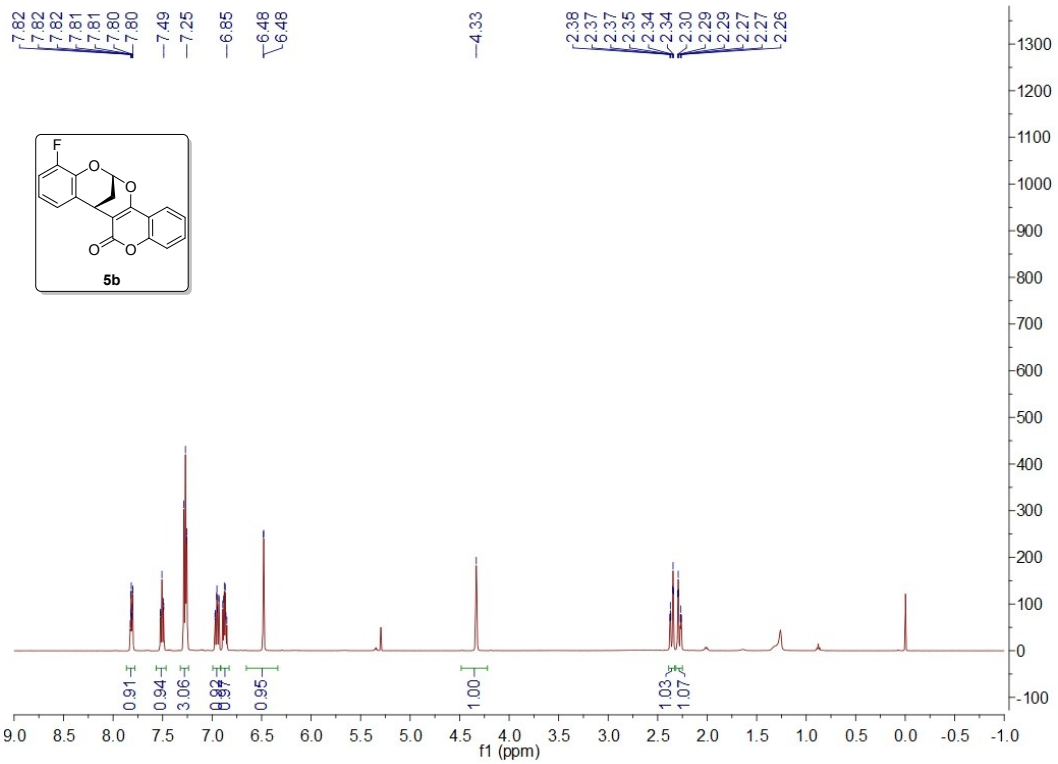
The HPLC of chiral 5a



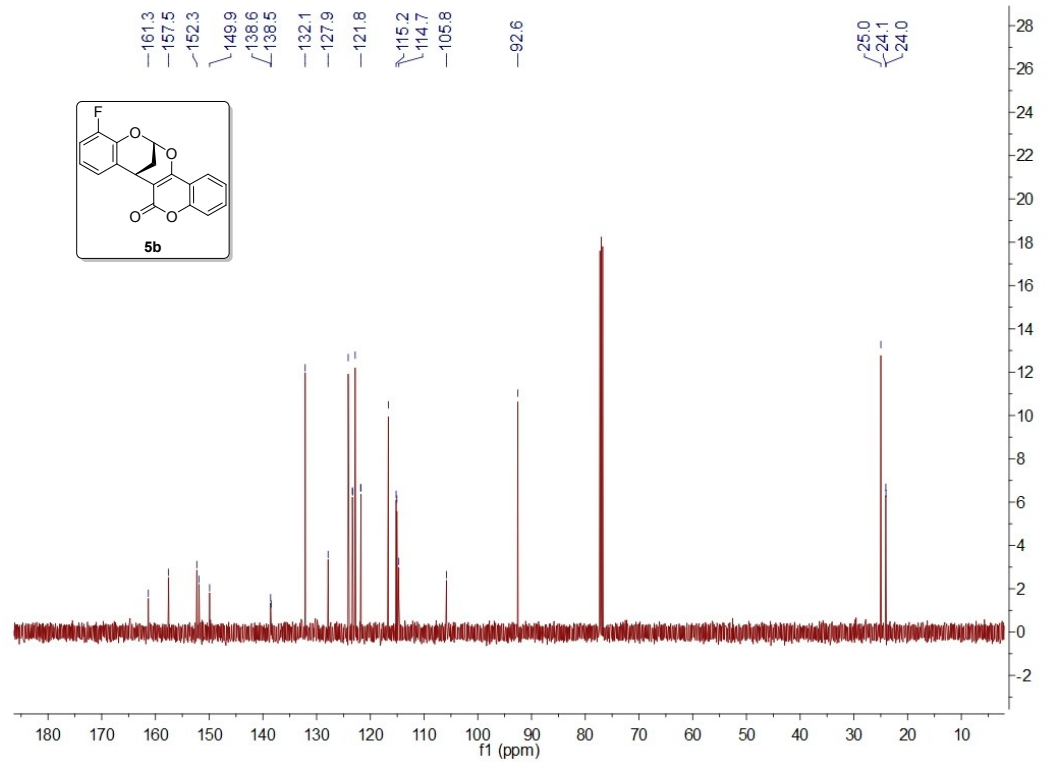
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	16.013	5318612	98.910	BB
2	18.693	58636	1.090	BB
		5377248	100.000	

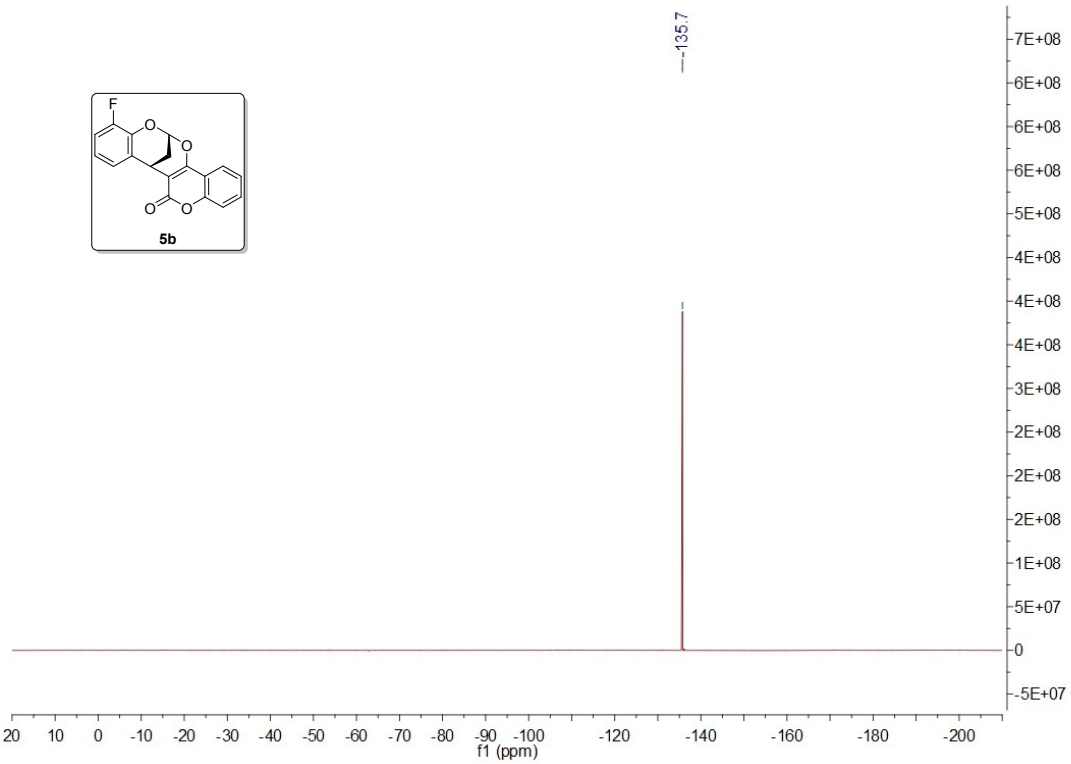
The ^{1}H NMR spectrum of 5b (500 MHz, $CDCl_3$)



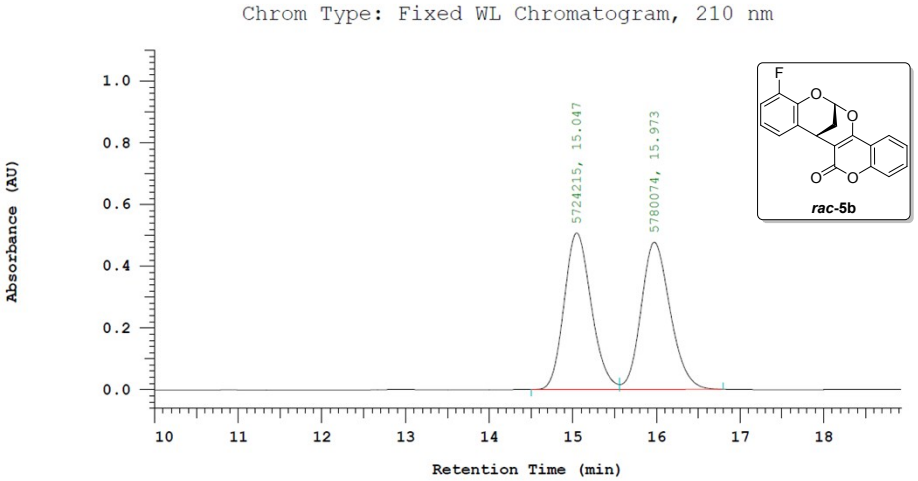
The ^{13}C NMR spectrum of 5b (125 MHz, $CDCl_3$)



The ^{19}F NMR spectrum of 5b (400 MHz, $CDCl_3$)


-135.7
F
O
O
O
O
5b
7E+08
6E+08
6E+08
6E+08
5E+08
4E+08
4E+08
4E+08
3E+08
2E+08
2E+08
2E+08
1E+08
5E+07
0
-5E+07
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -120 -140 -160 -180 -200
f1 (ppm)

The HPLC of racemic 5b



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

No.	RT	Area	Area %	BC
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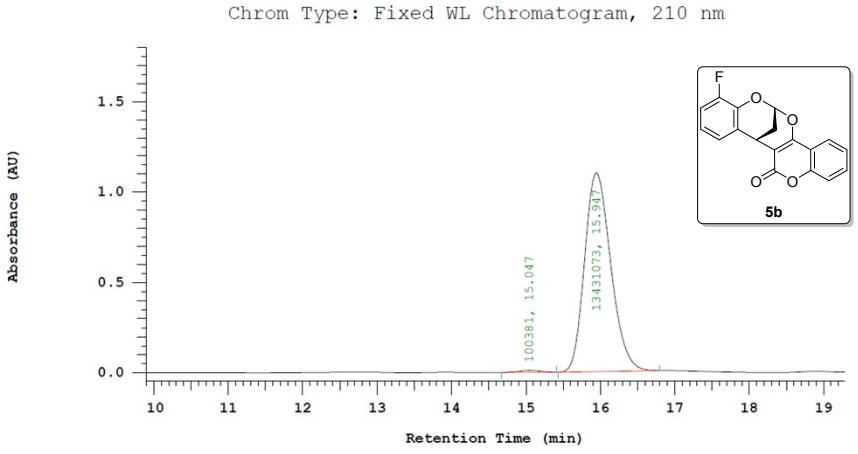
2	15.973	5780074	50.243	VB
		11504289	100.000	

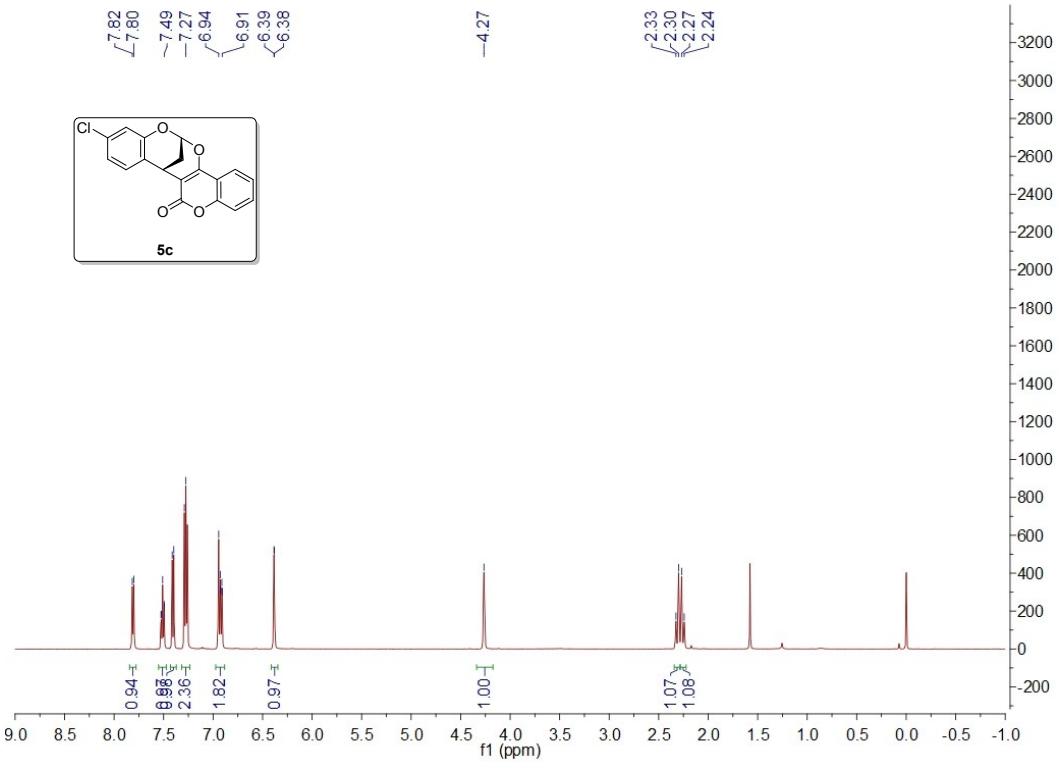
The HPLC of chiral 5b



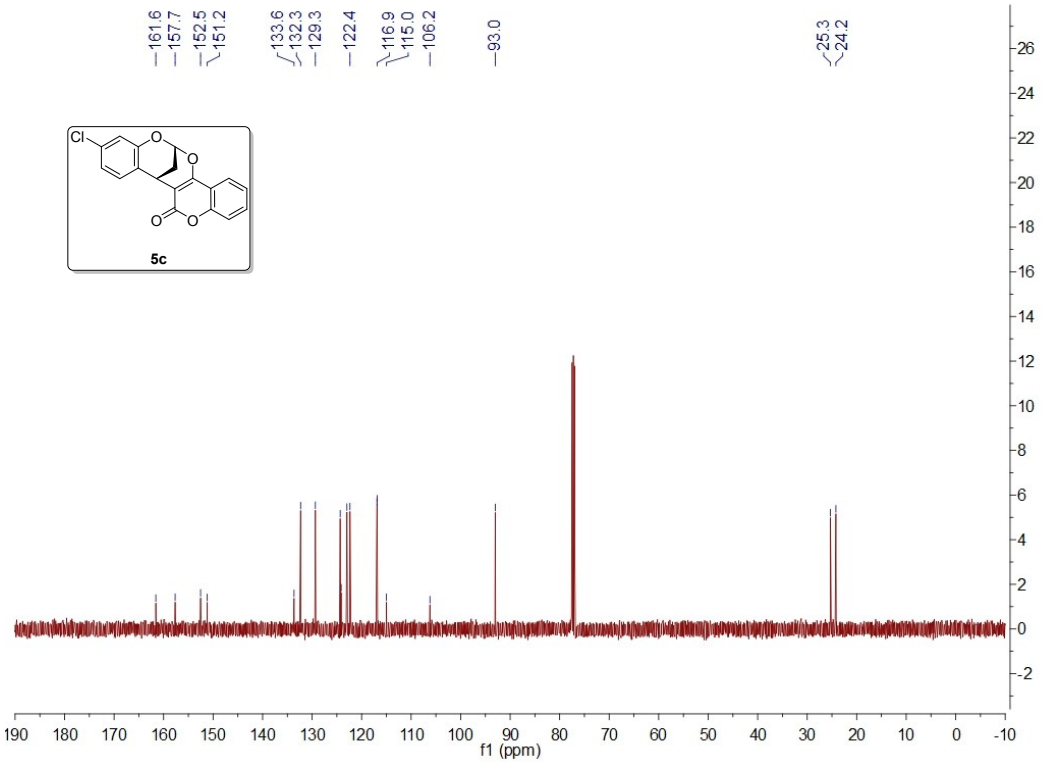
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	15.047	100381	0.742	BB
2	15.947	13431073	99.258	BB
		13531454	100.000	

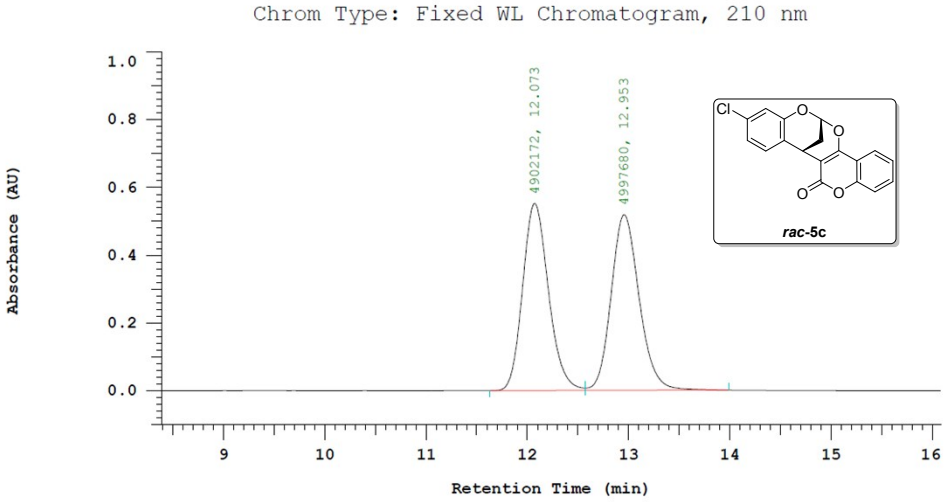
The ^{1}H NMR spectrum of 5c (500 MHz, $CDCl_3$)



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
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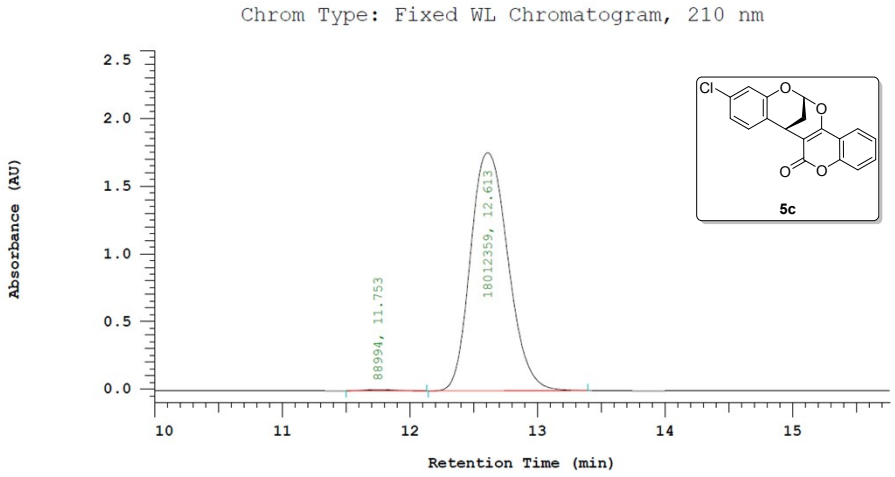
		9899852	100.000	

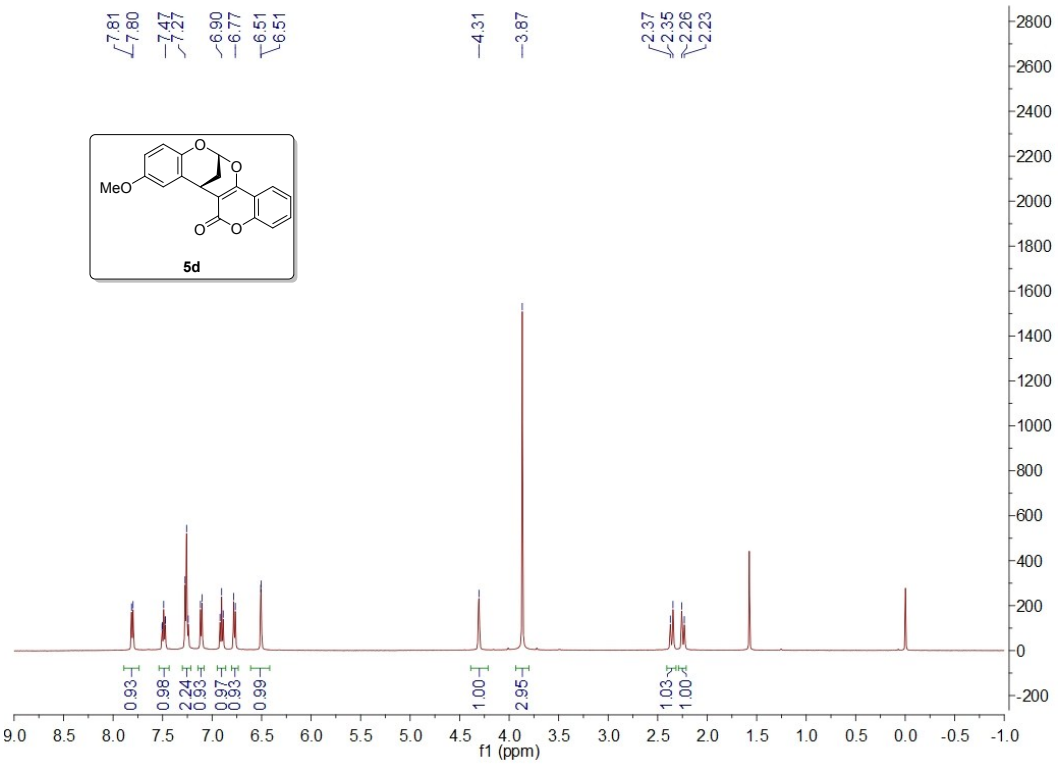
The HPLC of chiral 5c



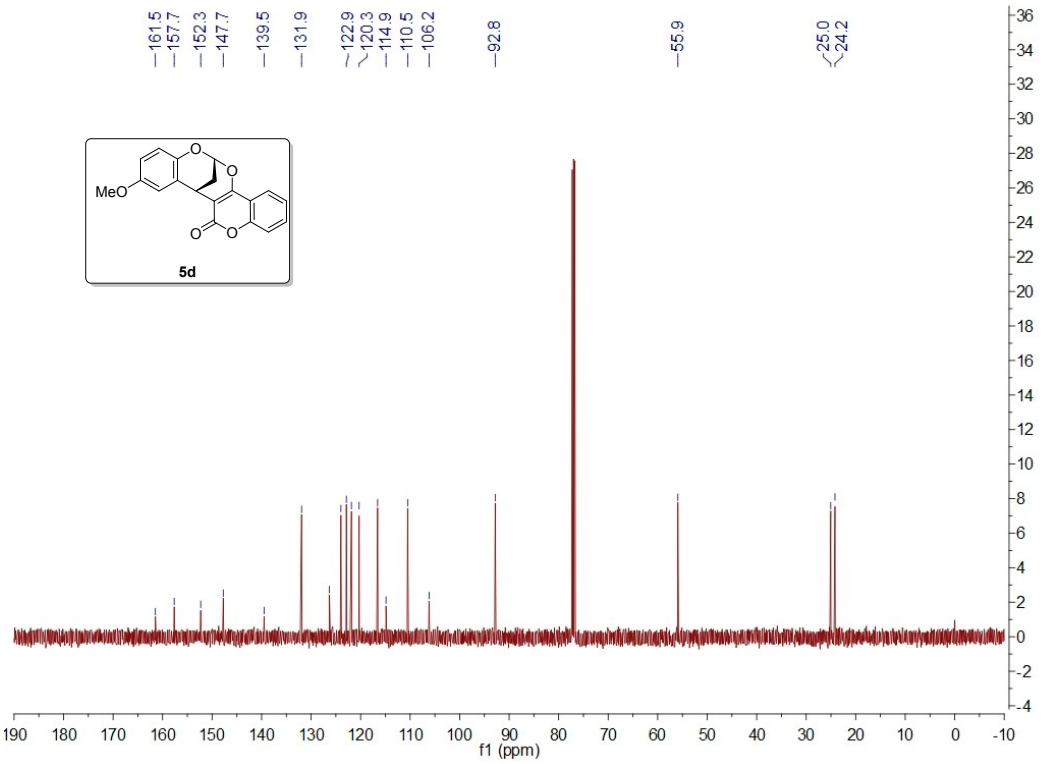
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	11.753	88994	0.492	BB
2	12.613	18012359	99.508	BB
		18101353	100.000	

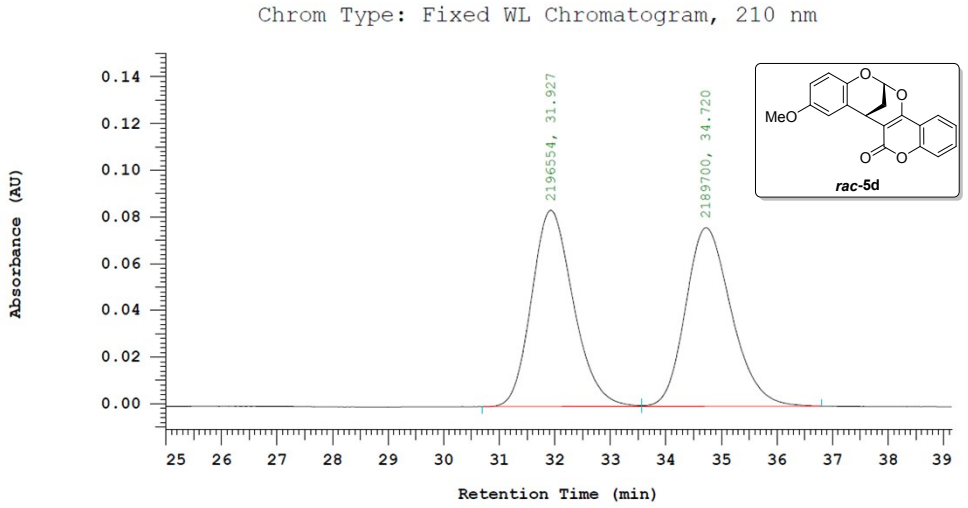
The ^{1}H NMR spectrum of 5d (500 MHz, $CDCl_3$)



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



The HPLC of racemic 5d



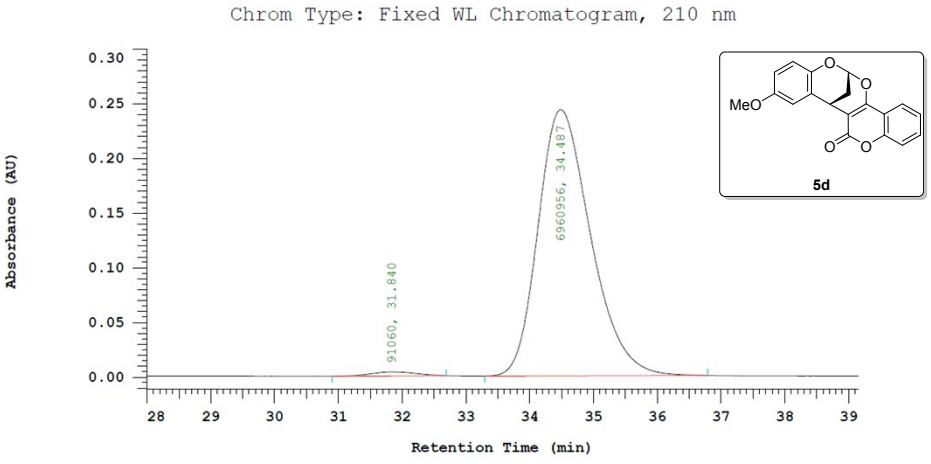
Chrom Type: Fixed WL Chromatogram, 210 nm

Peak Quantitation: AREA

Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	31.927	2196554	50.078	BV
2	34.720	2189700	49.922	VB
		4386254	100.000	

The HPLC of chiral 5d



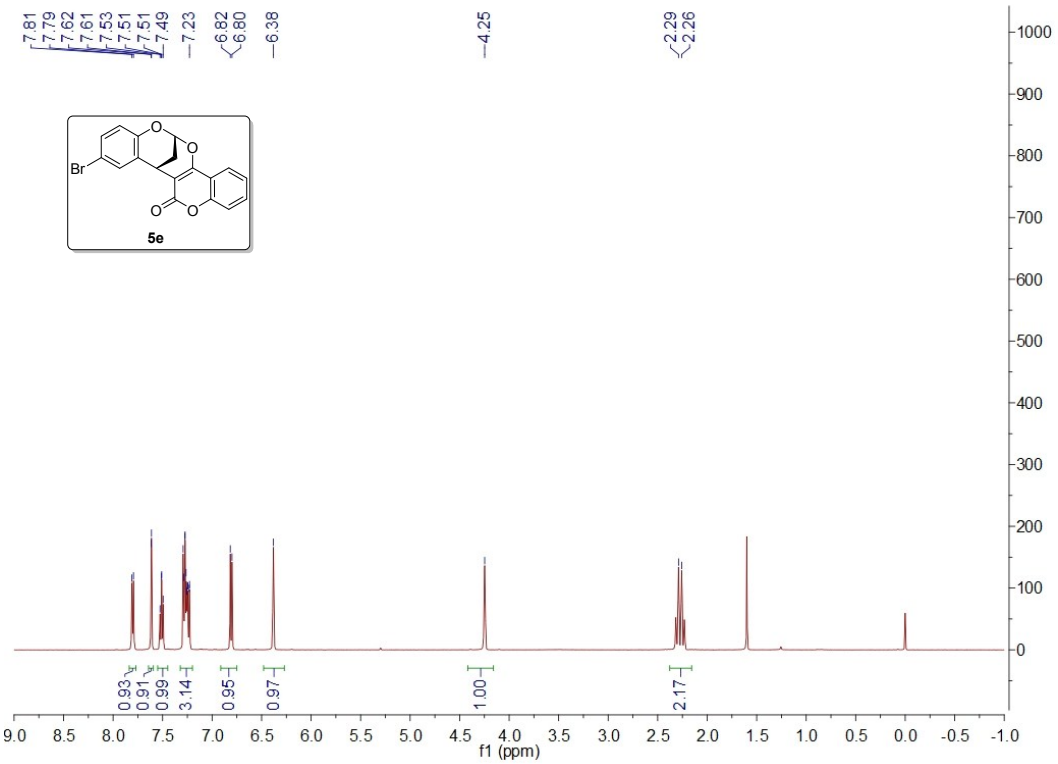
Chrom Type: Fixed WL Chromatogram, 210 nm

Peak Quantitation: AREA

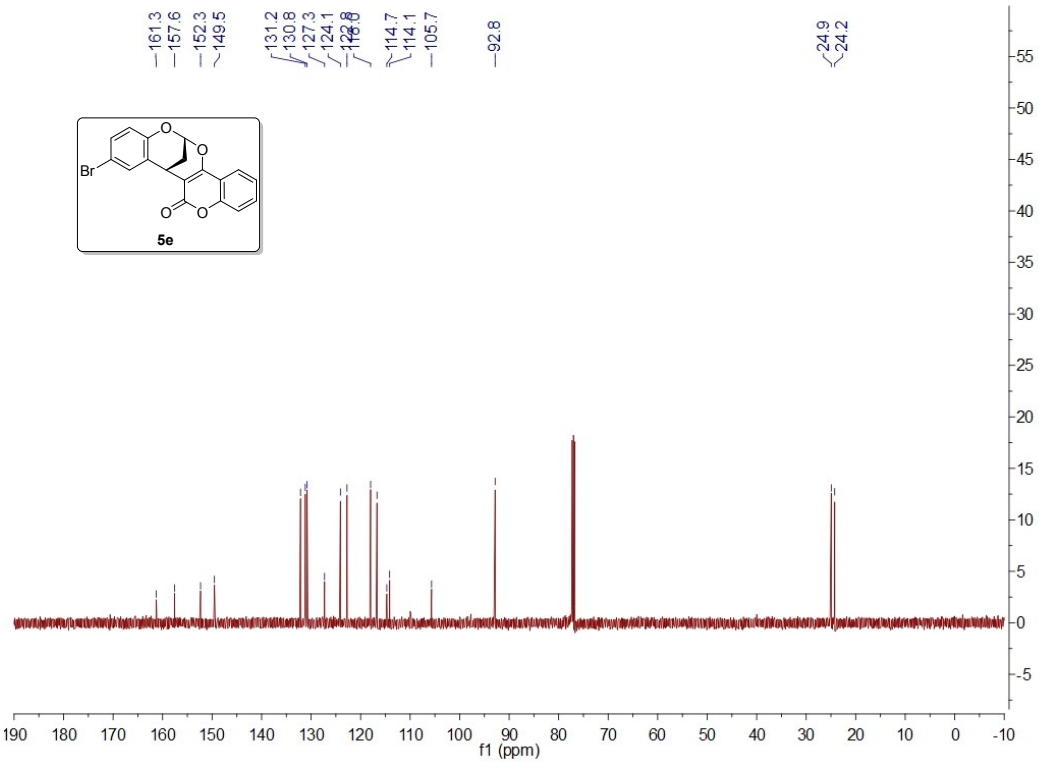
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	31.840	91060	1.291	BB
2	34.487	6960956	98.709	BB
		7052016	100.000	

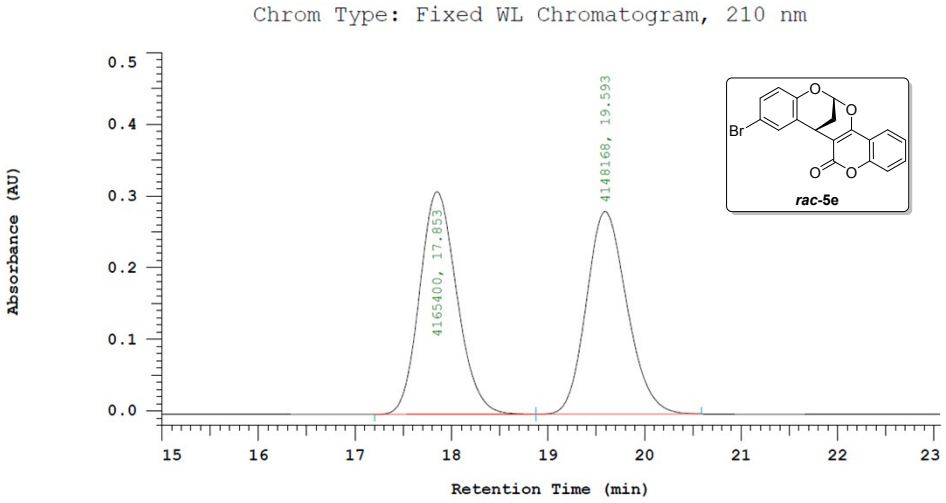
The ^{1}H NMR spectrum of 5e (500 MHz, $CDCl_3$)



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



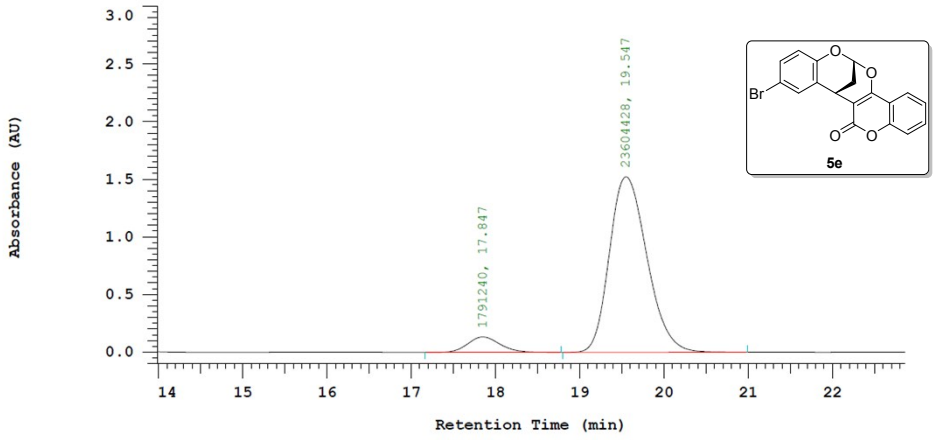
The HPLC of racemic 5e



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

No.	RT	Area	Area %	BC
1	17.853	4165400	50.104	BB
2	19.593	4148168	49.896	BB
		8313568	100.000	

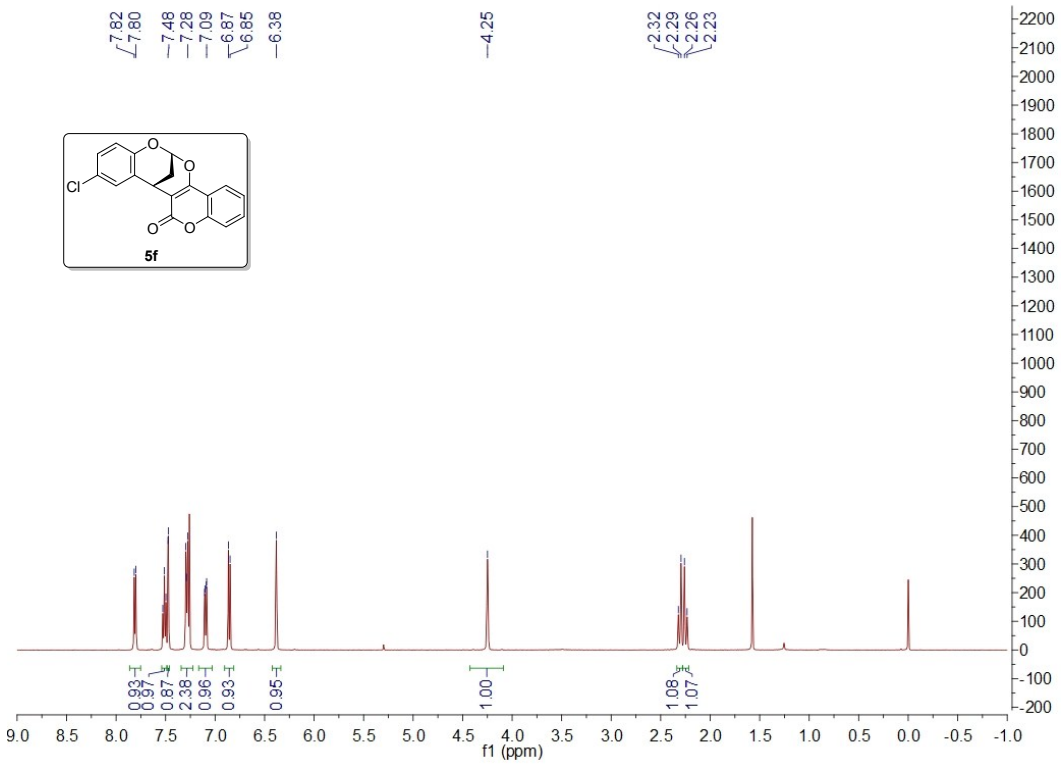
The HPLC of chiral 5e



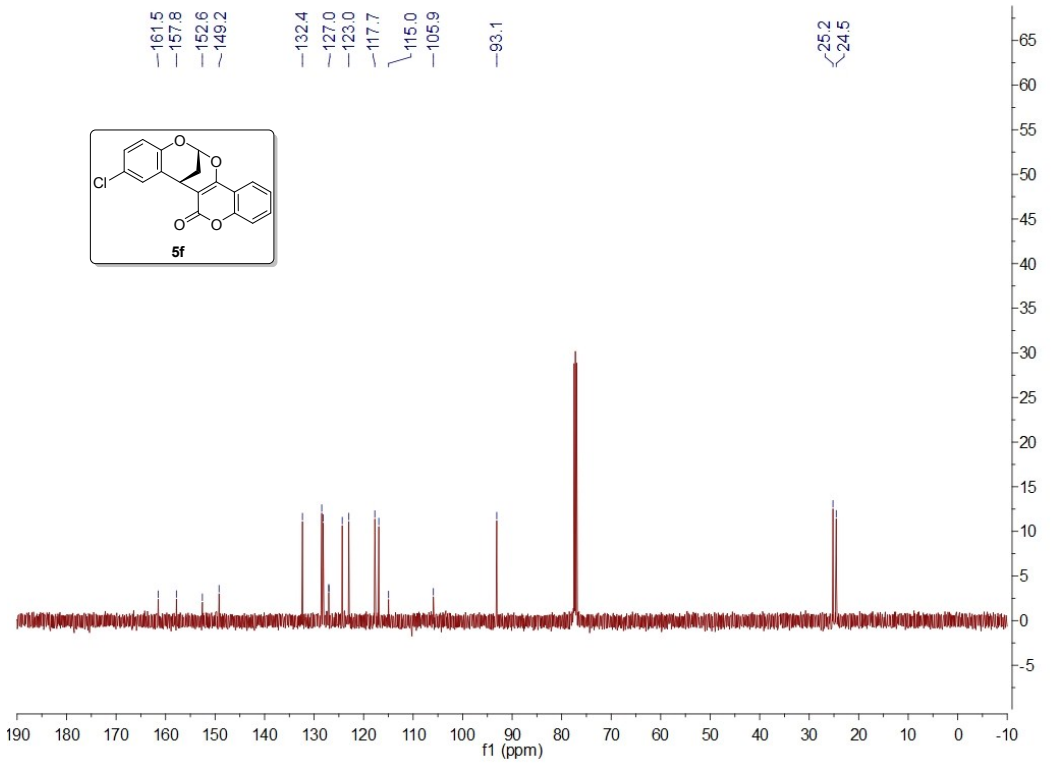
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	17.847	1791240	7.053	BB
2	19.547	23604428	92.947	BB
		25395668	100.000	

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

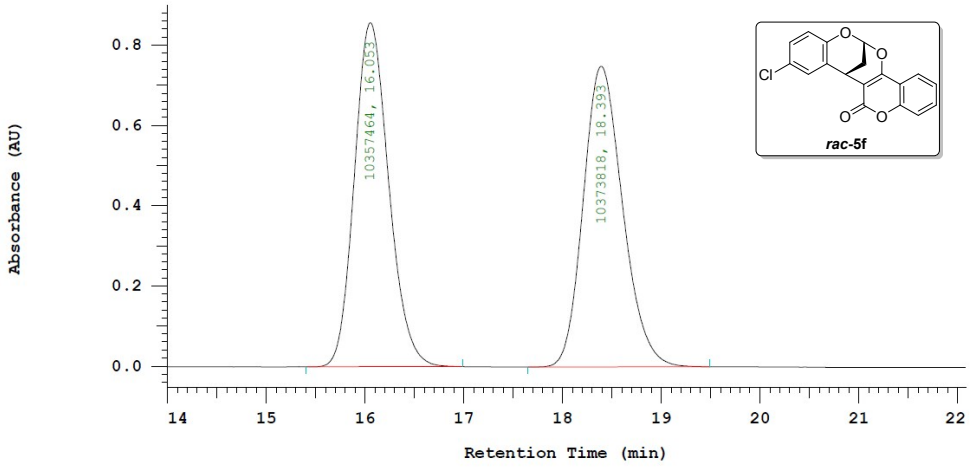


The ^{13}C NMR spectrum of 5f (125 MHz, $CDCl_3$)



The HPLC of racemic 5f

Chrom Type: Fixed WL Chromatogram, 210 nm



Chrom Type: Fixed WL Chromatogram, 210 nm

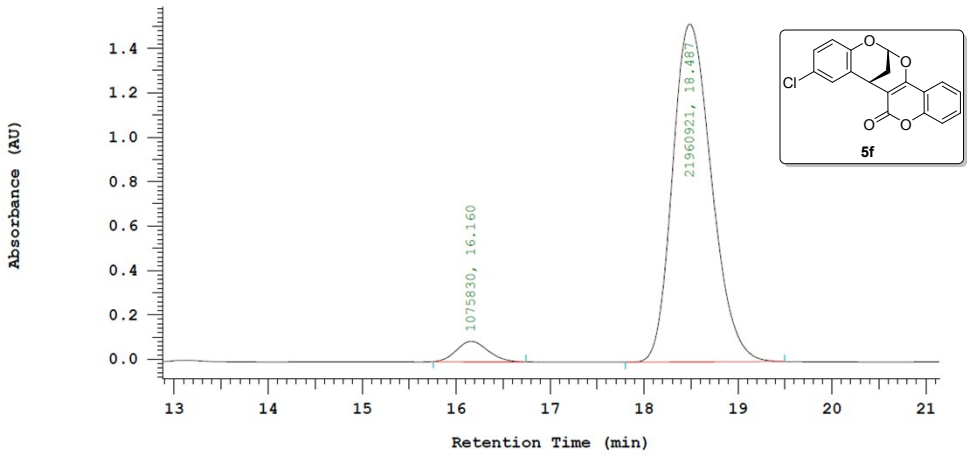
Peak Quantitation: AREA

Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	16.053	10357464	49.961	BB
2	18.393	10373818	50.039	BB
		20731282	100.000	

The HPLC of chiral 5f

Chrom Type: Fixed WL Chromatogram, 210 nm



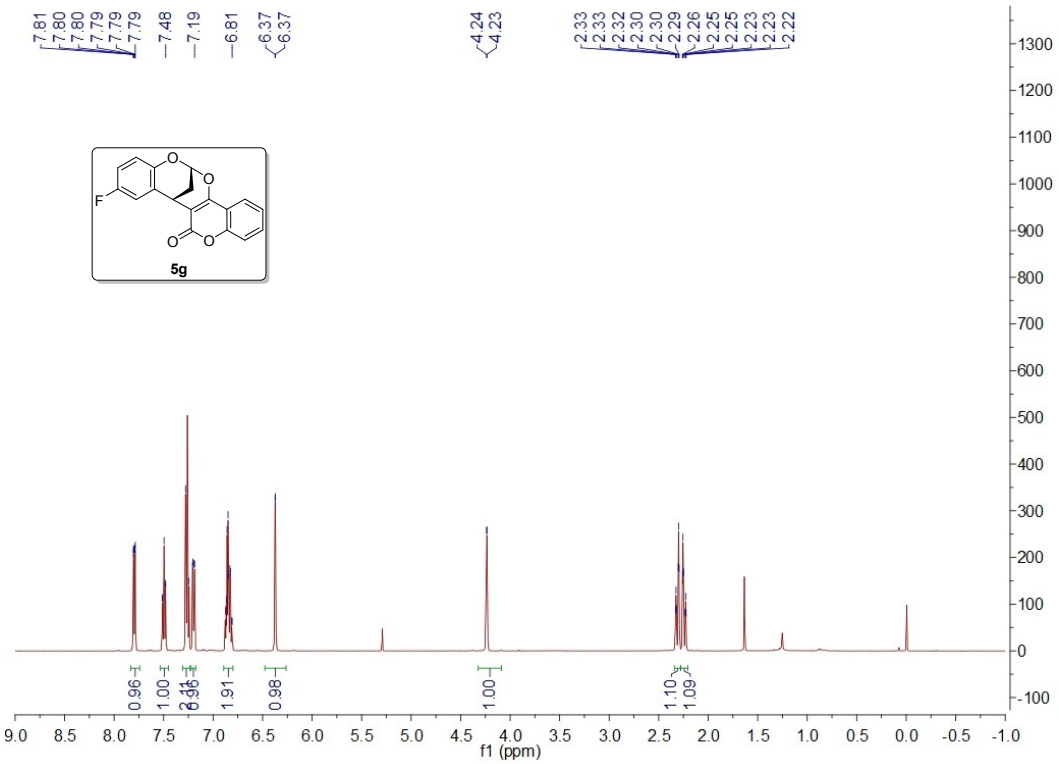
Chrom Type: Fixed WL Chromatogram, 210 nm

Peak Quantitation: AREA

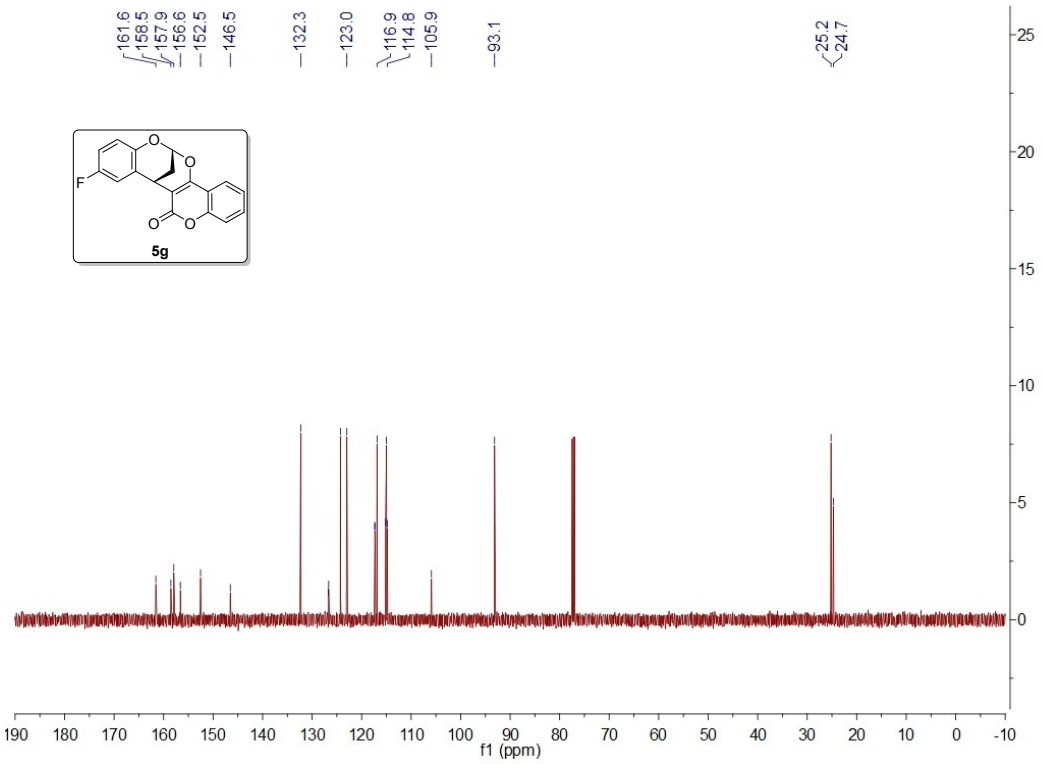
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	16.160	1075830	4.670	BB
2	18.487	21960921	95.330	BB
		23036751	100.000	

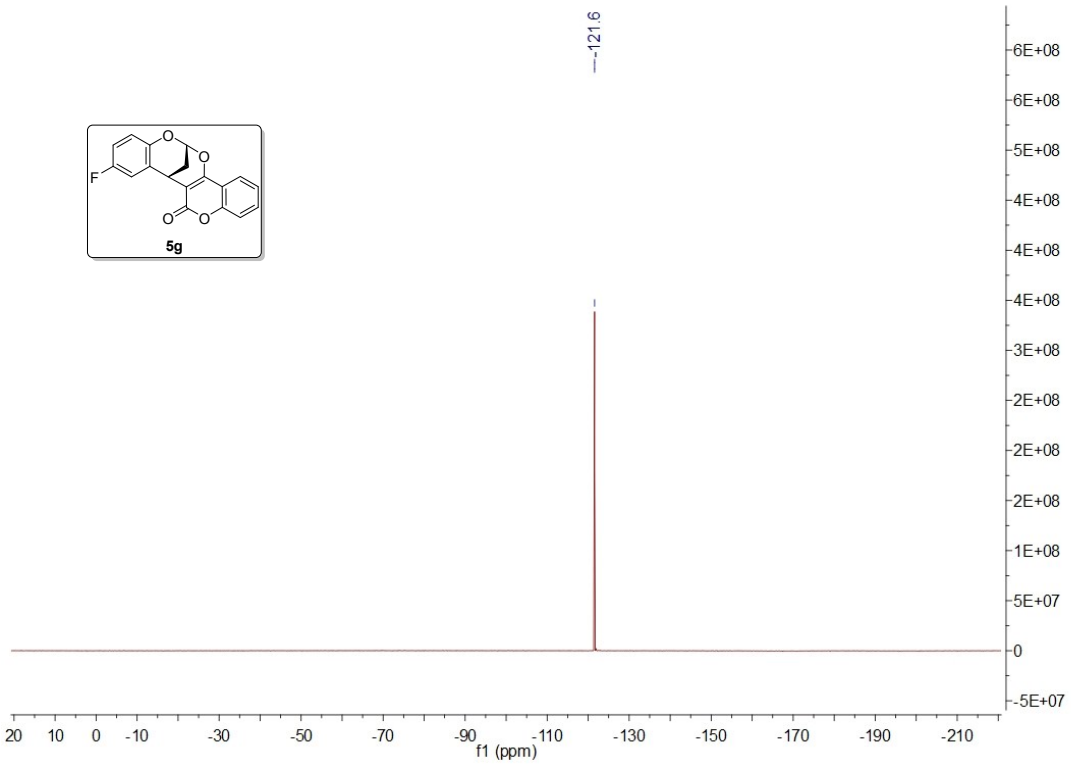
The ^{1}H NMR spectrum of 5g (500 MHz, $CDCl_3$)



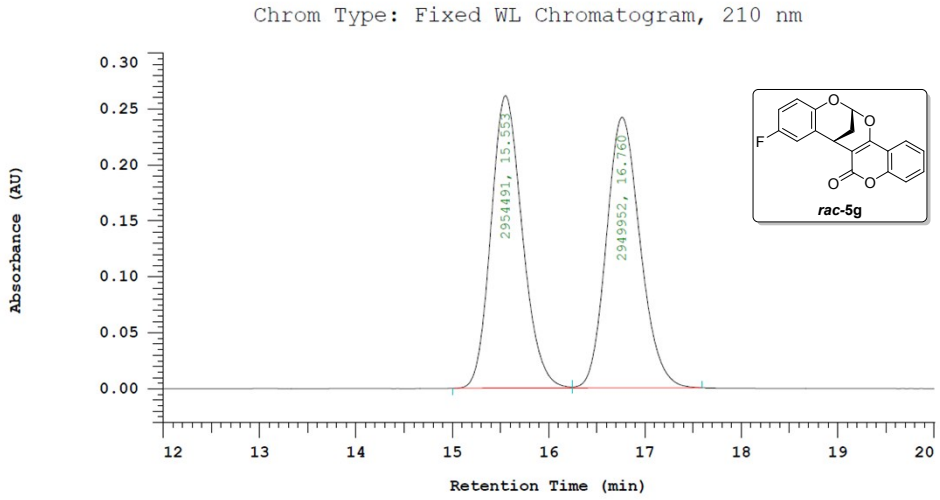
The ^{13}C NMR spectrum of 5g (125 MHz, $CDCl_3$)



The ^{19}F NMR spectrum of 5g (400 MHz, $CDCl_3$)


-121.6
6E+08
6E+08
5E+08
4E+08
4E+08
4E+08
3E+08
2E+08
2E+08
2E+08
1E+08
5E+07
0
-5E+07
F
O
O
O
O
5g
20
10
0
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

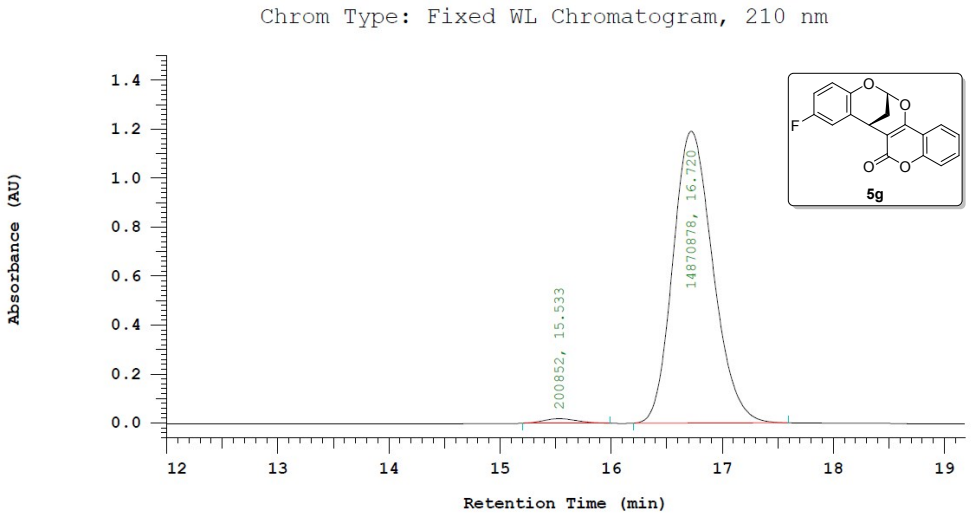
The HPLC of racemic 5g



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

No.	RT	Area	Area %	BC
1	15.553	2954491	50.038	BV
2	16.760	2949952	49.962	VB
		5904443	100.000	

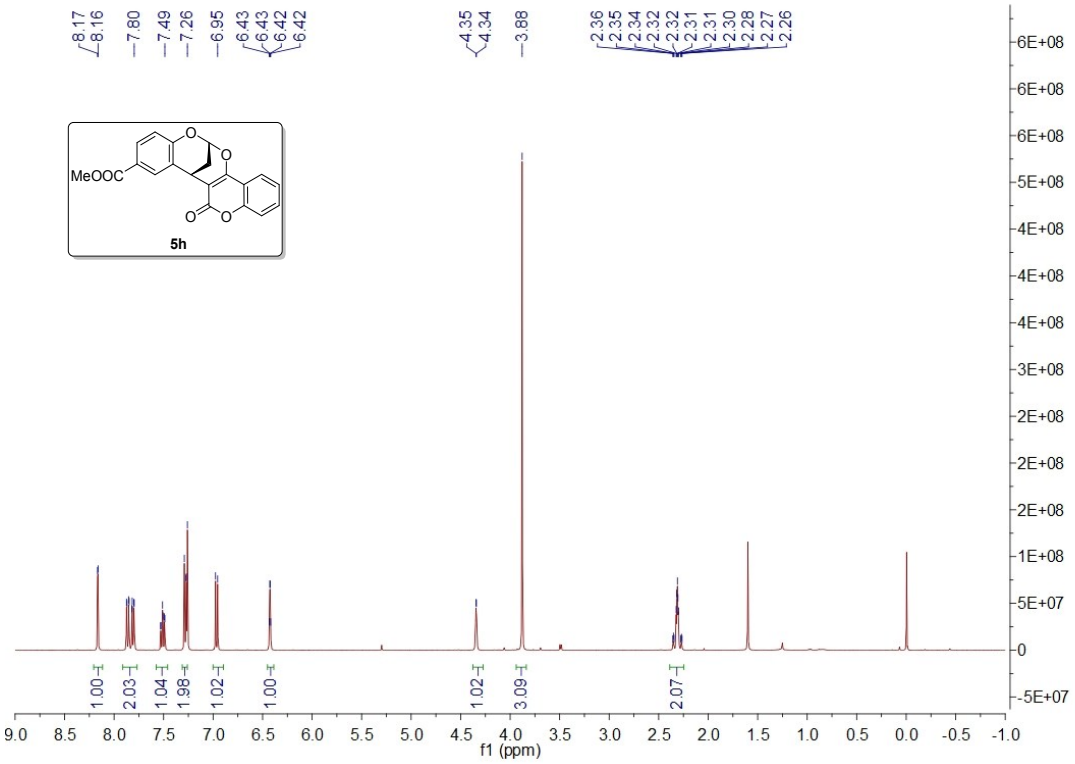
The HPLC of chiral 5g



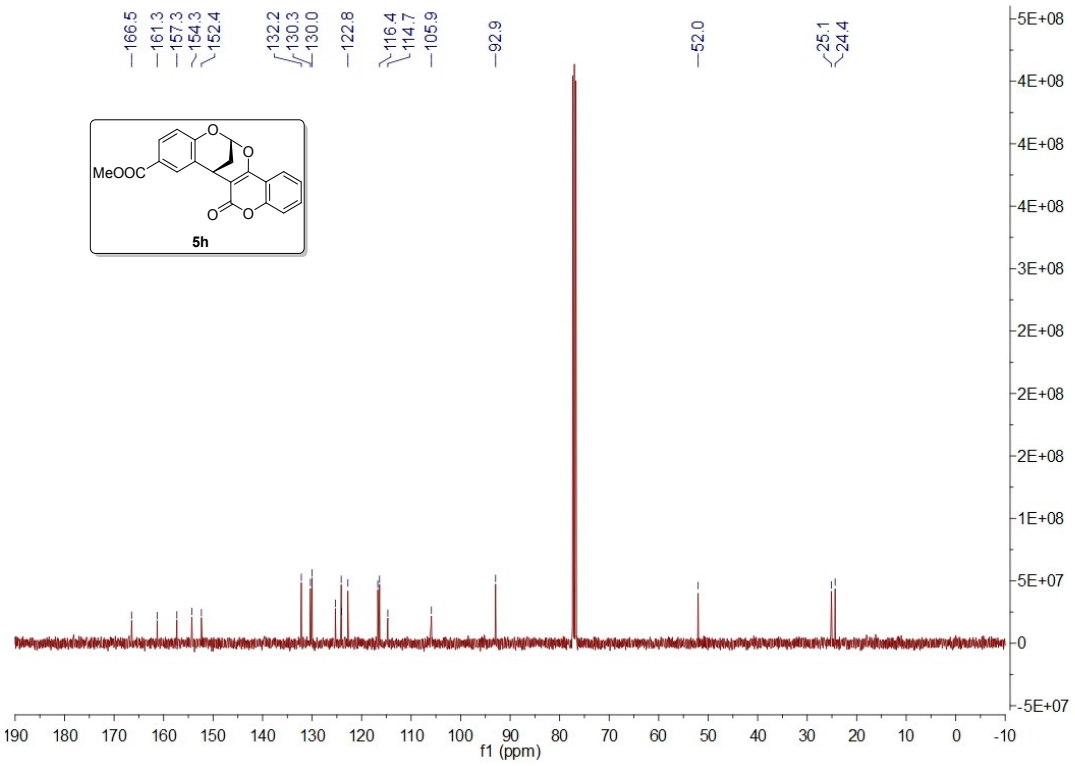
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	15.533	200852	1.333	BB
2	16.720	14870878	98.667	BB
		15071730	100.000	

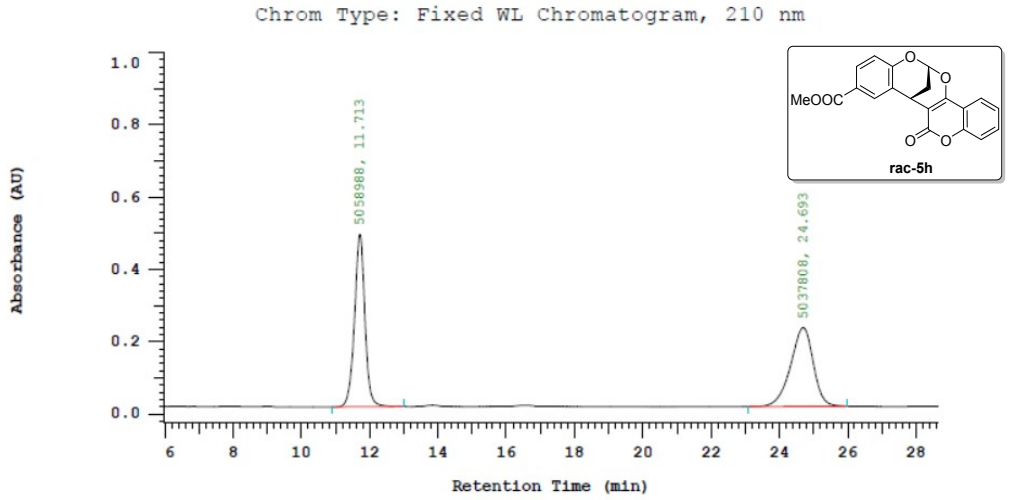
The ^{1}H NMR spectrum of 5h (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 5h (100 MHz, $CDCl_3$)



The HPLC of racemic 5h



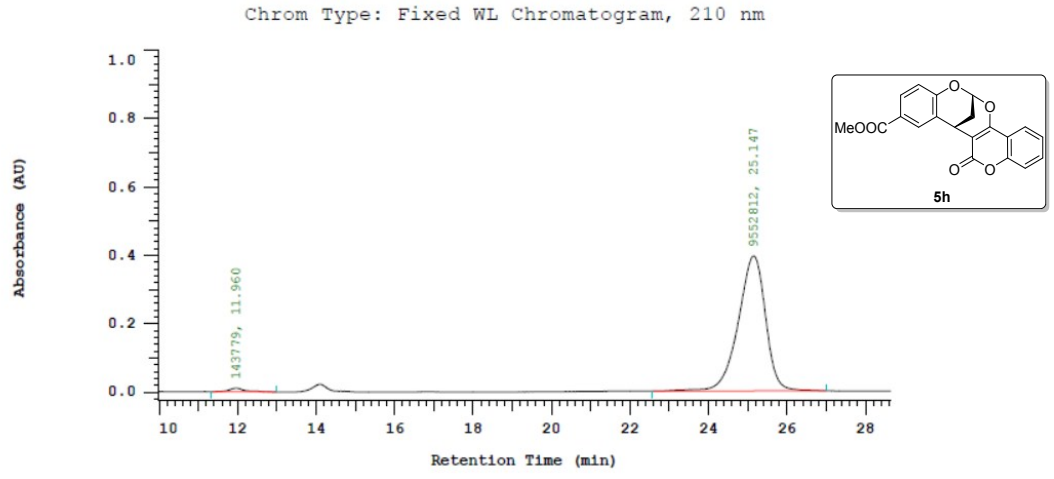
Chrom Type: Fixed WL Chromatogram, 210 nm

Peak Quantitation: AREA

Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	11.713	5058988	50.105	BB
2	24.693	5037808	49.895	BB
		10096796	100.000	

The HPLC of chiral 5h



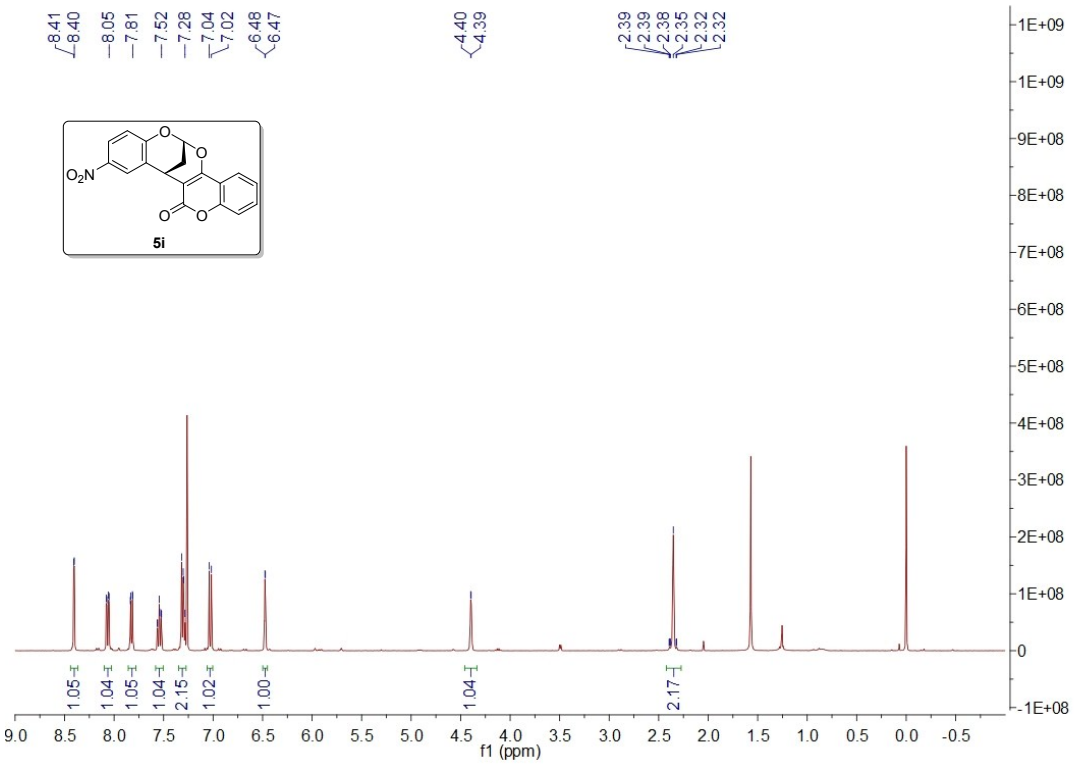
Chrom Type: Fixed WL Chromatogram, 210 nm

Peak Quantitation: AREA

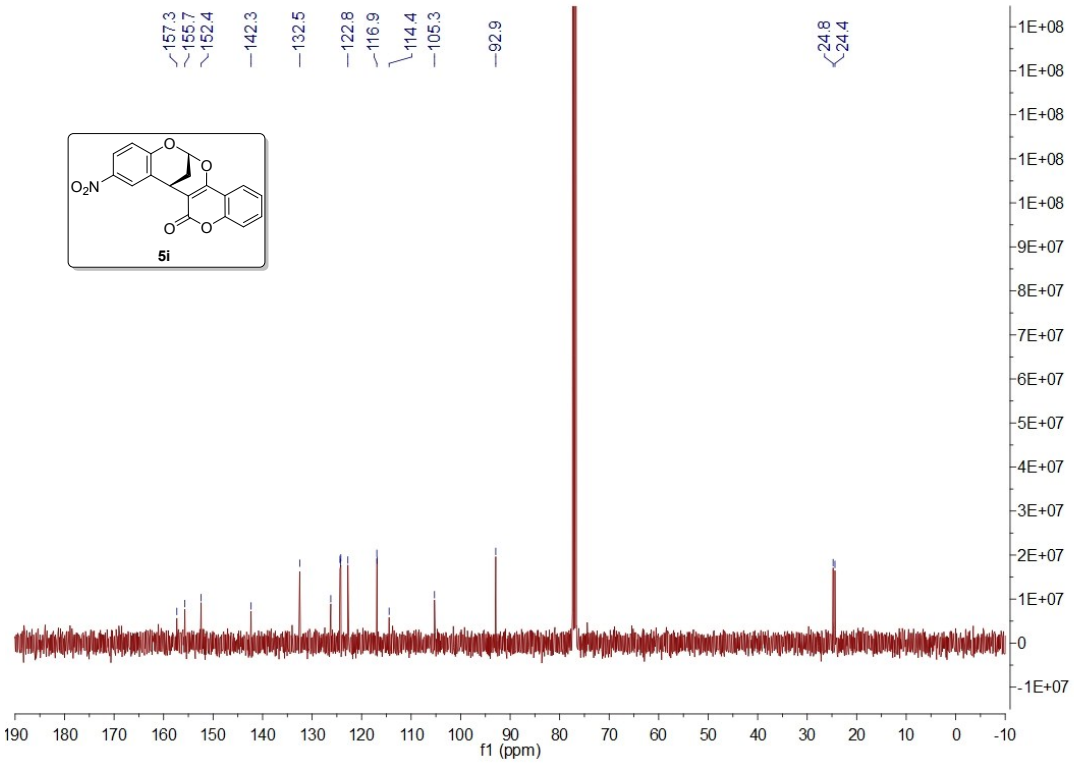
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	11.960	143779	1.483	BB
2	25.147	9552812	98.517	BB
		9696591	100.000	

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

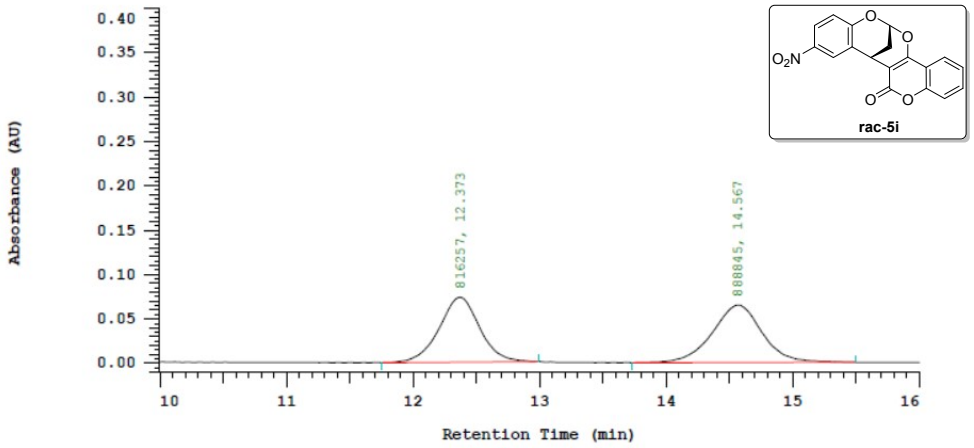


The ^{13}C NMR spectrum of 5i (100 MHz, $CDCl_3$)



The HPLC of racemic 5i

Chrom Type: Fixed WL Chromatogram, 210 nm



Chrom Type: Fixed WL Chromatogram, 210 nm

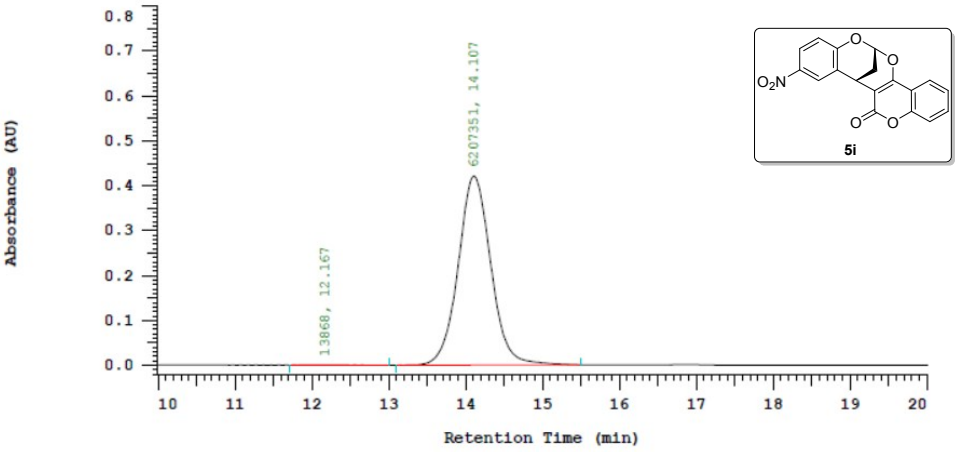
Peak Quantitation: AREA

Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	12.373	816257	47.871	BB
2	14.567	888845	52.129	BB
		1705102	100.000	

The HPLC of chiral 5i

Chrom Type: Fixed WL Chromatogram, 210 nm



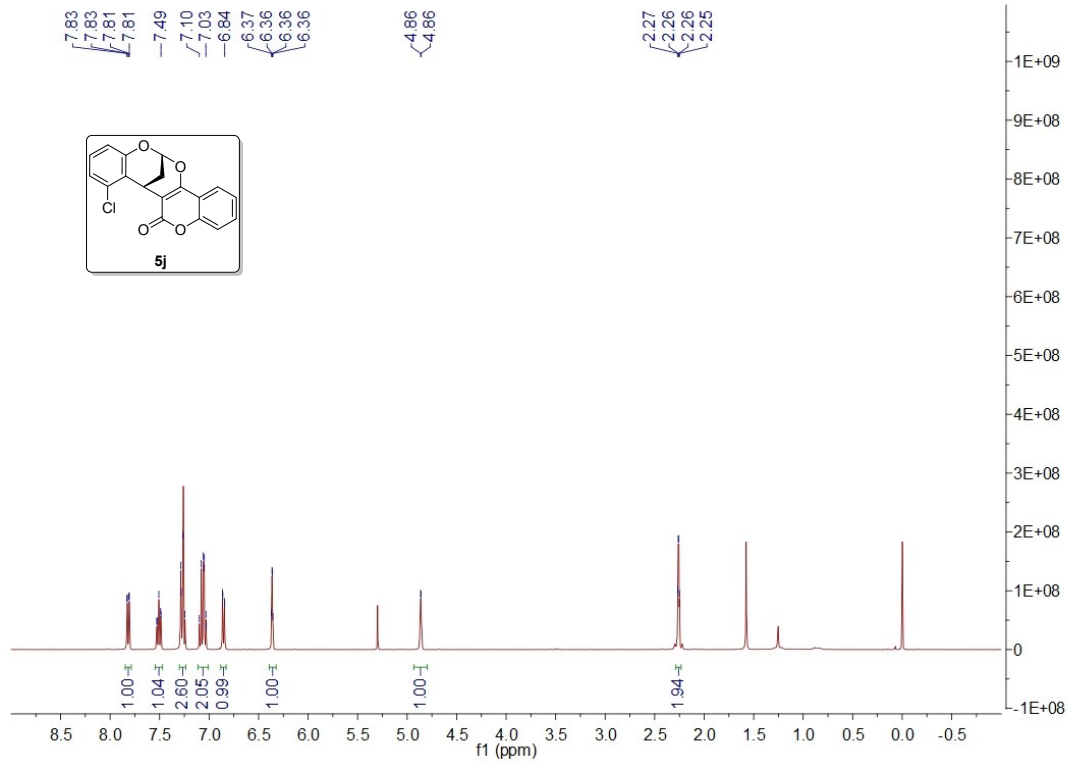
Chrom Type: Fixed WL Chromatogram, 210 nm

Peak Quantitation: AREA

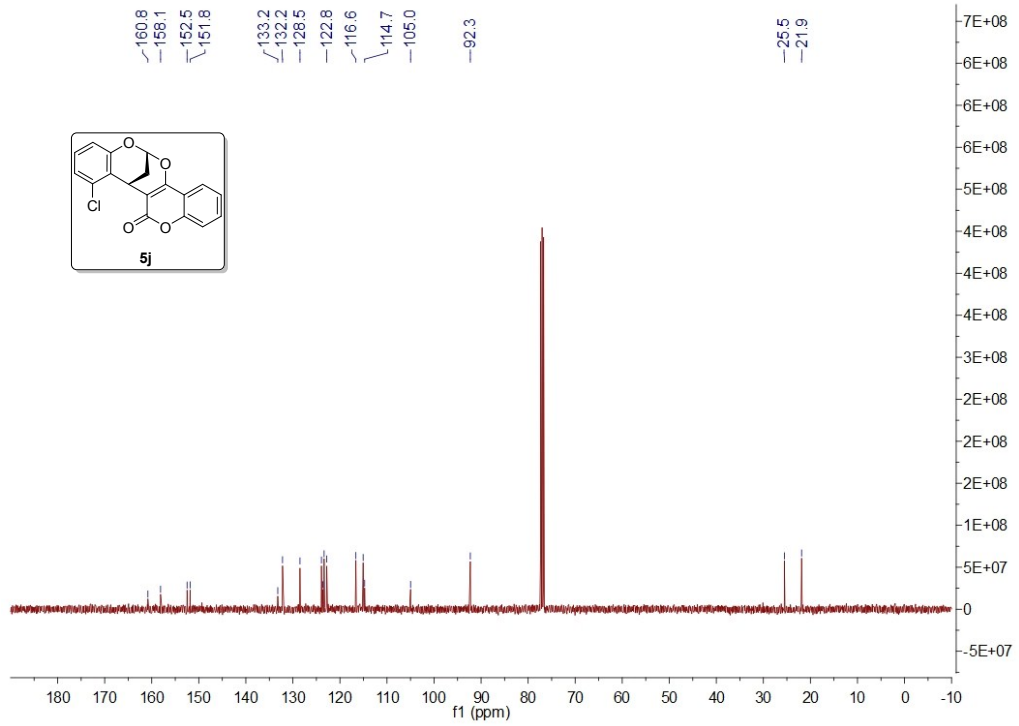
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	12.167	13868	0.223	BB
2	14.107	6207351	99.777	BB
		6221219	100.000	

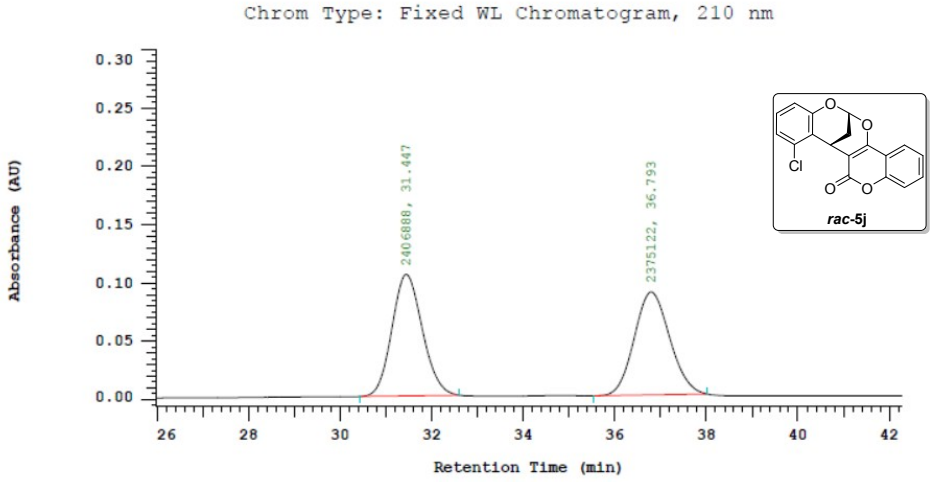
The ^{1}H NMR spectrum of 5j (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 5j (100 MHz, $CDCl_3$)



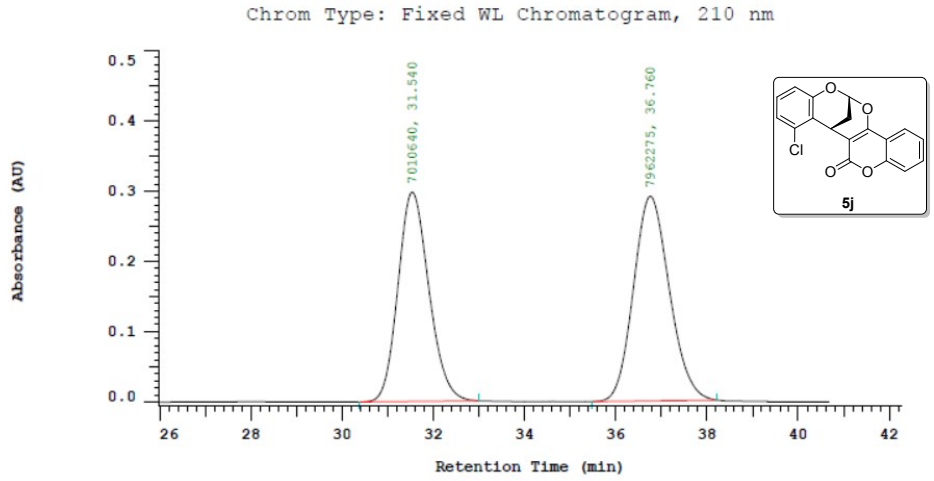
The HPLC of racemic 5j



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

No.	RT	Area	Area %	BC
1	31.447	2406888	50.332	BB
2	36.793	2375122	49.668	BB
		4782010	100.000	

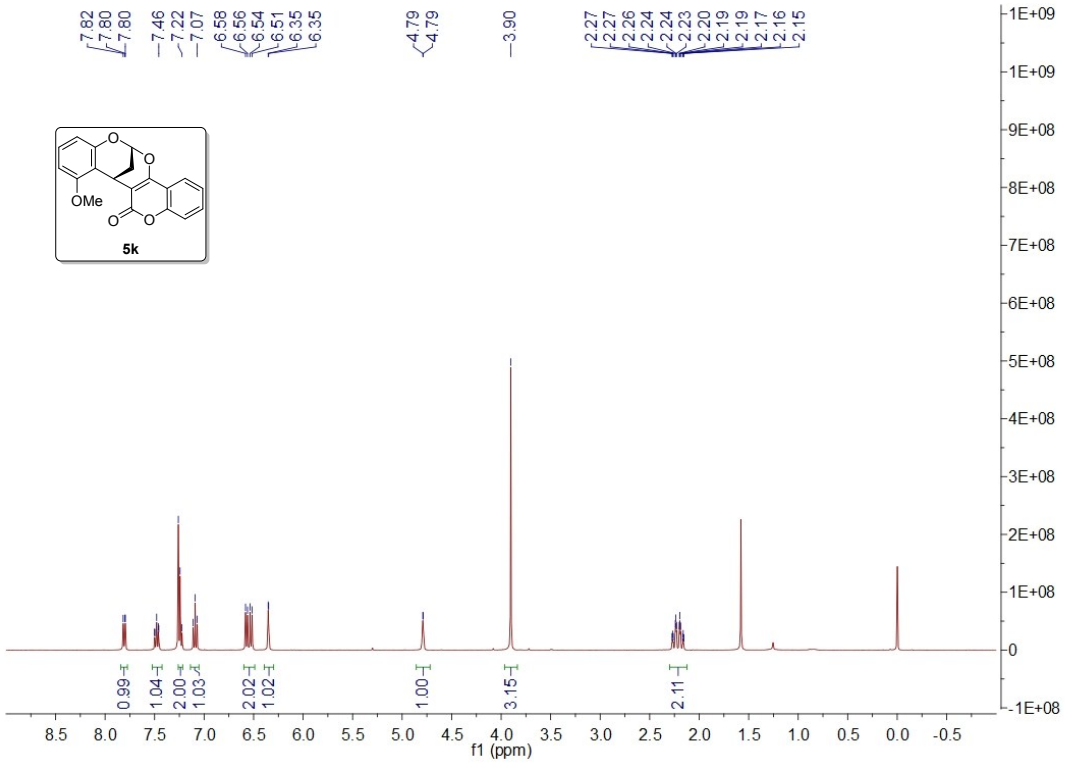
The HPLC of chiral 5j



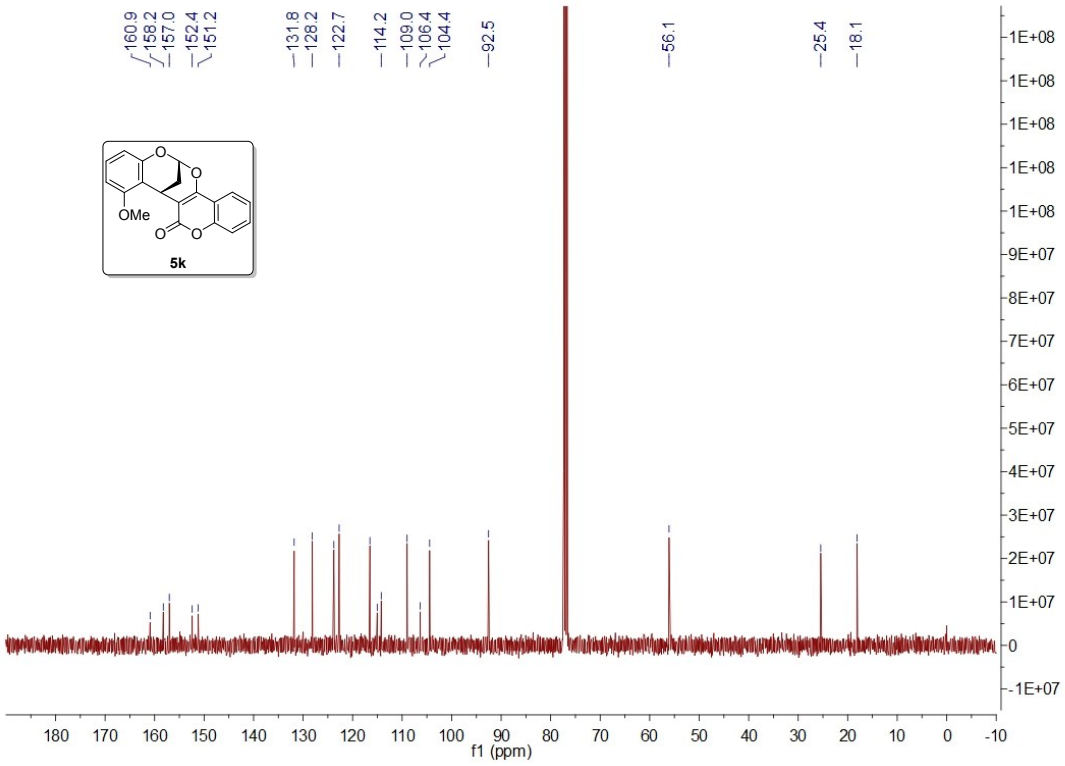
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	31.540	7010640	46.822	BB
2	36.760	7962275	53.178	BB
		14972915	100.000	

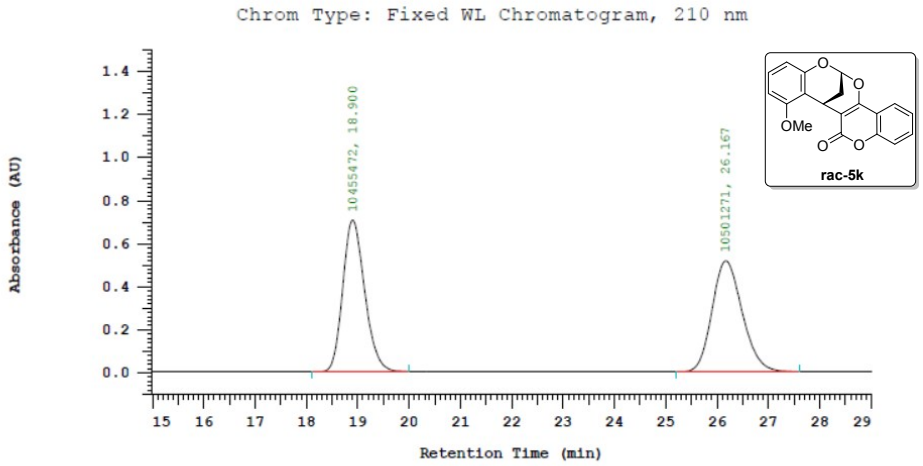
The ^{1}H NMR spectrum of 5k (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 5k (100 MHz, $CDCl_3$)



The HPLC of racemic 5k



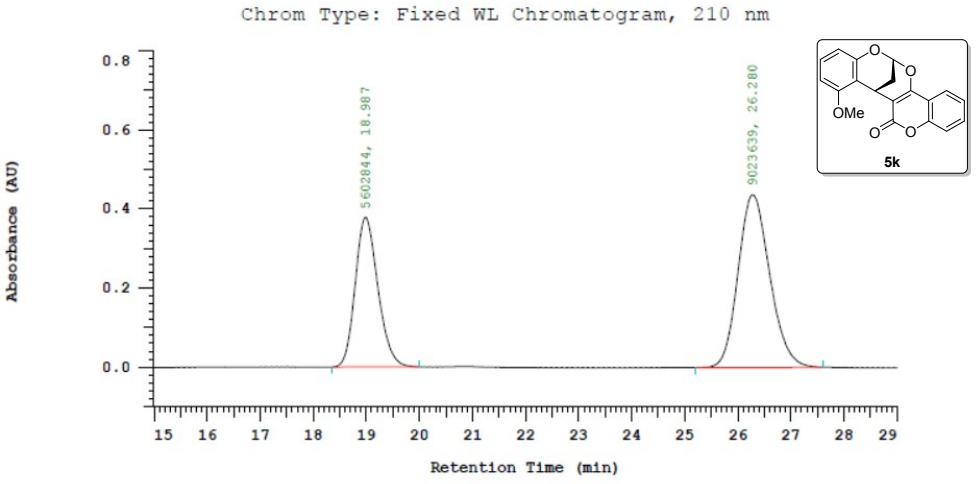
Chrom Type: Fixed WL Chromatogram, 210 nm

Peak Quantitation: AREA

Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	18.900	10455472	49.891	BB
2	26.167	10501271	50.109	BB
		20956743	100.000	

The HPLC of chiral 5k



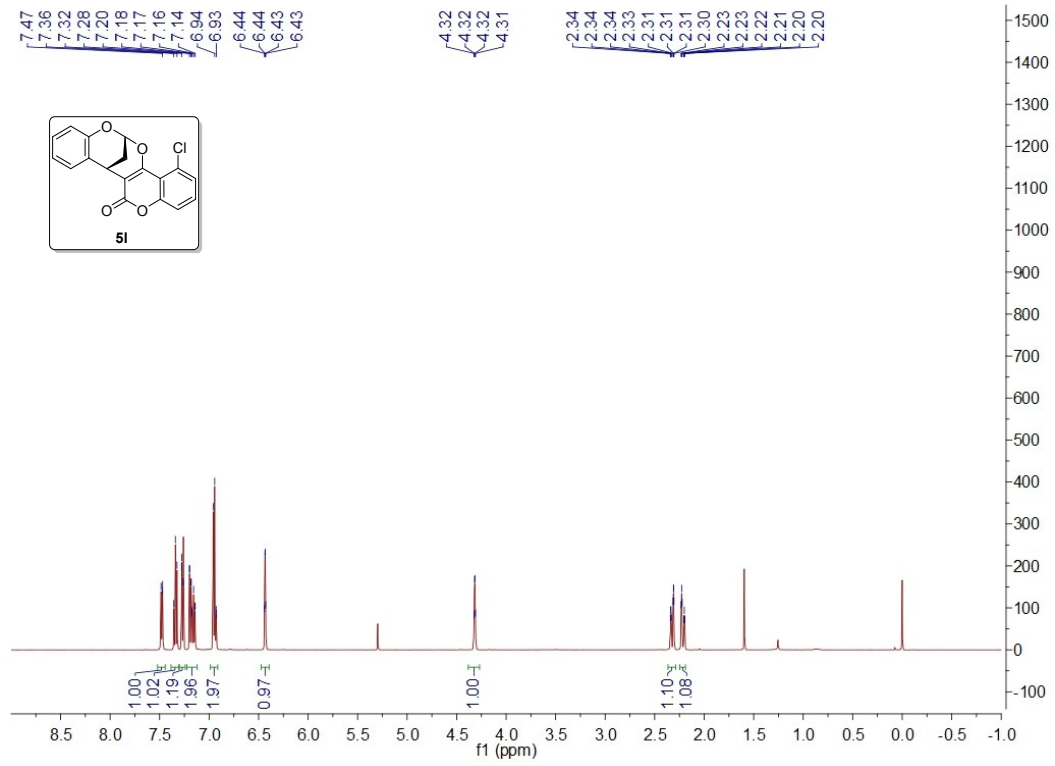
Chrom Type: Fixed WL Chromatogram, 210 nm

Peak Quantitation: AREA

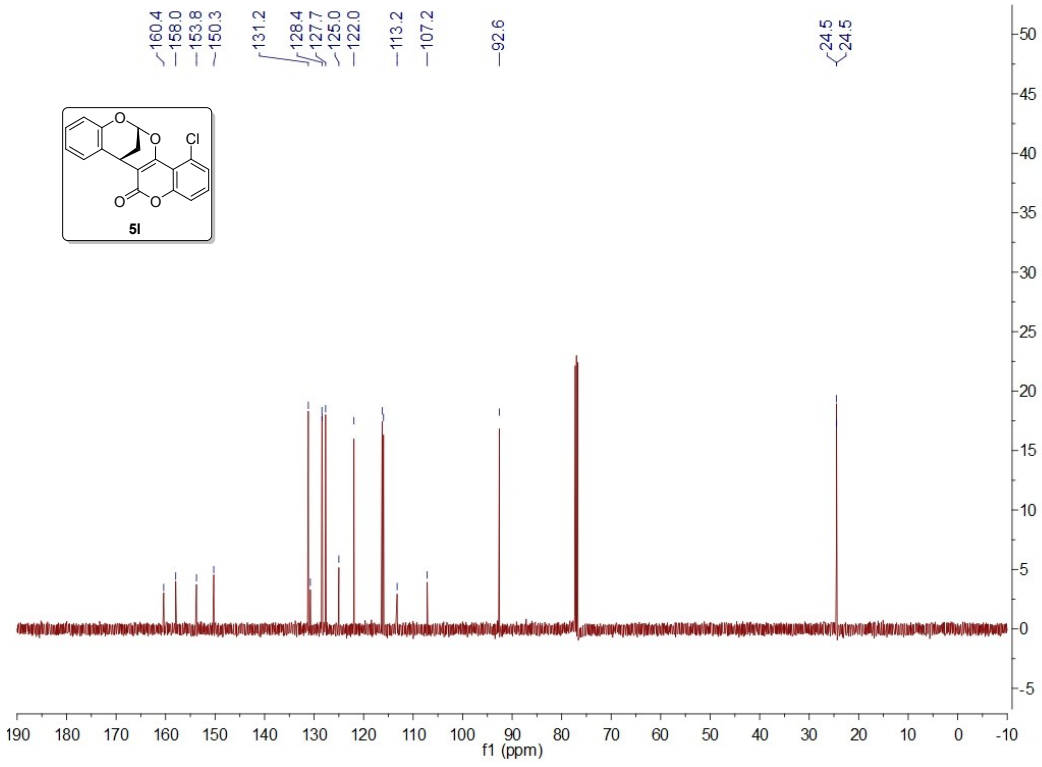
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	18.987	5602844	38.306	BB
2	26.280	9023639	61.694	BB
		14626483	100.000	

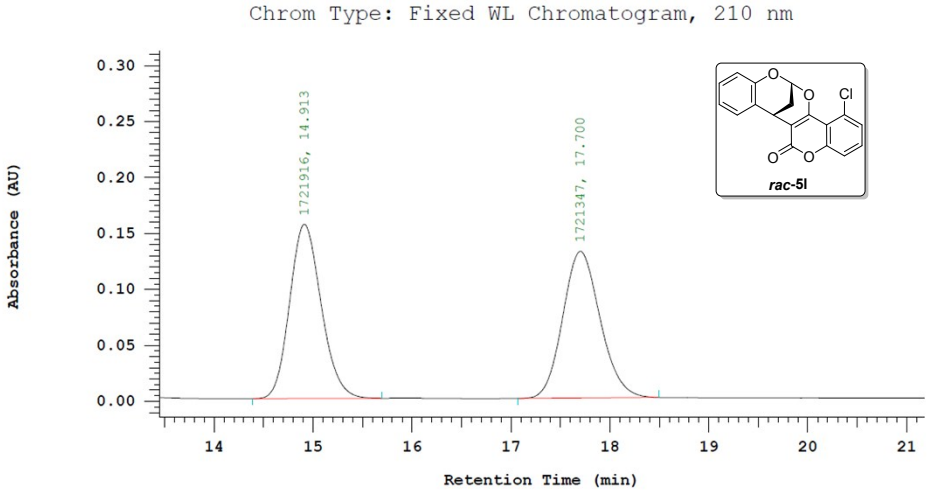
The ^{1}H NMR spectrum of 5l (500 MHz, $CDCl_3$)



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



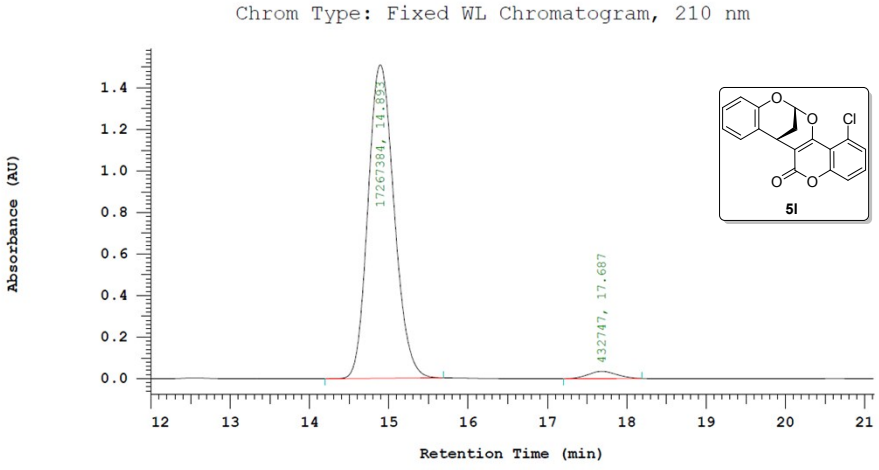
The HPLC of racemic 5l



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

No.	RT	Area	Area %	BC
1	14.913	1721916	50.008	BB
2	17.700	1721347	49.992	BB
		3443263	100.000	

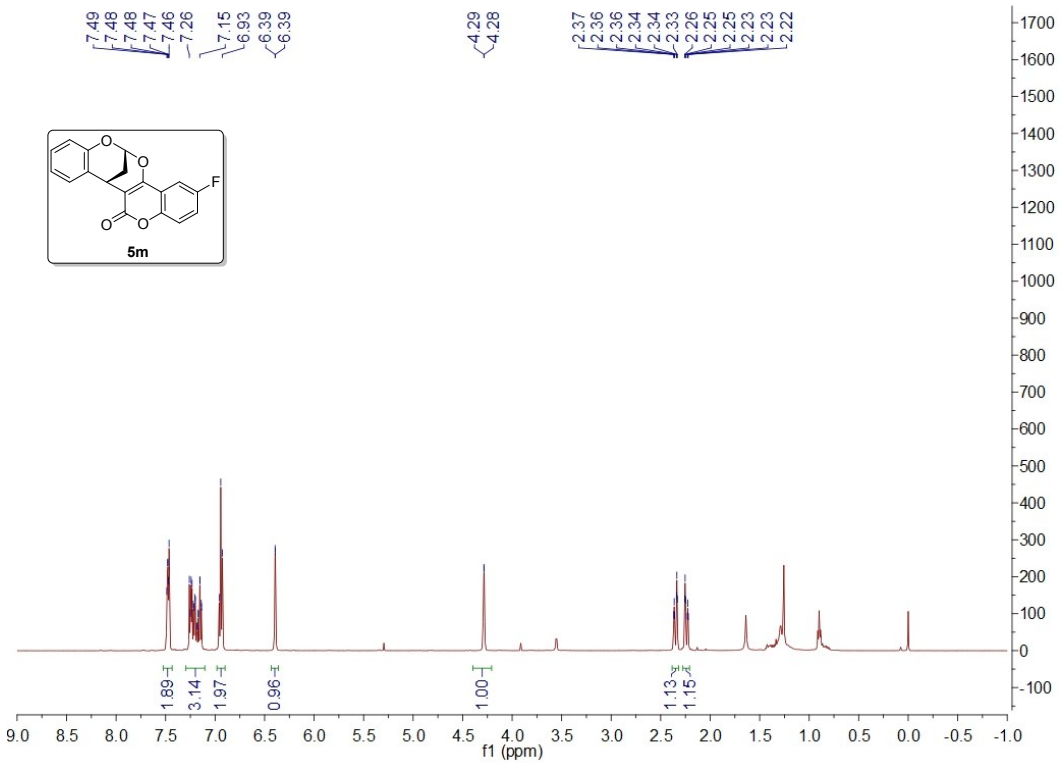
The HPLC of chiral 5l



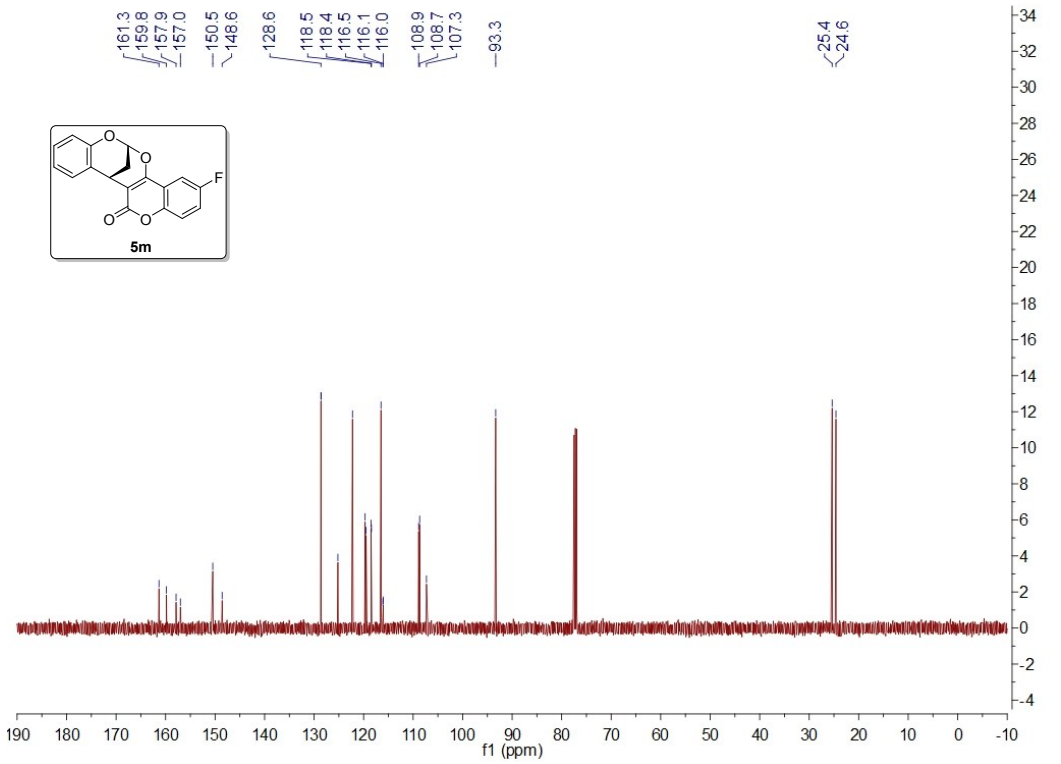
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	14.893	17267384	97.555	BB
2	17.687	432747	2.445	BB
		17700131	100.000	

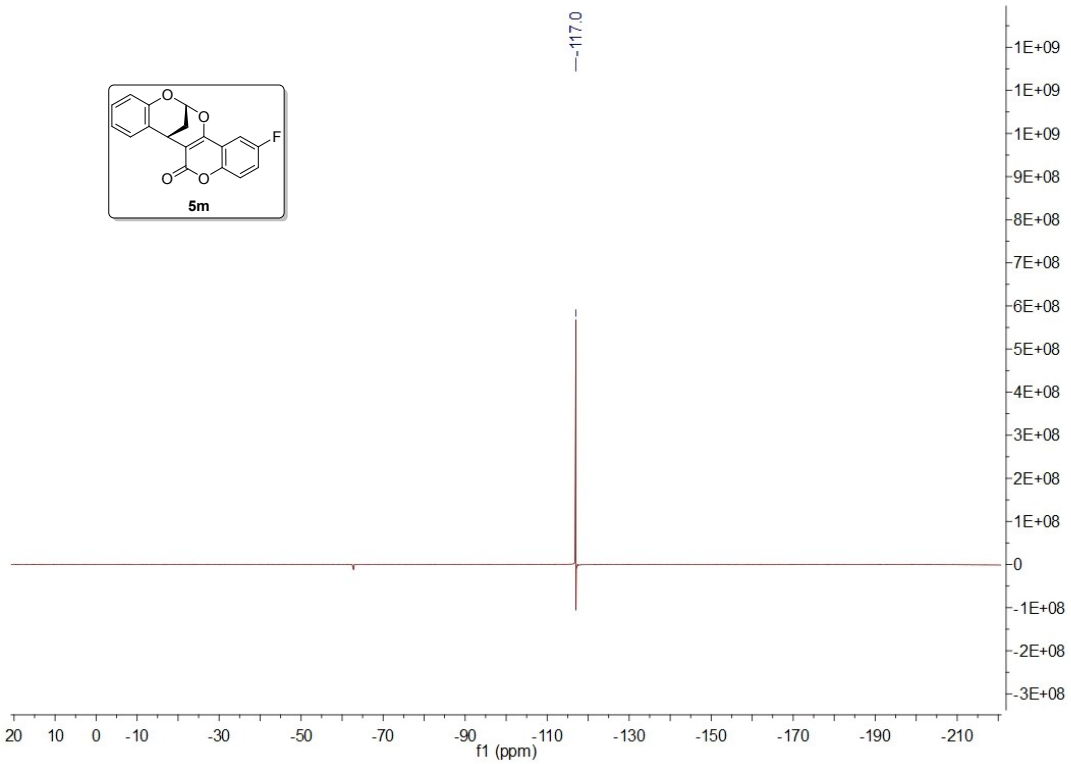
The ^{1}H NMR spectrum of 5m (500 MHz, $CDCl_3$)



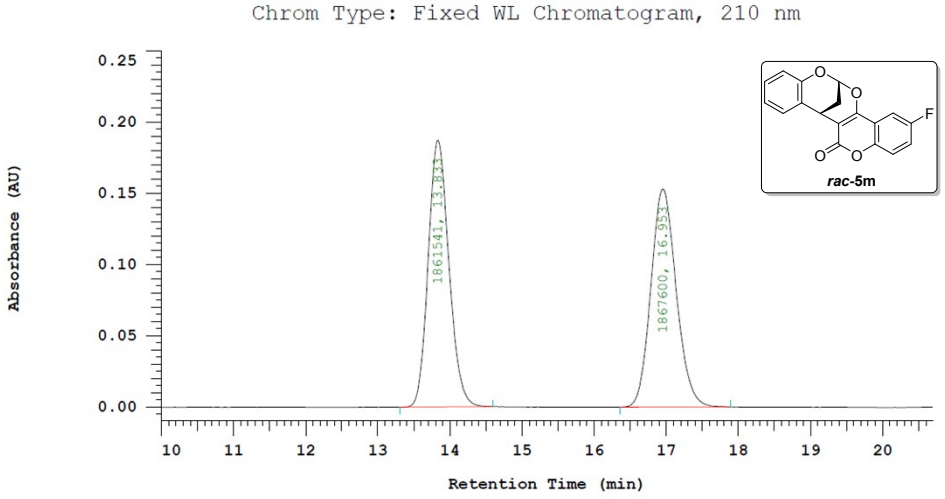
The ^{13}C NMR spectrum of 5m (125 MHz, $CDCl_3$)



The ^{19}F NMR spectrum of 5m (400 MHz, $CDCl_3$)


-117.0
1E+09
1E+09
1E+09
9E+08
8E+08
7E+08
6E+08
5E+08
4E+08
3E+08
2E+08
1E+08
0
-1E+08
-2E+08
-3E+08
20 10 0 -10 -30 -50 -70 -90 -110 -130 -150 -170 -190 -210
f1 (ppm)
O
O
F
O
O
5m

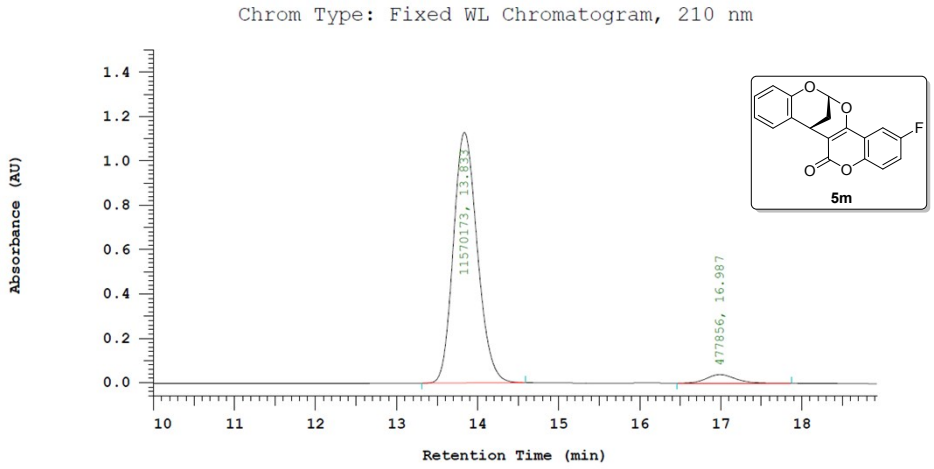
The HPLC of racemic 5m



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

No.	RT	Area	Area %	BC
1	13.833	1861541	49.919	BB
2	16.953	1867600	50.081	BB
		3729141	100.000	

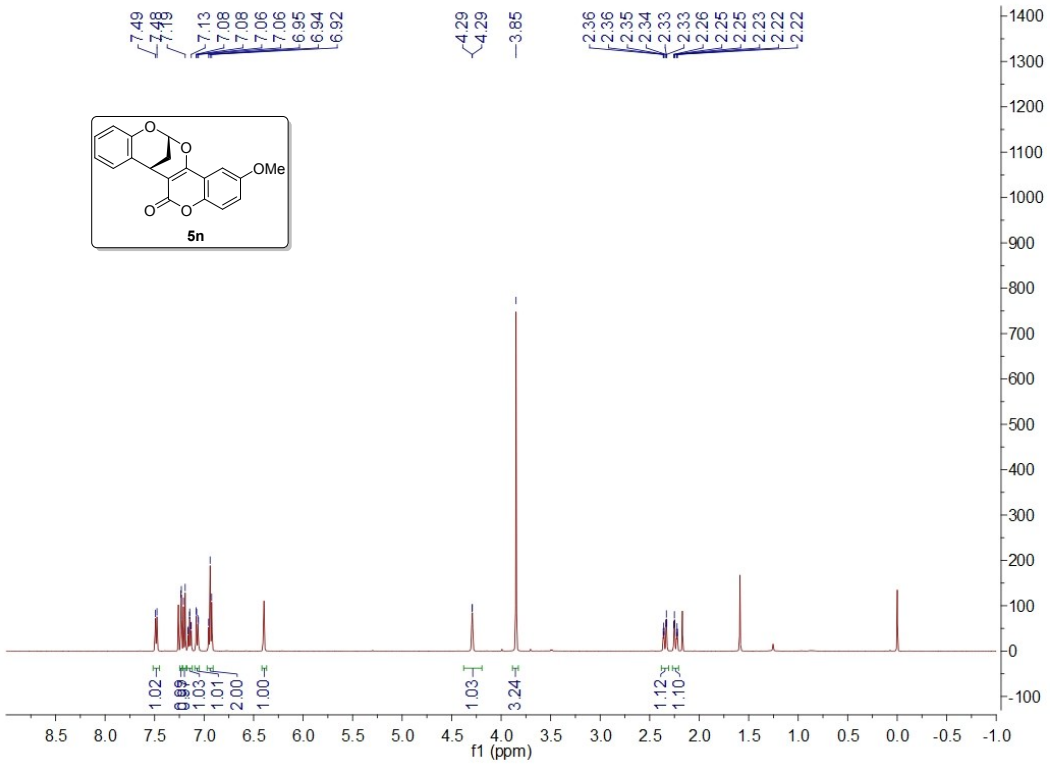
The HPLC of chiral 5m



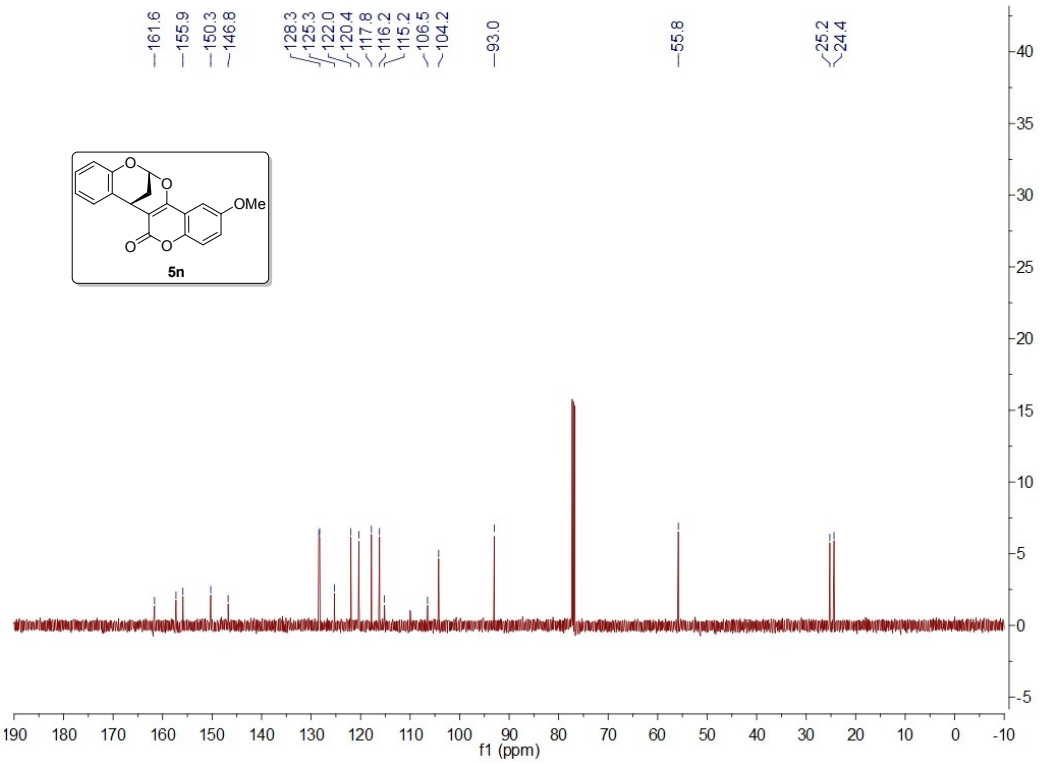
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	13.833	11570173	96.034	BB
2	16.987	477856	3.966	BB
		12048029	100.000	

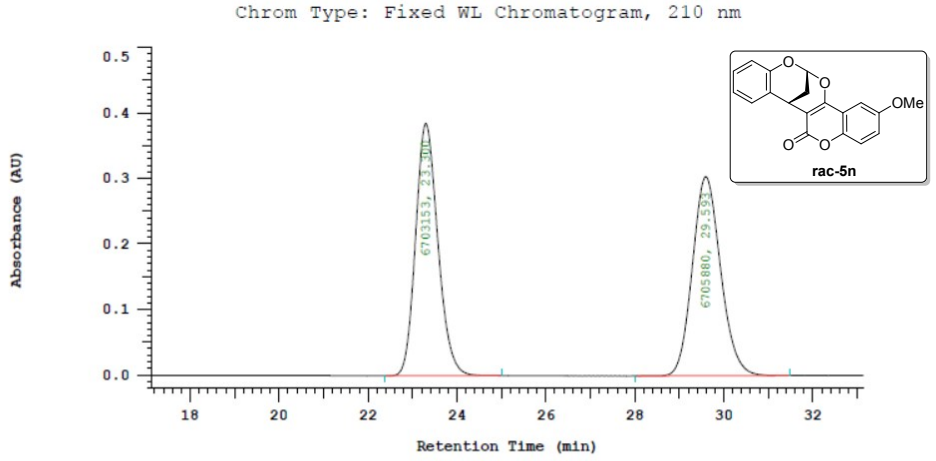
The ^{1}H NMR spectrum of 5n (500 MHz, $CDCl_3$)



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



The HPLC of racemic 5n



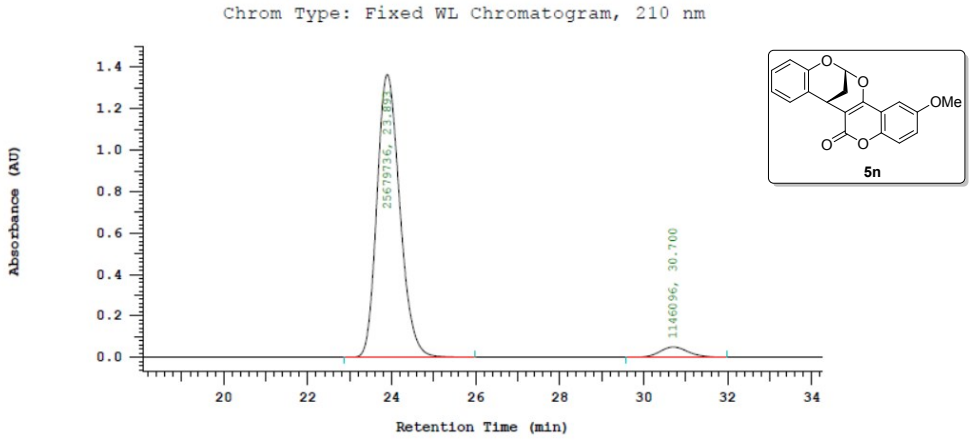
Chrom Type: Fixed WL Chromatogram, 210 nm

Peak Quantitation: AREA

Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	23.300	6703153	49.990	BB
2	29.593	6705880	50.010	BB
		13409033	100.000	

The HPLC of chiral 5n



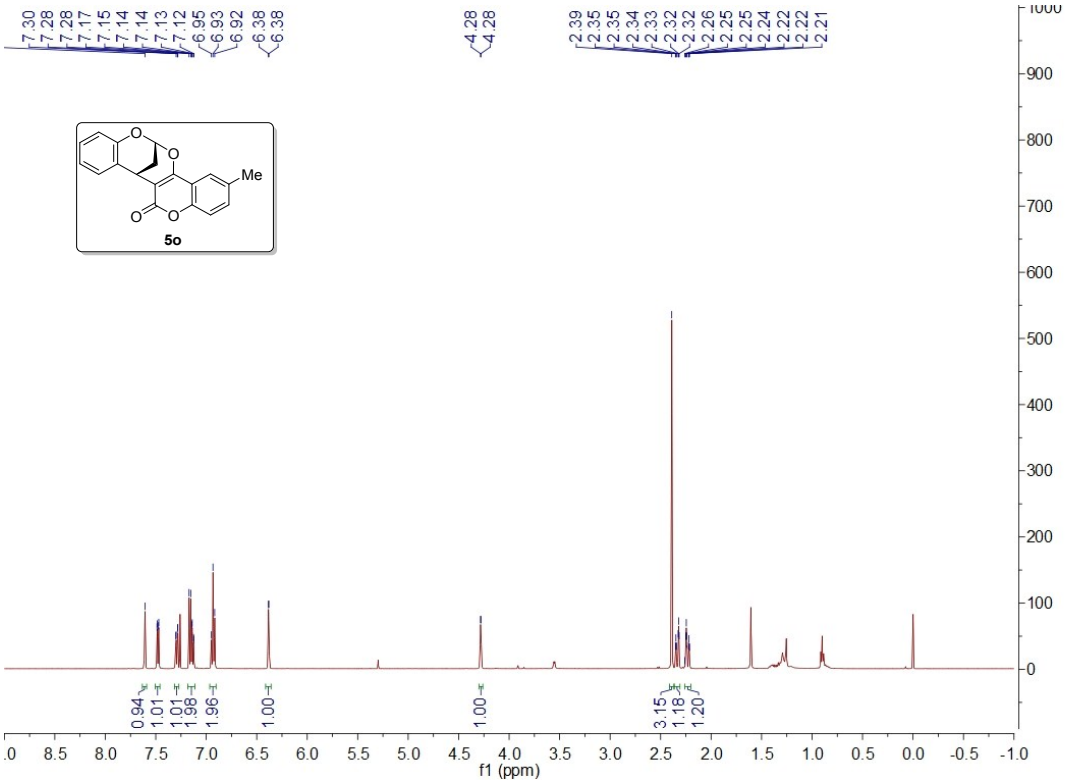
Chrom Type: Fixed WL Chromatogram, 210 nm

Peak Quantitation: AREA

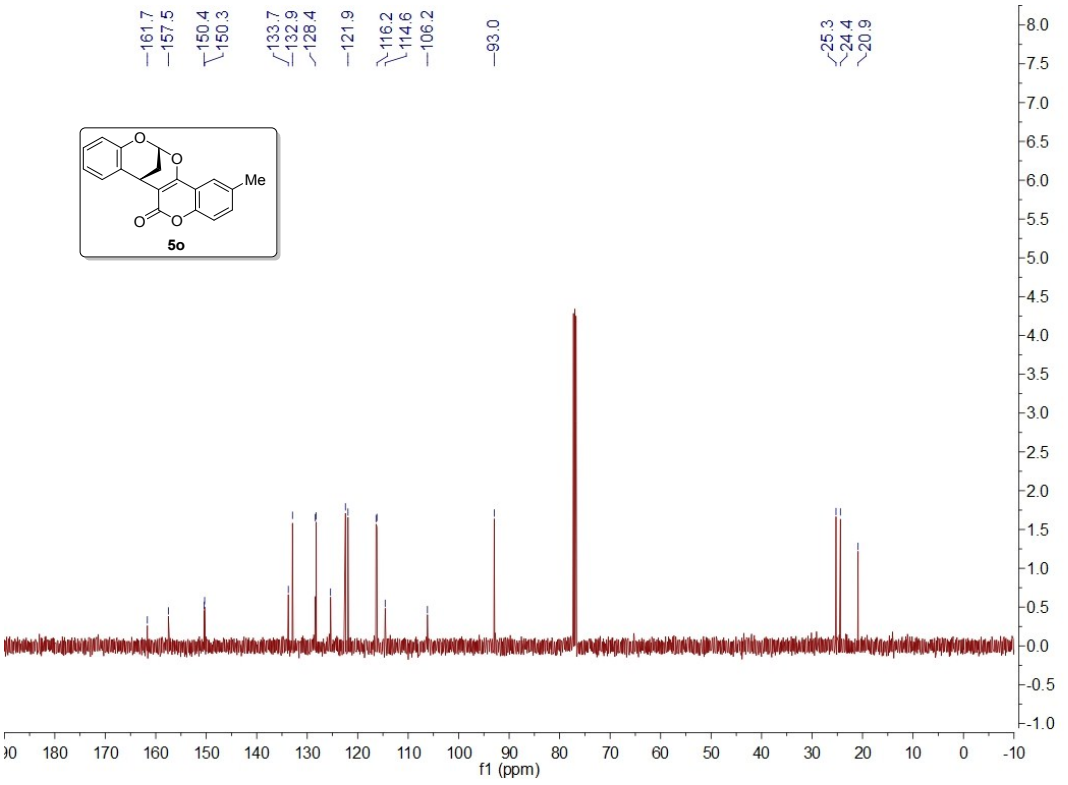
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	23.893	25679736	95.728	BB
2	30.700	1146096	4.272	BB
		26825832	100.000	

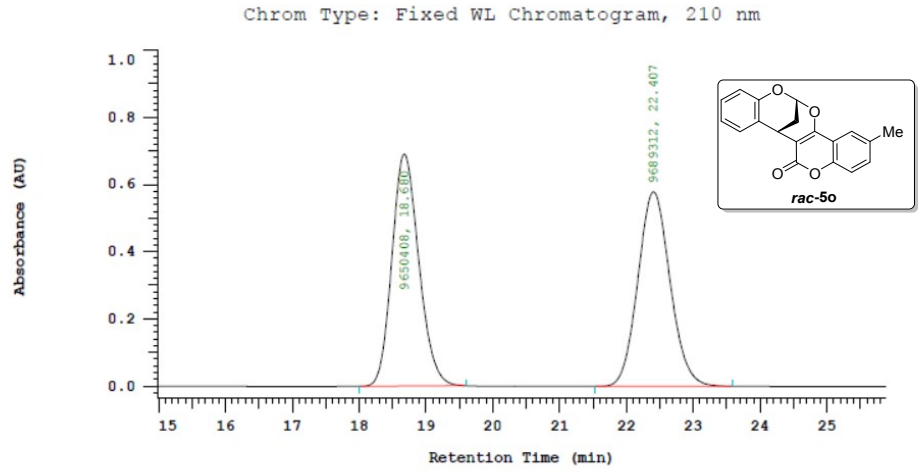
The ^{1}H NMR spectrum of 5o (500 MHz, $CDCl_3$)



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



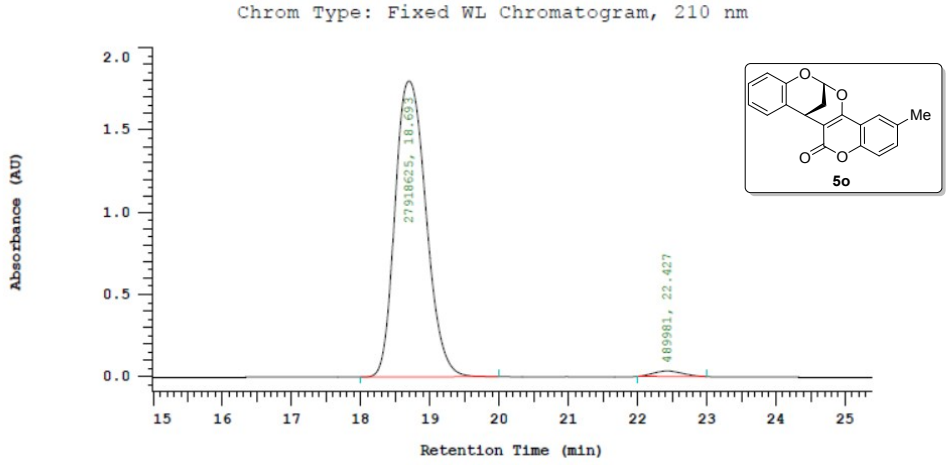
The HPLC of racemic 5o



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

No.	RT	Area	Area %	BC
1	18.680	9650408	49.899	BB
2	22.407	9689312	50.101	BB
		19339720	100.000	

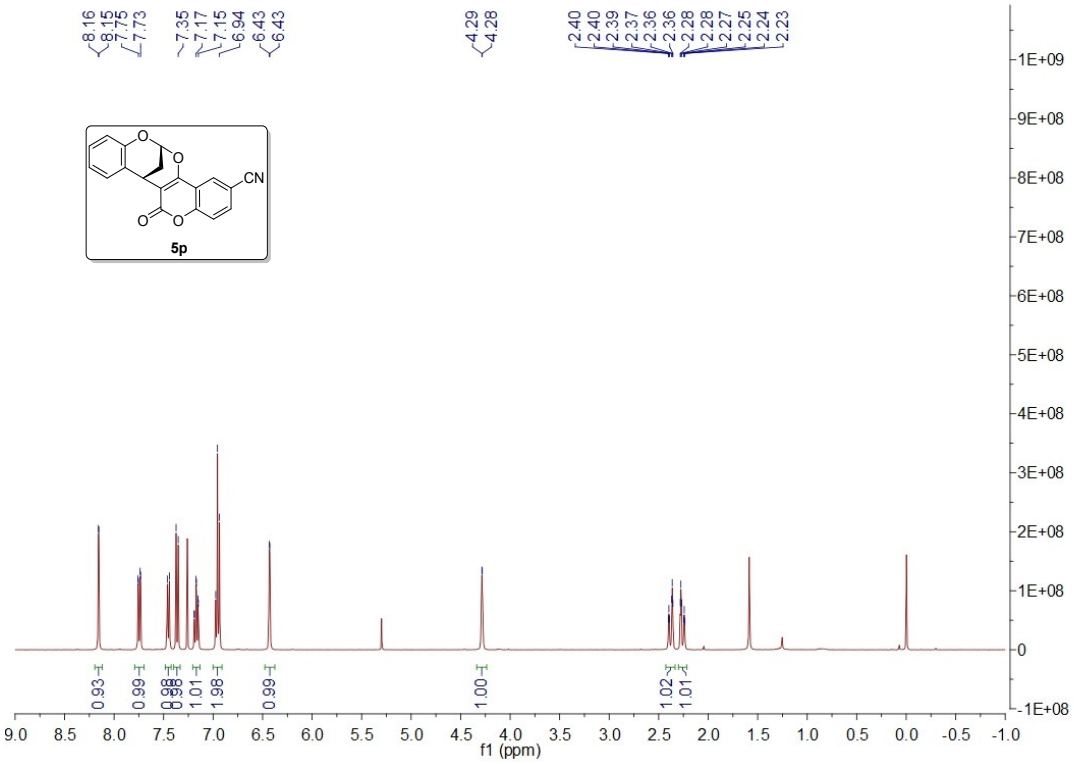
The HPLC of chiral 5o



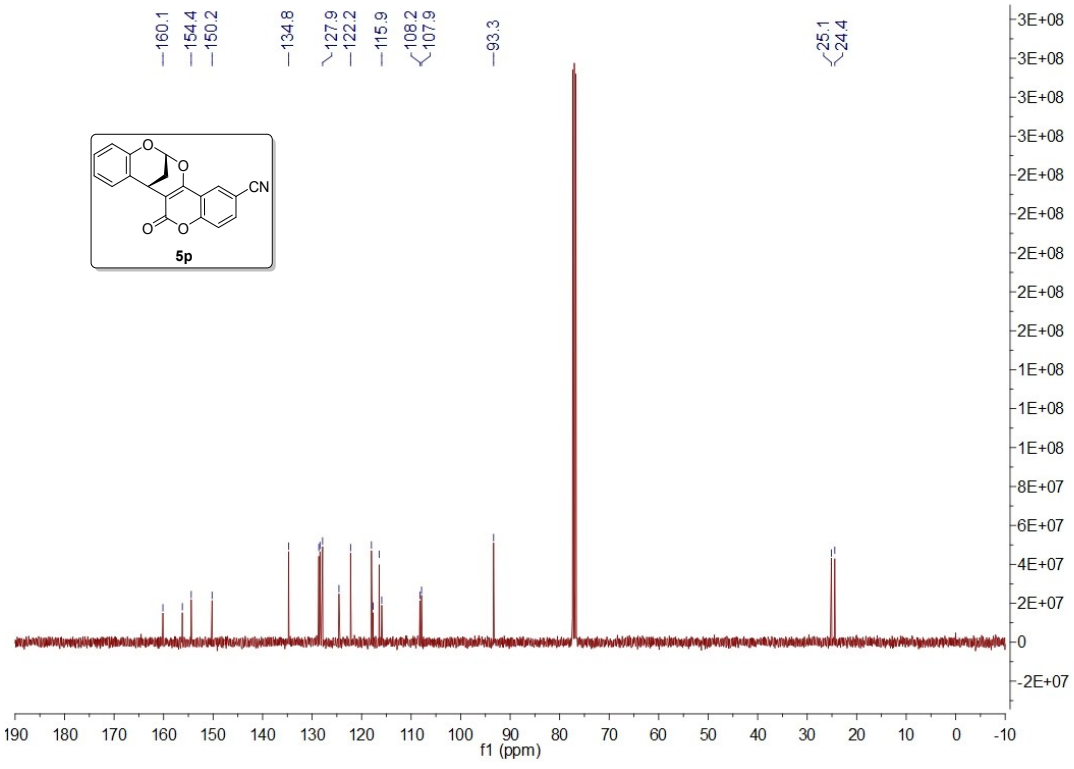
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	18.693	27918625	98.275	BB
2	22.427	489981	1.725	BB
		28408606	100.000	

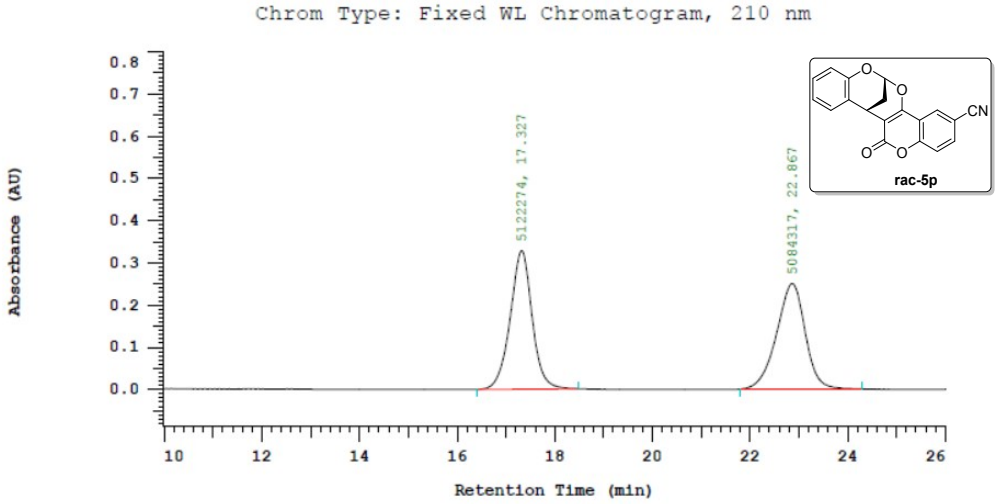
The ^{1}H NMR spectrum of 5p (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 5p (100 MHz, $CDCl_3$)



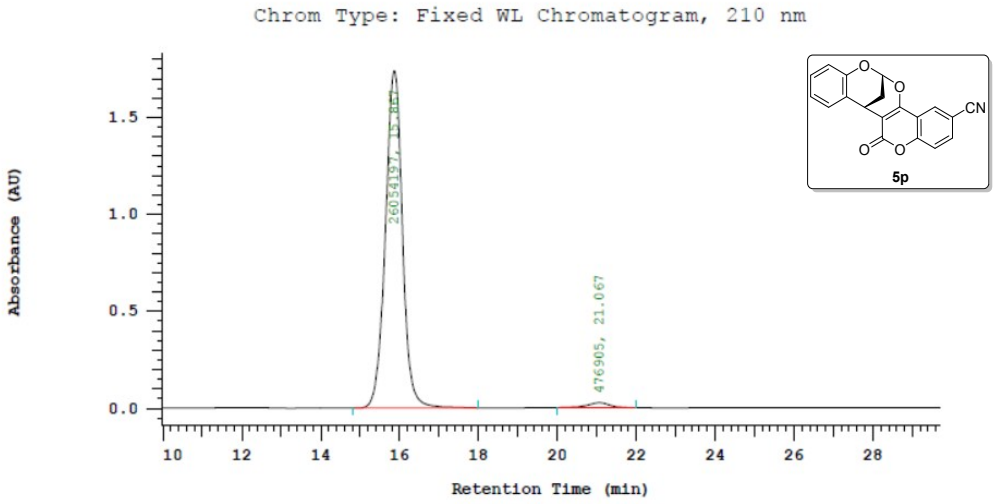
The HPLC of racemic 5p



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

No.	RT	Area	Area %	BC
1	17.327	5122274	50.186	BB
2	22.867	5084317	49.814	BB
		10206591	100.000	

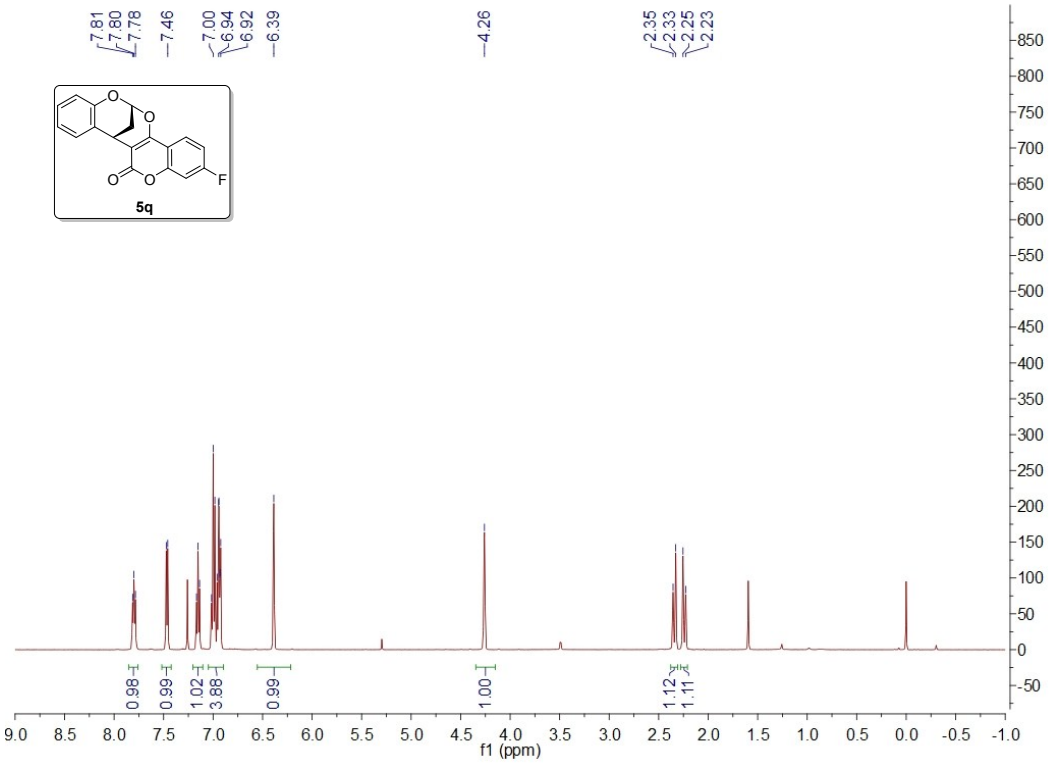
The HPLC of chiral 5p



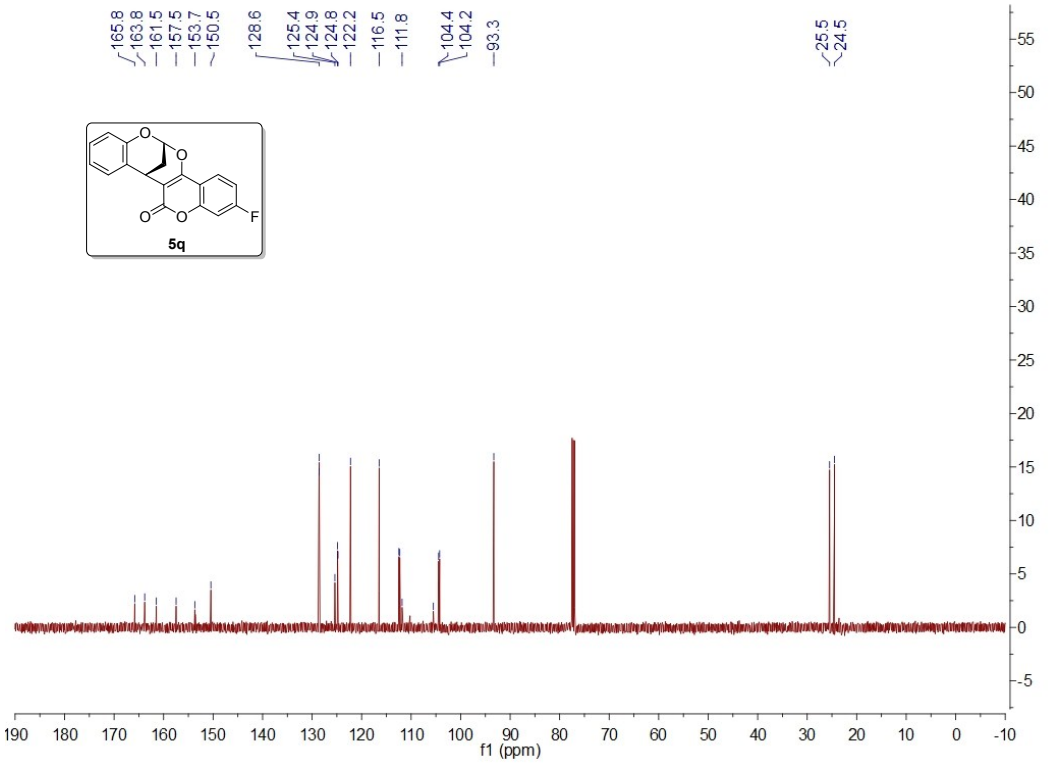
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	15.867	26054197	98.202	BB
2	21.067	476905	1.798	BB
		26531102	100.000	

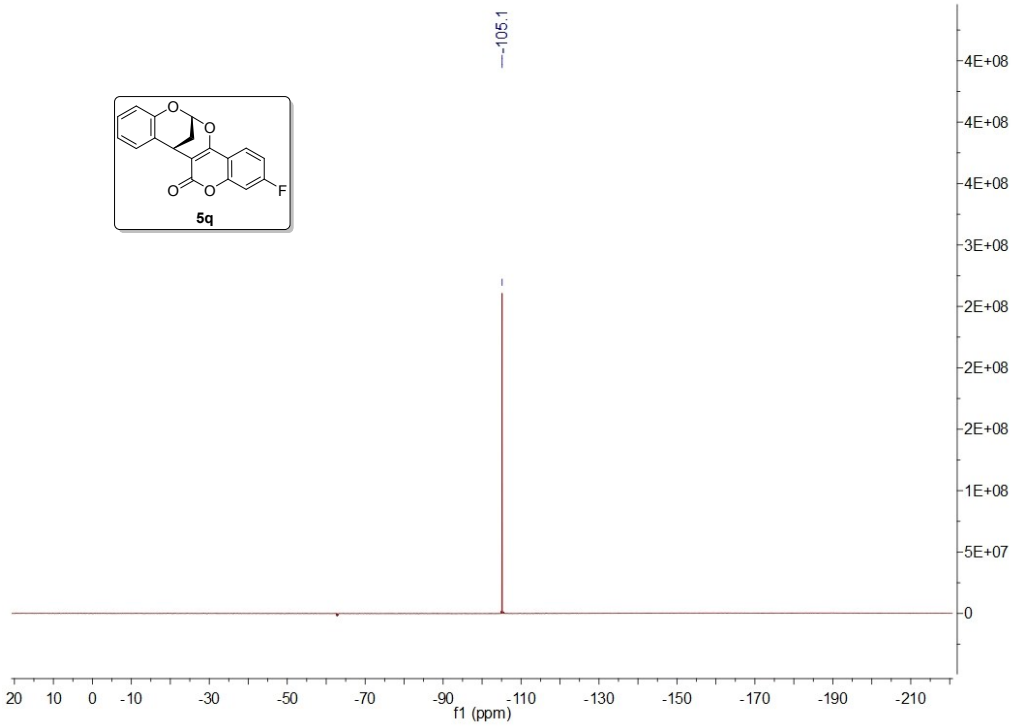
The ^{1}H NMR spectrum of 5q (500 MHz, $CDCl_3$)



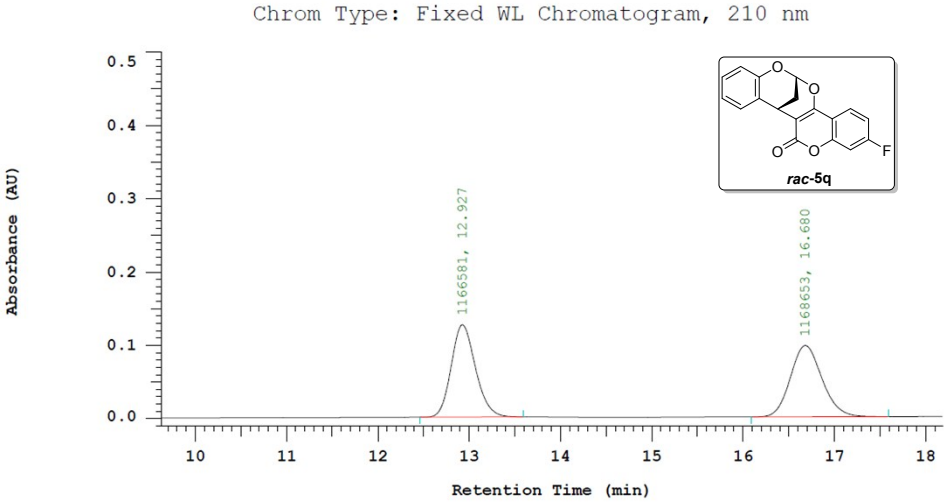
The ^{13}C NMR spectrum of 5q (125 MHz, $CDCl_3$)



The ^{19}F NMR spectrum of 5q (400 MHz, $CDCl_3$)



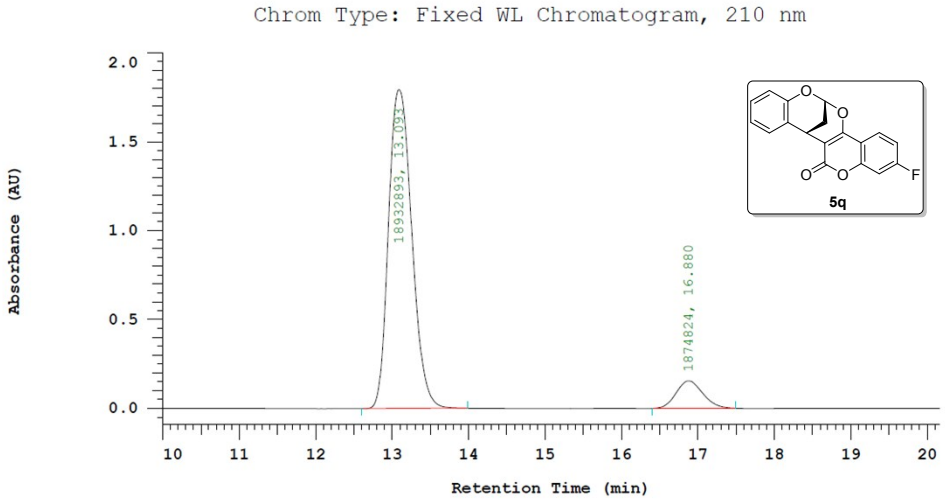
The HPLC of racemic 5q



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

No.	RT	Area	Area %	BC
1	12.927	1166581	49.956	BB
2	16.680	1168653	50.044	BB
		2335234	100.000	

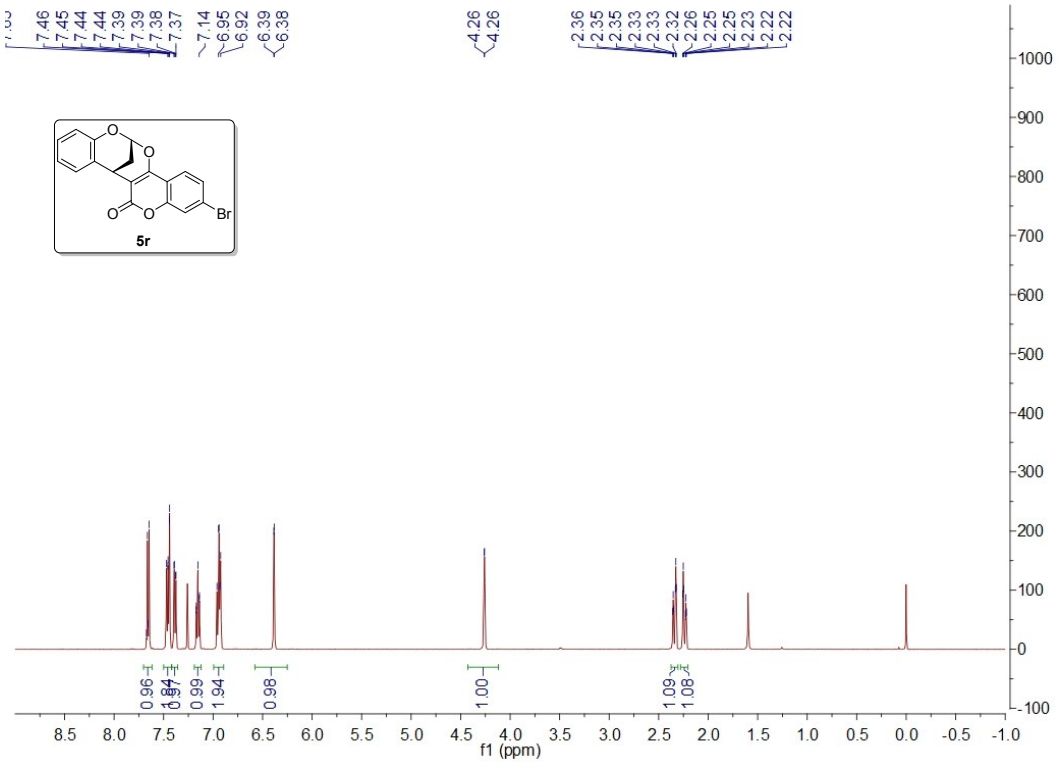
The HPLC of chiral 5q



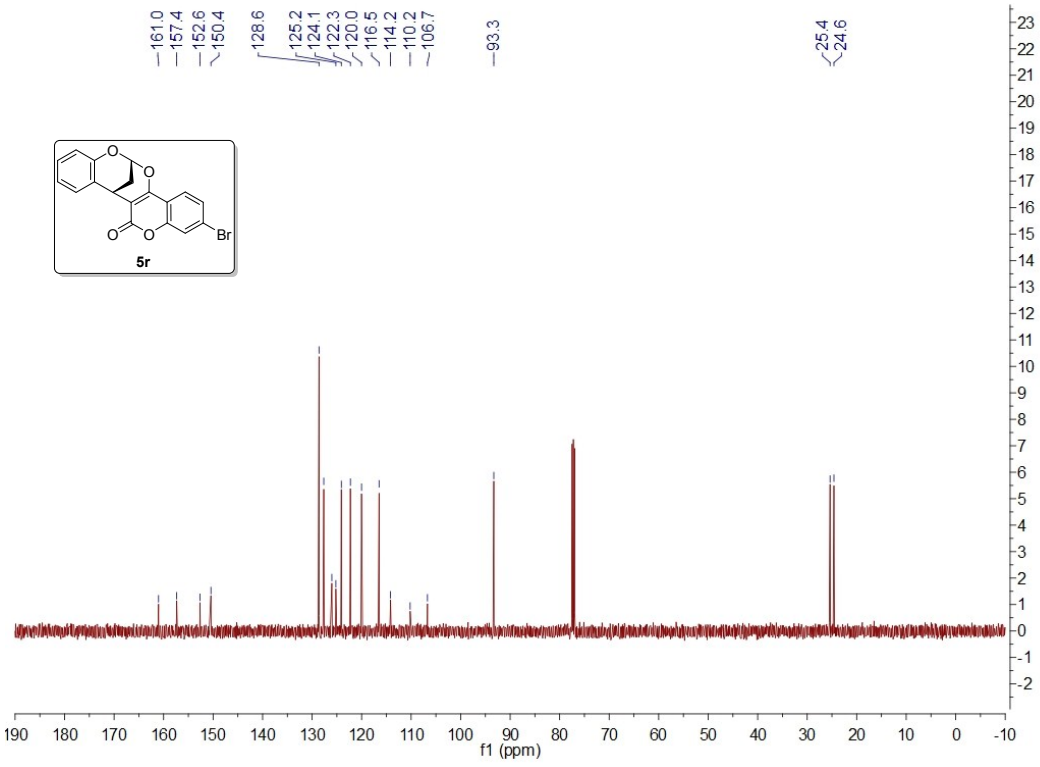
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	13.093	18932893	90.990	BB
2	16.880	1874824	9.010	BB
		20807717	100.000	

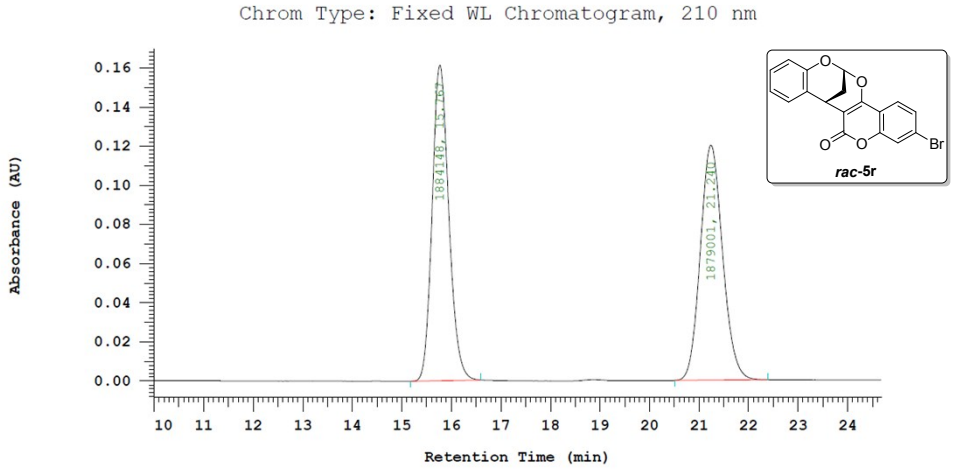
The ^{1}H NMR spectrum of 5r (500 MHz, $CDCl_3$)



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



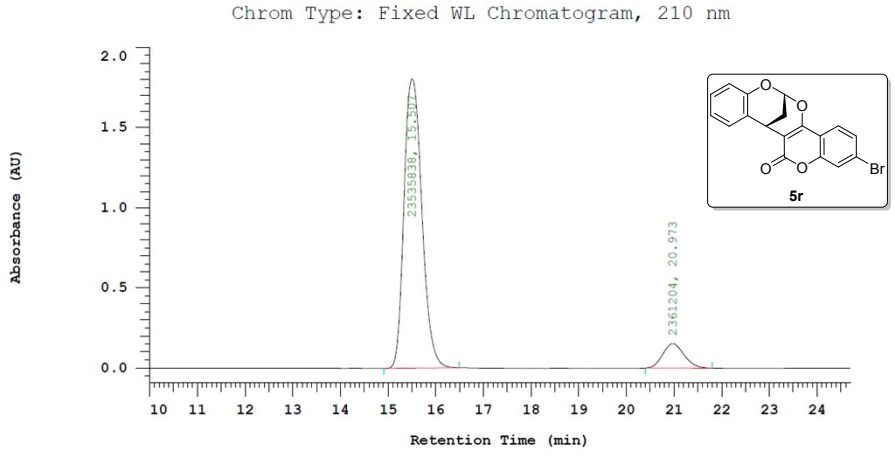
The HPLC of racemic 5r



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

No.	RT	Area	Area %	BC
1	15.767	1884148	50.068	BB
2	21.240	1879001	49.932	BB
		3763149	100.000	

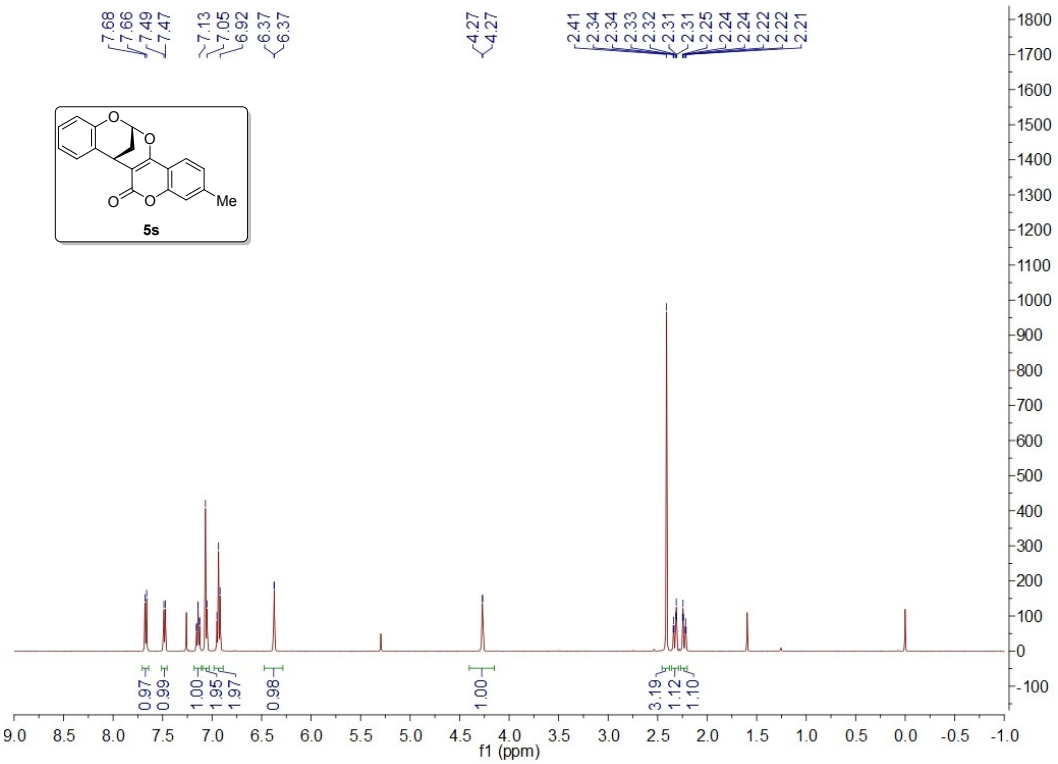
The HPLC of chiral 5r



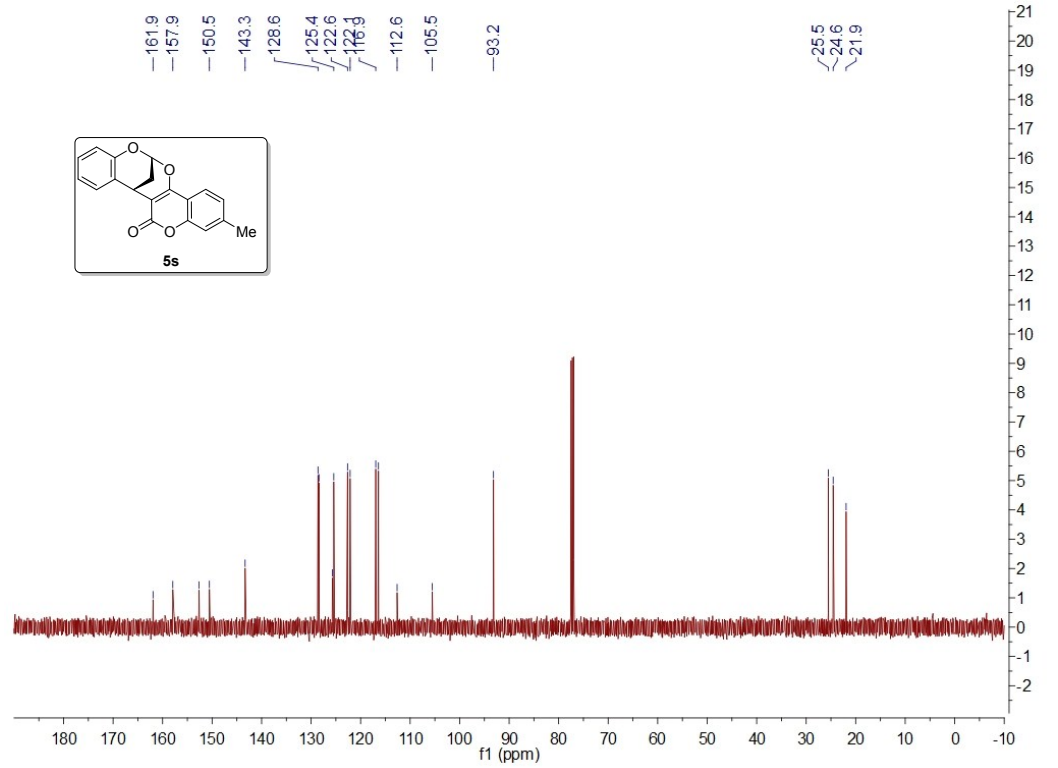
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	15.507	23535838	90.882	BB
2	20.973	2361204	9.118	BB
		25897042	100.000	

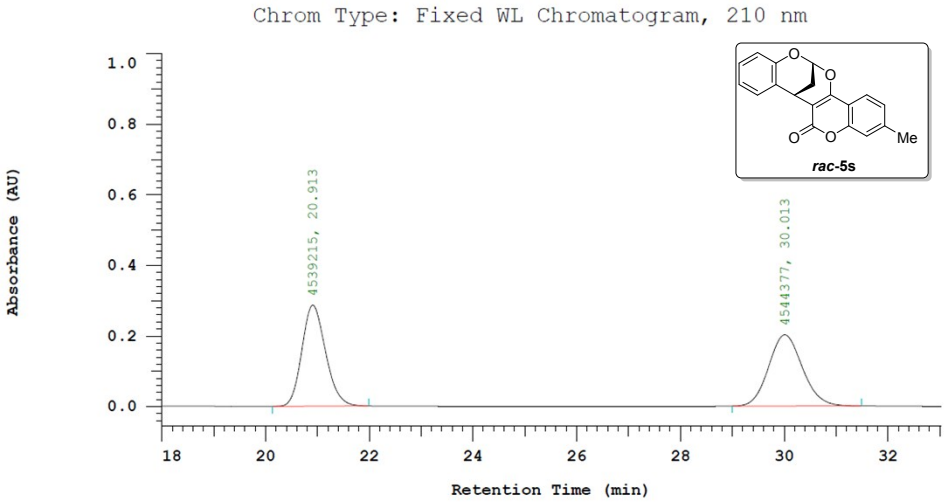
The ^{1}H NMR spectrum of 5s (500 MHz, $CDCl_3$)



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



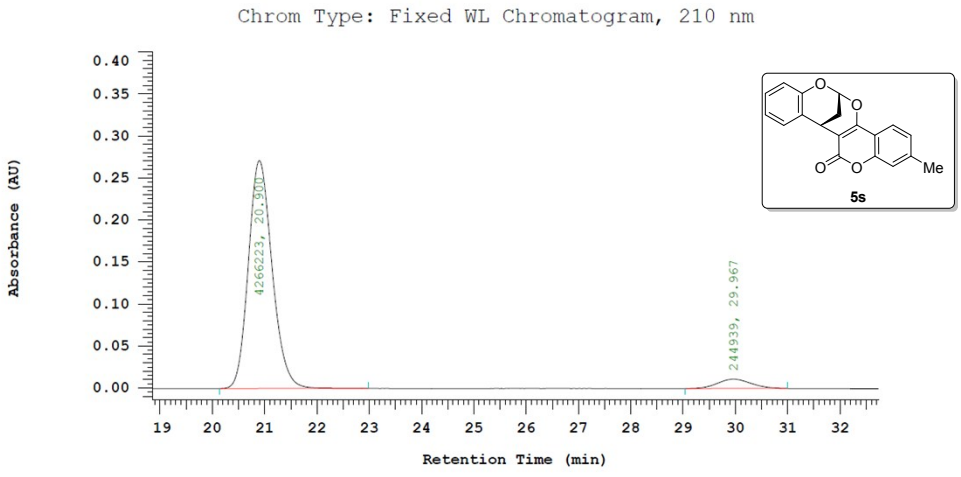
The HPLC of racemic 5s



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

No.	RT	Area	Area %	BC
1	20.913	4539215	49.972	BB
2	30.013	4544377	50.028	BB
		9083592	100.000	

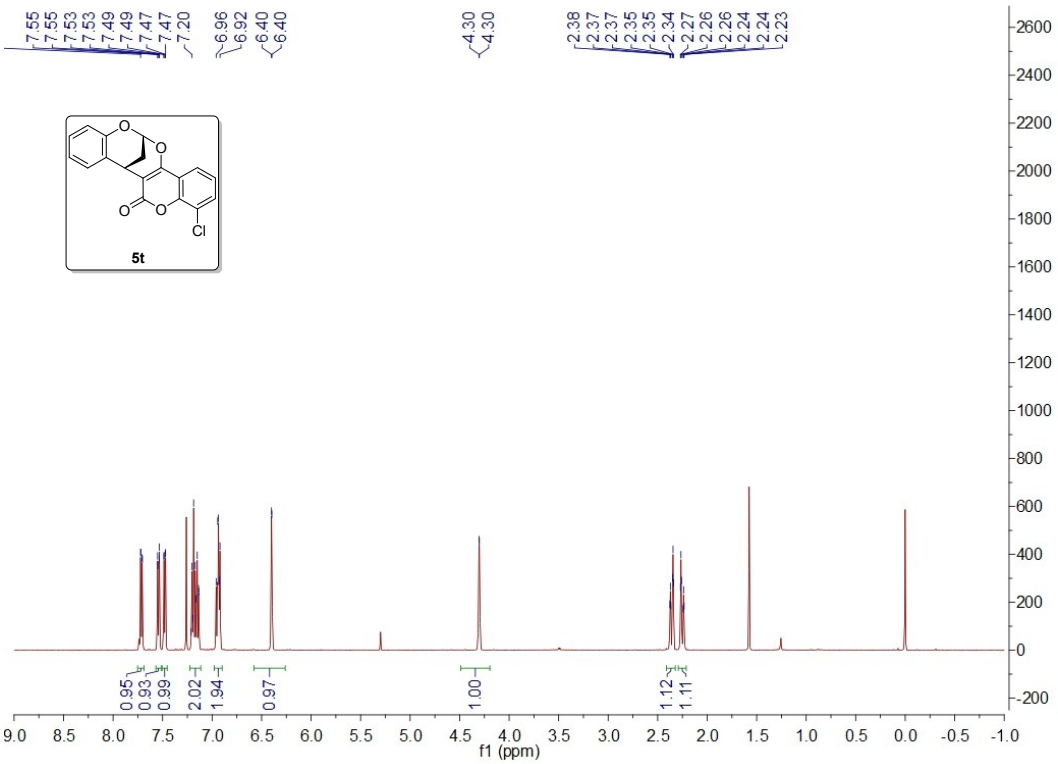
The HPLC of chiral 5s



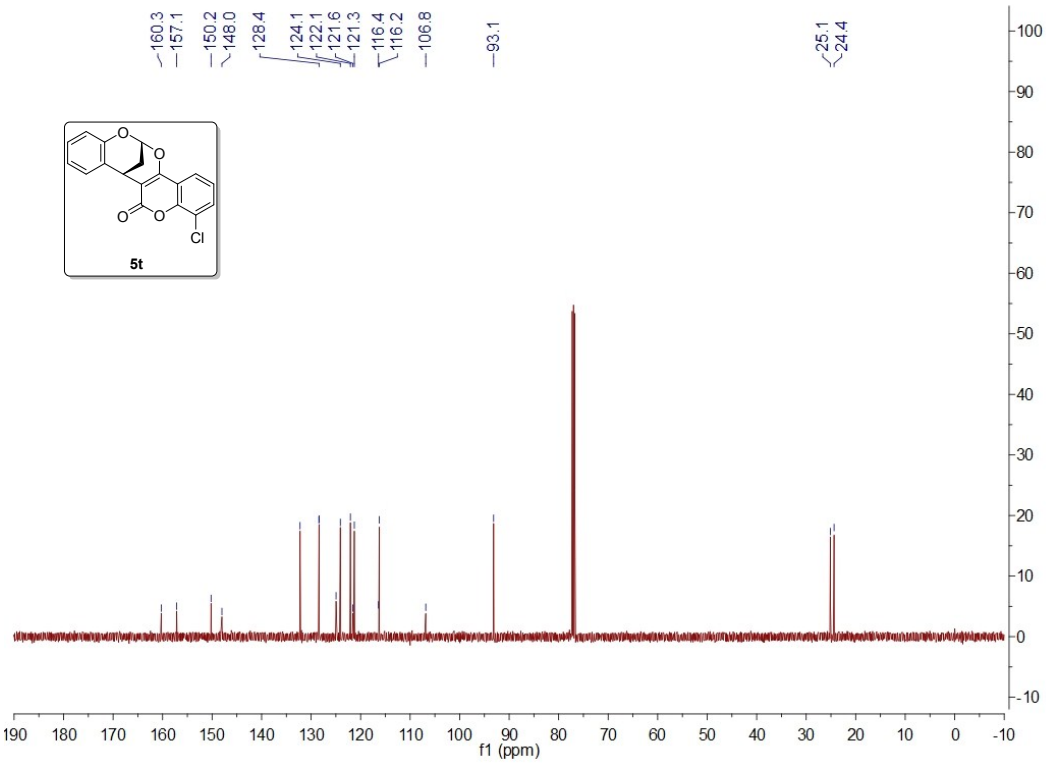
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	20.900	4266223	94.570	BB
2	29.967	244939	5.430	BB
		4511162	100.000	

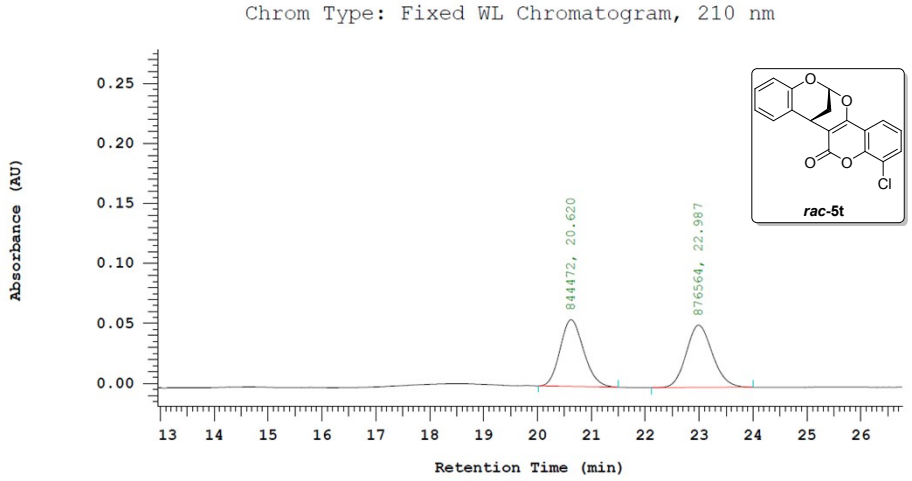
The ^{1}H NMR spectrum of 5t (500 MHz, $CDCl_3$)



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



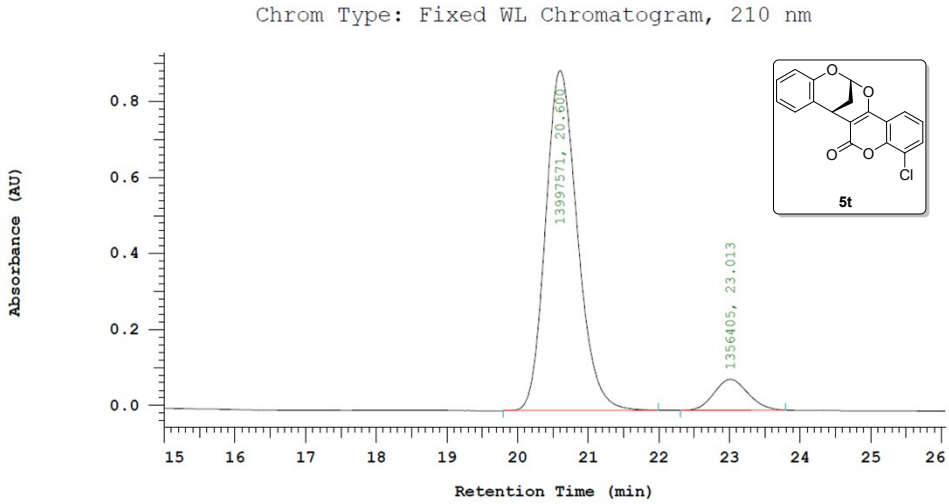
The HPLC of racemic 5t



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

No.	RT	Area	Area %	BC
1	20.620	844472	49.068	BB
2	22.987	876564	50.932	BB
		1721036	100.000	

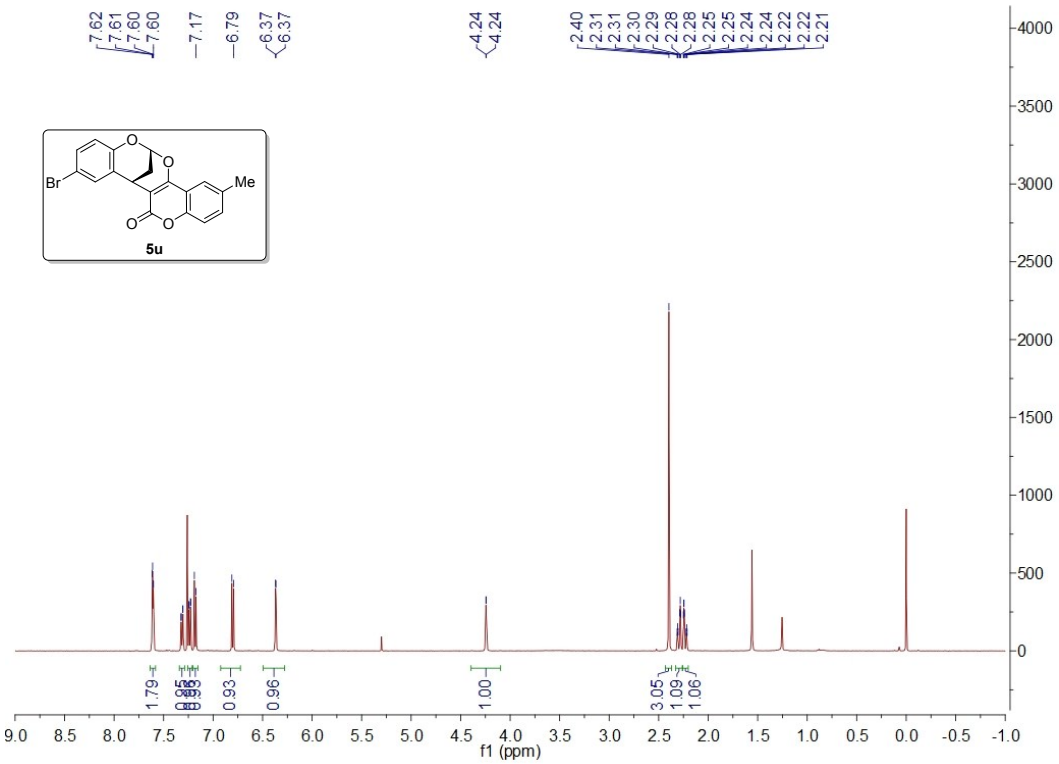
The HPLC of chiral 5t



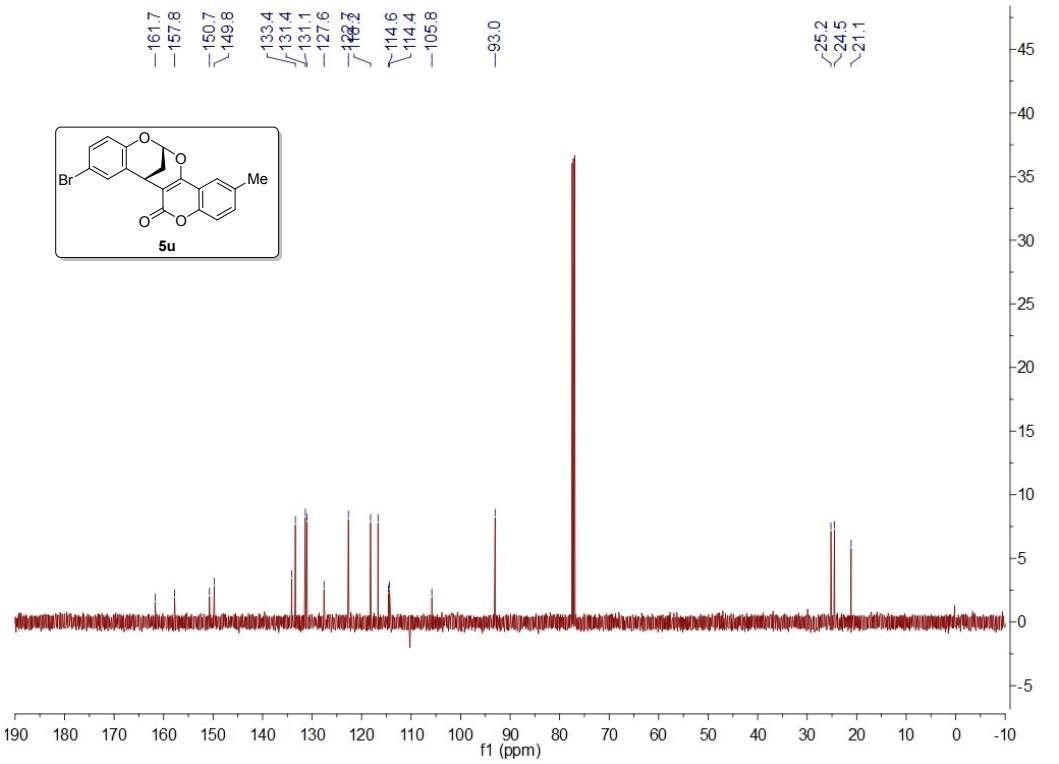
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	20.600	13997571	91.166	BB
2	23.013	1356405	8.834	BB
		15353976	100.000	

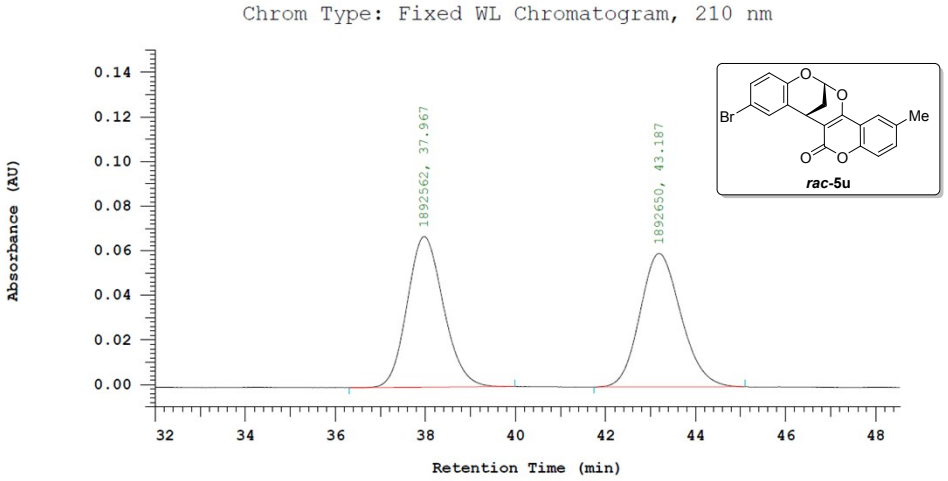
The ^{1}H NMR spectrum of 5u (500 MHz, $CDCl_3$)



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



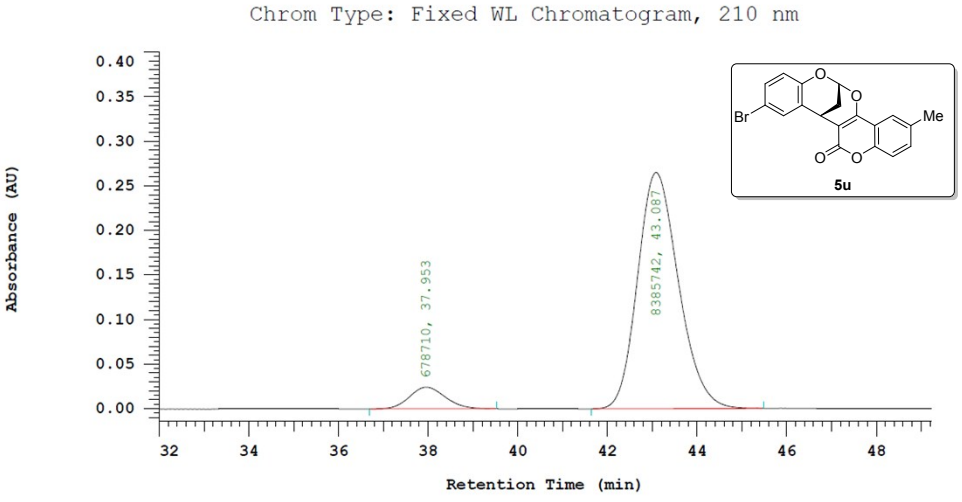
The HPLC of racemic 5u



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

No.	RT	Area	Area %	BC
1	37.967	1892562	49.999	BB
2	43.187	1892650	50.001	BB
		3785212	100.000	

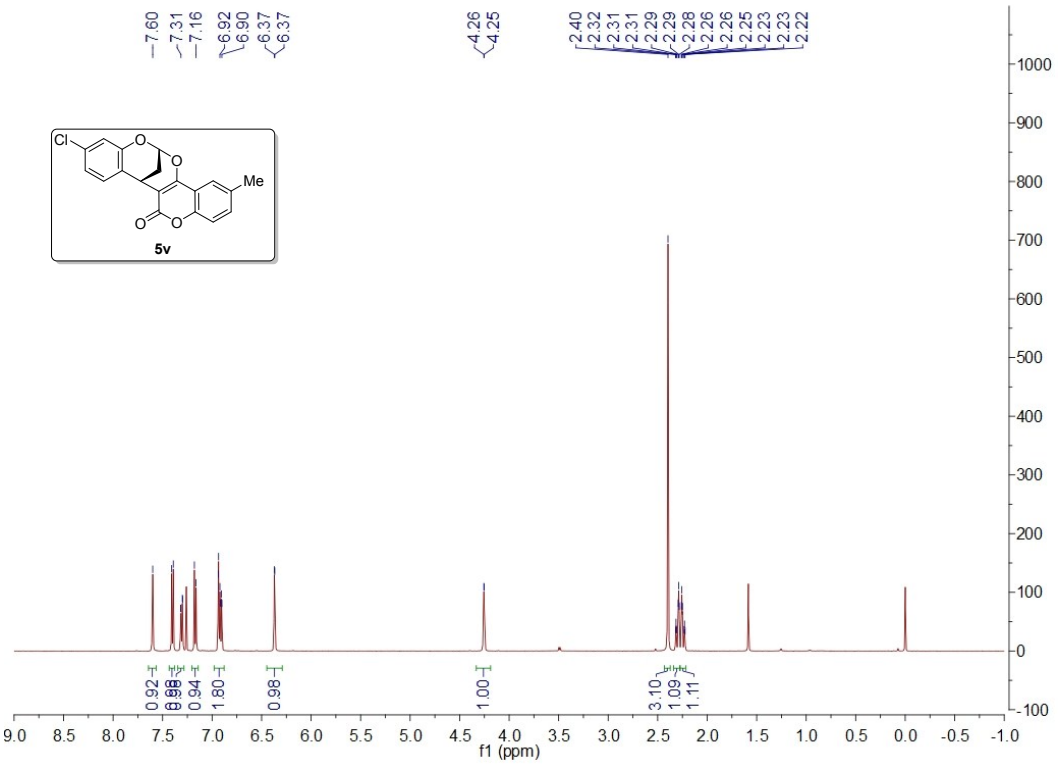
The HPLC of chiral 5u



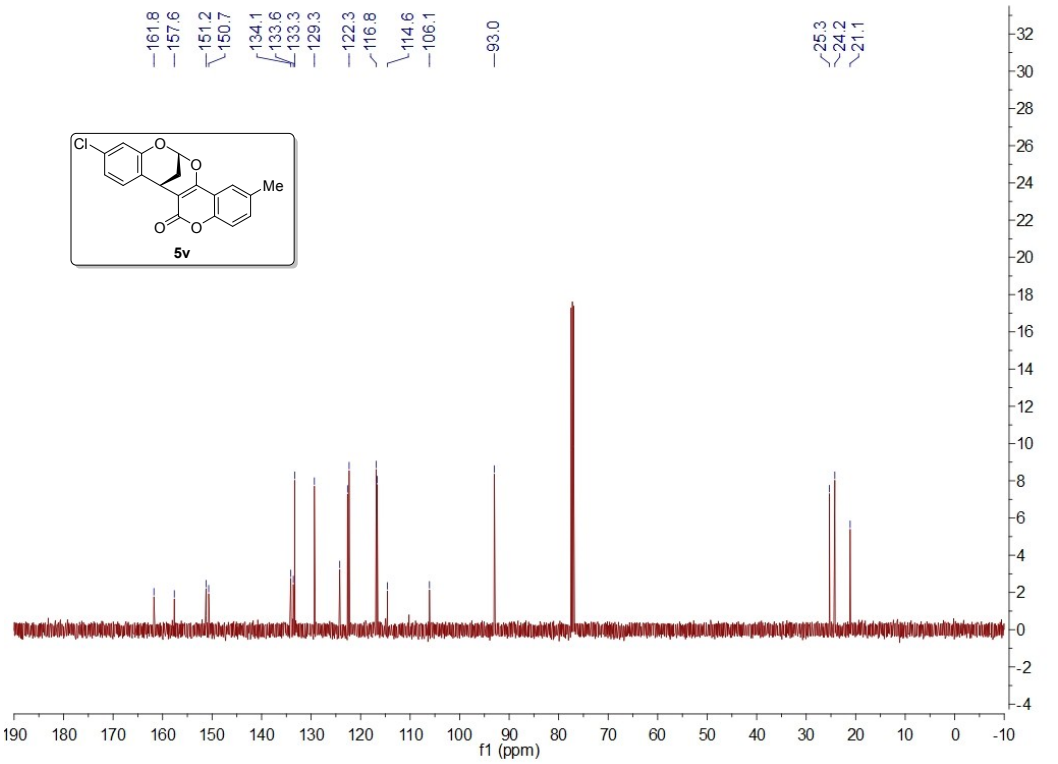
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	37.953	678710	7.488	BB
2	43.087	8385742	92.512	BB
		9064452	100.000	

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

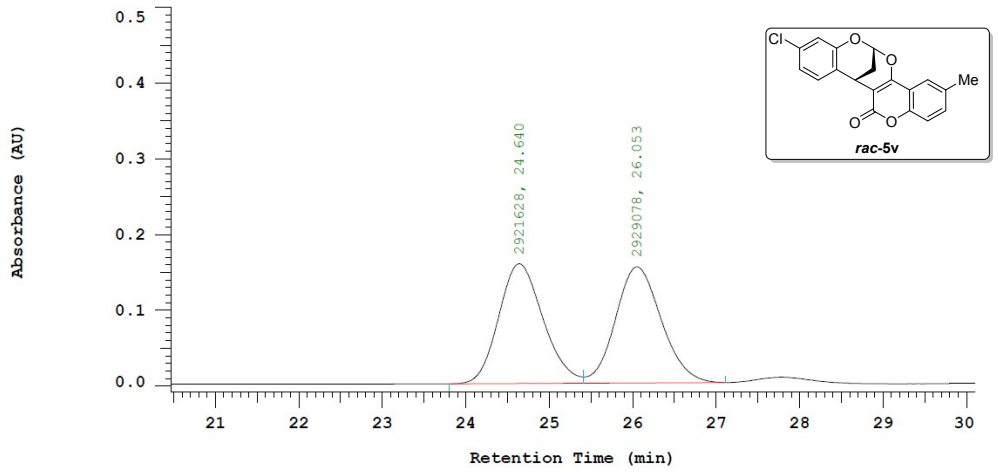


The ^{13}C NMR spectrum of 5v (125 MHz, $CDCl_3$)



The HPLC of racemic 5v

Chrom Type: Fixed WL Chromatogram, 210 nm

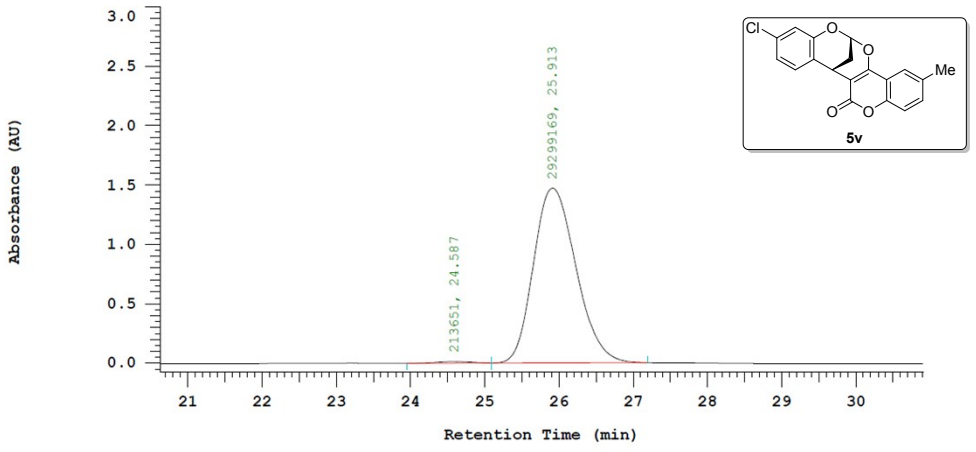


Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	24.640	2921628	49.936	BV
2	26.053	2929078	50.064	VB
		5850706	100.000	

The HPLC of chiral 5v

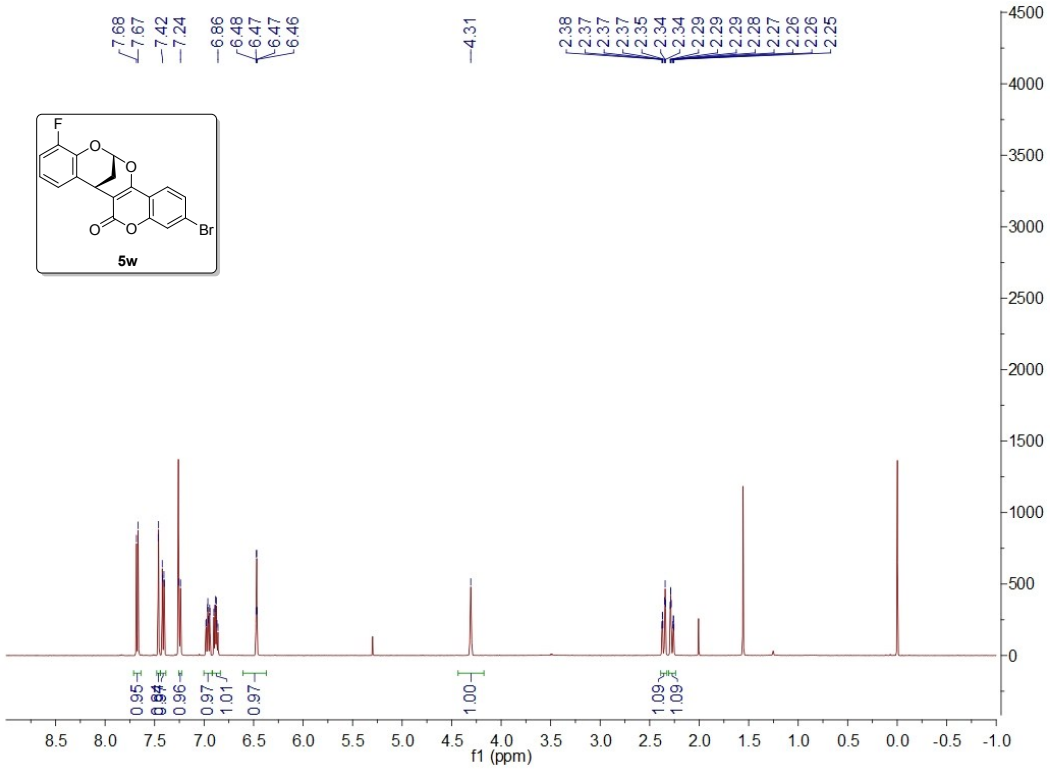
Chrom Type: Fixed WL Chromatogram, 210 nm



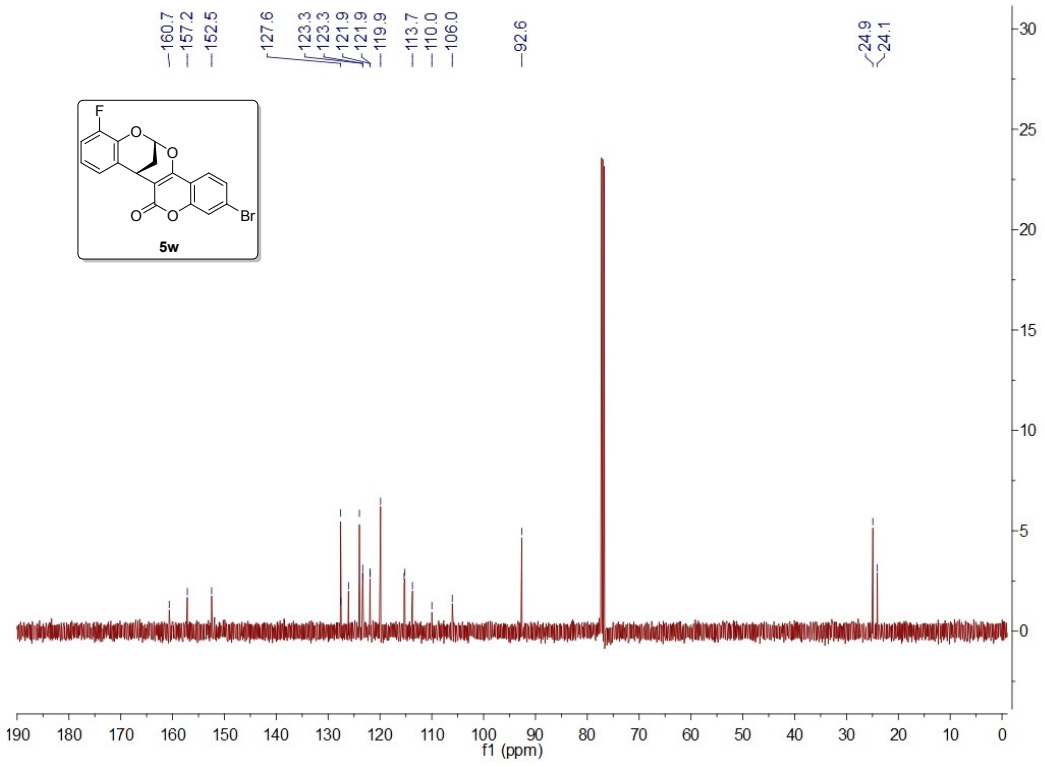
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	24.587	213651	0.724	BV
2	25.913	29299169	99.276	VB
		29512820	100.000	

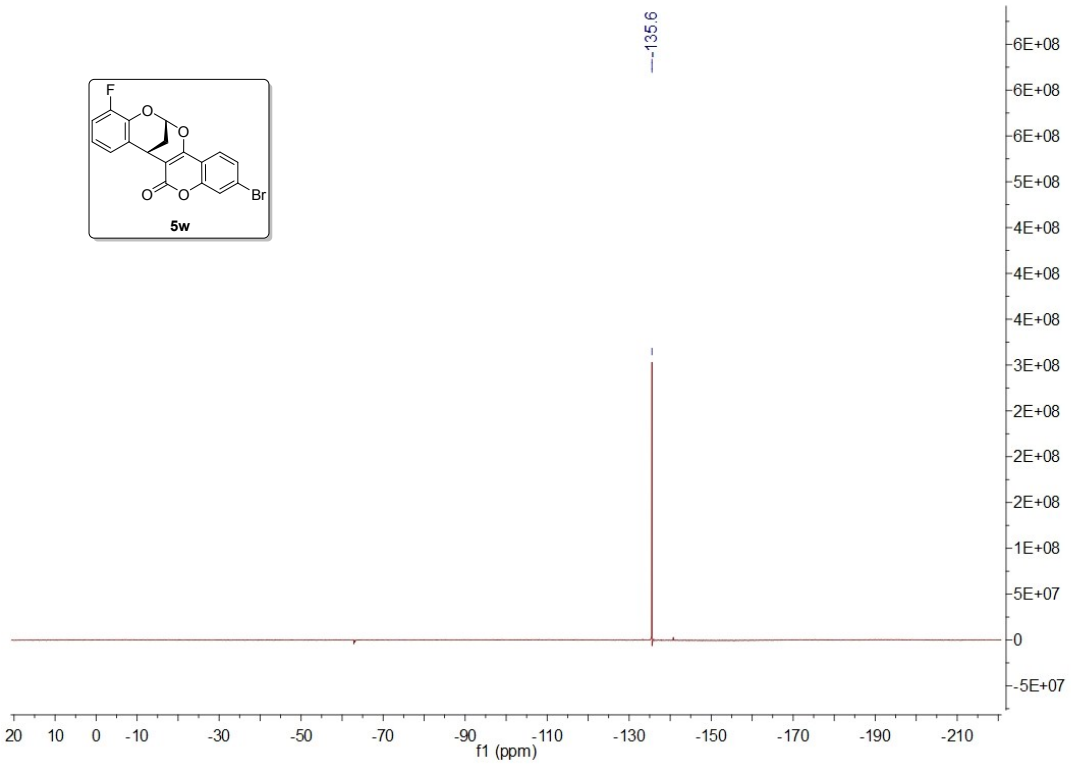
The ^{1}H NMR spectrum of 5w (500 MHz, $CDCl_3$)



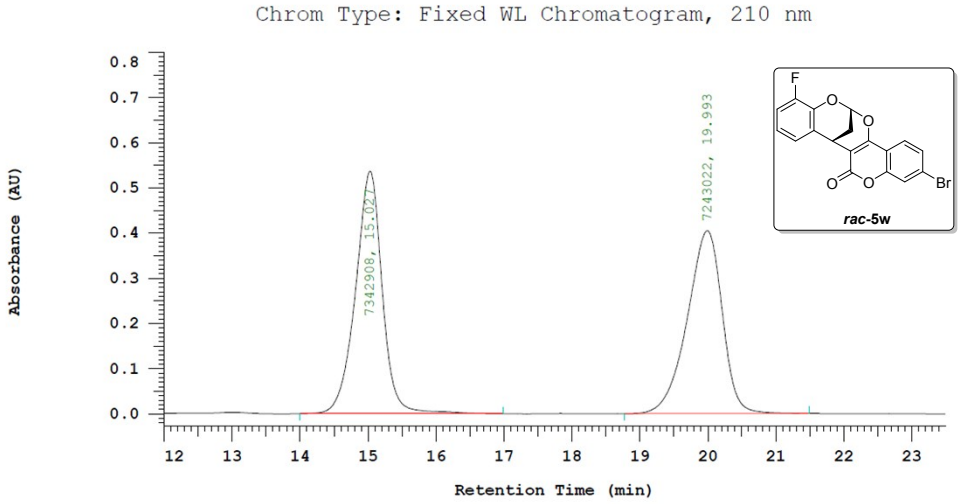
The ^{13}C NMR spectrum of 5w (125 MHz, $CDCl_3$)



The ^{19}F NMR spectrum of 5w (400 MHz, $CDCl_3$)


F
O
O
O
O
Br
5w
-135.6
6E+08
6E+08
6E+08
5E+08
4E+08
4E+08
4E+08
3E+08
2E+08
2E+08
2E+08
1E+08
5E+07
0
-5E+07
20
10
0
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

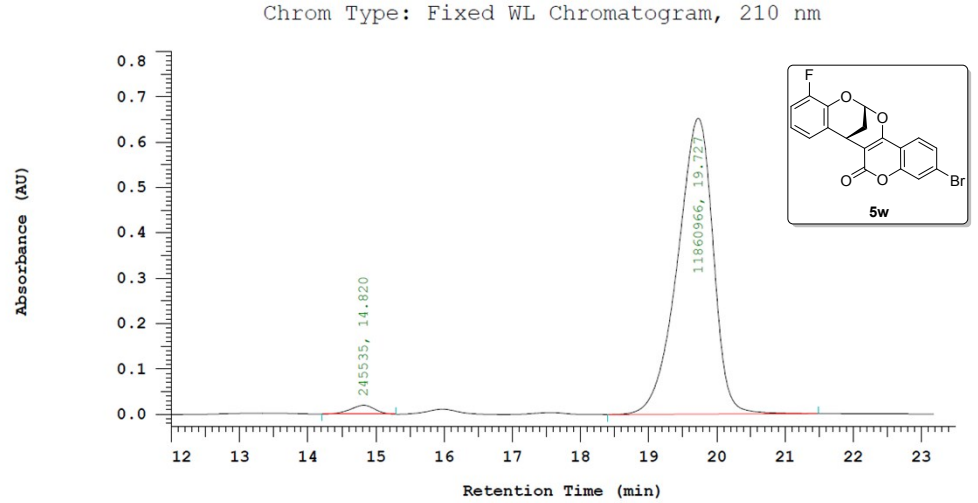
The HPLC of racemic 5w



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

No.	RT	Area	Area %	BC
1	15.027	7342908	50.342	BB
2	19.993	7243022	49.658	BB
		14585930	100.000	

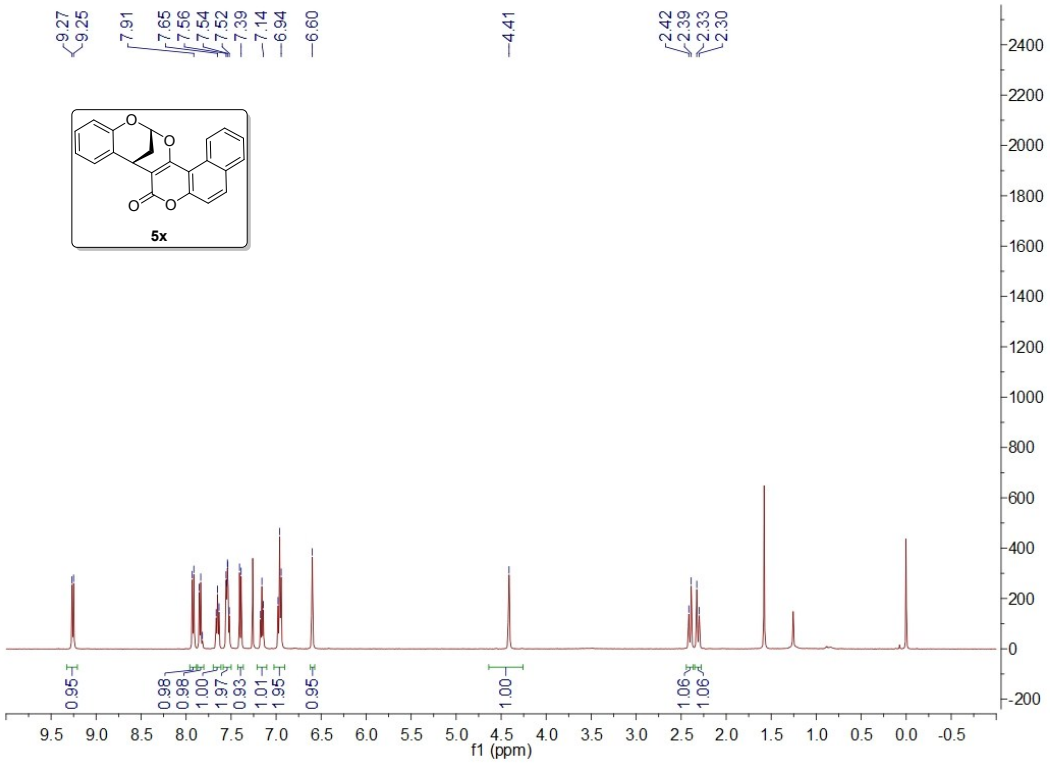
The HPLC of chiral 5w



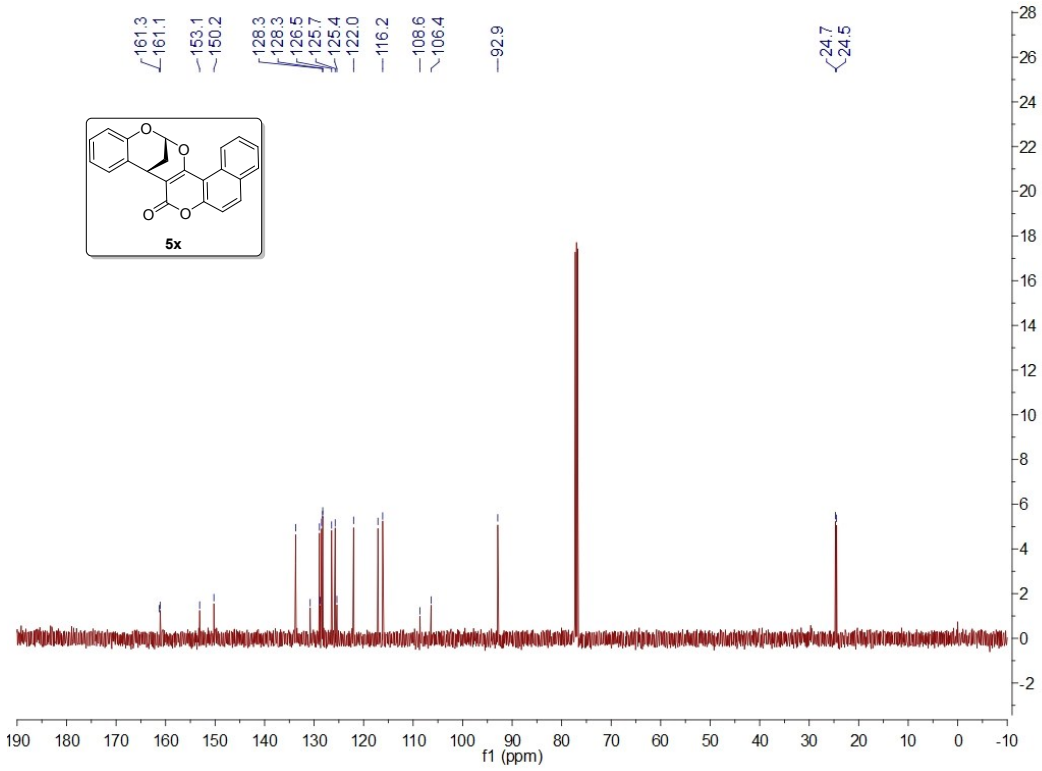
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	14.820	245535	2.028	BB
2	19.727	11860966	97.972	BB
		12106501	100.000	

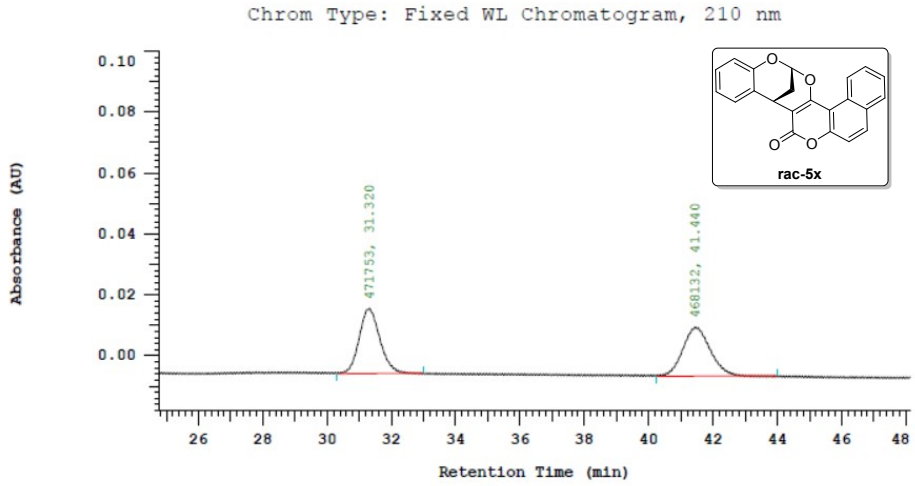
The ^{1}H NMR spectrum of 5x (500 MHz, $CDCl_3$)



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



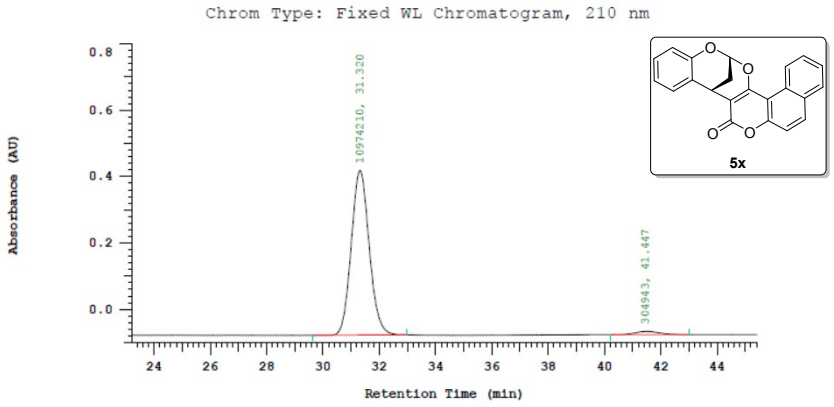
The HPLC of racemic 5x



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

No.	RT	Area	Area %	BC
1	31.320	471753	50.193	BB
2	41.440	468132	49.807	BB
		939885	100.000	

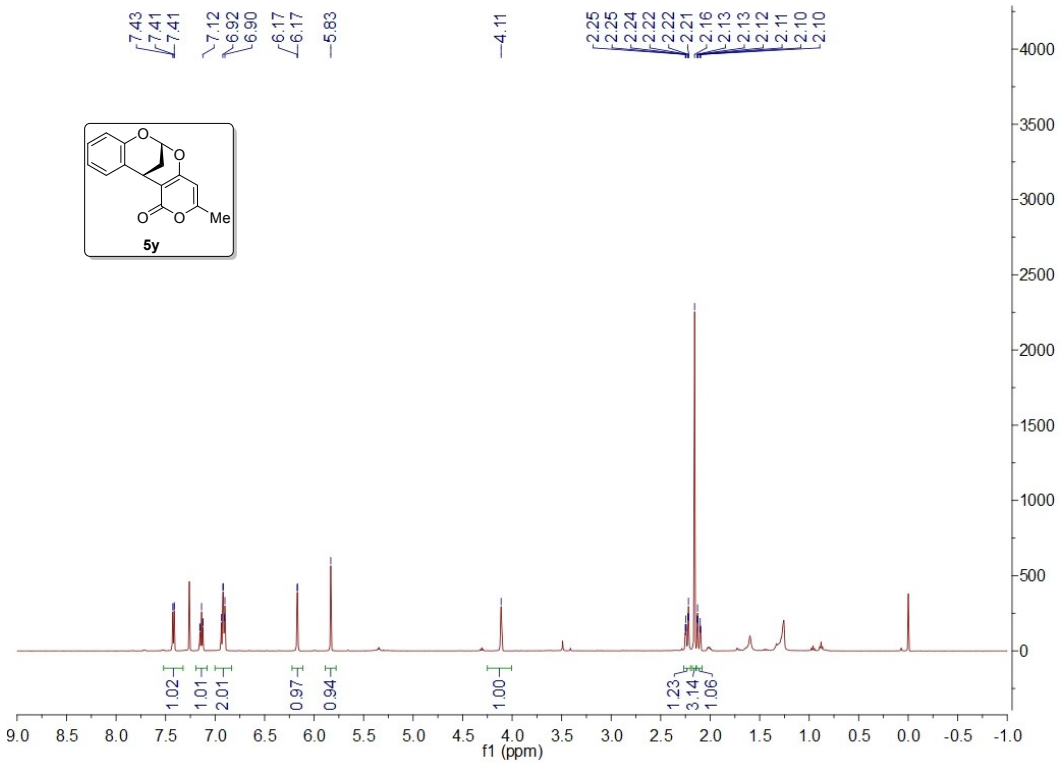
The HPLC of chiral 5x



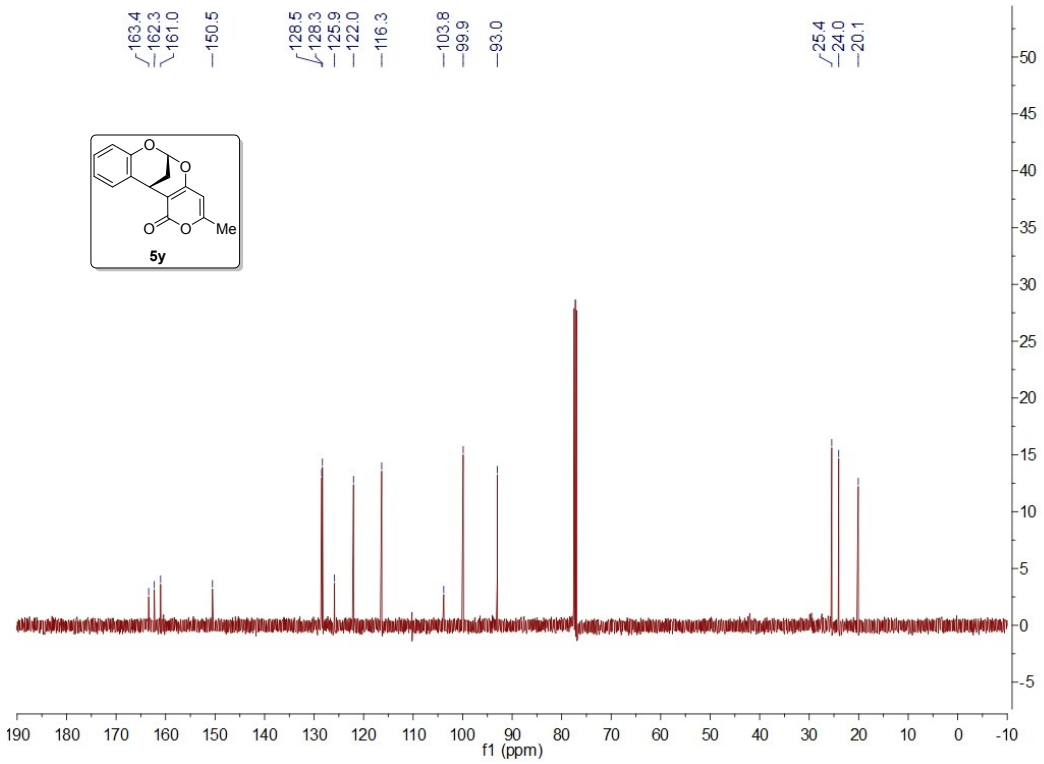
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	31.320	10974210	97.296	BB
2	41.447	304943	2.704	BB
		11279153	100.000	

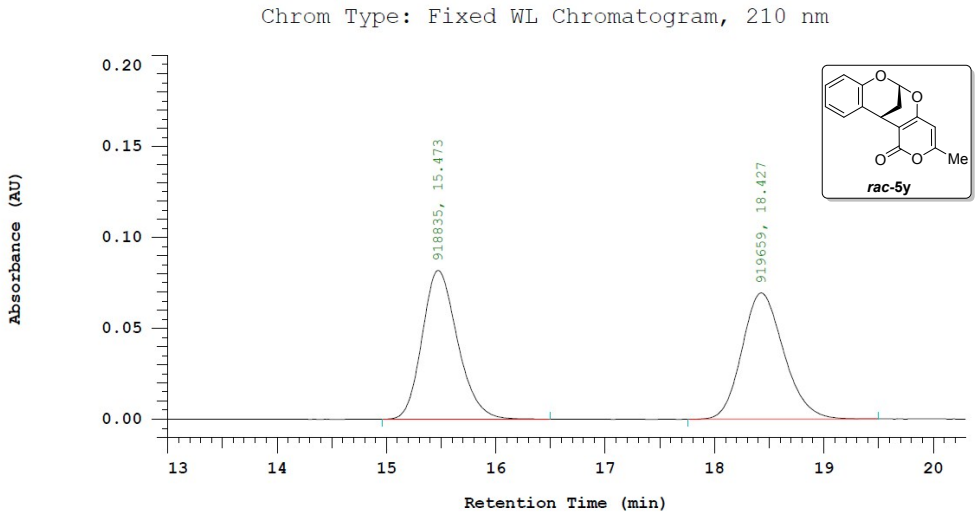
The ^{1}H NMR spectrum of 5y (500 MHz, $CDCl_3$)



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



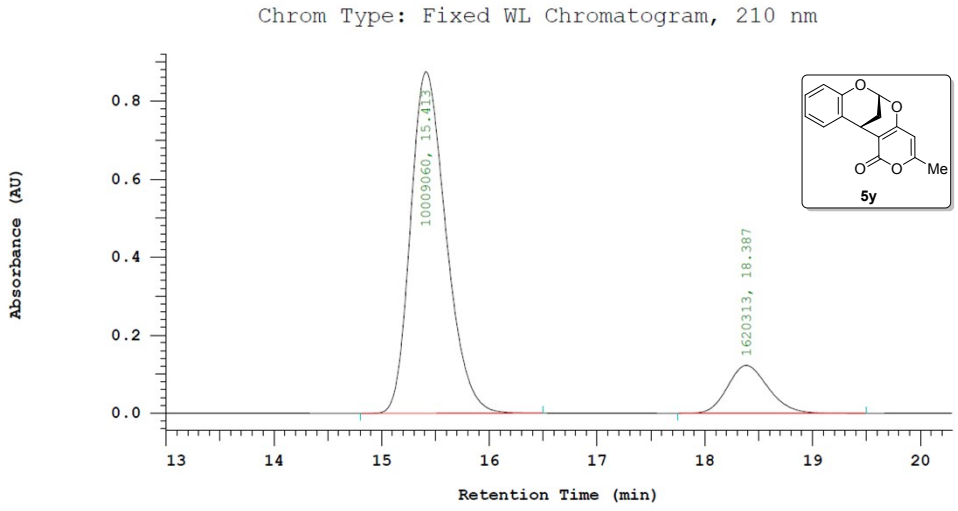
The HPLC of racemic 5y



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

No.	RT	Area	Area %	BC
1	15.473	918835	49.978	BB
2	18.427	919659	50.022	BB
		1838494	100.000	

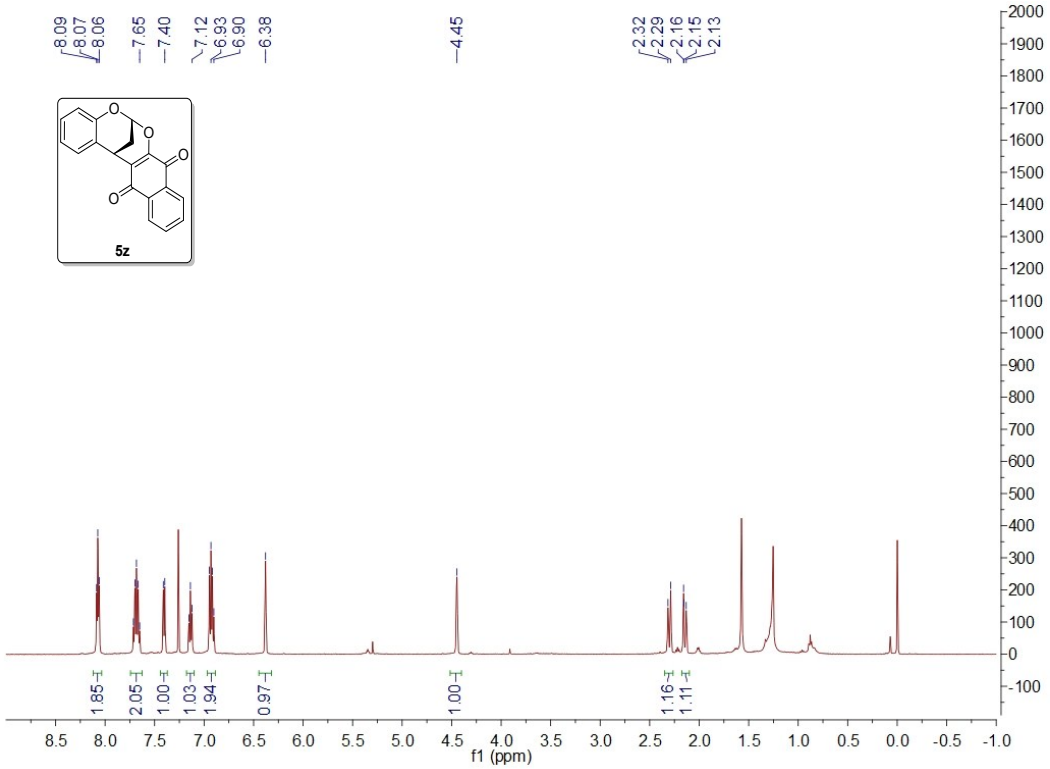
The HPLC of chiral 5y



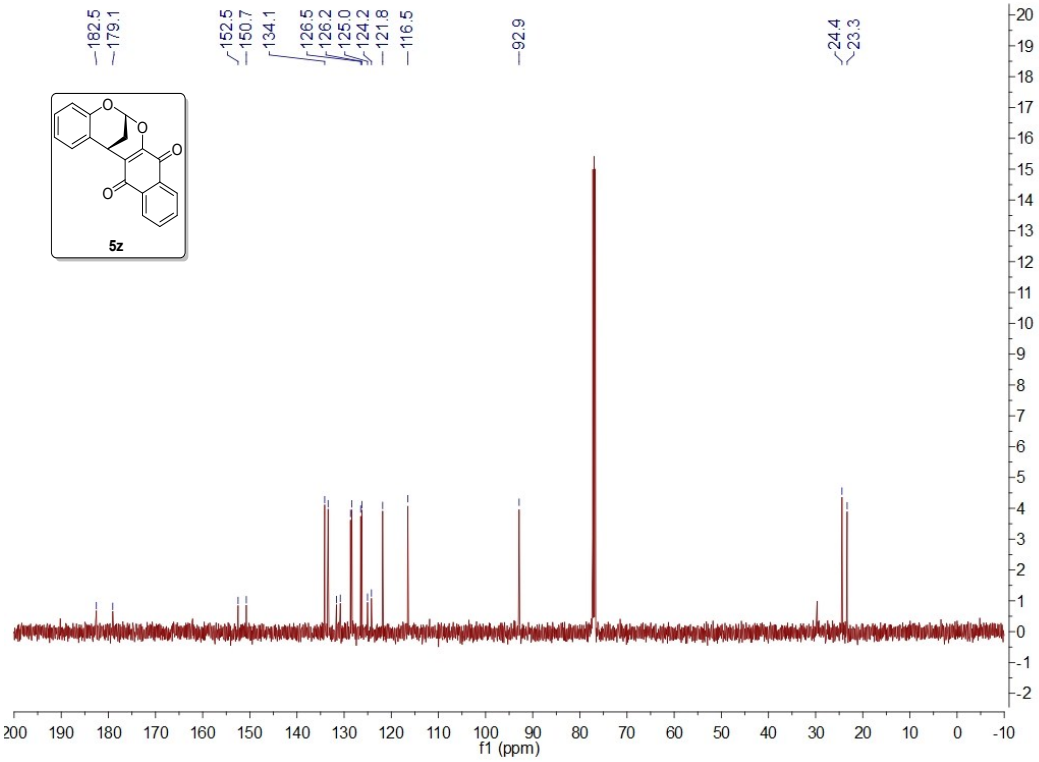
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	15.413	10009060	86.067	BB
2	18.387	1620313	13.933	BB
		11629373	100.000	

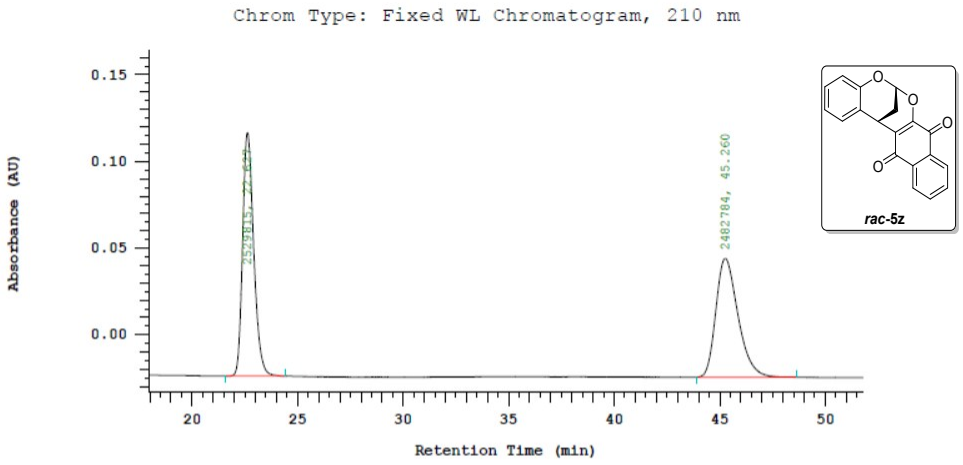
The ^{1}H NMR spectrum of 5z (500 MHz, $CDCl_3$)



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



The HPLC of racemic 5z



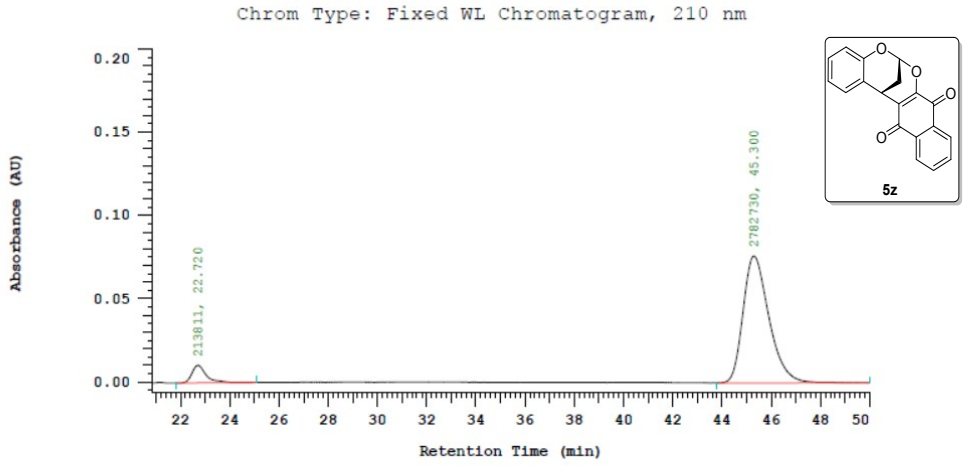
Chrom Type: Fixed WL Chromatogram, 210 nm

Peak Quantitation: AREA

Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	22.627	2529815	50.469	BB
2	45.260	2482784	49.531	BB
		5012599	100.000	

The HPLC of chiral 5z



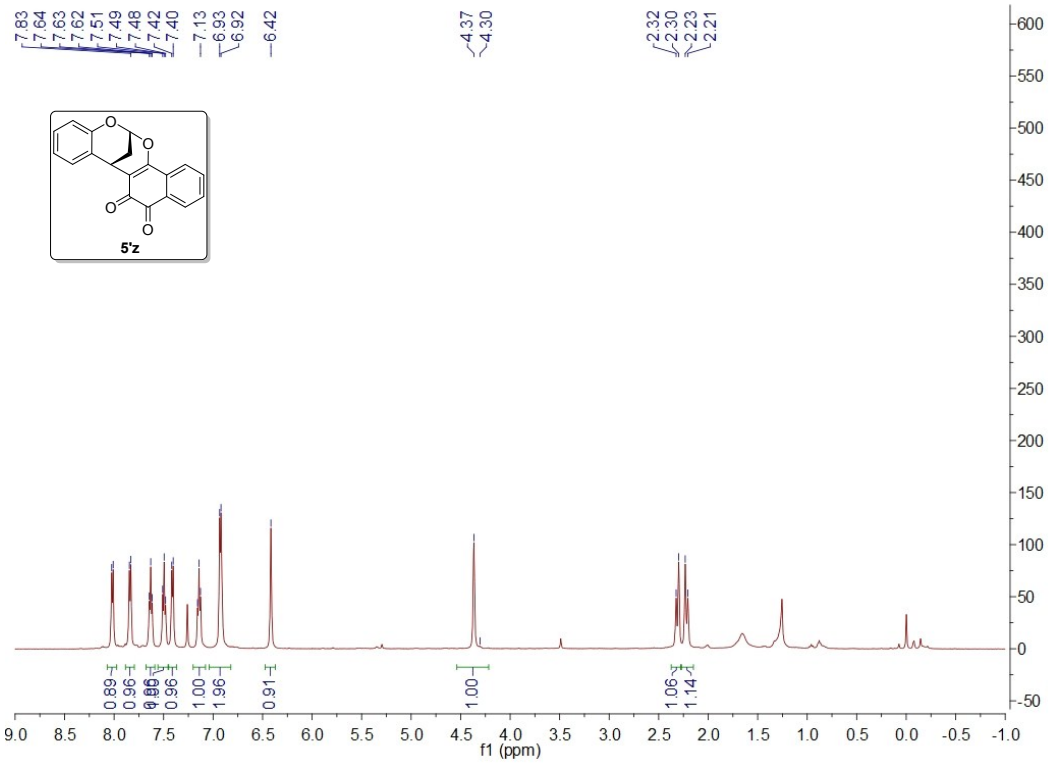
Chrom Type: Fixed WL Chromatogram, 210 nm

Peak Quantitation: AREA

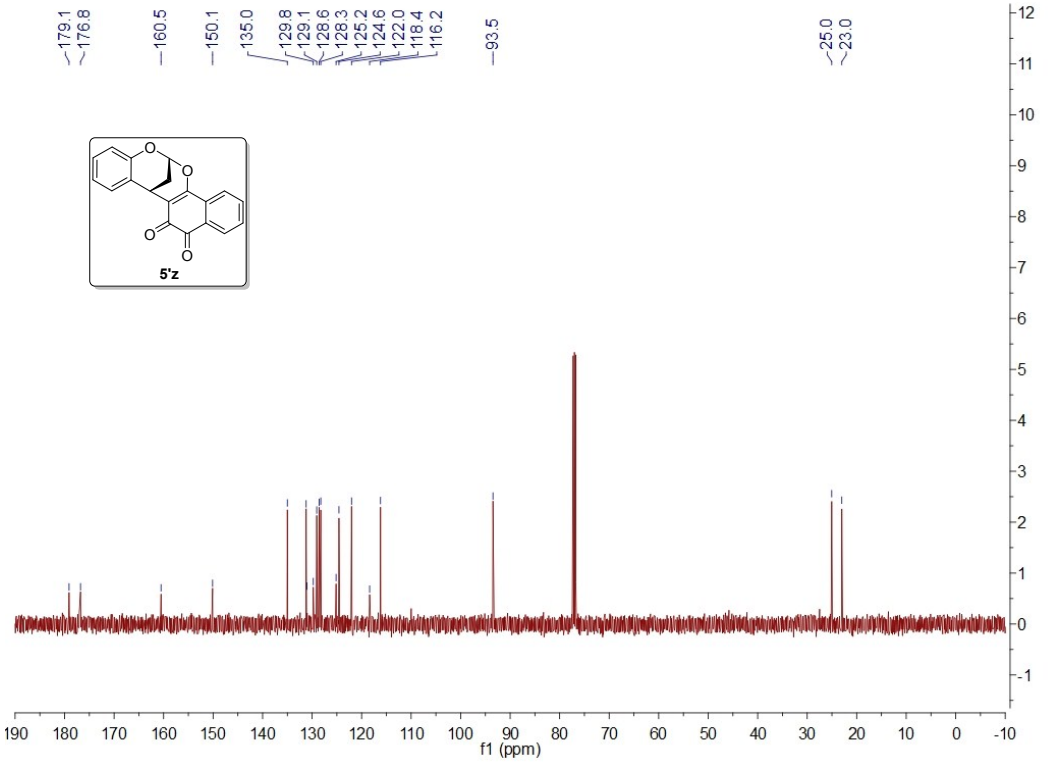
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	22.720	213811	7.135	BB
2	45.300	2782730	92.865	BB
		2996541	100.000	

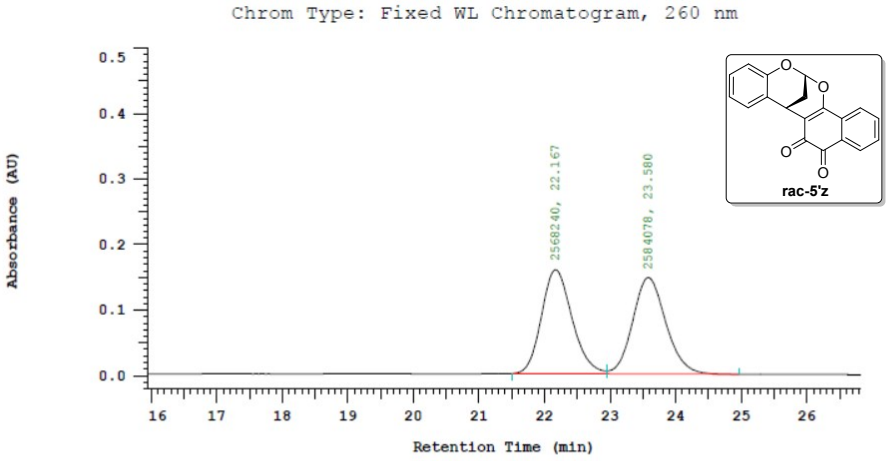
The ^{1}H NMR spectrum of 5'z (500 MHz, $CDCl_3$)



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



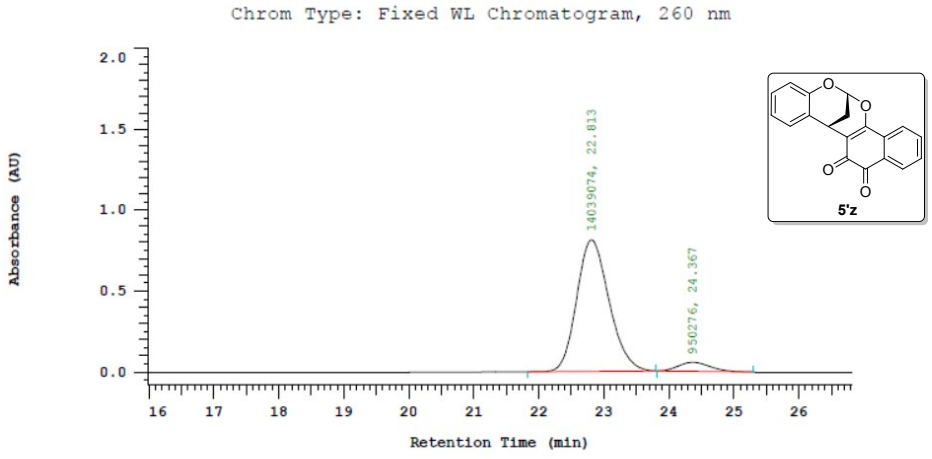
The HPLC of racemic 5'z



Chrom Type: Fixed WL Chromatogram, 260 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	22.167	2568240	49.846	BV
2	23.580	2584078	50.154	VB
		5152318	100.000	

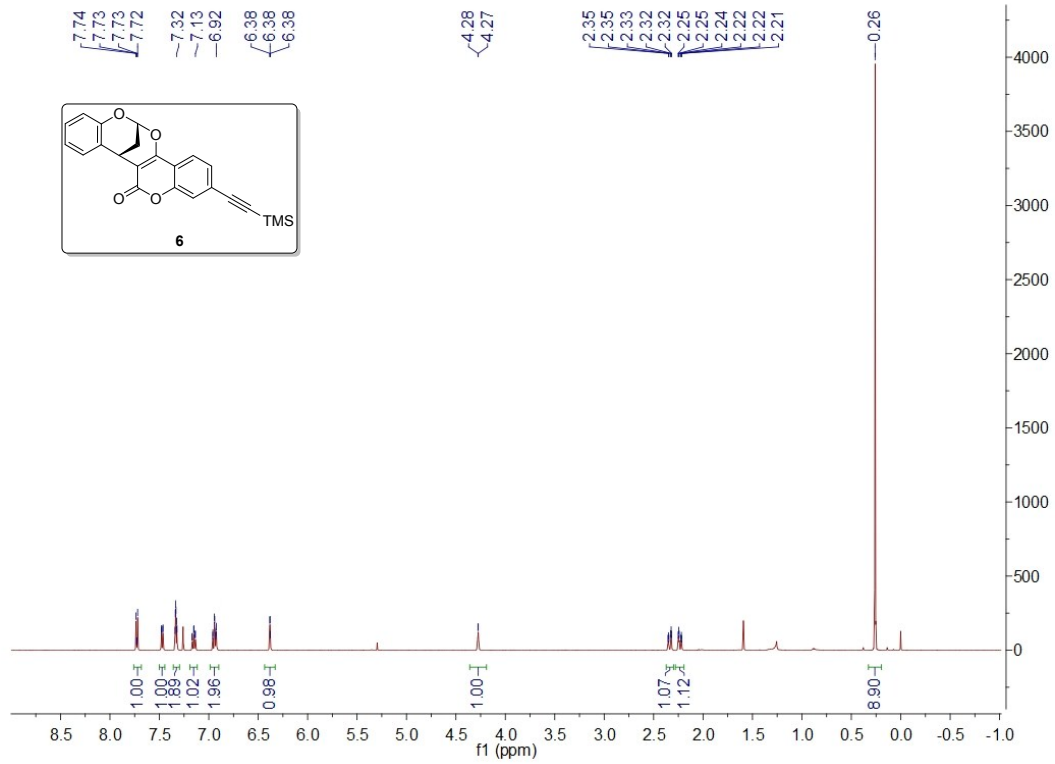
The HPLC of chiral 5'z



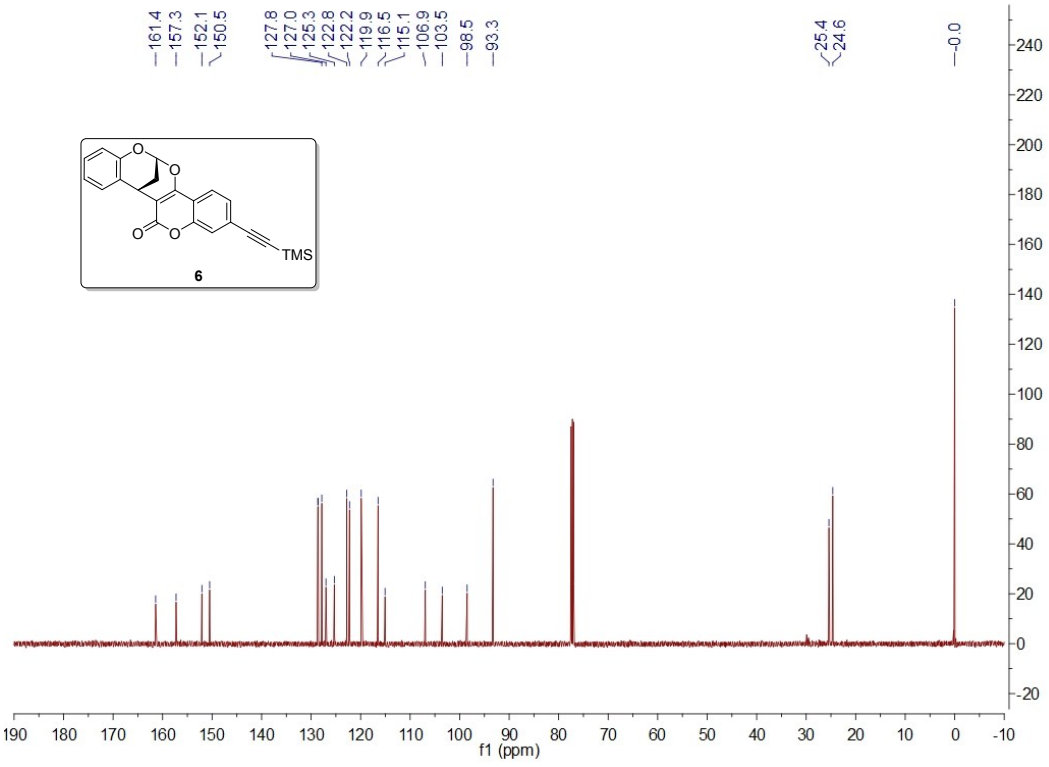
Chrom Type: Fixed WL Chromatogram, 260 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	22.813	14039074	93.660	BB
2	24.367	950276	6.340	BB
		14989350	100.000	

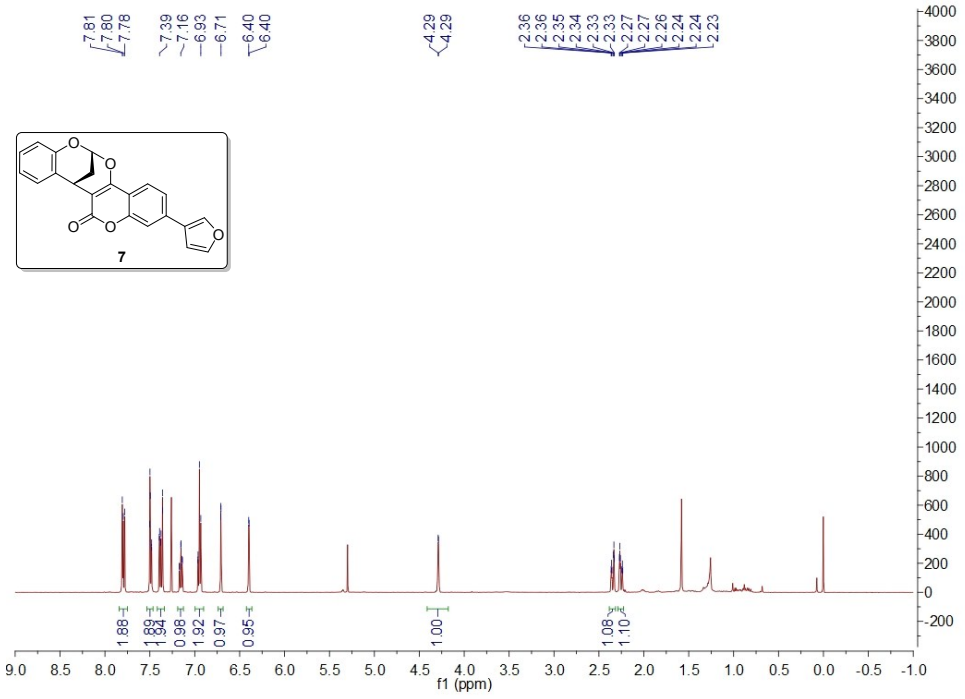
The ^{1}H NMR spectrum of 6 (500 MHz, $CDCl_3$)



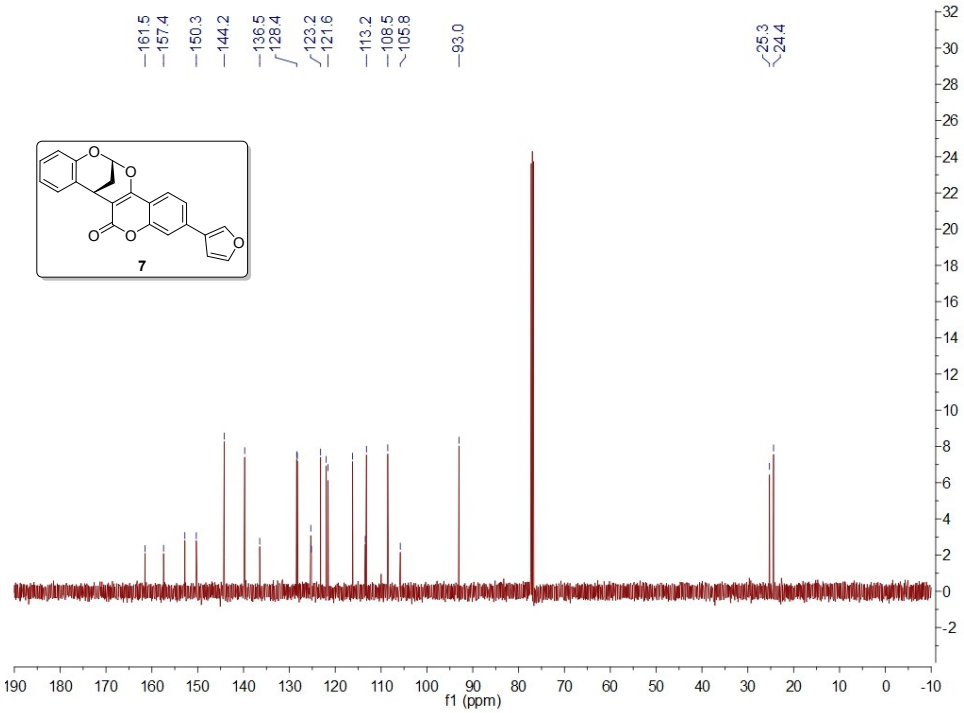
The ^{13}C NMR spectrum of 6 (125 MHz, $CDCl_3$)



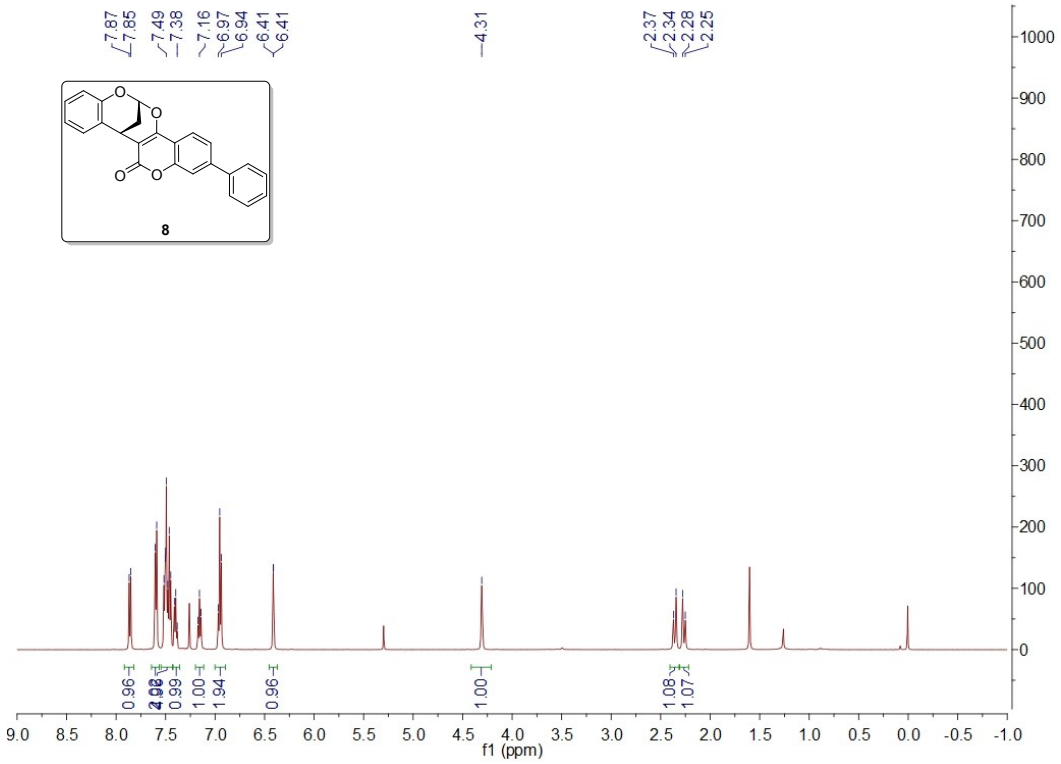
The ^{1}H NMR spectrum of 7 (500 MHz, $CDCl_3$)



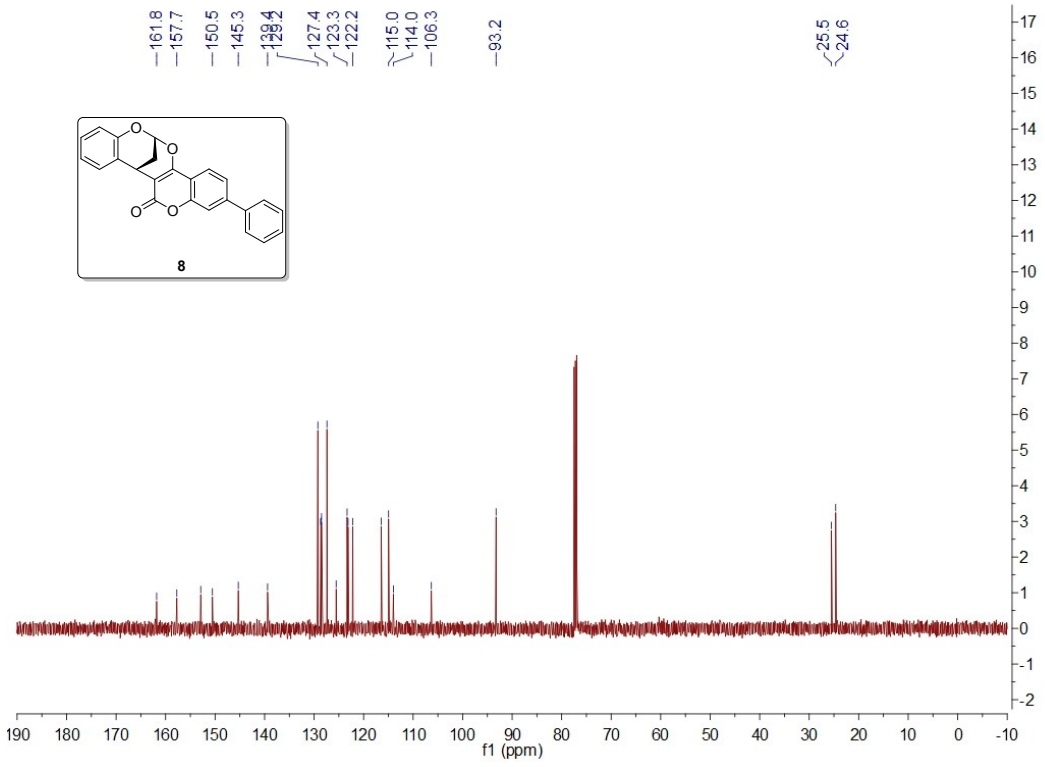
The ^{13}C NMR spectrum of 7 (125 MHz, $CDCl_3$)



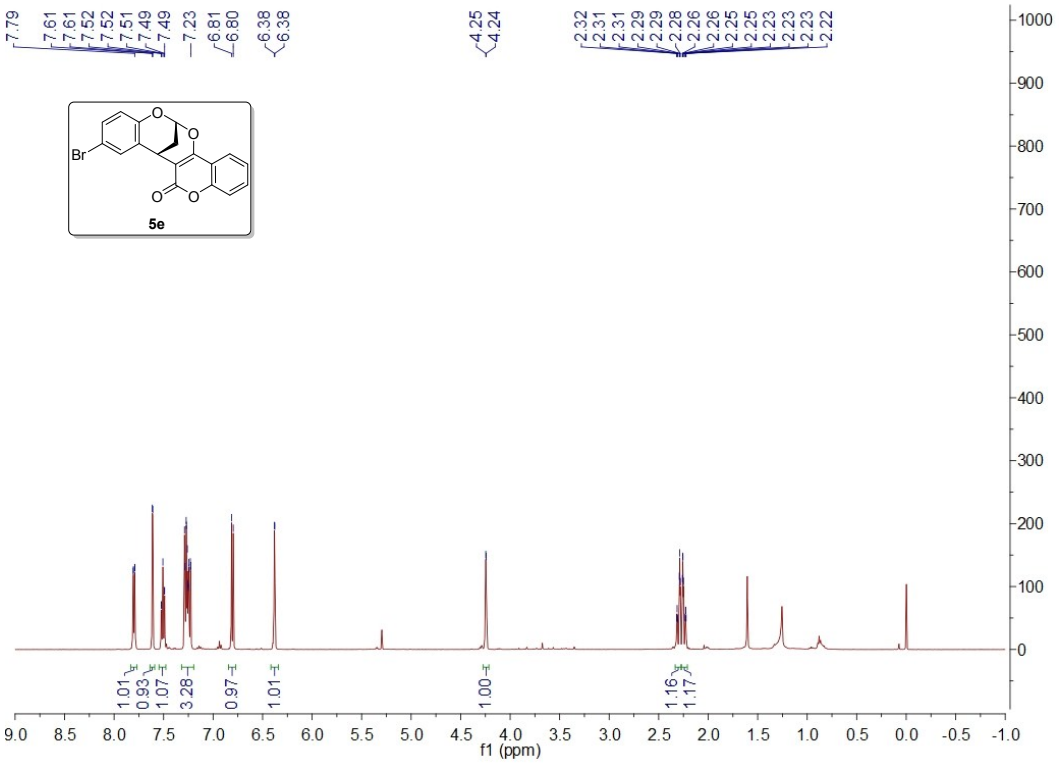
The ^{1}H NMR spectrum of 8 (500 MHz, $CDCl_3$)



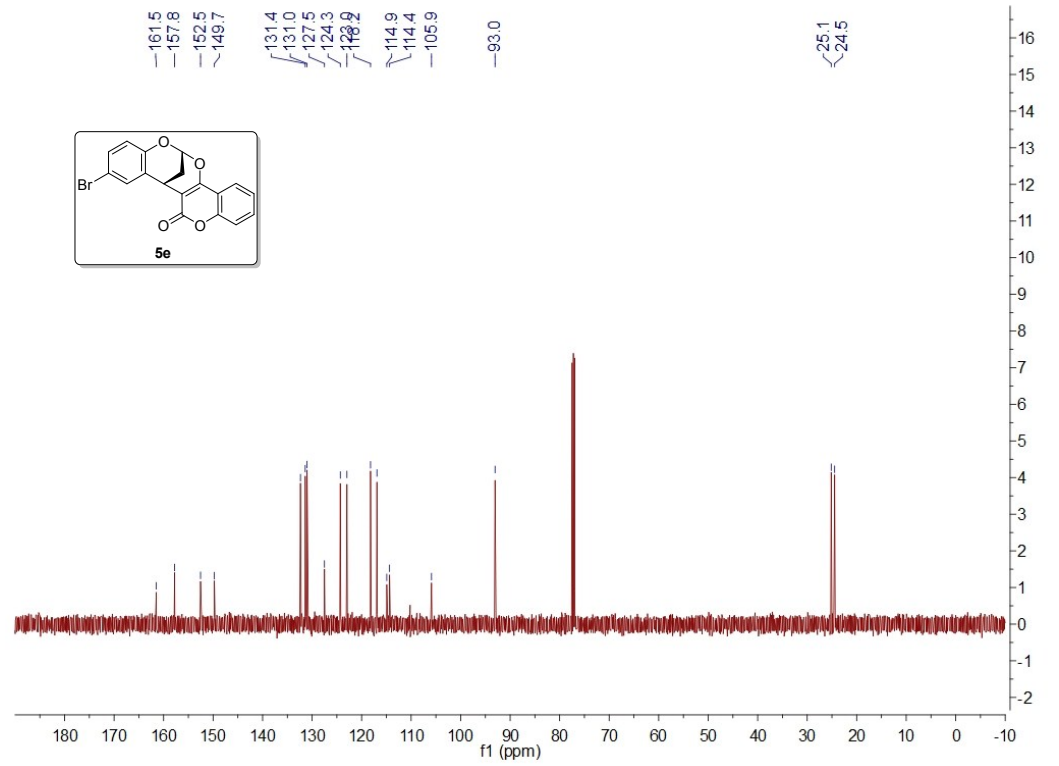
The ^{13}C NMR spectrum of 8 (125 MHz, $CDCl_3$)



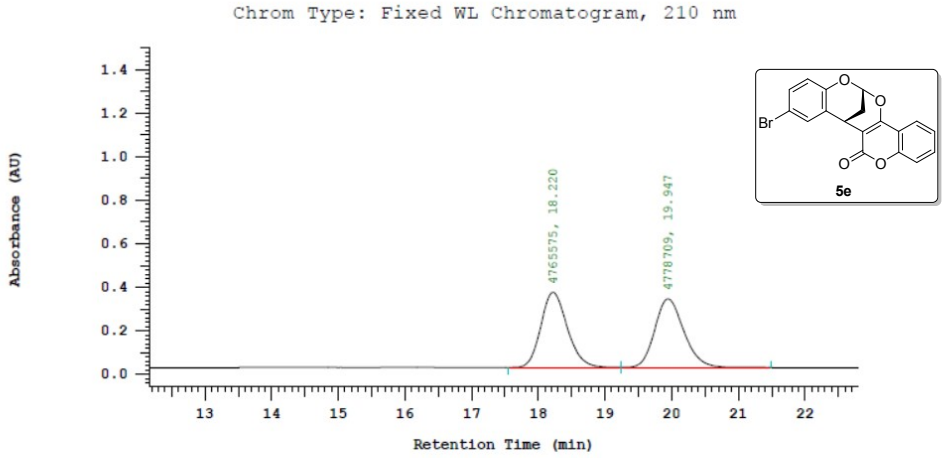
The ^{1}H NMR spectrum of 5e (500 MHz, $CDCl_3$)



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



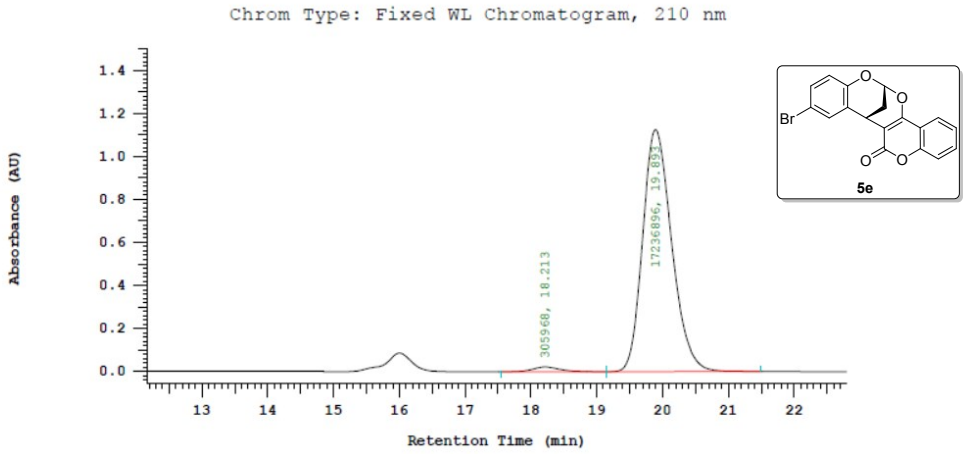
The HPLC of racemic 5e



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

No.	RT	Area	Area %	BC
1	18.220	4765575	49.931	BV
2	19.947	4778709	50.069	VB
		9544284	100.000	

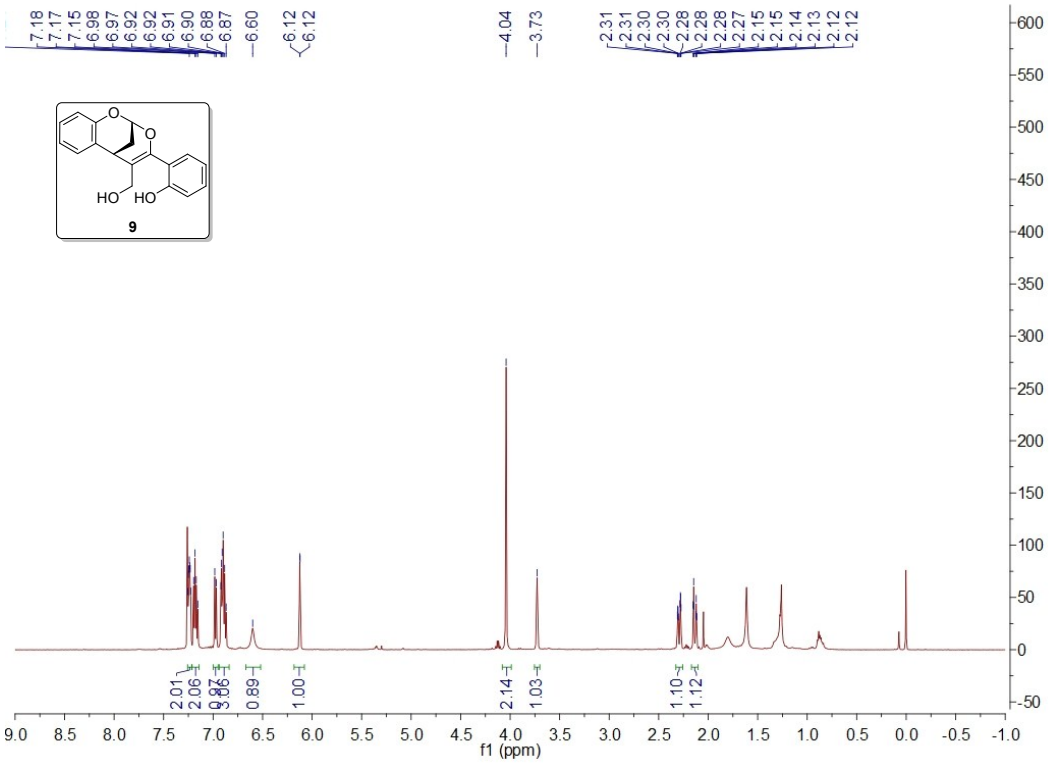
The HPLC of chiral 5e



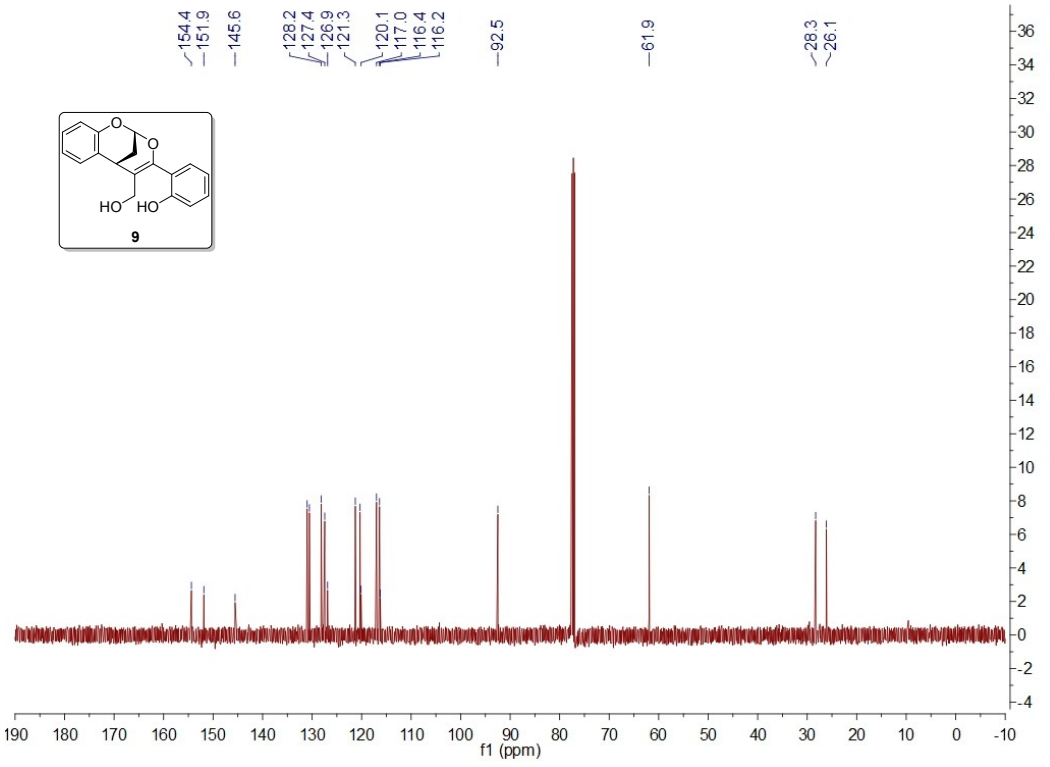
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	18.213	305968	1.744	BB
2	19.893	17236896	98.256	BB
		17542864	100.000	

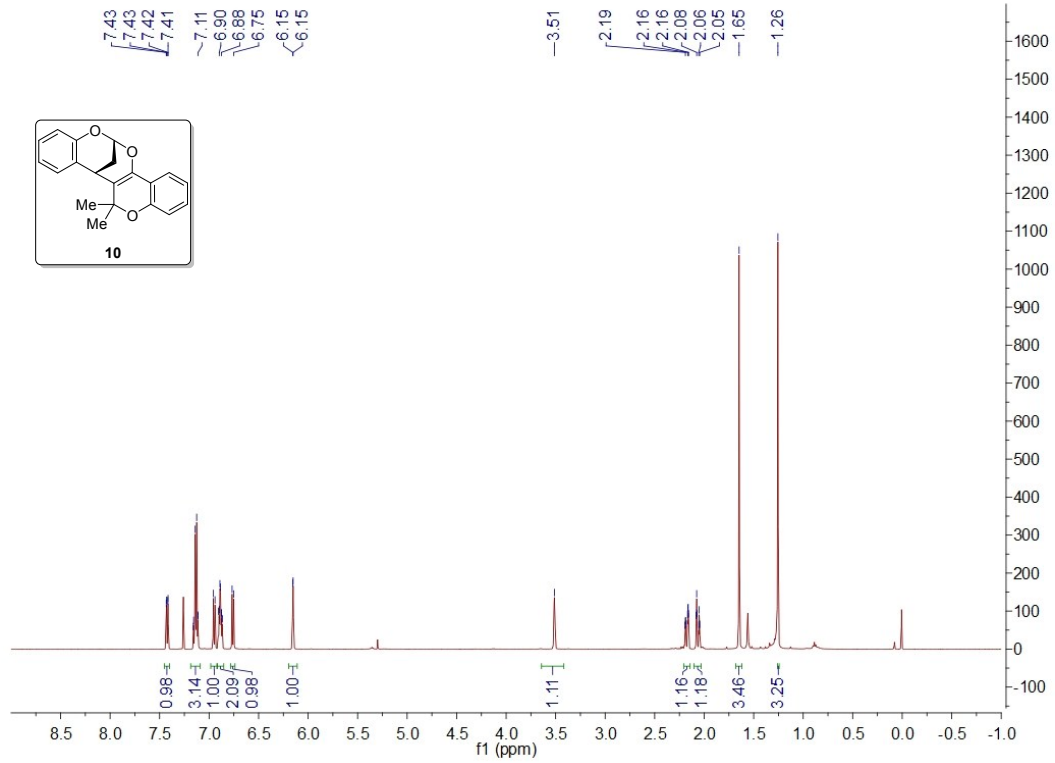
The ^{1}H NMR spectrum of 9 (500 MHz, $CDCl_3$)



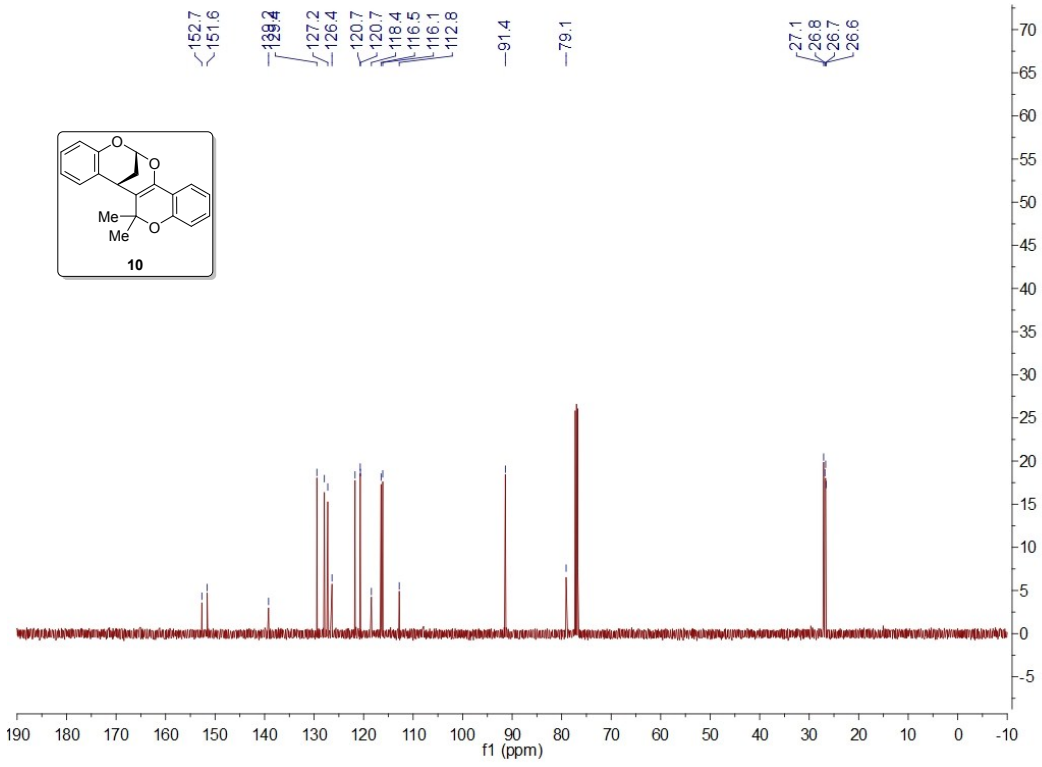
The ^{13}C NMR spectrum of 9 (125 MHz, $CDCl_3$)



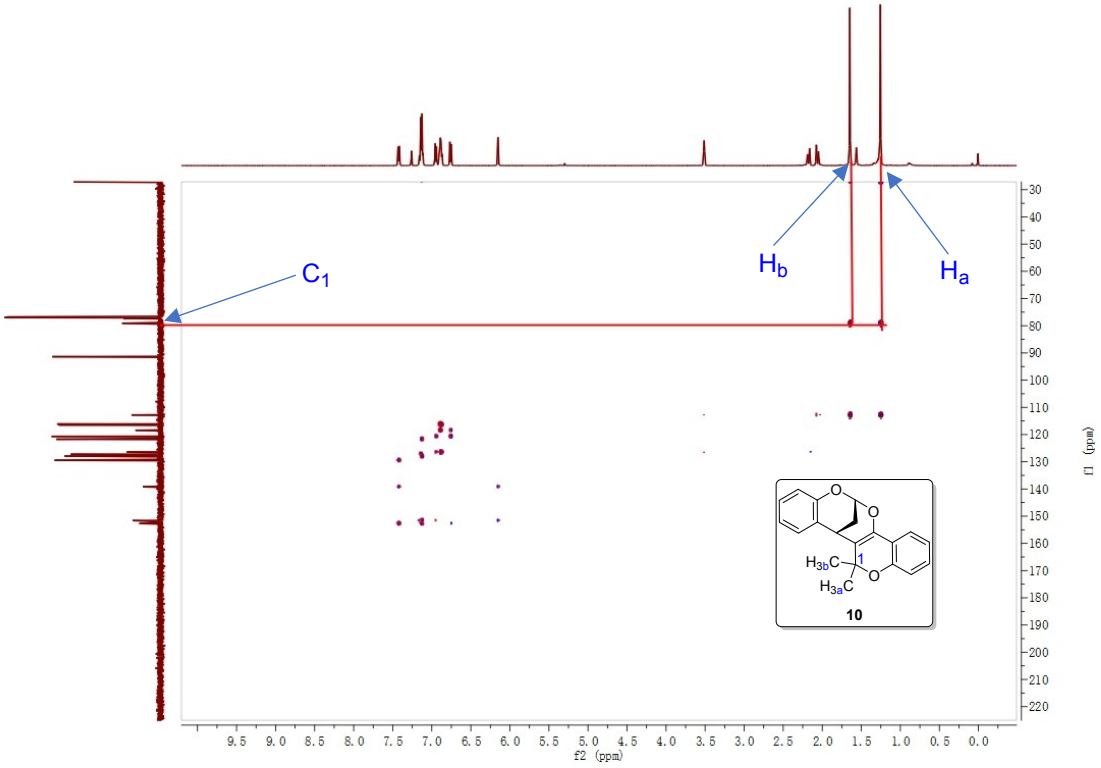
The ^{1}H NMR spectrum of 10 (500 MHz, $CDCl_3$)



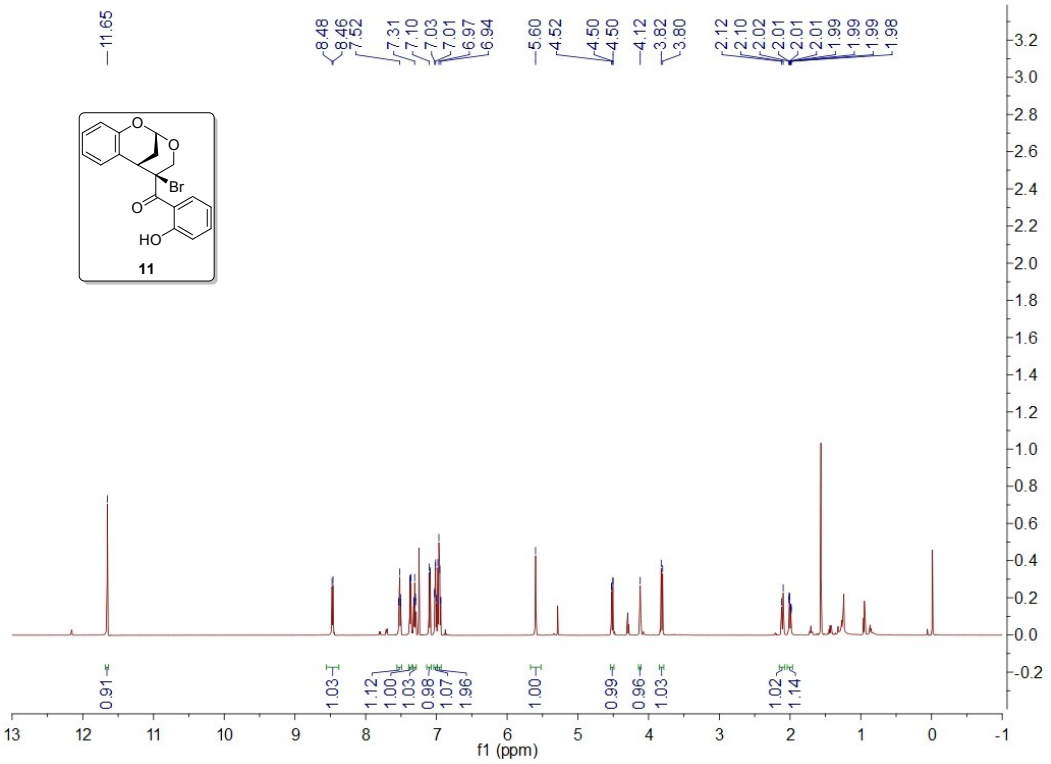
The ^{13}C NMR spectrum of 10 (125 MHz, $CDCl_3$)



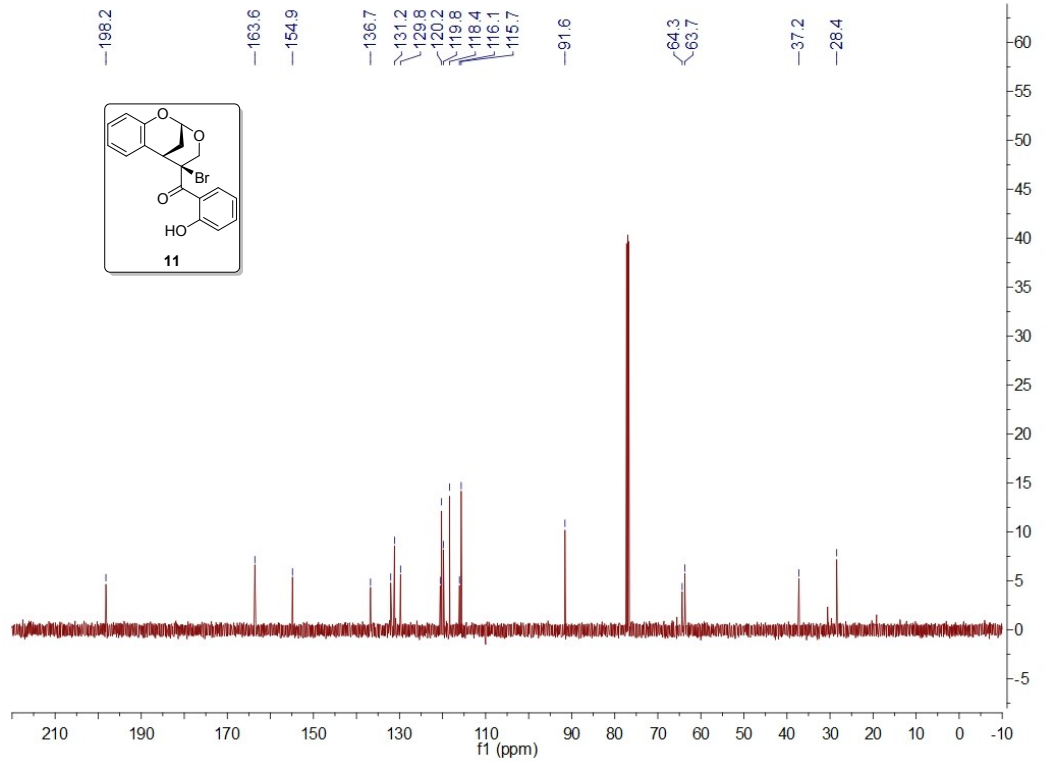
The HMBC spectrum of 10 (500 MHz, $CDCl_3$)



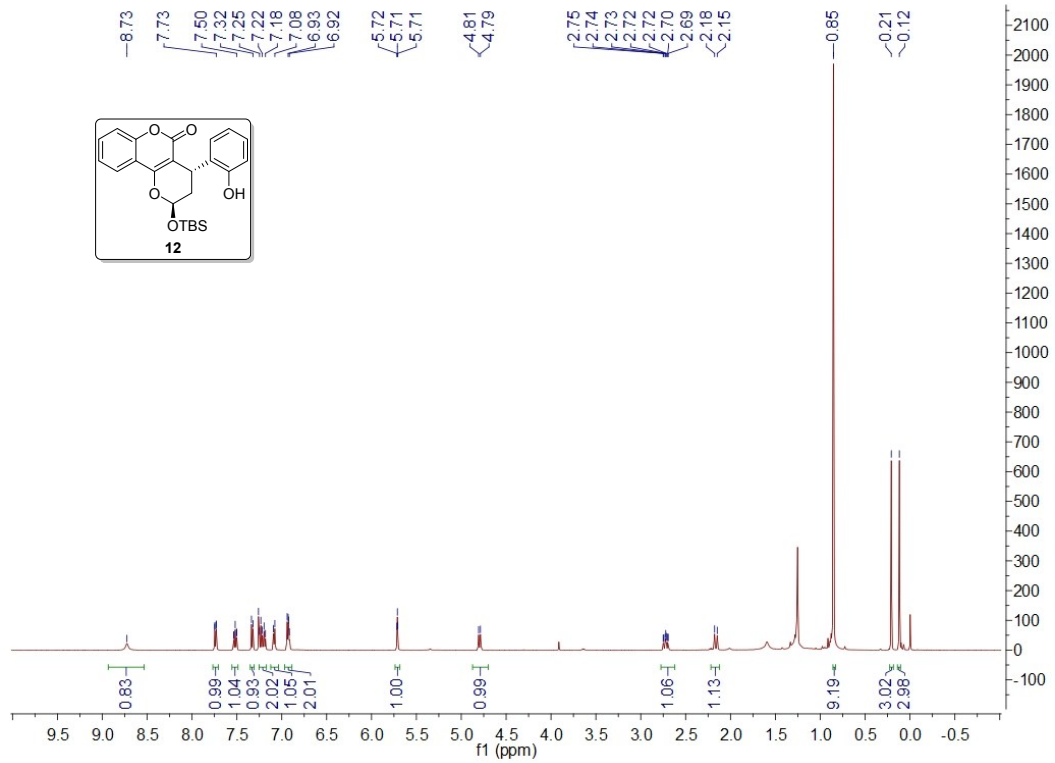
The ^{1}H NMR spectrum of 11 (600 MHz, $CDCl_3$)



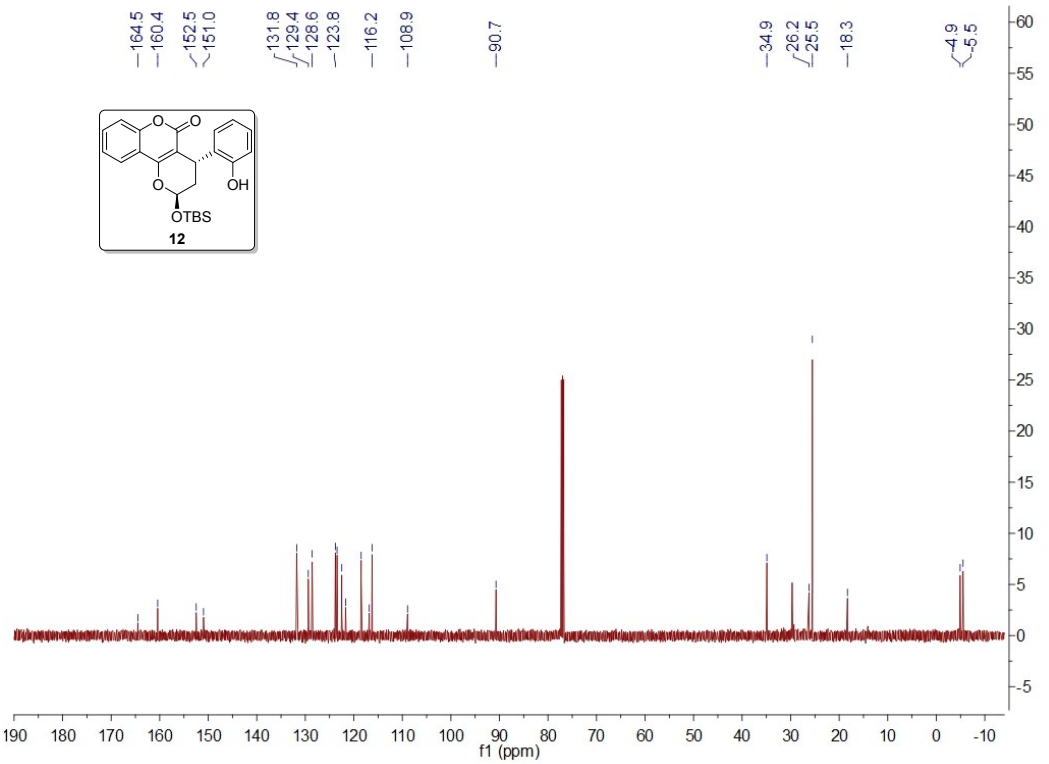
The ^{13}C NMR spectrum of 11 (125 MHz, $CDCl_3$)



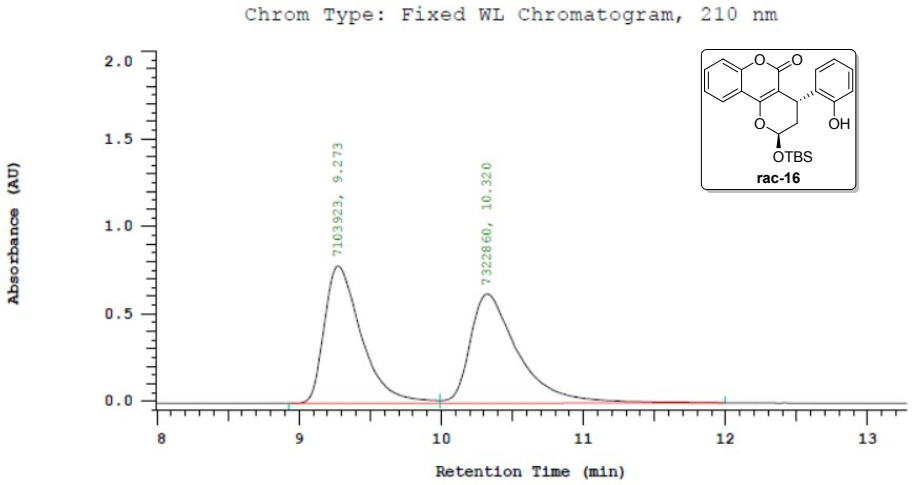
The ^{1}H NMR spectrum of 16 (500 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 16 (125 MHz, $CDCl_3$)



The HPLC of racemic 16

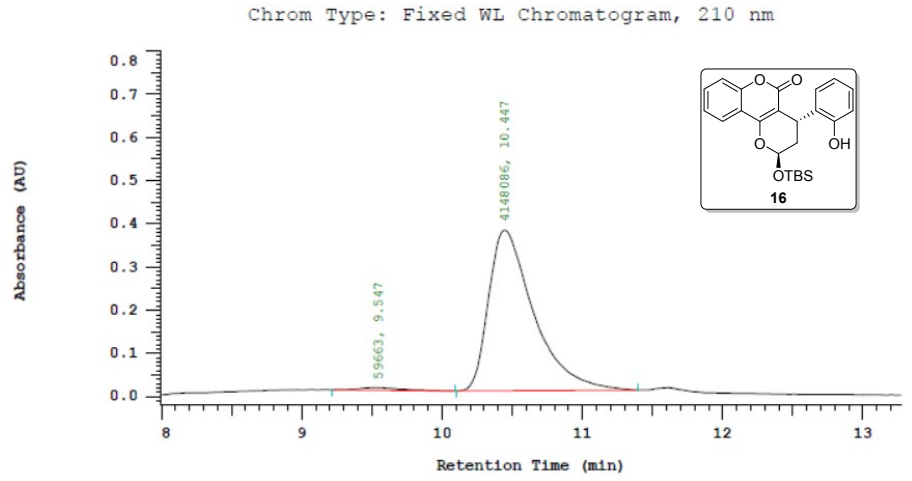


Chrom Type: Fixed WL Chromatogram, 210 nm

Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	9.273	7103923	49.241	BV
2	10.320	7322860	50.759	VB
		14426783	100.000	

The HPLC of chiral 16

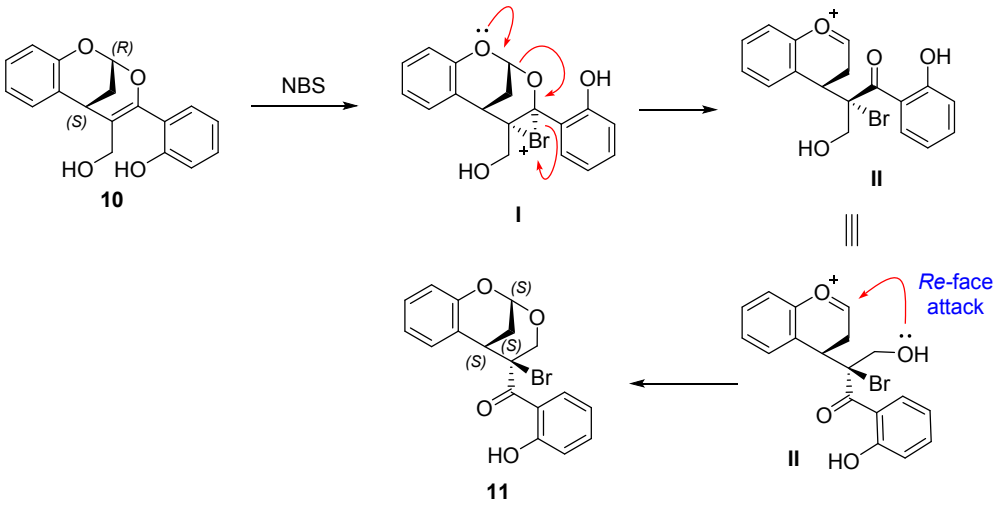


Chrom Type: Fixed WL Chromatogram, 210 nm

Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	9.547	59663	1.418	BB
2	10.447	4148086	98.582	BB
		4207749	100.000	

H. Proposed mechanism for the preparation of 11

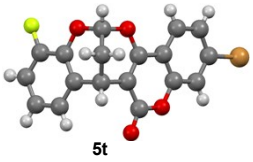


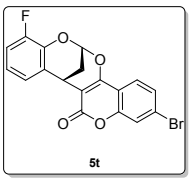
The reaction of the enantiopure dihydroxy compound **10** with NBS formed the electrophilic bromonium ion **I**, which could be converted into oxocarbenium ion **II** via electron transfer. Subsequently, the intramolecular *Re*-face attack of the aliphatic hydroxyl to the oxocarbenium ion moiety gave the new bicyclic acetal compound **11** with the proposed absolute configuration.

I. Single crystal X-Ray diffraction data

[CCDC 1959362 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.].

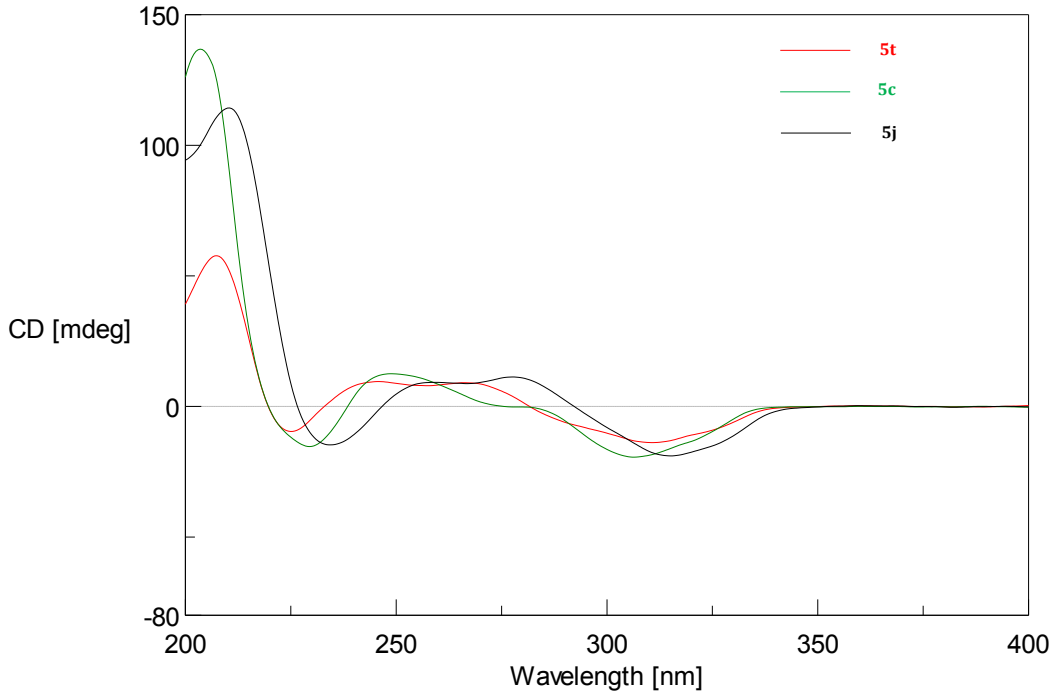
Absolute configuration of **5t**





```
Bond precision:  C-C = 0.0063 A          Wavelength=1.54184

Cell:            a=9.2599(2)     b=12.5261(3)     c=12.6868(4)
                 alpha=90        beta=90          gamma=90
Temperature:     293 K

                 Calculated                Reported
Volume           1471.55(7)                1471.54(6)
Space group      P 21 21 21                P 21 21 21
Hall group       P 2ac 2ab                 P 2ac 2ab
Moiety formula   C18 H10 Br F O4           ?
Sum formula      C18 H10 Br F O4           C18 H10 Br F O4
Mr               389.16                    389.17
Dx,g cm-3        1.757                     1.757
Z                4                         4
Mu (mm-1)        4.115                     4.115
F000             776.0                     776.0
F000'            775.60
h,k,lmax         11,14,15                  11,14,15
Nref             2631[ 1524]               2633
Tmin,Tmax        0.641,0.636               0.688,1.000
Tmin'            0.581

Correction method= # Reported T Limits: Tmin=0.688 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 1.73/1.00      Theta(max)= 67.195

R(reflections)= 0.0320( 2427)     wR2(reflections)= 0.0803( 2633)

S = 1.063                 Npar= 218
```

ECD analysis of compound **5c**, **5j** and **5t**



ECD spectrum were recorded in methanol on JASCO J-815 spectropolarim
eter (JASCO Corporation, Tokyo, Japan).
The nearly identical ECD spectra of **5t**, **5c** and **5j** indicate that they display same stereochemistry.