

**Supporting Information for**

**Chiral Organic Contact Ion Pairs in**

**Metal-free Catalytic Asymmetric Allylic Substitutions**

Magnus Rueping,\* Uxue Uria, Ming-Yuan Lin, Iuliana Atodiresei

*Institute of Organic Chemistry, RWTH Aachen University, Landoltweg 1, 52074, Aachen (Germany)*

Magnus.Rueping@rwth-aachen.de

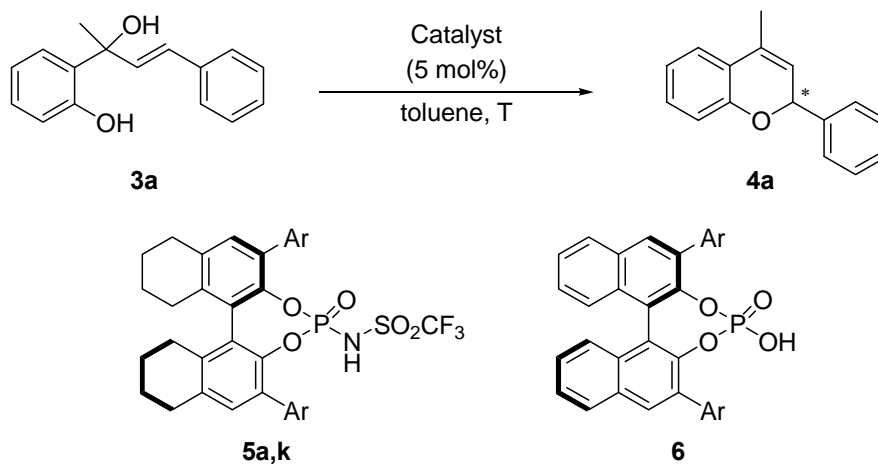
**Table of Contents**

General Methods	S2
Catalytic Metal-Free Allylic Substitution	S3
<b>Table S1.</b> Preliminary Evaluation of Brønsted Acid Nature, Catalyst Loading and Temperature in Asymmetric Allylic Substitution	S3
<b>Table S2.</b> Solvent and Molecular Sieves Effect on Asymmetric Allylic Substitution	S3
Functionalization of the Products	S4
<b>Figure S1.</b> EDX of Catalyst <b>5a</b>	S5
Representative Procedure for Enantioselective Allylic Substitution	S6
Characterization of Products <b>4a-o</b>	S6
General Procedure for the Reduction of <b>4a</b>	S13
Characterization of Product <b>7a</b>	S13
Determination of the Absolute Configuration	S13
NMR Spectra of Compounds <b>4a-o</b> and <b>7a</b>	S16
Chiral SFC Data of Compounds <b>4a-o</b> , <b>7a</b> and <b>3a</b>	S32

**General Methods.** Unless otherwise noted, all commercially available compounds were used as received. Solvents for chromatography were technical grade and distilled prior to use. Toluene used in reactions was analytical grade. Analytical thin-layer chromatography (TLC) was performed on Merck silica gel 60 aluminum plates with F-254 indicator, visualized by UV irradiation. Column chromatography was performed using MN silica gel (particle size 0.040-0.063 mm).  $^1\text{H}$ -NMR and  $^{13}\text{C}$ -NMR were recorded on a Mercury 300 or Inova 400 spectrometer in  $\text{CDCl}_3$  or  $\text{CD}_2\text{Cl}_2$  with residual proton signal of the deuterated solvents as the internal reference ( $\delta_{\text{H}} = 7.26$  ppm and  $\delta_{\text{C}} = 77.0$  ppm for  $\text{CDCl}_3$  and  $\delta_{\text{H}} = 5.32$  ppm and  $\delta_{\text{C}} = 53.8$  ppm for  $\text{CD}_2\text{Cl}_2$ ). Data are reported in the following order: chemical shift ( $\delta$ ) in ppm; multiplicities are indicated s (singlet), d (doublet), t (triplet), dd (doublet of doublets), td (triplet of doublets), qt (quartet of triplets), ddd (doublet of doublet of doublets), m (multiplet); coupling constants ( $J$ ) are in Hertz (Hz).  $^{13}\text{C}$  NMR spectra were acquired on a broad band decoupled mode. Mass spectra was conducted on GC-MS Shimadzu QP2010 (column: Equity<sup>®</sup>-5, length  $\times$  I.D. 30 m  $\times$  0.25 mm,  $d_{\text{f}}$  0.25  $\mu\text{m}$ , lot # 28089-U, Supelco). HRMS were measured on a Finnigan MAT 95 or LTQ Orbitrap XL spectrometer. IR spectra were measured in a Perkin-Elmer ATR apparatus and are reported in terms of frequency of absorption ( $\text{cm}^{-1}$ ). Optical rotations were measured on a Perkin-Elmer 241 polarimeter. The enantiomeric excess (ee) of the products was determined by Supercritical Fluid Chromatography (SFC) analysis using Daicel Chiralpak IA, Daicel Chiralcel ODH or OJH and (S,S)-Whelk-01 columns. The chiral SFC methods were calibrated with the corresponding racemic mixtures. The CD-spectrum for the 2H-chromene **4m** was recorded on a circular dichroism spectrometer (AVIV Model 62DS) at room temperature in acetonitrile. The starting materials **3a-o** were readily prepared by using established Claisen-Schmidt condensation and subsequent alkylation reactions (1-3). The two enantiomers of **3a** have been separated by preparative SFC on a Chiralpak IA column 250  $\times$  20 mm,  $\text{CO}_2$  (60g) and 12% *n*-Hexan:*iso*-Propanol 1:1.

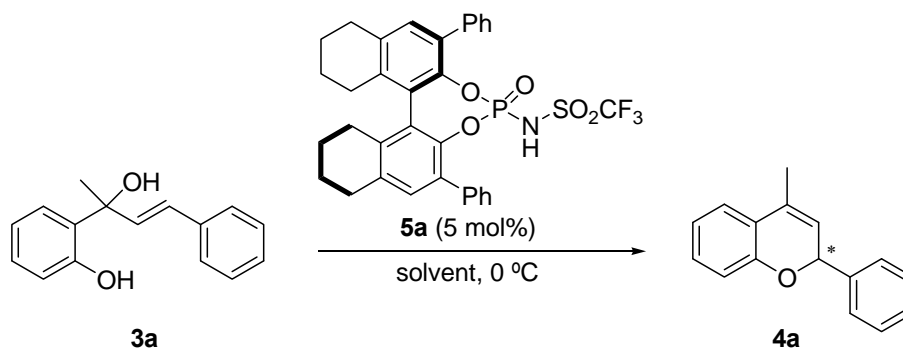
## Catalytic Metal-free Allylic Substitution

**Table S1.** Preliminary Evaluation of Brønsted Acid Nature, Catalyst Loading and Temperature in Asymmetric Allylic Substitution.



Entry	Catalyst Ar	Catalyst (mol%)	Temp (°C)	t (h)	Yield (%)	ee (%)
1	phenyl ( <b>6</b> )	10	rt	312	16	0
2	phenyl ( <b>5a</b> )	10	35	0.5	71	34
3	phenyl ( <b>5a</b> )	10	rt	1.5	97	36
4	phenyl ( <b>5a</b> )	5	0	13	77	56
5	biphenyl ( <b>5k</b> )	10	rt	1.5	77	26
6	biphenyl ( <b>5k</b> )	5	rt	4	83	22
7	biphenyl ( <b>5k</b> )	2	rt	312	54	1

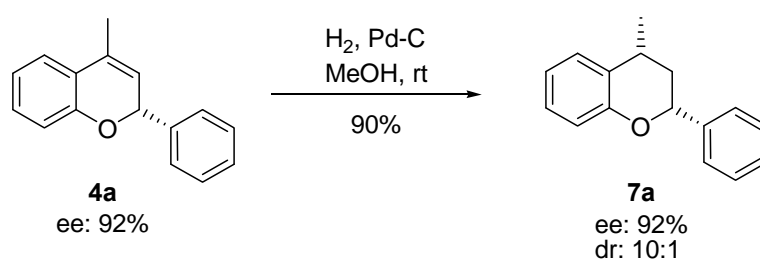
**Table S2.** Solvent and Molecular Sieves Effect on Asymmetric Allylic Alkylation.



Entry	Solvent	T (h)	Yield (%)	Ee (%)
1	toluene	13	77	56
2	m-xylene	17	97	30
3	o-xylene	17	76	46
4	CH <sub>2</sub> Cl <sub>2</sub>	17	97	42
5	CF <sub>3</sub> Ph	17	97	46
6	toluene/ MS(3A)	17	68	46

## Functionalization of the Products.

We have also gained some insight into the ability of the chromene structure to undergo chemical modifications. In this respect, the presence of a C-C double bond in the chromene skeleton provides great flexibility for further structural modifications. For instance, compounds containing a chroman scaffold, which are chemotherapeutic (antiviral) agents (**4**), are readily available by a simple reduction from adducts **4** (Scheme 1S). For example during the reduction of **4a** a new stereogenic center is formed in a diastereoselective way, affording the flavan derivative **7a** in an excellent yield.

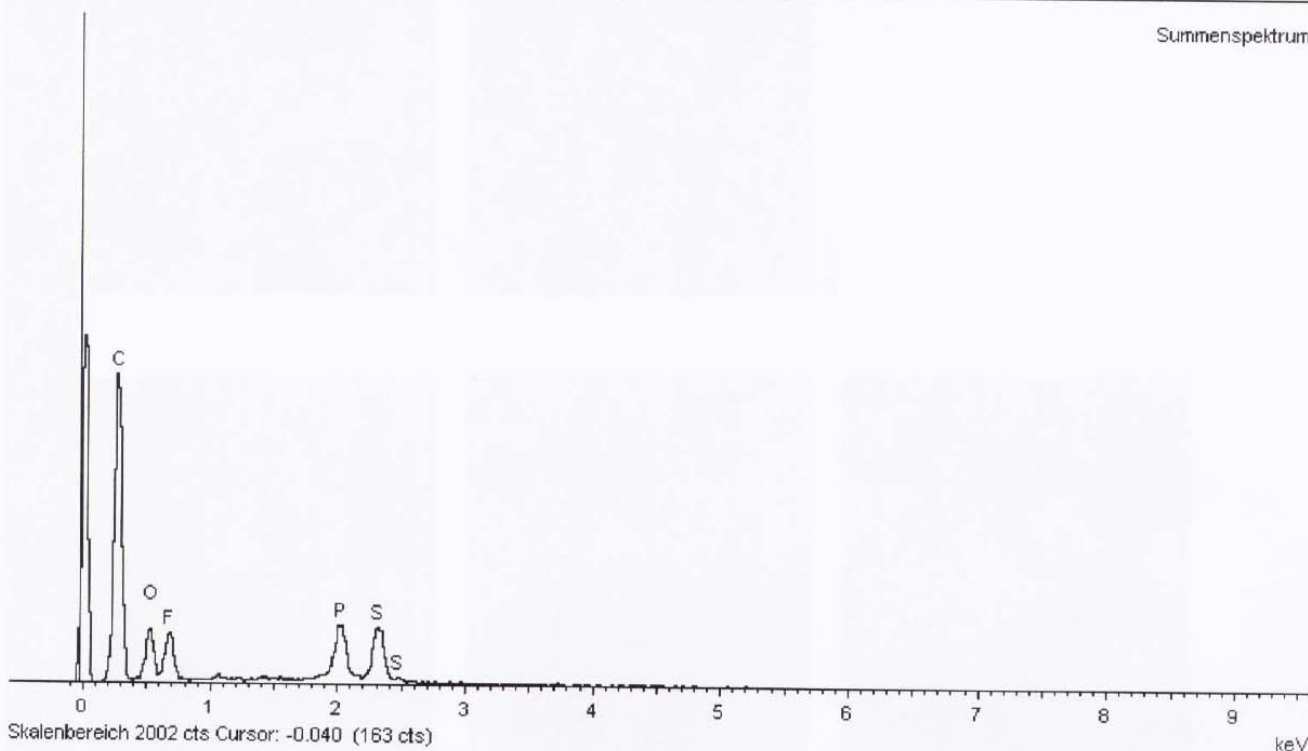


**Scheme 1S.** Reduction of chromene **4a** to the corresponding chromane **7a**.

Probe: 1  
Typ: Vorgabe  
ID:

Projekt: Guest 21.07.10  
Besitzer: SEM  
Bereich: 1\_01.tif

Summenspektrum



Spektrumverarbeitung :  
Keine Peaks weggelassen

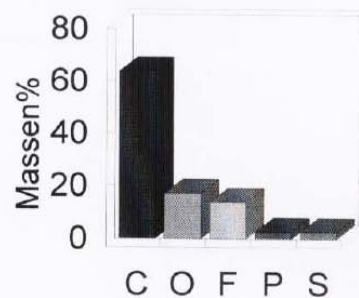
Verarbeitungsoption : Alle Elemente analysiert (Normalisiert)  
Anzahl Iterationen = 6

Standard :

C CaCO<sub>3</sub> 1-Jun-1999 12:00 AM  
O SiO<sub>2</sub> 1-Jun-1999 12:00 AM  
F MgF<sub>2</sub> 1-Jun-1999 12:00 AM  
P GaP 1-Jun-1999 12:00 AM  
S FeS<sub>2</sub> 1-Jun-1999 12:00 AM

Element	Offstl. Konz.	Intensität Korrektur	Massen%	Massen% Sigma	Atom%
C K	213.20	0.7775	63.83	1.07	73.03
O K	30.77	0.4191	17.09	0.97	14.68
F K	13.55	0.2284	13.81	0.83	9.99
P K	15.16	1.3411	2.63	0.15	1.17
S K	10.77	0.9461	2.65	0.14	1.14
Insgesamt			100.00		

Quantitative Resultate



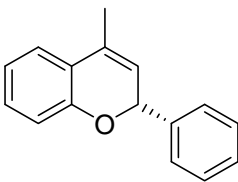
Kommentar:

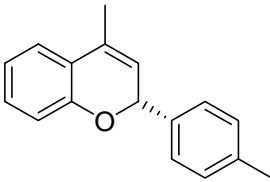
**Figure S1.** EDX of catalyst **5a**.

## Representative procedure for the Enantioselective Allylic Substitution.

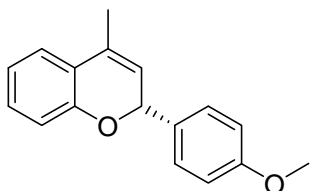
To a solution of the corresponding freshly prepared substituted phenol compound in toluene (0.08 M) was added the catalyst (5-10 mol%) at the temperature indicated and the resulting mixture was stirred until being completed (TLC monitoring). The crude reaction mixture was directly charged on silica gel and purified by column chromatography (cyclohexane/AcOEt 19:1) to afford the corresponding product **4a-o**. To avoid the decomposition of these products, they were stored at -26 °C.

### Characterization of Products 4a-o

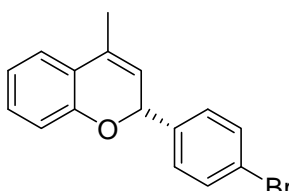
 **(2R)- 4-Methyl-2-phenyl-2H-chromene (4a).** Following the general procedure **4a** (34 mg, 0.15 mmol) was isolated as a colorless oil after 20 hours in 92% yield starting from (*E*)-2-(2-hydroxy-4-phenylbut-3-en-2-yl)phenol (40 mg, 0.17 mmol) in the presence of **5a** (10 mg, 10 mol%) and using toluene (2.08 mL) as solvent at -78 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.41-6.99 (m, 7H), 6.83 (t, *J*=7.5 Hz, 1H), 6.74 (m, 1H), 5.77 (m, 1H), 5.53 (m, 1H), 2.00 (t, *J*=1.7 Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 153.2, 141.3, 129.6, 129.3, 128.6, 128.2, 127.0, 123.5, 123.2, 121.7, 121.0, 116.0, 77.1, 18.2. IR (KBr):  $\tilde{\nu}$  = 3062, 3036, 2920, 2852, 1648, 1605, 1486, 1450, 1222, 754, 699 cm<sup>-1</sup>. MS (EI) *m/z* (%): 222.0 (M<sup>+</sup>, 22), 221.0 (32), 207.0 (77), 202.0 (18), 178.0 (43), 145.1 (55), 115.0 (37), 91.0 (18), 77.9 (19), 77.0 (100), 63.0 (16). HRMS (EI) calculated for C<sub>16</sub>H<sub>14</sub>O 222.10392 found 222.10353. [ $\alpha$ ]<sub>D</sub><sup>25</sup>: +182.4 (c = 1.0, MeOH). The enantiomeric excess was determined by chiral SFC using a Chiralpak IA column, 2% MeOH/CO<sub>2</sub>, 4 mL/min, 244nm;  $\tau_{\text{major}}$  = 3.86 min,  $\tau_{\text{minor}}$  = 3.49 min (92% ee).

 **(2R)- 4-Methyl-2-*p*-tolyl-2H-chromene (4b).** Following the general procedure **4b** (31 mg, 0.16 mmol) was isolated as a colorless oil after 17 hours in 84% yield starting from (*E*)-2-(2-hydroxy-4-*p*-tolylbut-3-en-2-yl)phenol (40 mg, 0.16 mmol) in the presence of **5a** (5 mg, 5 mol%) and using toluene (1.96 mL) as solvent at -78 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.33 (d, *J*=8.0 Hz, 2H), 7.24-7.08 (m, 4H), 6.91 (td, *J*=7.5, 1.2 Hz, 1H), 6.81 (dd, *J*=8.0, 1.2 Hz, 1H), 5.83 (dd, *J*=3.2, 1.6 Hz, 1H), 5.61 (dd, *J*=3.2, 1.6 Hz, 1H), 2.35 (s, 3H), 2.09 (t, *J*=1.6 Hz, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 153.3, 138.3, 138.0, 129.5, 129.2, 127.0, 123.4, 123.2, 121.8, 120.9, 116.0, 76.9, 21.2, 18.0. IR (KBr):  $\tilde{\nu}$  = 3033, 2920, 2857, 1648, 1608, 1485, 1449, 1222, 753 cm<sup>-1</sup>. MS (EI) *m/z* (%): 236.0 (M<sup>+</sup>, 28), 235.1 (35), 221.0 (100), 201.9 (23), 178.1 (29), 145.1 (44), 115.1 (30), 91.1 (32),

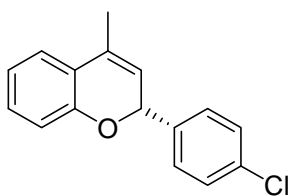
77.1 (10), 65.0 (16). HRMS (ESI<sup>+</sup>) calculated for C<sub>17</sub>H<sub>16</sub>O<sub>1</sub>+H (C<sub>17</sub>H<sub>17</sub>O<sub>1</sub>) 237.12739 found 237.12685. [ $\alpha$ ]<sub>D</sub><sup>25</sup>: +187.5 (c = 1.0, MeOH). The enantiomeric excess was determined by chiral SFC using a Chiralpak IA column, 2% MeOH/CO<sub>2</sub>, 4 mL/min, 244nm;  $\tau_{\text{major}}$  = 4.32 min,  $\tau_{\text{minor}}$  = 3.80 min (93% ee).



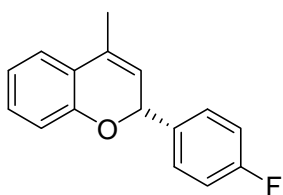
**(2R)- 2-(4-Methoxyphenyl)-4-methyl-2H-chromene (4c).** Following the general procedure **4c** (42 mg, 0.17 mmol) was isolated as a colorless oil after 17 hours in 91% yield starting from (*E*)-2-(2-hydroxy-4-(4-methoxyphenyl)but-3-en-2-yl)phenol (50 mg, 0.19 mmol) in the presence of **5a** (6 mg, 5 mol%) and using toluene (2.31 mL) as solvent at -78 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.31-7.23 (m, 2H), 7.12-6.98 (m, 2H), 6.85-6.75 (m, 3H), 6.73-6.67 (m, 1H), 5.77-5.66 (m, 1H), 5.50 (dd, *J*=3.2, 1.4 Hz, 1H), 3.69 (s, 3H), 2.00 (t, *J*=1.7 Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  159.5, 153.2, 133.3, 129.6, 129.2, 128.6, 123.4, 123.2, 121.8, 120.9, 116.0, 113.9, 76.7, 55.4, 18.2. IR (KBr):  $\tilde{\nu}$  = 3036, 2919, 2840, 1650, 1608, 1511, 1486, 1450, 1248, 755 cm<sup>-1</sup>. MS (EI) *m/z* (%): 252.1 (M<sup>+</sup>, 40), 251.0 (40), 237.0 (100), 221.1 (15), 208.0 (30), 194.0 (22), 165.0 (18), 145.0 (34), 115.1 (23), 91.2 (13). HRMS (EI) calculated for C<sub>17</sub>H<sub>16</sub>O<sub>2</sub> 252.11448 found 252.11378. [ $\alpha$ ]<sub>D</sub><sup>25</sup>: +108.2 (c = 1.0, MeOH). The enantiomeric excess was determined by chiral SFC using a Chiralpak IA column, 2% MeOH/CO<sub>2</sub>, 4 mL/min, 249nm;  $\tau_{\text{major}}$  = 6.58 min,  $\tau_{\text{minor}}$  = 6.07 min (90% ee).



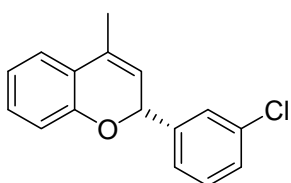
**(2R)-2-(4-bromophenyl)-4-methyl-2H-chromene (4d).** Following the general procedure **4d** (34 mg, 0.11 mmol) was isolated as a colorless oil after 3 days in 80% yield starting from (*E*)-2-(4-(4-bromophenyl)-2-hydroxybut-3-en-2-yl)phenol (45 mg, 0.14 mmol) in the presence of **5a** (9 mg, 10 mol%) and using toluene (1.76 mL) as solvent at -78 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.43-7.36 (m, 2H), 7.26-7.20 (m, 2H), 7.14-7.03 (m, 2H), 6.84 (td, *J*=7.5, 1.2 Hz, 1H), 6.73 (dd, *J*=8.0, 1.2 Hz, 1H), 5.75-5.71 (m, 1H), 5.52-5.48 (m, 1H), 2.01 (t, *J*=1.6 Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  152.9, 140.2, 131.6, 130.1, 129.4, 128.7, 123.5, 123.0, 122.1, 121.2, 120.9, 116.0, 76.2, 18.2. IR (KBr):  $\tilde{\nu}$  = 3064, 3039, 2971, 2918, 2851, 1644, 1600, 1485, 1451, 1222, 754 cm<sup>-1</sup>. MS (EI) *m/z* (%): 300.8 (M<sup>+</sup>, 24), 298.9 (31), 286.9 (100), 284.9 (92), 219.0 (27), 204.9 (70), 178.1 (34), 145.0 (79), 115.0 (42), 91.2 (17), 78.1 (16). HRMS (EI) calculated for C<sub>16</sub>H<sub>11</sub>O<sub>1</sub>Br 300.01443 found 300.01328. [ $\alpha$ ]<sub>D</sub><sup>25</sup>: +180.3 (c = 0.5, MeOH). The enantiomeric excess was determined by chiral SFC using a Chiralpak IA column, 8% MeOH/CO<sub>2</sub>, 2.5 mL/min, 250nm;  $\tau_{\text{major}}$  = 5.5 min,  $\tau_{\text{minor}}$  = 5.25 min (94% ee).



**(2R)-2-(4-chlorophenyl)-4-methyl-2H-chromene (4e).** Following the general procedure **4e** (32 mg, 0.13 mmol) was isolated as a colorless oil after 3 days in 86% yield starting from (*E*)-2-(4-(4-chlorophenyl)-2-hydroxybut-3-en-2-yl)phenol (40 mg, 0.15 mmol) in the presence of **5a** (9 mg, 10 mol%) and using toluene (1.83 mL) as solvent at -78 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.41-7.30 (m, 4H), 7.23-7.11 (m, 2H), 6.93 (td, *J*=7.4, 1.1 Hz, 1H), 6.82 (dd, *J*=8.0, 1.1 Hz, 1H), 5.87-5.78 (m, 1H), 5.64-5.54 (m, 1H), 2.10 (t, *J*=1.6 Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 152.9, 139.7, 133.9, 130.1, 129.4, 128.7, 128.3, 123.5, 123.1, 121.1, 121.0, 116.0, 76.2, 18.2. IR (KBr):  $\tilde{\nu}$  = 3068, 2975, 1626, 1594, 1486, 1457, 1223, 752 cm<sup>-1</sup>. MS (EI) *m/z* (%): 256.0 (M<sup>+</sup>, 20), 254.9 (32), 240.9 (100), 205.0 (19), 201.9 (18), 178.1 (31), 164.9 (10), 145.1 (52), 115.1 (28), 90.9 (14), 76.9 (12). HRMS (ESI<sup>+</sup>) calculated for C<sub>16</sub>H<sub>13</sub>O<sub>1</sub>Cl<sub>1</sub>+H (C<sub>17</sub>H<sub>14</sub>O<sub>1</sub>Cl<sub>1</sub>) 257.07277 found 257.07266. [α]<sub>D</sub><sup>25</sup>: +174.9 (c = 1.0, MeOH). The enantiomeric excess was determined by chiral SFC using a Chiralpak IA column, 8% MeOH/CO<sub>2</sub>, 2.5 mL/min, 250nm; τ<sub>major</sub> = 4.45 min, τ<sub>minor</sub> = 4.24 min (94% ee).



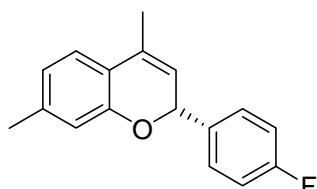
**(2R)-2-(4-fluorophenyl)-4-methyl-2H-chromene (4f).** Following the general procedure **4f** (30 mg, 0.13 mmol) was isolated as a colorless oil after 27 hours in 81% yield starting from (*E*)-2-(4-(4-fluorophenyl)-2-hydroxybut-3-en-2-yl)phenol (40 mg, 0.16 mmol) in the presence of **5a** (10 mg, 10 mol%) and using toluene (1.94 mL) as solvent at -78 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.46-7.37 (m, 2H), 7.23-7.10 (m, 2H), 7.09-6.99 (m, 2H), 6.92 (td, *J*=7.5, 1.2 Hz, 1H), 6.81 (dd, *J*=8.0, 1.2 Hz, 1H), 5.90-5.78 (m, 1H), 5.64-5.55 (m, 1H), 2.10 (t, *J*=1.6 Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 162.5 (d, *J*<sub>CF</sub> = 245.1 Hz), 152.9, 137.0, 129.9, 129.3, 128.9, 128.8, 123.5, 123.1, 121.1 (d, *J*<sub>CF</sub> = 23.6 Hz), 116.0, 115.3 (d, *J*<sub>CF</sub> = 21.3 Hz), 76.3, 18.2. IR (KBr):  $\tilde{\nu}$  = 3065, 2919, 2851, 1647, 1604, 1504, 1450, 1223, 755 cm<sup>-1</sup>. MS (EI) *m/z* (%): 240.0 (M<sup>+</sup>, 23), 239.2 (31), 224.8 (100), 197.0 (22), 195.9 (56), 145.1 (64), 115.1 (42), 113.1 (18), 91.3 (27), 75.1 (21), 64.6 (20). HRMS (EI) calculated for C<sub>16</sub>H<sub>13</sub>O<sub>1</sub>F<sub>1</sub> 240.09449 Found 240.09471. [α]<sub>D</sub><sup>25</sup>: +210.4 (c = 1.0, MeOH). The enantiomeric excess was determined by chiral SFC using a Chiralpak IA column, 8% MeOH/CO<sub>2</sub>, 2.5 mL/min, 250 nm; τ<sub>major</sub> = 3.1 min, τ<sub>minor</sub> = 2.97 min (94% ee).



**(2R)-2-(3-chlorophenyl)-4-methyl-2H-chromene (4g).** Following the general procedure **4g** (40 mg, 0.16 mmol) was isolated as a colorless oil after 15 hours in 95% yield starting from (*E*)-2-(4-(3-chlorophenyl)-2-

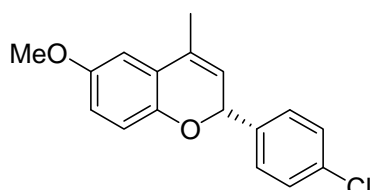


hydroxybut-3-en-2-yl)phenol (45 mg, 0.16 mmol) in the presence of **5a** (10 mg, 10 mol%) and using toluene (2.05 mL) as solvent at -48 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.44 (d, *J*=1.5 Hz, 1H), 7.36-7.23 (m, 3H), 7.23-7.08 (m, 2H), 6.93 (td, *J*=7.5, 1.2 Hz, 1H), 6.84 (dd, *J*=8.0, 1.2 Hz, 1H), 5.88-5.79 (m, 1H), 5.64-5.55 (m, 1H), 2.10 (t, *J*=1.6 Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 152.9, 143.3, 134.4, 130.1, 129.8, 129.4, 128.2, 127.1, 125.0, 123.6, 123.0, 121.2, 120.8, 116.0, 76.2, 18.2. IR (KBr):  $\tilde{\nu}$  = 3066, 2920, 2852, 1650, 1600, 1576, 1481, 1447, 1220, 754 cm<sup>-1</sup>. MS (EI) *m/z* (%): 255.8 (M<sup>+</sup>, 20), 255.0 (36), 241.0 (92), 205.0 (25), 201.9 (31), 178.0 (28), 145.1 (100), 115.0 (41), 91.1 (20), 76.9 (15). HRMS (EI) calculated for C<sub>16</sub>H<sub>13</sub>O<sub>1</sub>Cl<sub>1</sub> 256.06494 found 256.06452. [α]<sub>D</sub><sup>25</sup>: +273.4 (c = 1.0, MeOH). The enantiomeric excess was determined by chiral SFC using a Chiralpak IA column, 8% MeOH/CO<sub>2</sub>, 2.5 mL/min, 250 nm; τ<sub>major</sub> = 4.52 min, τ<sub>minor</sub> = 4.05 min (84% ee).



**(2R)-2-(4-fluorophenyl)-4,7-dimethyl-2H-chromene (4h).** Following the general procedure **4h** (23 mg, 0.09 mmol) was isolated as a colorless oil after 22 hours in 82% yield starting from (*E*)-2-(4-(4-fluorophenyl)-2-hydroxybut-3-en-2-yl)-5-methylphenol (30 mg, 0.11

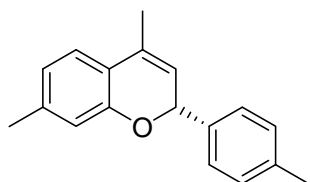
mmol) in the presence of **5a** (7 mg, 10 mol%) and using toluene (1.38 mL) as solvent at -78 °C. <sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 7.36-7.28 (m, 2H), 7.02-6.92 (m, 3H), 6.67-6.61 (m, 1H), 6.53-6.49 (m, 1H), 5.74-5.66 (m, 1H), 5.51-5.46 (m, 1H), 2.17 (s, 3H), 1.99 (t, *J*=1.6 Hz, 3H). <sup>13</sup>C NMR (100 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 162.4 (d, *J*<sub>CF</sub> = 243.5 Hz), 152.7, 139.7, 137.3, 130.0, 128.8 (d, *J*<sub>CF</sub> = 8.4 Hz), 123.3, 121.7, 120.5, 120.0, 116.4, 115.1 (d, *J*<sub>CF</sub> = 21.2 Hz), 76.0, 21.1, 17.8. IR (KBr):  $\tilde{\nu}$  = 3038, 2969, 2920, 2857, 1651, 1611, 1507, 1442, 1229, 1151, 820 cm<sup>-1</sup>. MS (EI) *m/z* (%): 254.1 (M<sup>+</sup>, 21), 253.0 (32), 239.0 (100), 220.0 (14), 196.1 (37), 159.0 (49), 129.1 (10), 115 (16), 91.2 (16). HRMS (EI) calculated for C<sub>17</sub>H<sub>15</sub>O<sub>1</sub>F<sub>1</sub> 254.11015 found 254.10968. [α]<sub>D</sub><sup>25</sup>: +210.1 (c = 1.0, MeOH). The enantiomeric excess was determined by chiral SFC using a Chiralpak IA column, 1% *i*PrOH/CO<sub>2</sub>, 2.5 mL/min, 229 nm; τ<sub>major</sub> = 7.28 min, τ<sub>minor</sub> = 7.92 min (90% ee).



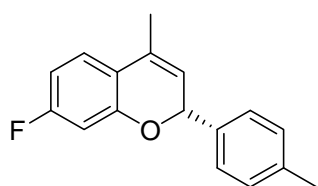
**(2R)-2-(4-chlorophenyl)-6-methoxy-4-methyl-2H-chromene (4i).**

Following the general procedure **4i** (35 mg, 0.12 mmol) was isolated as a colorless oil after 5 days in 83% yield starting from (*E*)-2-(4-(4-chlorophenyl)but-2-en-2-yl)-4-methoxyphenol (45 mg, 0.15 mmol) in the presence of **5a** (9 mg, 10 mol%) and using toluene (1.85 mL) as solvent at -78 °C. <sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 7.41-7.28 (m, 4H), 6.82-6.65 (m, 3H), 5.77-5.73 (m, 1H), 5.65-5.61 (m, 1H), 3.78 (s, 3H), 2.08 (t, *J*=1.6 Hz, 3H). <sup>13</sup>C NMR (100 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 154.0, 146.8,

139.5, 133.9, 130.2, 128.6, 128.4, 124.0, 122.0, 116.4, 113.8, 109.6, 76.0, 55.8, 18.2. IR (KBr):  $\tilde{\nu}$  = 2919, 2850, 1680, 1488, 1433, 1210, 821  $\text{cm}^{-1}$ . MS (EI)  $m/z$  (%): 285.9 ( $\text{M}^+$ , 29), 285.0 (49), 273.1 (33), 270.9 (100), 252.0 (17), 242.0 (19), 227.8 (22), 175.1 (65), 165.1 (39), 132.1 (25), 77.0 (13). HRMS (EI) calculated for  $\text{C}_{17}\text{H}_{15}\text{O}_2\text{Cl}_1$  286.07551 found 286.07550.  $[\alpha]_{\text{D}}^{25}$ : +65.5 ( $c$  = 1.0, MeOH). The enantiomeric excess was determined by chiral SFC using a Chiralcel OJH column, 2%  $i$ PrOH/ $\text{CO}_2$ , 4 mL/min, 250 nm;  $\tau_{\text{major}}$  = 14.11 min,  $\tau_{\text{minor}}$  = 12.49 min (84% ee).

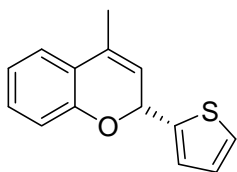


**(2R)-4,7-dimethyl-2-p-tolyl-2H-chromene (4j).** Following the general procedure **4j** (25 mg, 0.10 mmol) was isolated as a colorless oil after 4 days in 87% yield starting from (*E*)-2-(2-hydroxy-4-*p*-tolylbut-3-en-2-yl)-5-methylphenol (30 mg, 0.11 mmol) in the presence of **5a** (7 mg, 10 mol%) and using toluene (1.40 mL) as solvent at -78 °C.  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_2\text{Cl}_2$ )  $\delta$  7.19 (d,  $J$ =7.7 Hz, 2H), 7.05 (d,  $J$ =7.9 Hz, 2H), 6.97 (d,  $J$ =7.7 Hz, 1H), 6.64-6.58 (m, 1H), 6.52-6.47 (m, 1H), 5.70-5.63 (m, 1H), 5.50-5.44 (m, 1H), 2.22 (s, 3H), 2.15 (s, 3H), 1.98-1.94 (m, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CD}_2\text{Cl}_2$ )  $\delta$  152.9, 139.5, 138.3, 138.0, 129.6, 129.0, 126.9, 123.3, 121.5, 120.7, 120.5, 116.4, 76.6, 21.1, 21.0, 17.9. IR (KBr):  $\tilde{\nu}$  = 3028, 2919, 2855, 1652, 1616, 1444, 1242, 814  $\text{cm}^{-1}$ . MS (EI)  $m/z$  (%): 250.1 ( $\text{M}^+$ , 28), 249.0 (43), 235.0 (100), 219.1 (13), 192.1 (20), 159.1 (45), 129.1 (10), 115.0 (12), 91.0 (18). HRMS (EI) calculated for  $\text{C}_{18}\text{H}_{18}\text{O}_1$  250.13522 found 250.13488.  $[\alpha]_{\text{D}}^{25}$ : +266.9 ( $c$  = 0.5, MeOH). The enantiomeric excess was determined by chiral SFC using a **(S,S)** Whelk-01 column, 2% MeOH/ $\text{CO}_2$ , 4 mL/min, 249 nm;  $\tau_{\text{major}}$  = 6.94 min,  $\tau_{\text{minor}}$  = 6.17 min (84% ee).

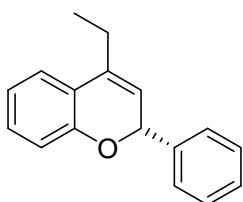


**(2R)-7-fluoro-4-methyl-2-p-tolyl-2H-chromene (4k).** Following the general procedure **4k** (26 mg, 0.10 mmol) was isolated as a colorless oil after 22 hours in 94% yield starting from (*E*)-5-fluoro-2-(2-hydroxy-4-*p*-tolylbut-3-en-2-yl)phenol (30 mg, 0.11 mmol) in the presence of **5a** (7 mg, 10 mol%) and using toluene (1.34 mL) as solvent at -78 °C.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.34-7.28 (m, 2H), 6.22-7.08 (m, 3H), 6.60 (td,  $J$ =8.5, 2.6 Hz, 1H), 6.54 (dd,  $J$ =10.0, 2.6 Hz, 1H), 5.87-5.81 (m, 1H), 5.59-5.54 (m, 1H), 2.35 (s, 3H), 2.08 (t,  $J$ =1.6 Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  163.1 (d,  $J_{\text{CF}}$  = 244.3 Hz), 154.5 (d,  $J_{\text{CF}}$  = 12.2 Hz), 138.0 (d,  $J_{\text{CF}}$  = 35.7 Hz), 129.3, 128.9, 127.0, 124.4, 120.5, 119.5, 107.4 (d,  $J_{\text{CF}}$  = 21.2 Hz), 103.7 (d,  $J_{\text{CF}}$  = 25.0 Hz), 77.3, 21.3, 18.2. IR (KBr):  $\tilde{\nu}$  = 3026, 2921, 2857, 1605, 1499, 1431, 1145, 1119, 814  $\text{cm}^{-1}$ . MS (EI)  $m/z$  (%): 254.0 ( $\text{M}^+$ , 34), 253.0 (54), 240.1 (32), 239.0 (100), 223.0 (24), 219.9 (23), 195.9 (28), 163.1 (45), 132.8 (14), 115.0 (18), 91.0 (16). HRMS (EI) calculated for  $\text{C}_{17}\text{H}_{15}\text{O}_1\text{F}_1$  254.11015 found

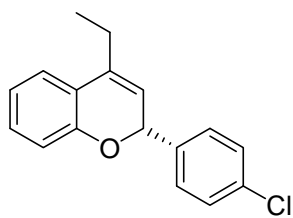
254.10993.  $[\alpha]_D^{25}$ : +215.9 ( $c = 1.0$ , MeOH). The enantiomeric excess was determined by chiral SFC using a Chiralpak IA column, 2% MeOH/CO<sub>2</sub>, 4 mL/min, 229 nm;  $\tau_{\text{major}} = 3.63$  min,  $\tau_{\text{minor}} = 3.12$  min (92% ee).



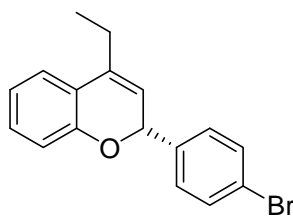
**(2R)-4-methyl-2-(thiophen-2-yl)-2H-chromene (4l).** Following the general procedure **4l** (26 mg, 0.11 mmol) was isolated as a yellow oil after 24 hours in 94% yield starting from (*E*)-2-(2-hydroxy-4-(thiophen-2-yl)but-3-en-2-yl)phenol (30 mg, 0.122 mmol) in the presence of **5a** (4 mg, 5 mol%) and using toluene (1.53 mL) as solvent at -78 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.32-7.21 (m, 2H), 7.20-7.07 (m, 2H), 7.02-6.91 (m, 2H), 6.85 (dd,  $J=8.0, 1.2$  Hz, 1H), 6.11-6.04 (m, 1H), 5.80-5.72 (m, 1H), 2.14 (t,  $J=1.5$  Hz, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  152.6, 144.4, 130.4, 129.4, 126.7, 126.1, 125.9, 123.6, 123.3, 121.3, 120.7, 116.4, 71.7, 18.0. IR (KBr):  $\tilde{\nu} = 2918, 2851, 1652, 1484, 1447, 1216, 831$  cm<sup>-1</sup>. MS (EI)  $m/z$  (%): 228.0 ( $M^+$ , 41), 227.1 (34), 213.0 (100), 183.9 (37), 165.1 (19), 152.0 (14), 145.1 (23), 115.0 (31), 91.0 (16). HRMS (EI) calculated for C<sub>14</sub>H<sub>12</sub>O<sub>1</sub><sup>32</sup>S<sub>1</sub> 228.06034 found 228.06044.  $[\alpha]_D^{25}$ : +102.2 ( $c = 1.0$ , MeOH). The enantiomeric excess was determined by chiral SFC using a Chiralpak IA column, 2% MeOH/CO<sub>2</sub>, 4 mL/min, 250 nm;  $\tau_{\text{major}} = 4.49$  min,  $\tau_{\text{minor}} = 3.79$  min (90% ee).



**(2R)-4-ethyl-2-phenyl-2H-chromene (4m).** Following the general procedure **4m** (33 mg, 0.14 mmol) was isolated as a white solid after 3 days in 88% yield starting from (*E*)-2-(3-hydroxy-1-phenylpent-1-en-3-yl)phenol (40 mg, 0.16 mmol) in the presence of **5a** (10 mg, 10 mol%) and using toluene (1.96 mL) as solvent at -78 °C. <sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>)  $\delta$  7.48-7.19 (m, 6H), 7.18-7.07 (m, 1H), 6.90 (td,  $J=7.5, 1.3$  Hz, 1H), 6.84-6.75 (m, 1H), 5.87-5.82 (m, 1H), 5.67-5.62 (m, 1H), 2.49 (qt,  $J=7.4, 1.6$  Hz, 2H), 1.19 (t,  $J=7.4$  Hz, 3H). <sup>13</sup>C NMR (100 MHz, CD<sub>2</sub>Cl<sub>2</sub>)  $\delta$  153.2, 141.2, 135.1, 128.9, 128.4, 128.1, 126.9, 123.1, 122.7, 120.9, 119.6, 116.0, 76.8, 24.0, 12.2. IR (KBr):  $\tilde{\nu} = 3068, 3031, 2965, 2910, 1648, 1601, 1485, 1449, 1208, 747$  cm<sup>-1</sup>. MS (EI)  $m/z$  (%): 236.1 ( $M^+$ , 21), 235.1 (19), 208.1 (26), 207.1 (100), 178.0 (46), 159.1 (38), 144.2 (19), 131.0 (18), 115.1 (22), 90.9 (25). HRMS (ESI<sup>+</sup>) calculated for C<sub>17</sub>H<sub>16</sub>O<sub>1</sub>+H (C<sub>17</sub>H<sub>17</sub>O<sub>1</sub>) 237.12739 Found 237.12730.  $[\alpha]_D^{25}$ : +210.7 ( $c = 1.0$ , MeOH). The enantiomeric excess was determined by chiral SFC using a Chiralcel OJH column, 5% MeOH/CO<sub>2</sub>, 3 mL/min, 265 nm;  $\tau_{\text{major}} = 6.05$  min,  $\tau_{\text{minor}} = 5.60$  min (91% ee; 98% ee after crystallization).



**(2R)-2-(4-chlorophenyl)-4-ethyl-2H-chromene (4n).** Following the general procedure **4n** (20 mg, 0.07 mmol) was isolated as a colorless oil after 6 days in 71% yield starting from (*E*)-2-(1-(4-chlorophenyl)-3-hydroxypent-1-en-3-yl)phenol (30 mg, 0.10 mmol) in the presence of **5a** (6 mg, 10 mol%) and using toluene (1.30 mL) as solvent at -78 °C. <sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 7.36-7.22 (m, 4H), 7.16 (dd, *J*=7.7, 1.5 Hz, 1H), 7.04 (td, *J*=7.7, 1.5 Hz, 1H), 6.83 (td, *J*=7.7, 1.2 Hz, 1H), 6.76-6.66 (m, 1H), 5.81-5.70 (m, 1H), 5.56-5.51 (m, 1H), 2.41 (qt, *J*=7.3, 1.5 Hz, 2H), 1.11 (t, *J*=7.4 Hz, 3H). <sup>13</sup>C NMR (100 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 152.9, 139.8, 135.6, 129.0, 128.5, 128.4, 127.5, 123.1, 121.0, 119.1, 116.1, 75.9, 24.0, 12.1. IR (KBr):  $\tilde{\nu}$  = 3066, 2967, 2922, 2852, 1598, 1486, 1455, 1221, 753 cm<sup>-1</sup>. MS (EI) *m/z* (%): 269.9 (M<sup>+</sup>, 15), 269.0 (15), 243.0 (37), 241.0 (100), 205.0 (29), 178.0 (27), 159.3 (32), 144.0 (20), 114.8 (22), 107.2 (19), 91.2 (21), 68.5 (14). HRMS (EI) calculated for C<sub>17</sub>H<sub>15</sub>O<sub>1</sub>Cl<sub>1</sub> 270.08059 found 270.08019. [ $\alpha$ ]<sub>D</sub><sup>25</sup>: +217.3 (*c* = 1.0, MeOH). The enantiomeric excess was determined by chiral SFC using a Chiralcel OJH column, 5% *i*PrOH/CO<sub>2</sub>, 3 mL/min, 250 nm;  $\tau_{\text{major}}$  = 9.91 min,  $\tau_{\text{minor}}$  = 8.73 min (96% ee).

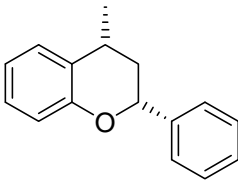


**(2R)-2-(4-bromophenyl)-4-ethyl-2H-chromene (4o).** Following the general procedure **4o** (23 mg, 0.07 mmol) was isolated as a colorless oil after 6 days in 61% yield starting from (*E*)-2-(1-(4-bromophenyl)-3-hydroxypent-1-en-3-yl)phenol (40 mg, 0.12 mmol) in the presence of **5a** (7 mg, 10 mol%) and using toluene (1.50 mL) as solvent at -78 °C. <sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 7.53-7.44 (m, 2H), 7.37-7.28 (m, 2H), 7.24 (dd, *J*=7.7, 1.6 Hz, 1H), 7.12 (td, *J*=7.7, 1.6 Hz, 1H), 6.91 (td, *J*=7.5, 1.2 Hz, 1H), 6.78 (dd, *J*=8.0, 1.2 Hz, 1H), 5.84-5.77 (m, 1H), 5.69-5.58 (m, 1H), 2.49 (qt, *J*=7.4, 1.5 Hz, 2H), 1.18 (t, *J*=7.4 Hz, 3H). <sup>13</sup>C NMR (100 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 152.9, 140.3, 135.6, 131.5, 129.1, 128.7, 127.9, 123.2, 121.9, 121.1, 119.0, 116.1, 76.0, 24.0, 12.1. IR (KBr):  $\tilde{\nu}$  = 2966, 2921, 2851, 1592, 1485, 1453, 1221, 753 cm<sup>-1</sup>. MS (EI) *m/z* (%): 313.9 (M<sup>+</sup>, 16), 313.0 (16), 286.9 (89), 284.9 (100), 219.1 (41), 205.1 (72), 191.2 (29), 159.1 (45), 144.1 (20), 115.2 (24), 91.0 (19). HRMS (ESI<sup>+</sup>) calculated for C<sub>17</sub>H<sub>15</sub>O<sub>1</sub>Br<sub>1</sub>+H (C<sub>17</sub>H<sub>16</sub>O<sub>1</sub>Br<sub>1</sub>) 315.03790 found 315.03793. [ $\alpha$ ]<sub>D</sub><sup>25</sup>: +162.6 (*c* = 0.25, MeOH). The enantiomeric excess was determined by chiral SFC using a Chiralcel OJH column, 5% *i*PrOH/CO<sub>2</sub>, 3 mL/min, 229 nm;  $\tau_{\text{major}}$  = 9.33 min,  $\tau_{\text{minor}}$  = 8.13 min (93% ee).

## General procedure for reduction of product 4a.

To a solution of chromene **4a** (20 mg, 0.09 mmol) in MeOH (2.0 mL) was added Pd-C (3 mg, 5% in 50% water) and the resulting mixture was stirred under an atmosphere of H<sub>2</sub> at room temperature for 2 hours. The crude reaction mixture was filtrated, washed with MeOH several times (5 or 6) and purified by column chromatography (cyclohexane/AcOEt 19:1) to afford the corresponding product **7a** (18 mg, 0.08 mmol) in 90% yield.

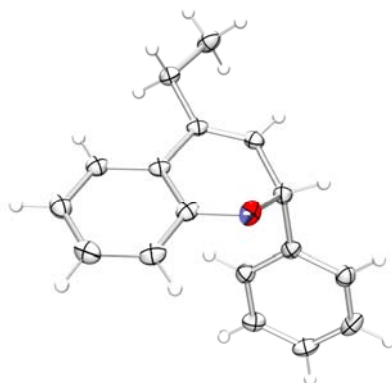
## Characterization of Product 7a

 **(2R,4R)- 4-methyl-2-phenylchroman (7a).** <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, major, *syn*) δ 7.52-7.27 (m, 6H), 7.19-7.11 (m, 1H), 6.99-6.89 (m, 2H), 5.09 (dd, *J*=11.6, 2.0 Hz, 1H), 3.32-3.12 (m, 1H), 2.23 (ddd, *J*=13.6, 5.7, 2.0 Hz, 1H), 1.92-1.76 (m, 1H), 1.39 (d, *J*=6.8 Hz, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, major, *syn*) δ 154.8, 141.7, 129.2, 128.5, 127.9, 127.4, 127.1, 126.1, 120.6, 116.9, 78.0, 40.0, 30.1, 20.2. IR (KBr):  $\tilde{\nu}$  = 3067, 3034, 2953, 2916, 2867, 1577, 1484, 1450, 1226, 749, 701 cm<sup>-1</sup>. MS (EI) *m/z* (%): 224.0 (M<sup>+</sup>, 34), 209.0 (29), 165.0 (7), 133.1 (21), 131.0 (21), 120.0 (22), 115.1 (25), 114.1 (44), 91.1 (100), 78.0 (24). The enantiomeric excess and diastereomeric ratio was determined by chiral SFC using a Chiralcel ODH column, 10% EtOH/CO<sub>2</sub>, 4 mL/min, 265nm;  $\tau_{anti,major}$  = 1.98 min,  $\tau_{syn,major}$  = 2.73 min,  $\tau_{syn,minor}$  = 2.31 min (92% ee; dr: 10:1).

## Determination of the absolute configuration

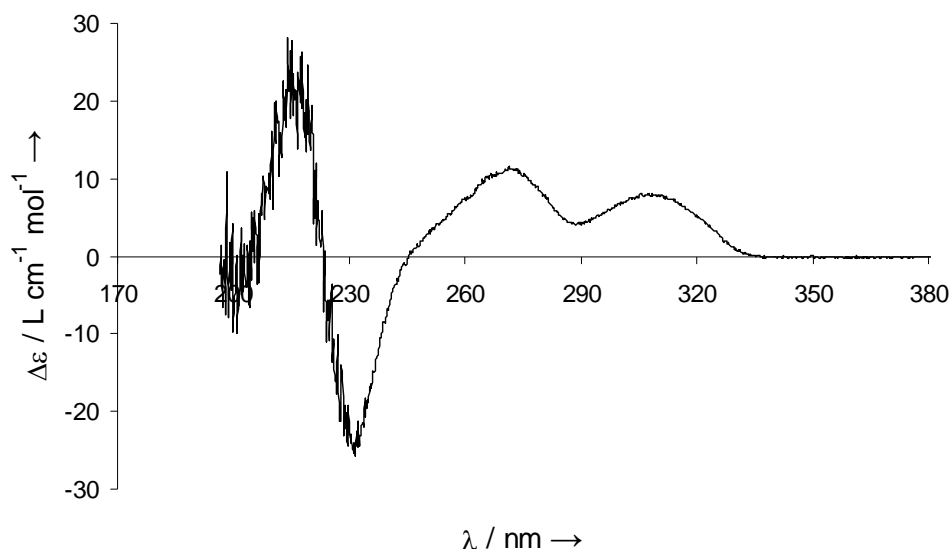
### X-ray Crystallographic Data.

The structure of the chromene **4m** was determined by single-crystal X-ray analysis.

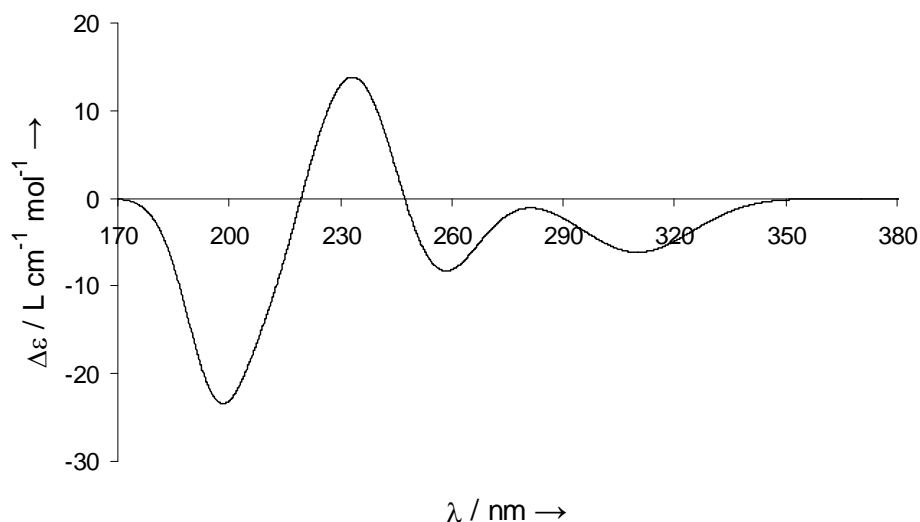


**Fig. S2.** Structure of **4m** in the solid state  $X_{abs} = 0.003(267)$ .

However, the values of the Flack parameter and standard uncertainty did not allow unambiguous determination of the absolute configuration. As an alternative, CD-spectroscopy was considered and the recorded and theoretically calculated CD-spectra of compound **4m** were analyzed (Fig. S3 a, b). The theoretical CD-spectrum has been obtained as an average of the spectra of the most stable five conformers lying in a range of 2 kcal/mol. Single spectra of the corresponding conformers have been obtained at the TD-DFT/B3LYP/6-31+G\*\*//B3LYP/6-31+G\*\* level using Gaussian 09 program package (5-6). Since the measured spectrum resembles the mirror image of the spectrum calculated for the (*S*)-enantiomer, we conclude that the absolute configuration of the compound present in our sample is (*R*).



a) Recorded CD-spectrum of **4m**.



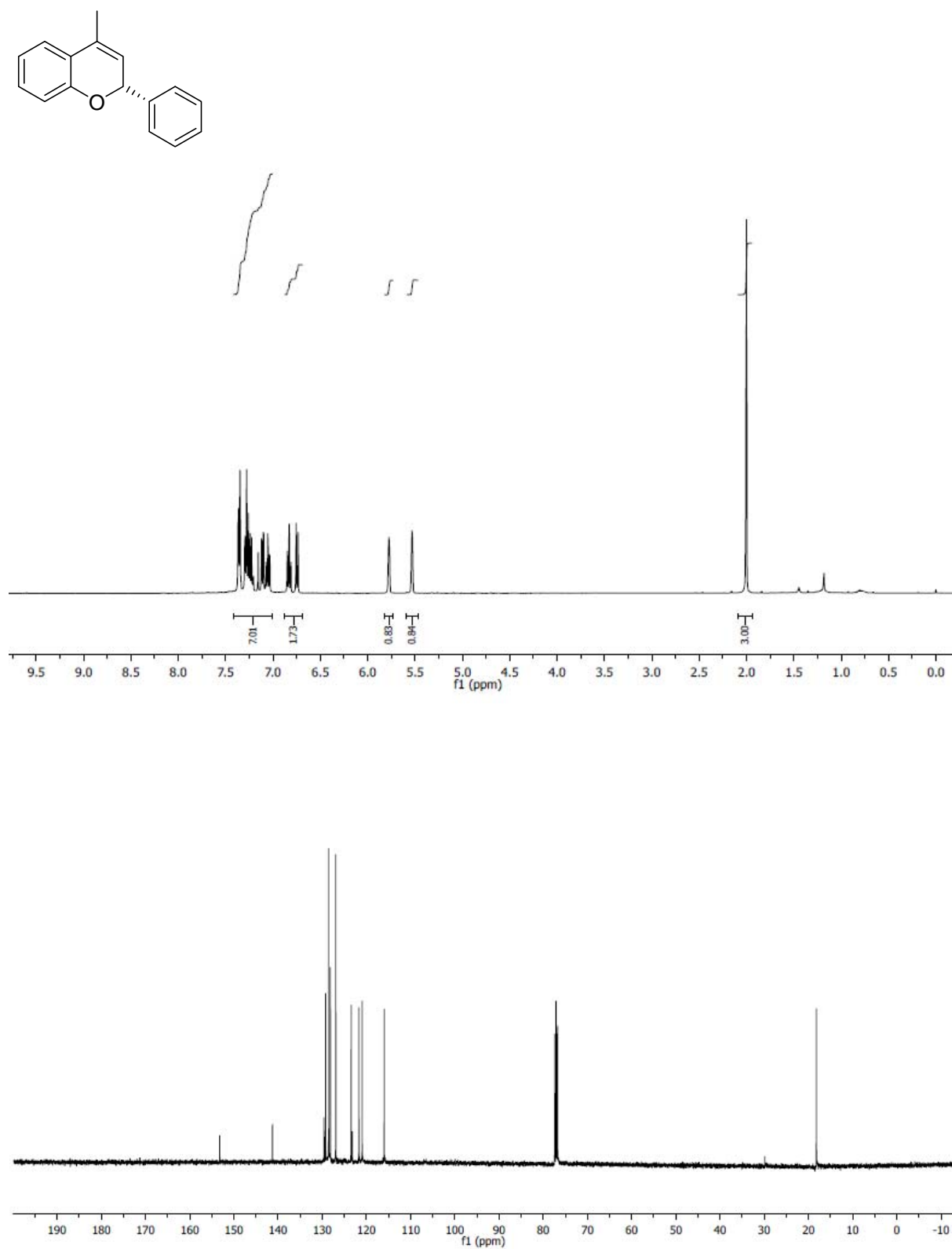
b) Averaged calculated CD-spectrum for (*S*)-**4m** at the TD-DFT/B3LYP/6-31+G\*\*//B3LYP/6-31+G\*\* level.

**Fig. S3.** Recorded and calculated CD-spectra for **4m**.

## References

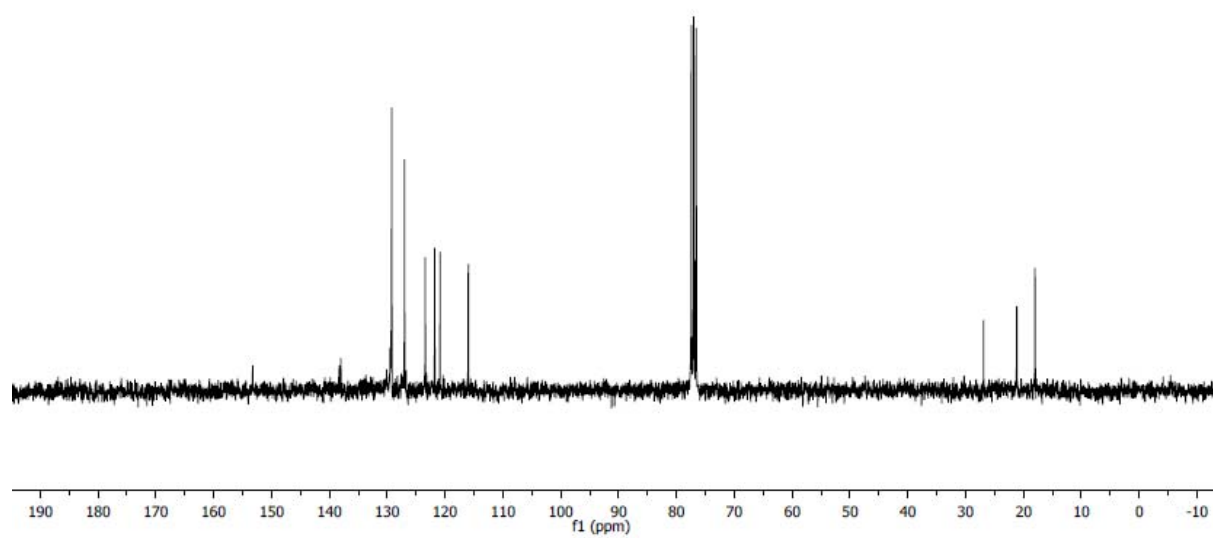
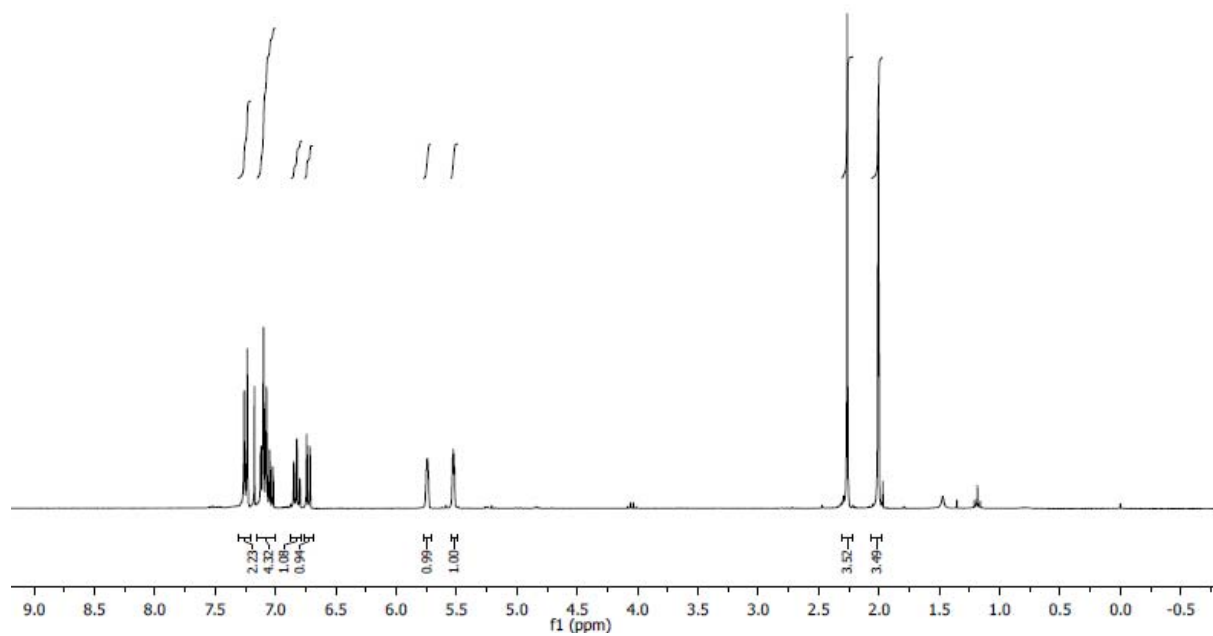
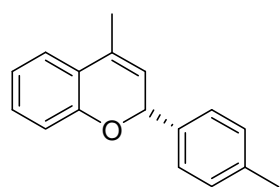
1. Barros, A. I. R. N. A. ; Silva, A. M. S.; Alkorta, I.; Elguero, J. *Tetradron* **2004**, *60*, 6513-6521.
2. Cabrera, M.; Simoens, M.; Falchi, G.; Lavaggi, M. L.; Piro, O. E.; Castellano, E. E.; Vidal, A.; Azqueta, A.; Monge, A.; de Cerain, A. L.; Sagrera, G.; Seoane, G.; Cerecetto H.; Gonzalez, M. *Bioorg. Med. Chem.* **2007**, *15*, 3356-3367.
3. Dennis, L.; George, Z. *J. Org. Chem.* **1980**, *45*, 2551-2553.
4. Patent J. F. Batchelor, H. F. Hodson, J. G. Vinter, Benzopyran compounds, useful as chemotherapeutic agents. Eur. Pat. Appl. EP 25599, CAN 95, 42910, **1981**.
5. The calculations have been performed by using the facilities and computing resources offered by the Center for Computing and Communication of the RWTH Aachen University.
6. Gaussian 09, Revision A.02, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2009.

# NMR Spectra of Compounds 4a-o and 7a.

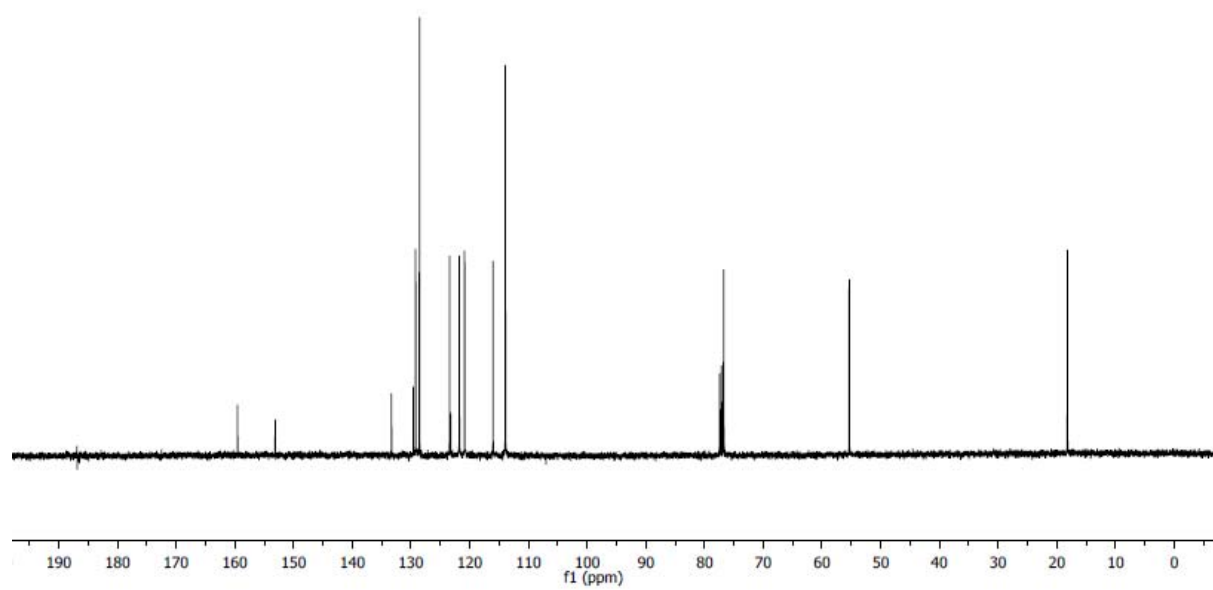
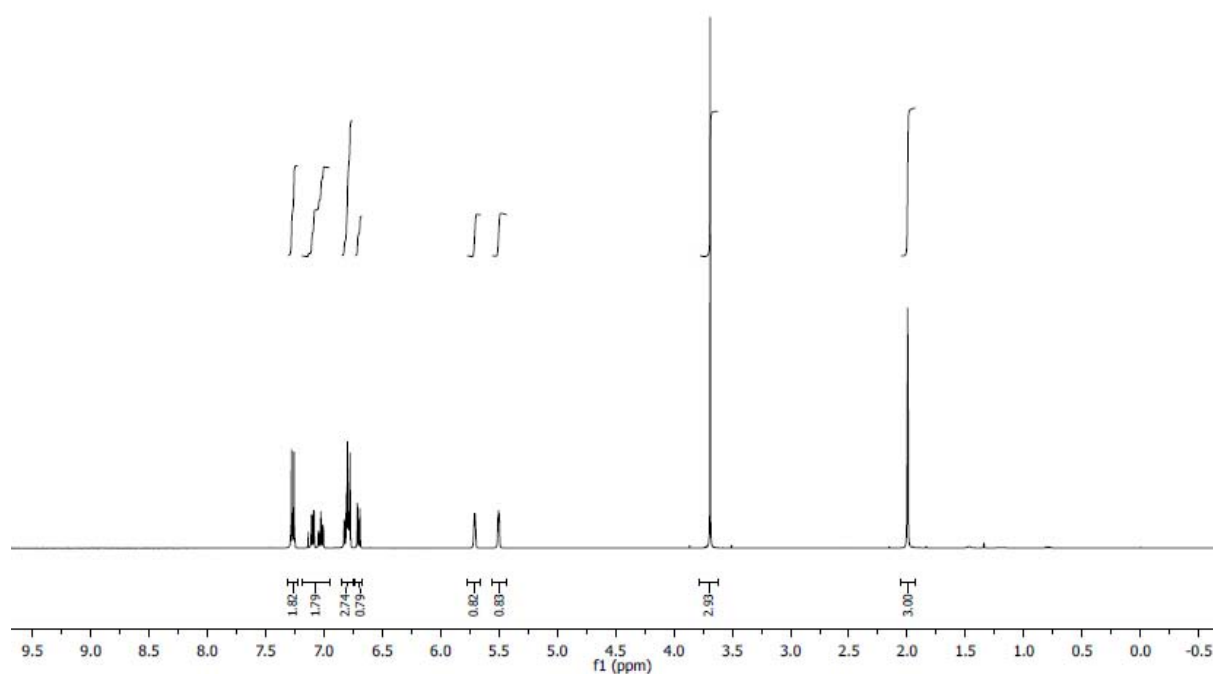
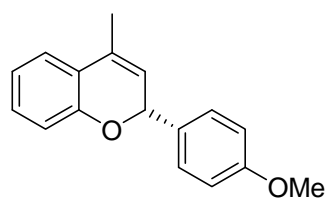


**Figure S4:** NMR spectra of compound 4a.

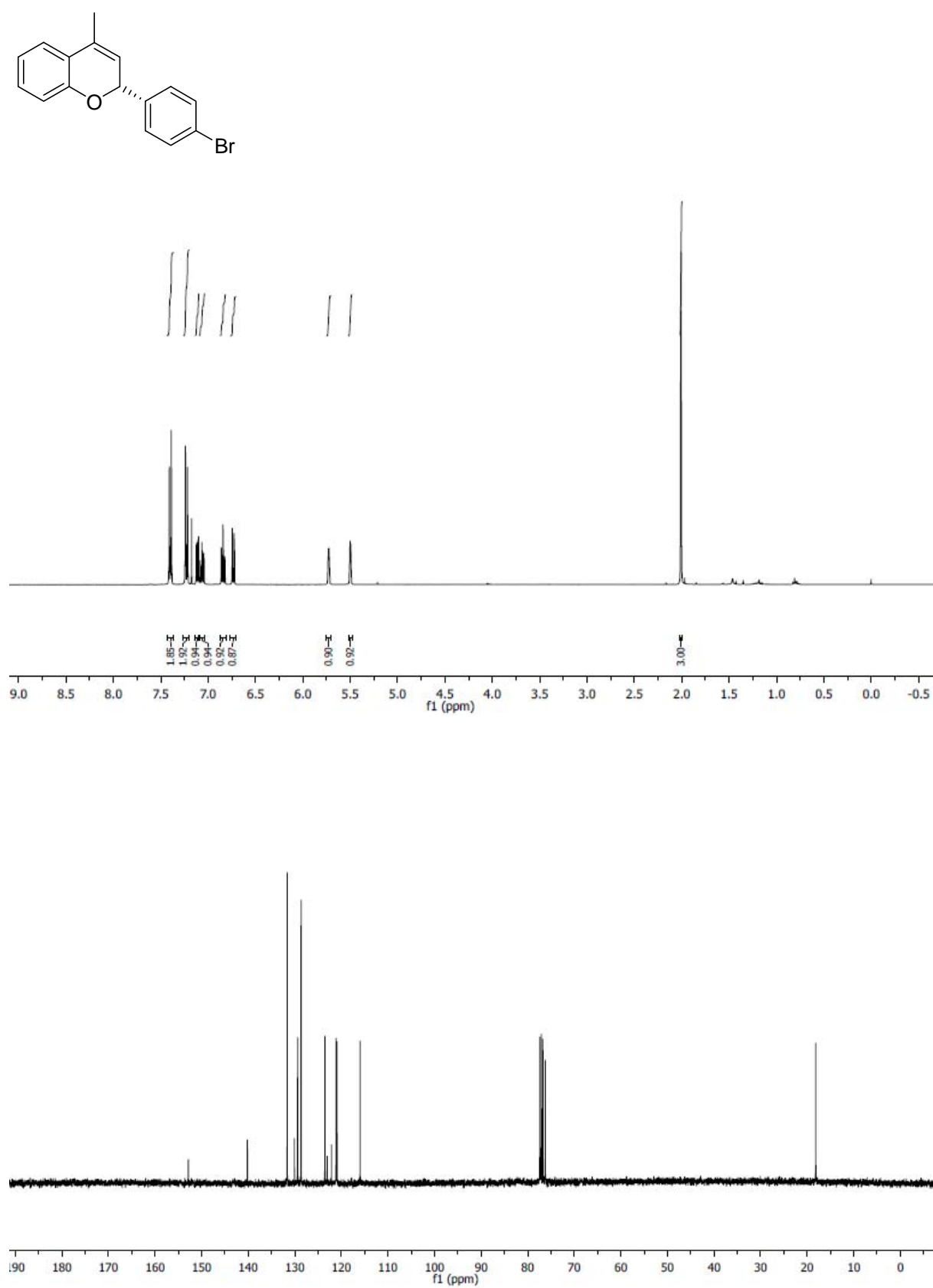




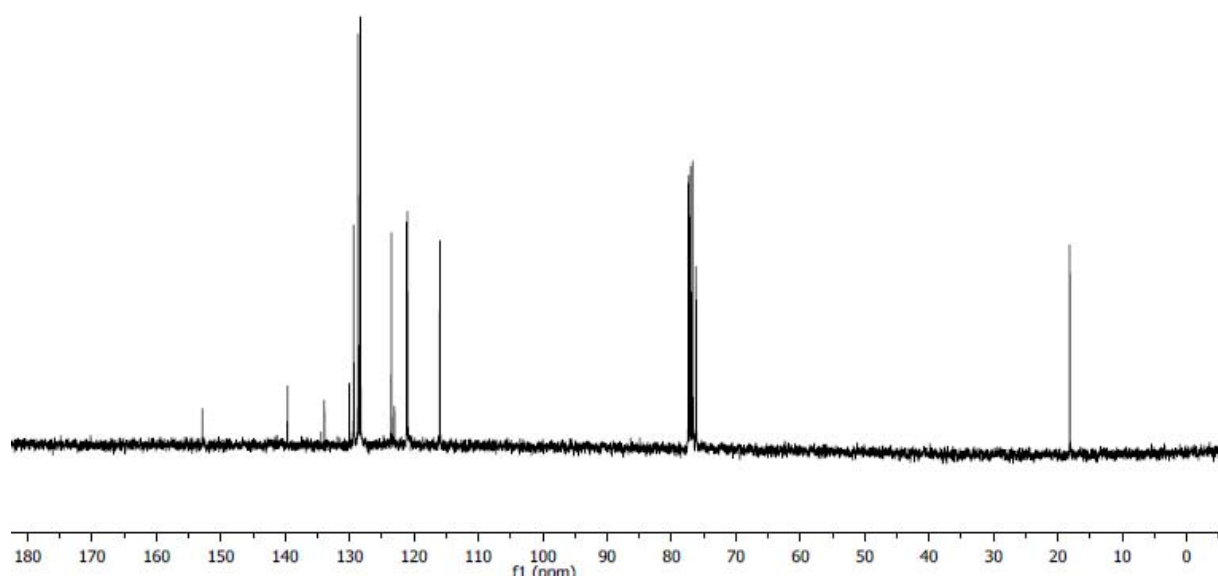
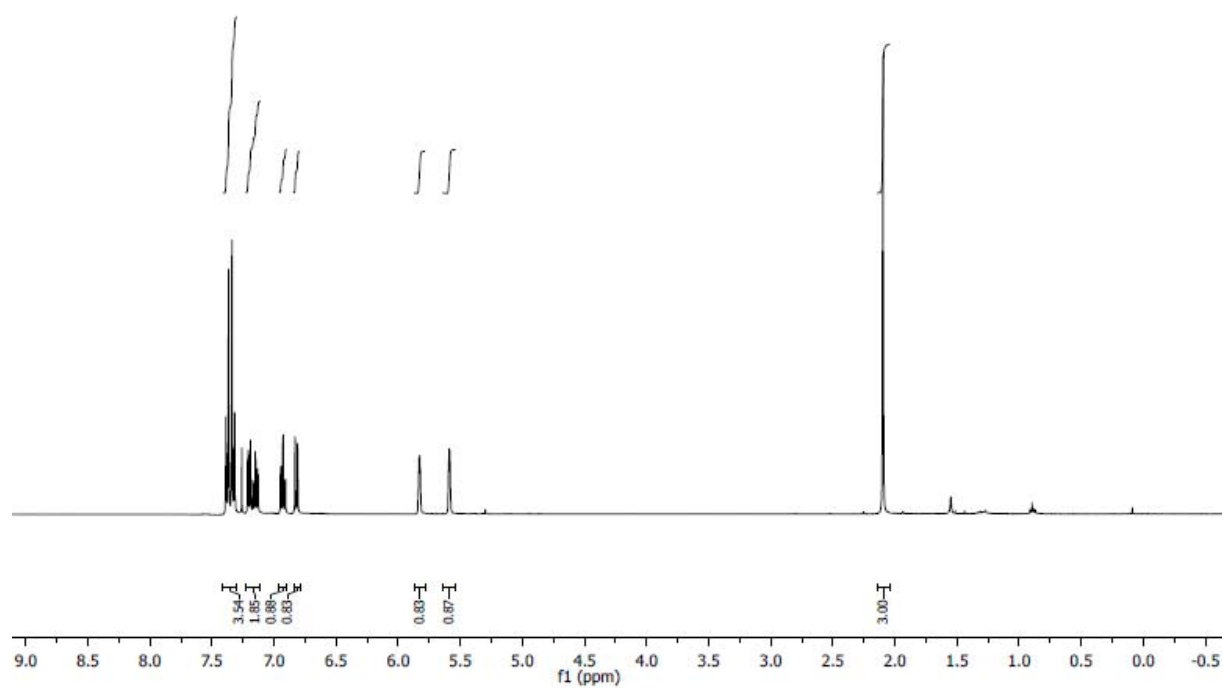
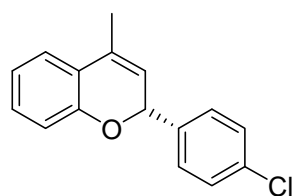
**Figure S5:** NMR spectra of compound 4b.



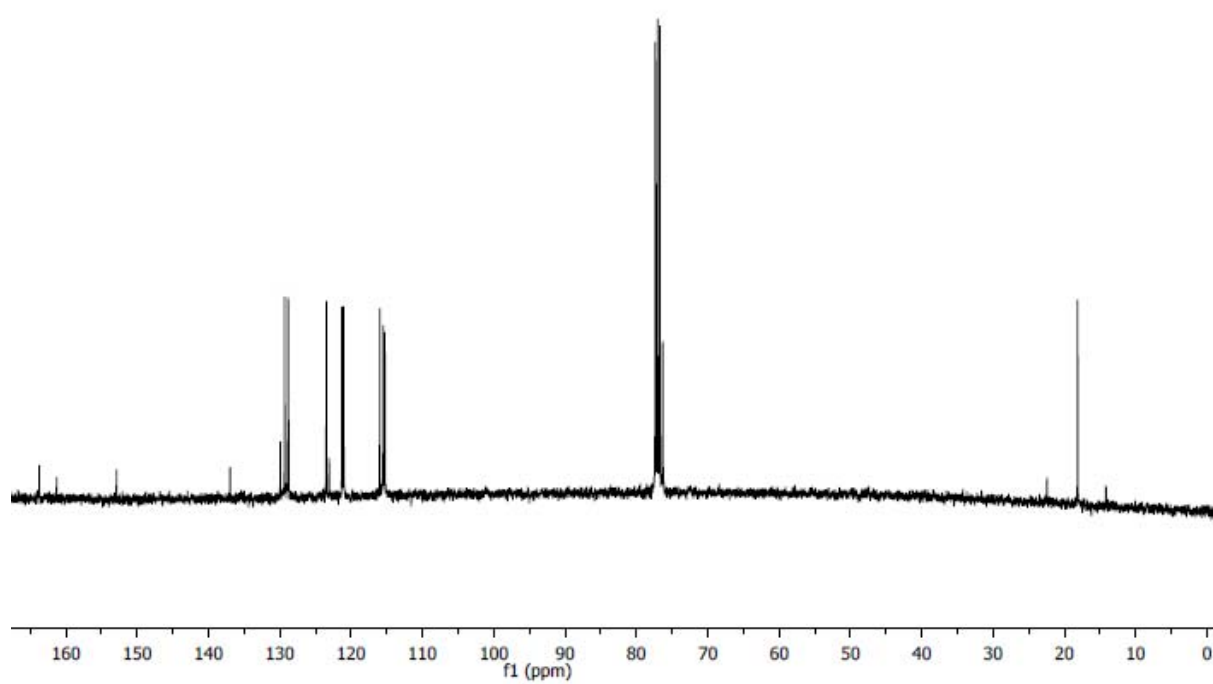
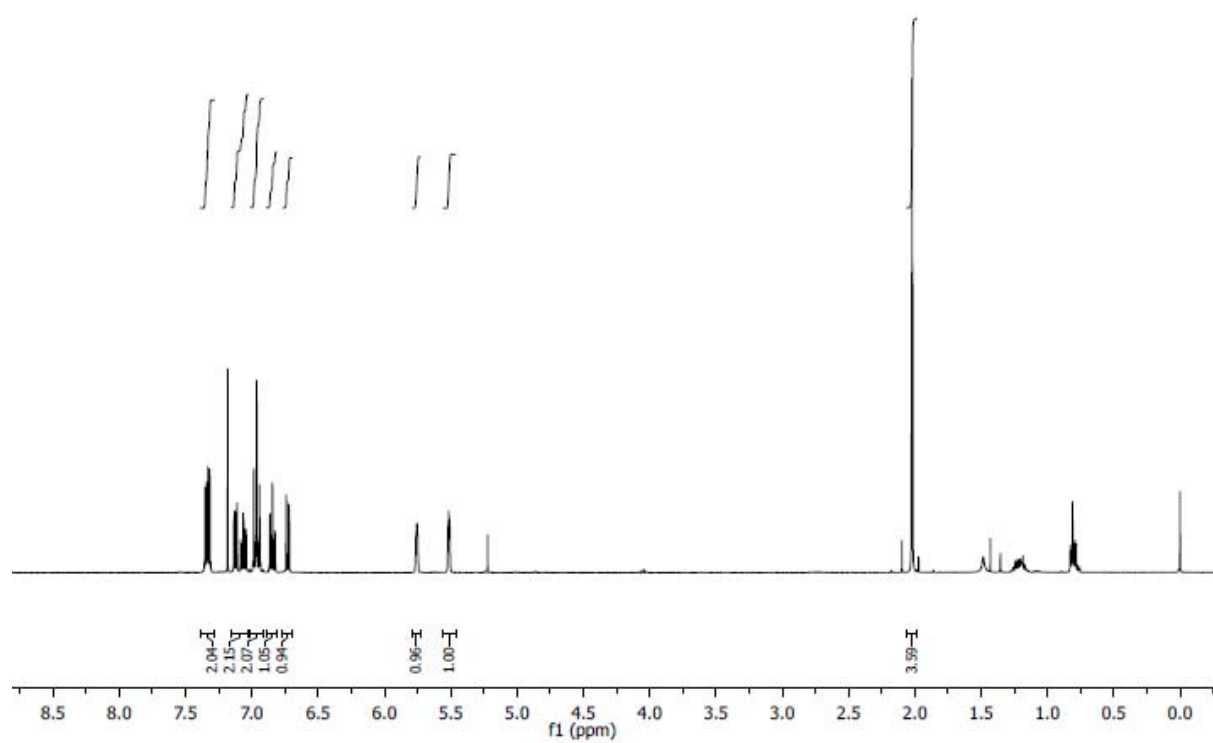
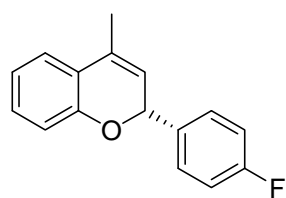
**Figure S6:** NMR spectra of compound 4c.



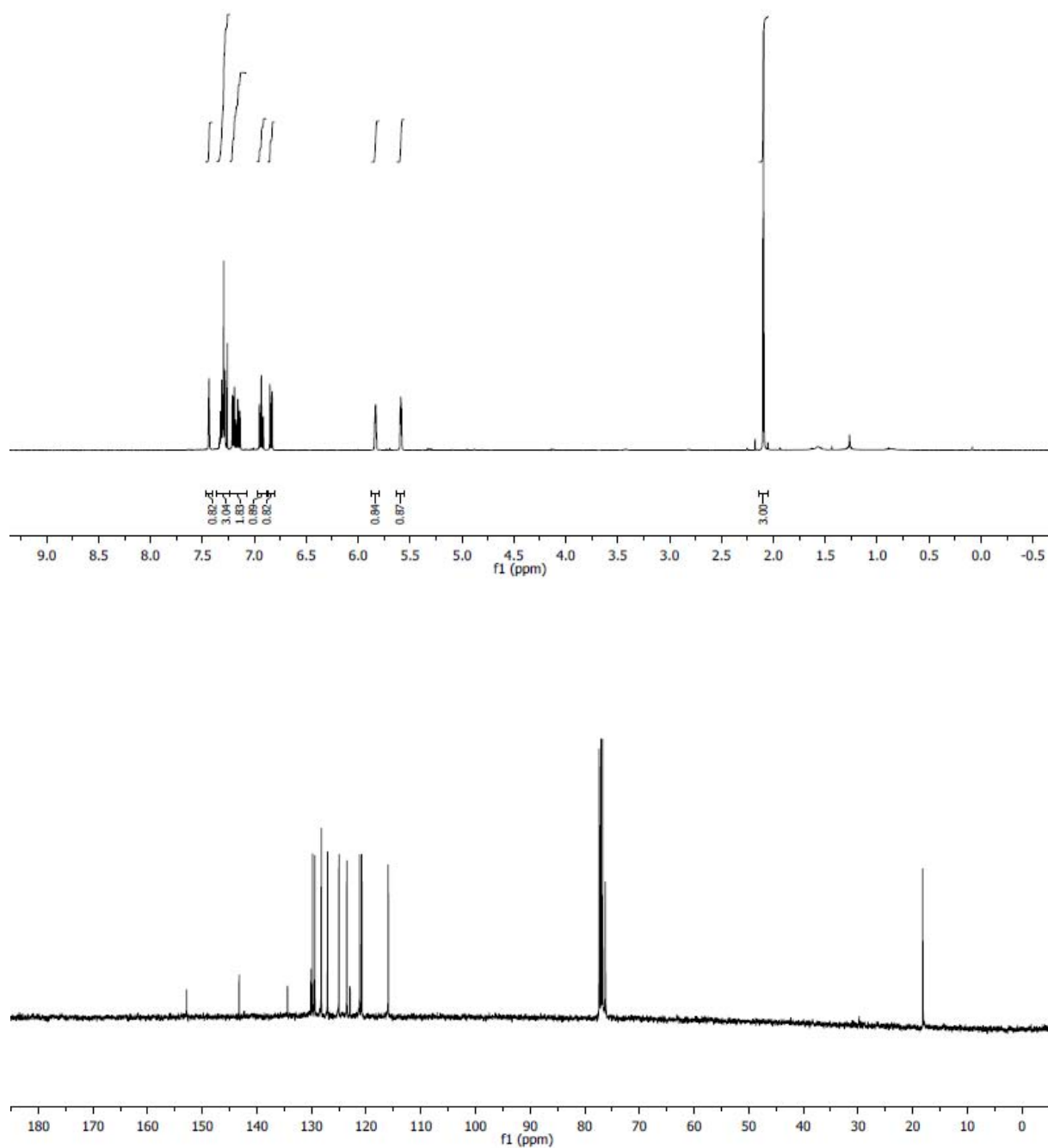
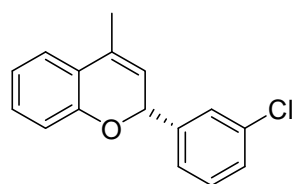
**Figure S7:** NMR spectra of compound **4d**.



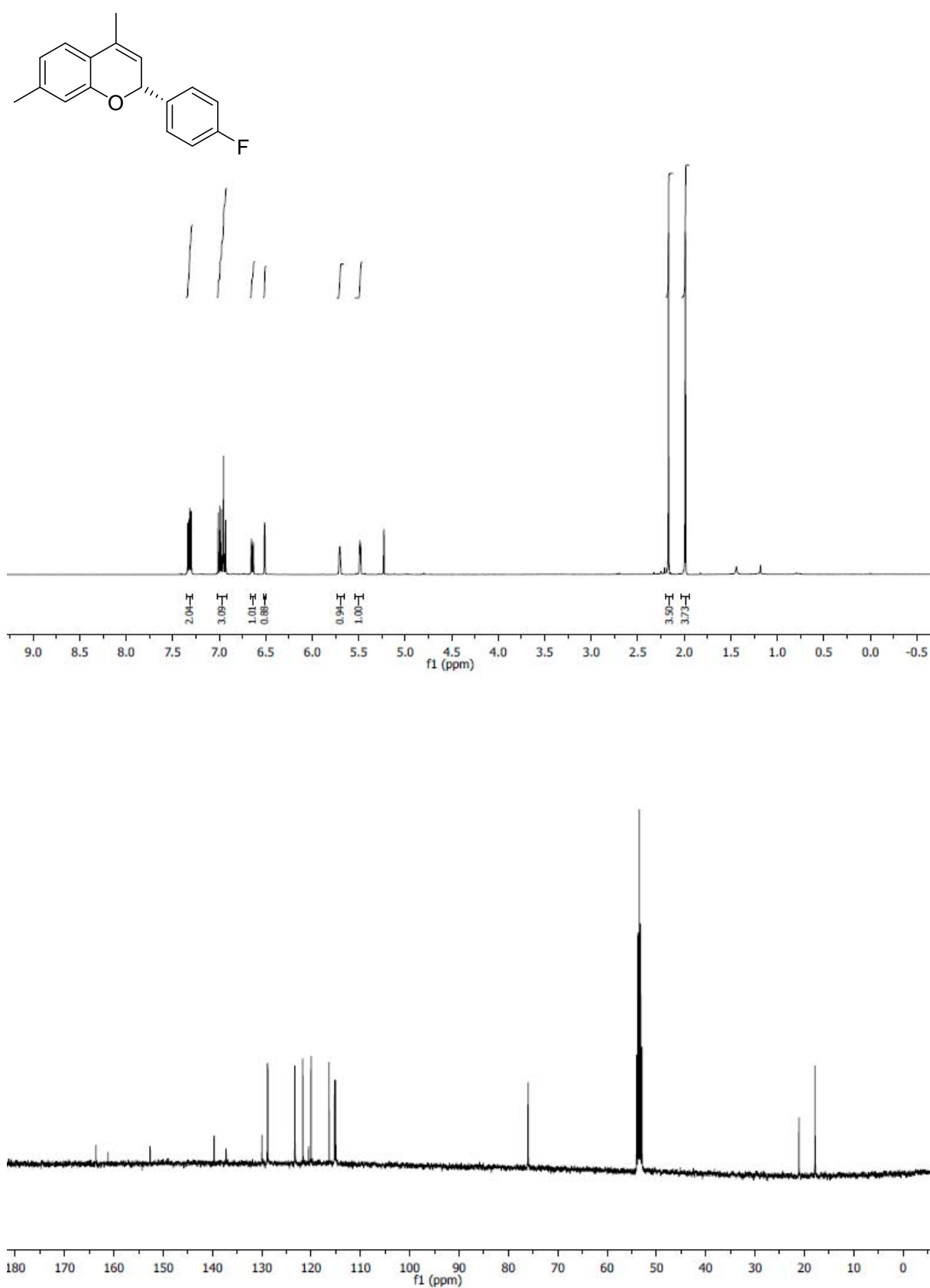
**Figure S8:** NMR spectra of compound 4e.



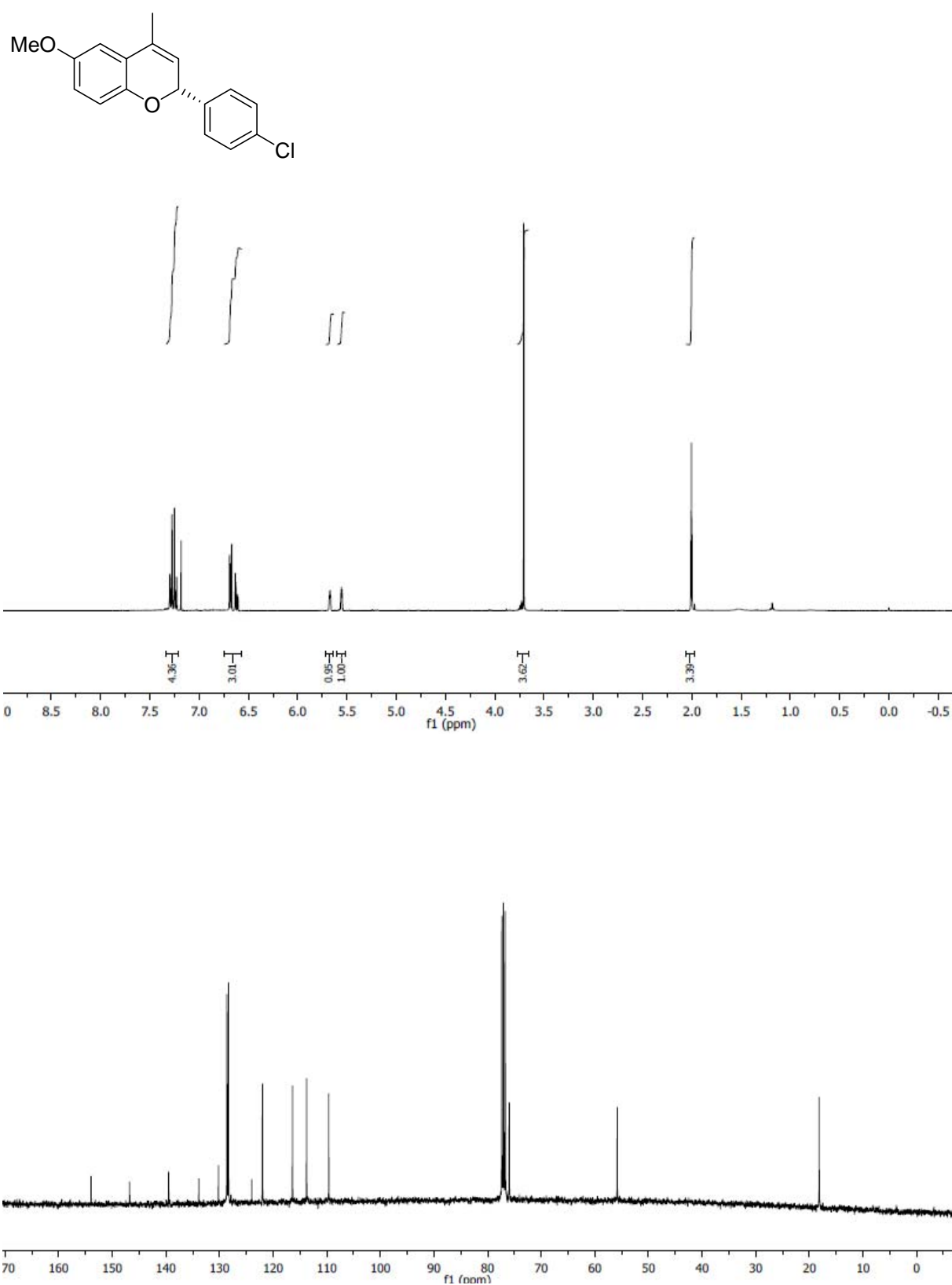
**Figure S9:** NMR spectra of compound **4f**.



**Figure S10:** NMR spectra of compound **4g**

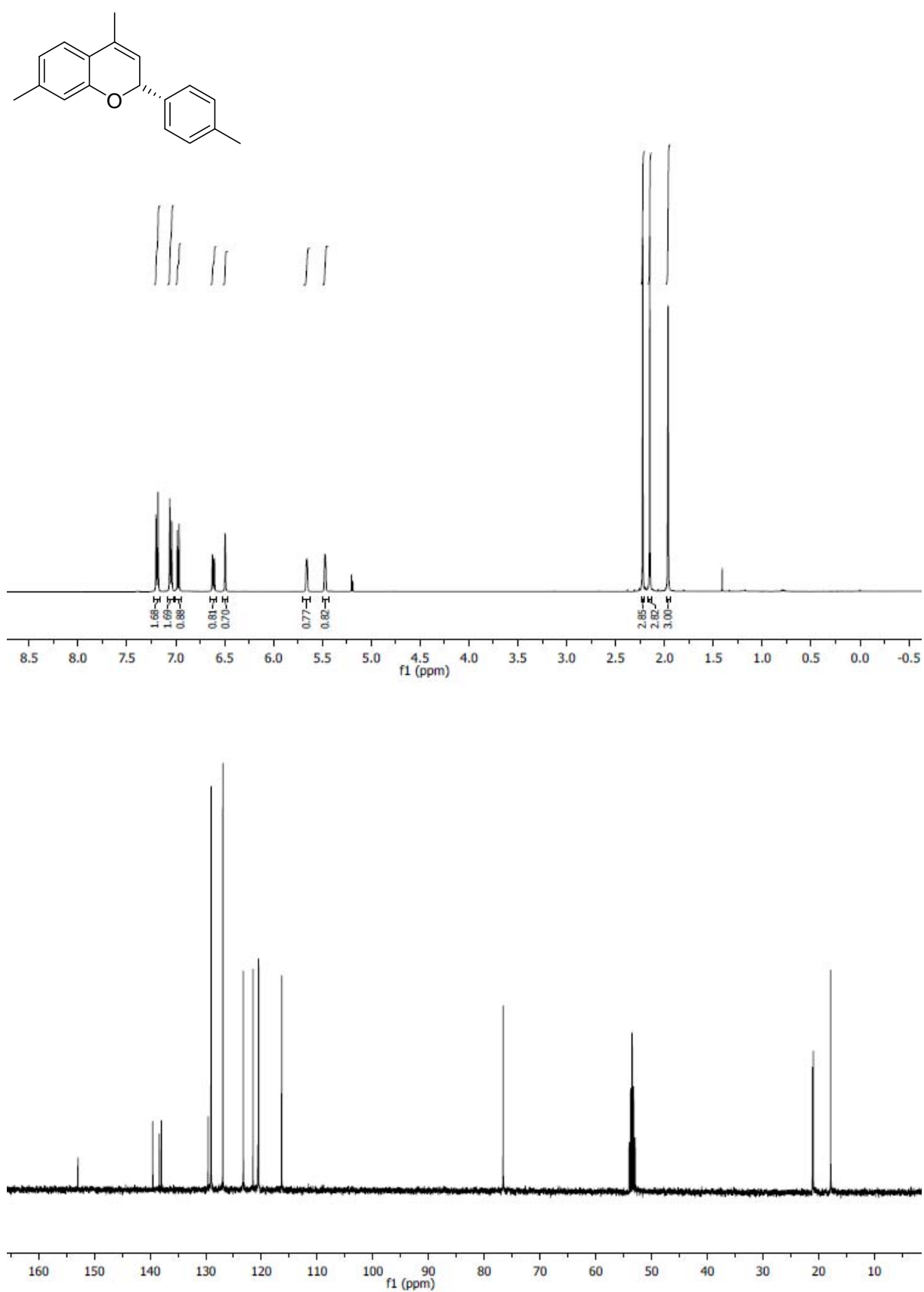


**Figure S11:** NMR spectra of compound **4h**

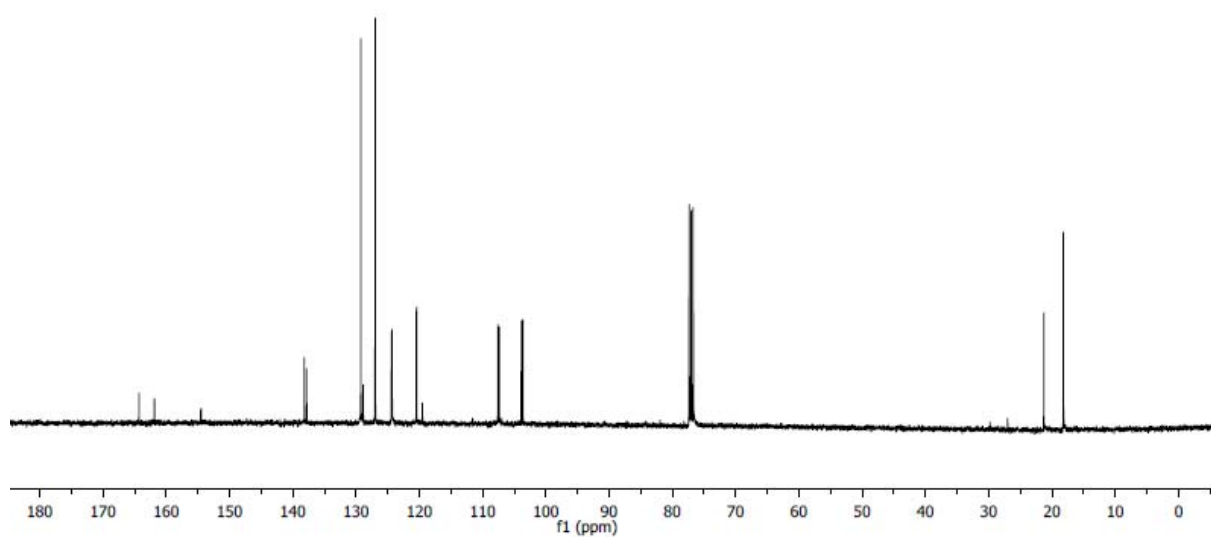
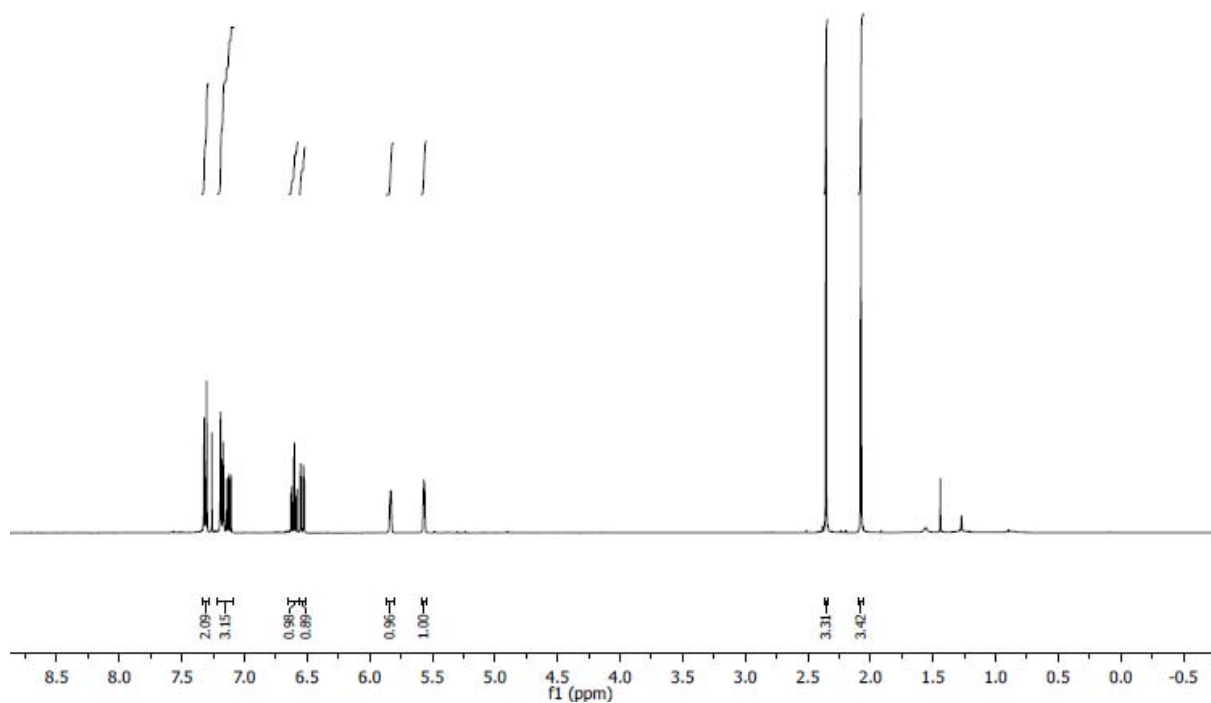
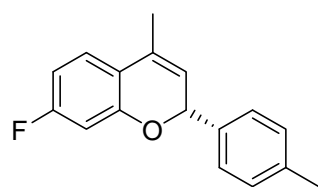


**Figure S12:** NMR spectra of compound **4i**

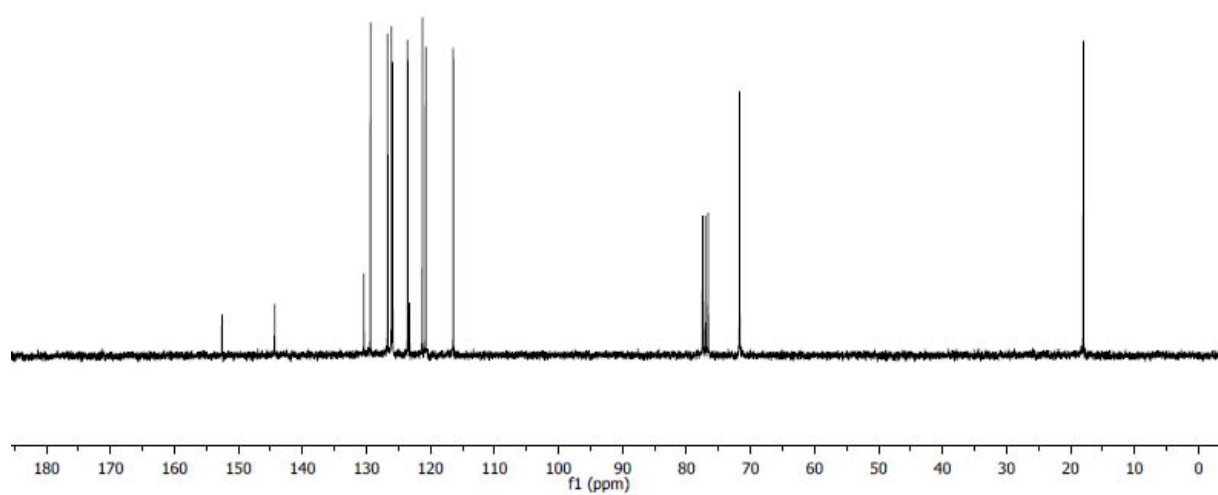
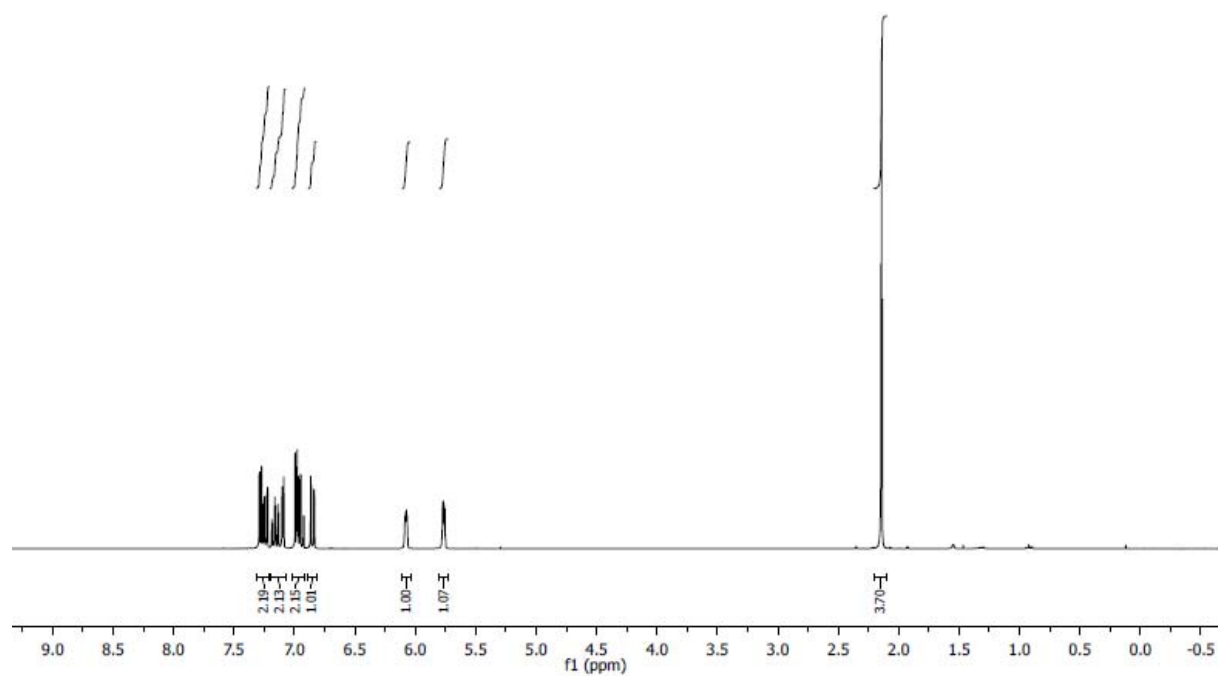
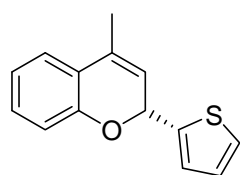




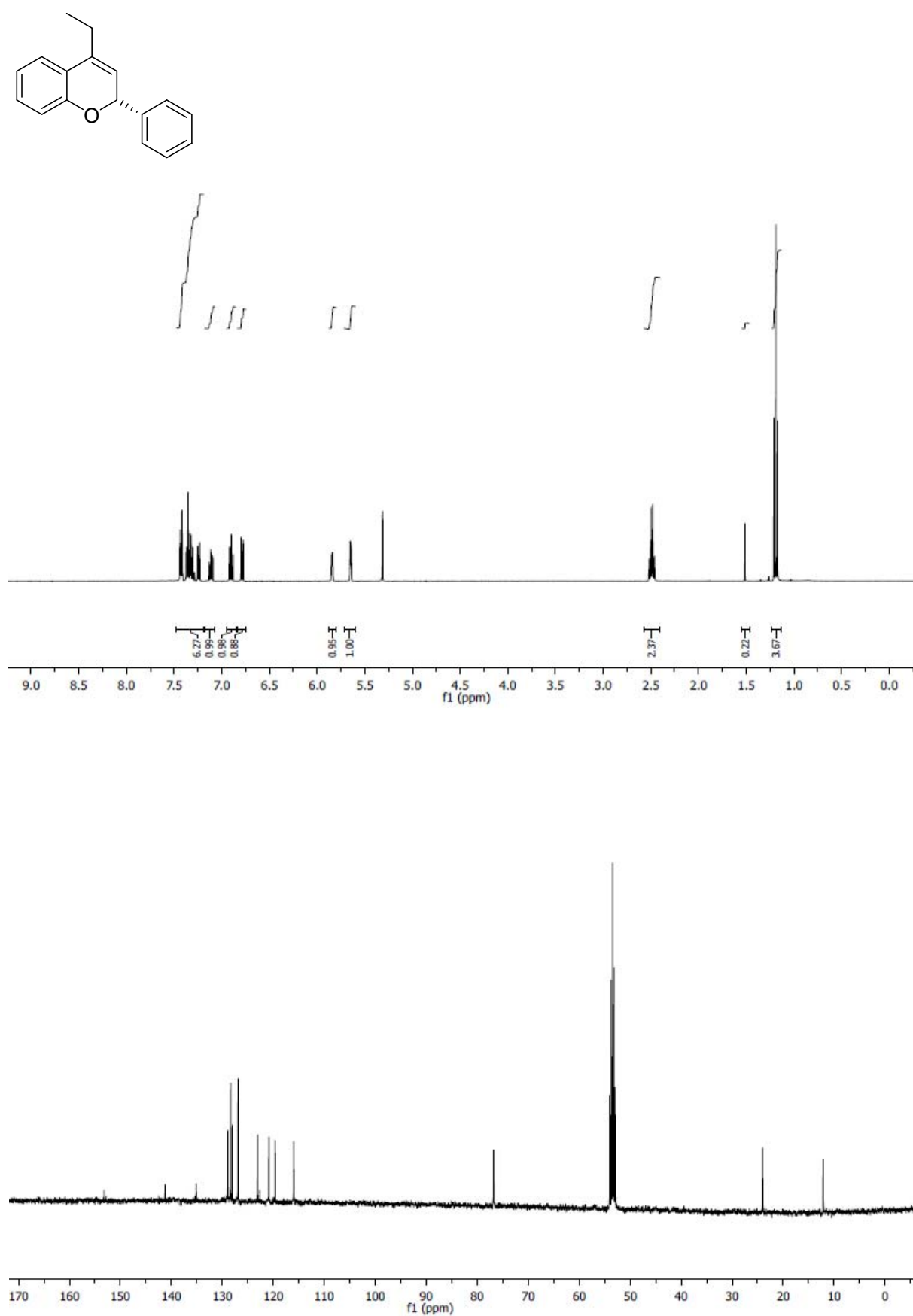
**Figure S13:** NMR spectra of compound 4j



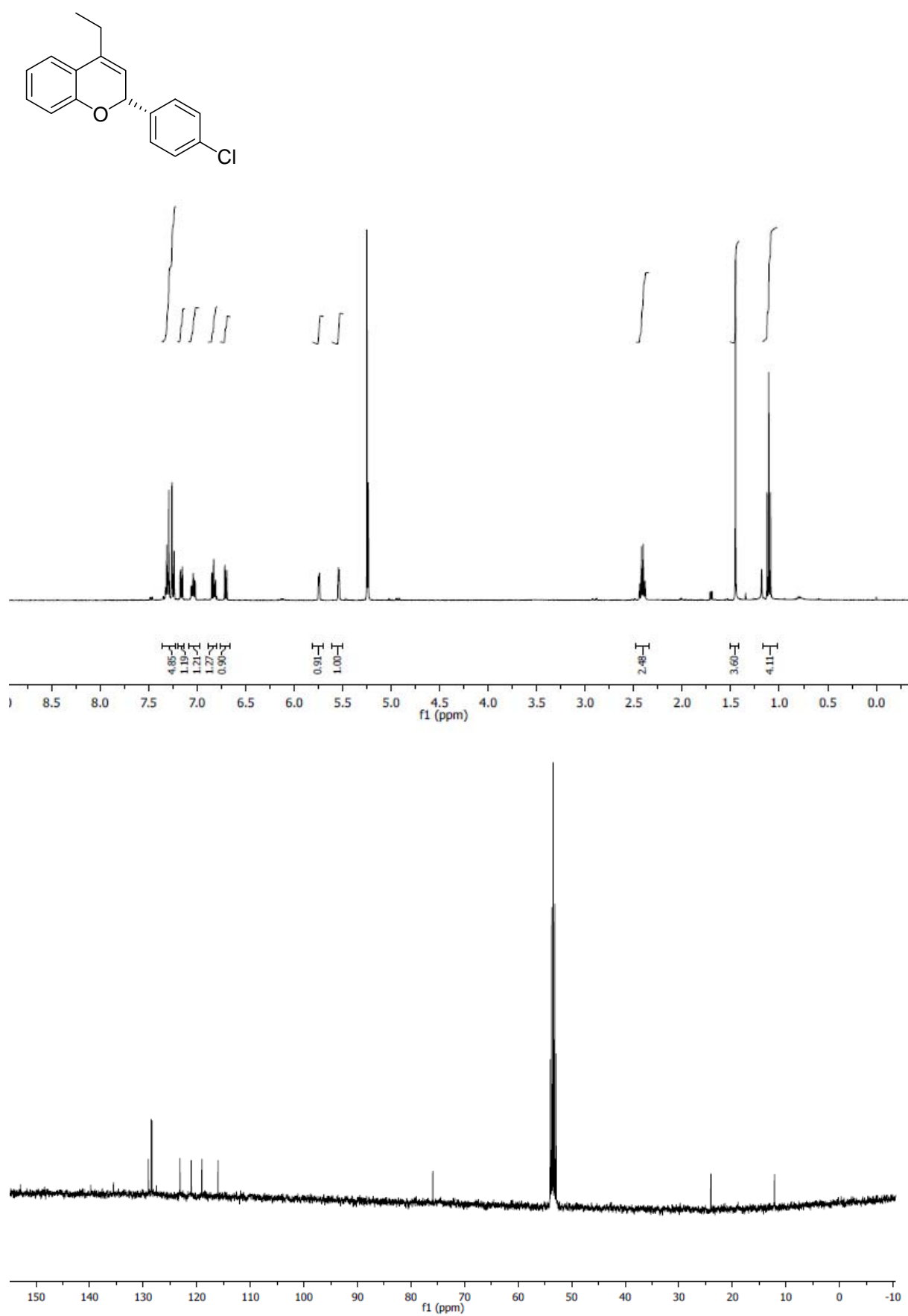
**Figure S14:** NMR spectra of compound **4k**



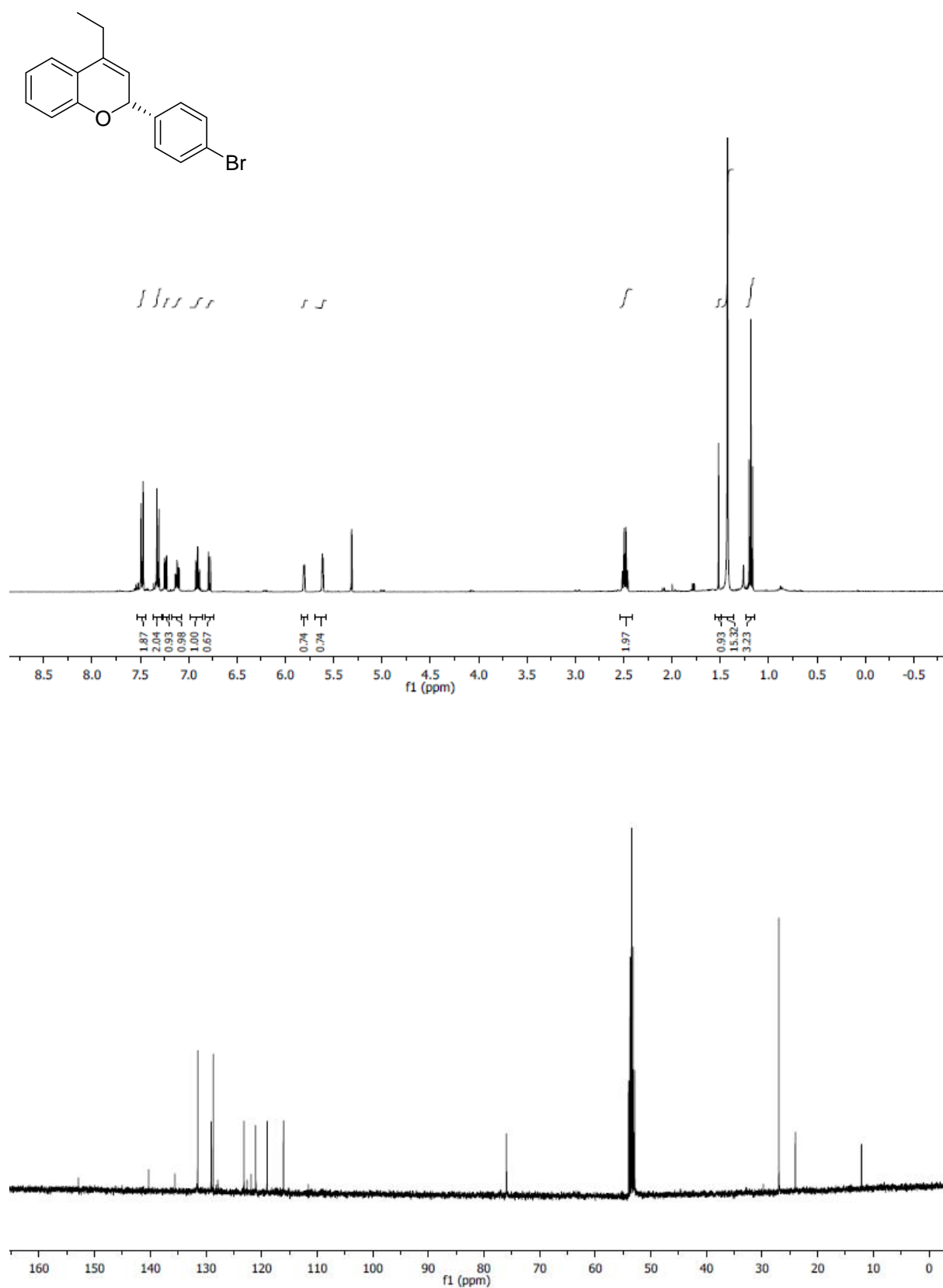
**Figure S15:** NMR spectra of compound **4l**



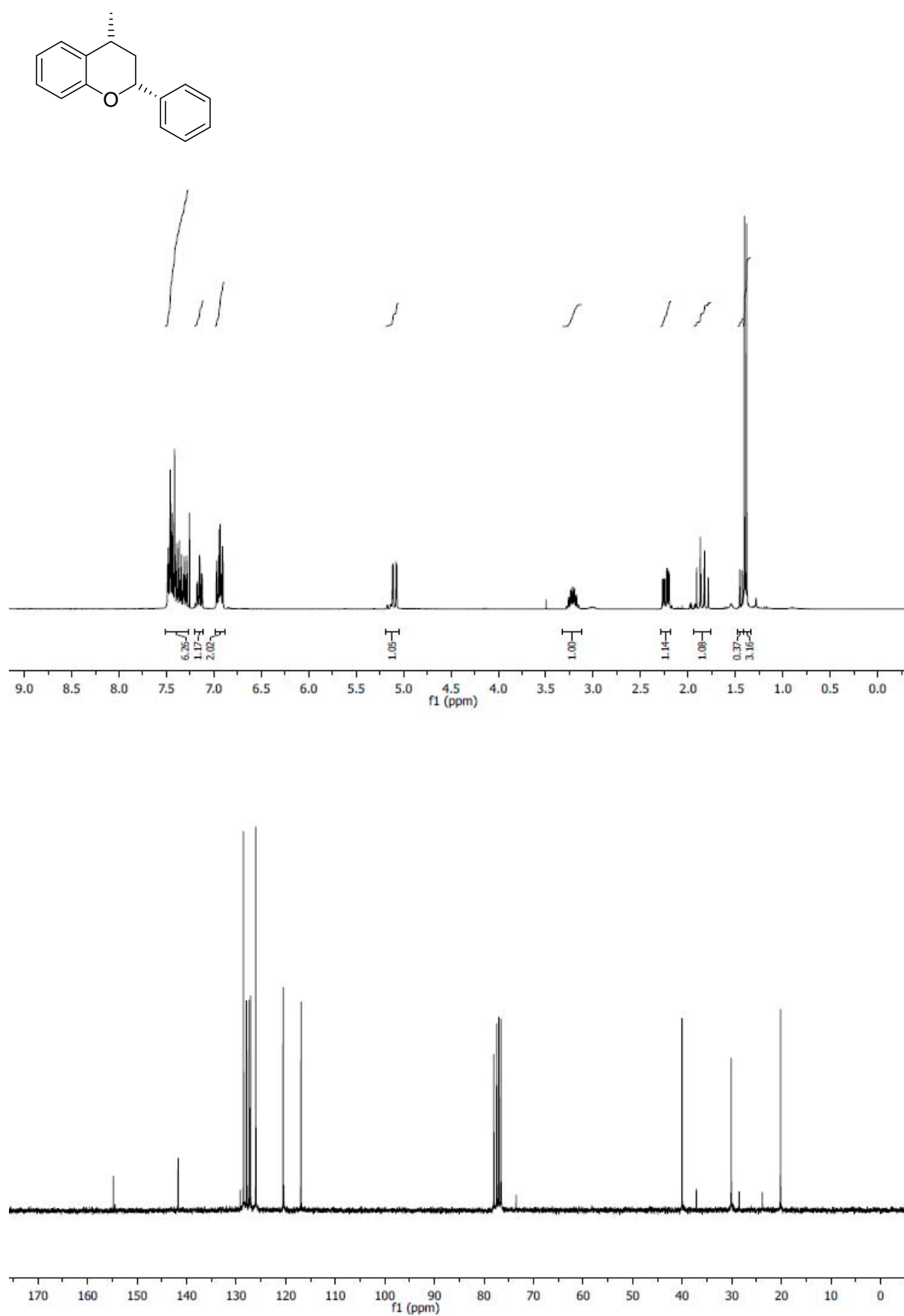
**Figure S16:** NMR spectra of compound **4m**



**Figure S17:** NMR spectra of compound **4n**

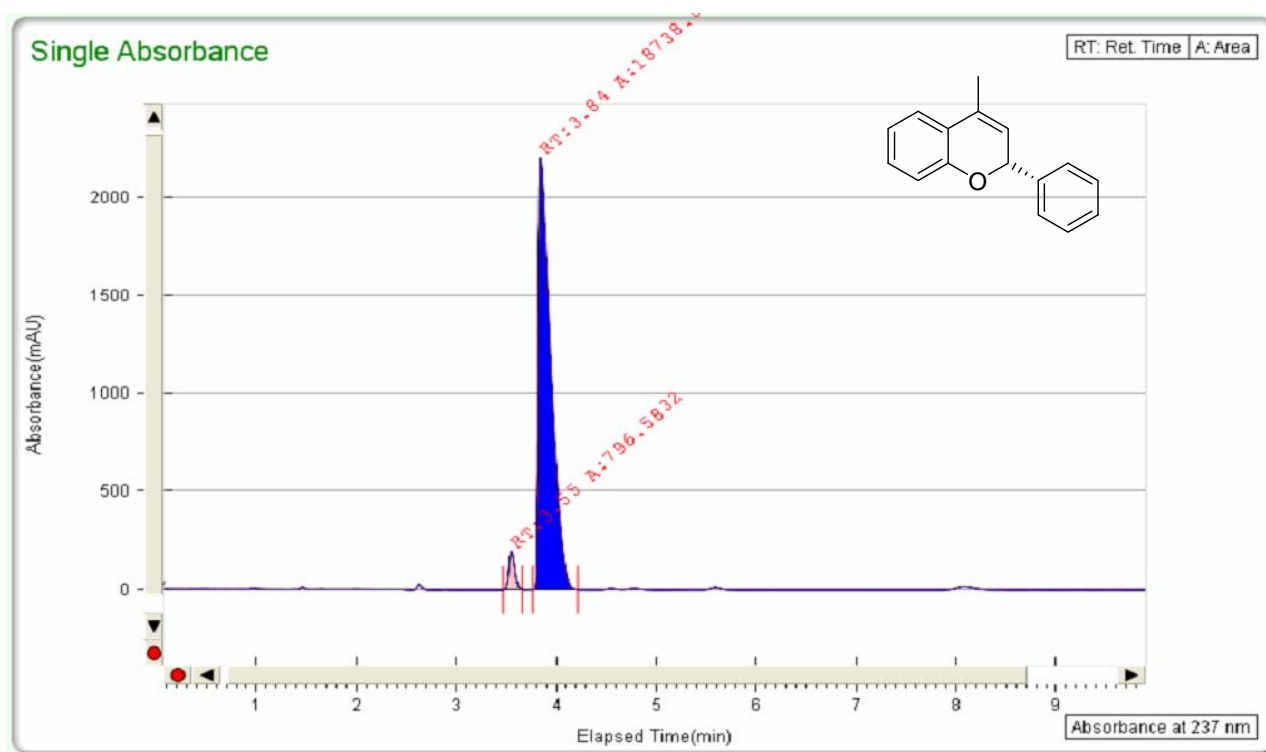
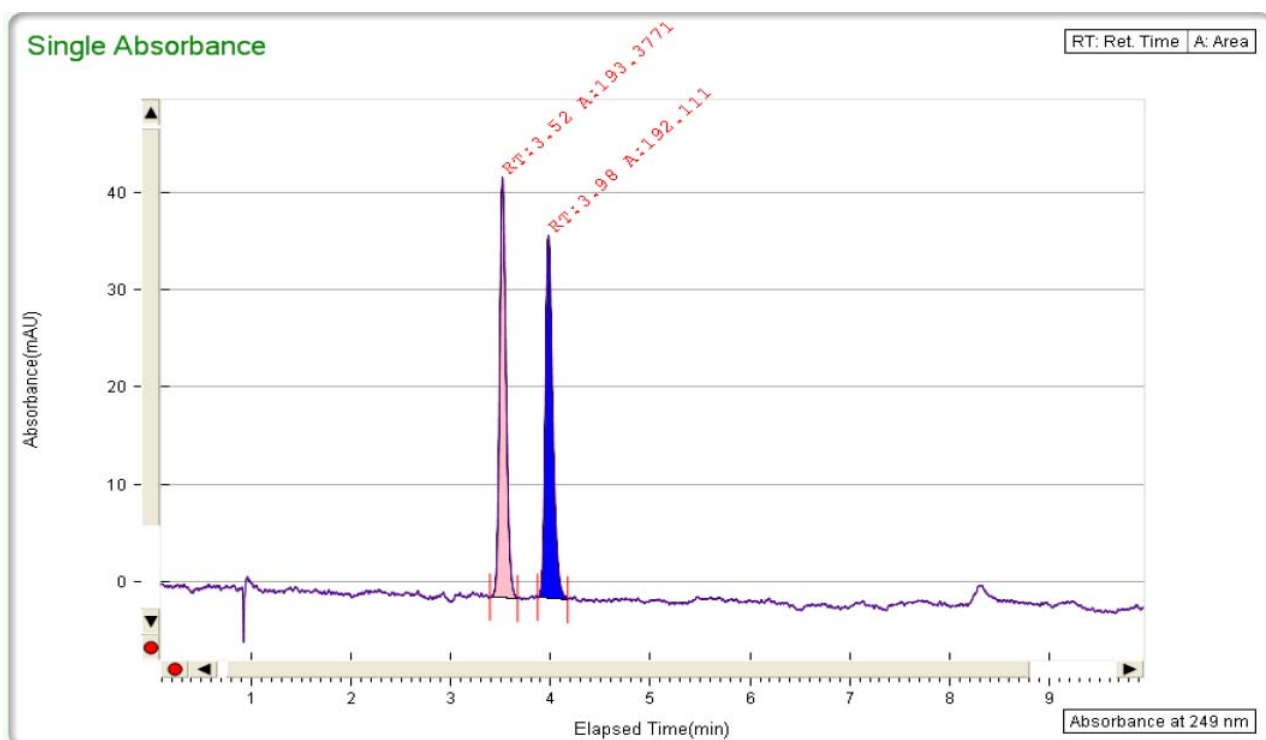


**Figure S18:** NMR spectra of compound **4o**



**Figure S19:** NMR spectra of compound **7a**

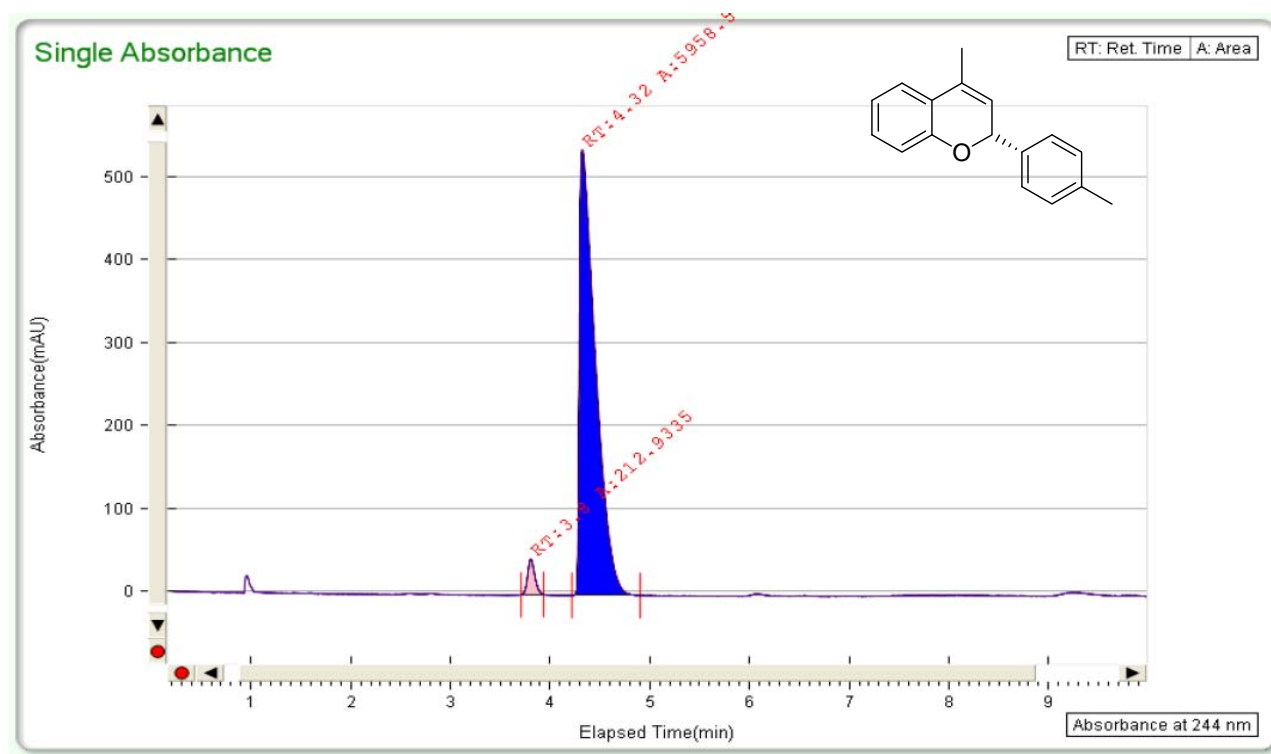
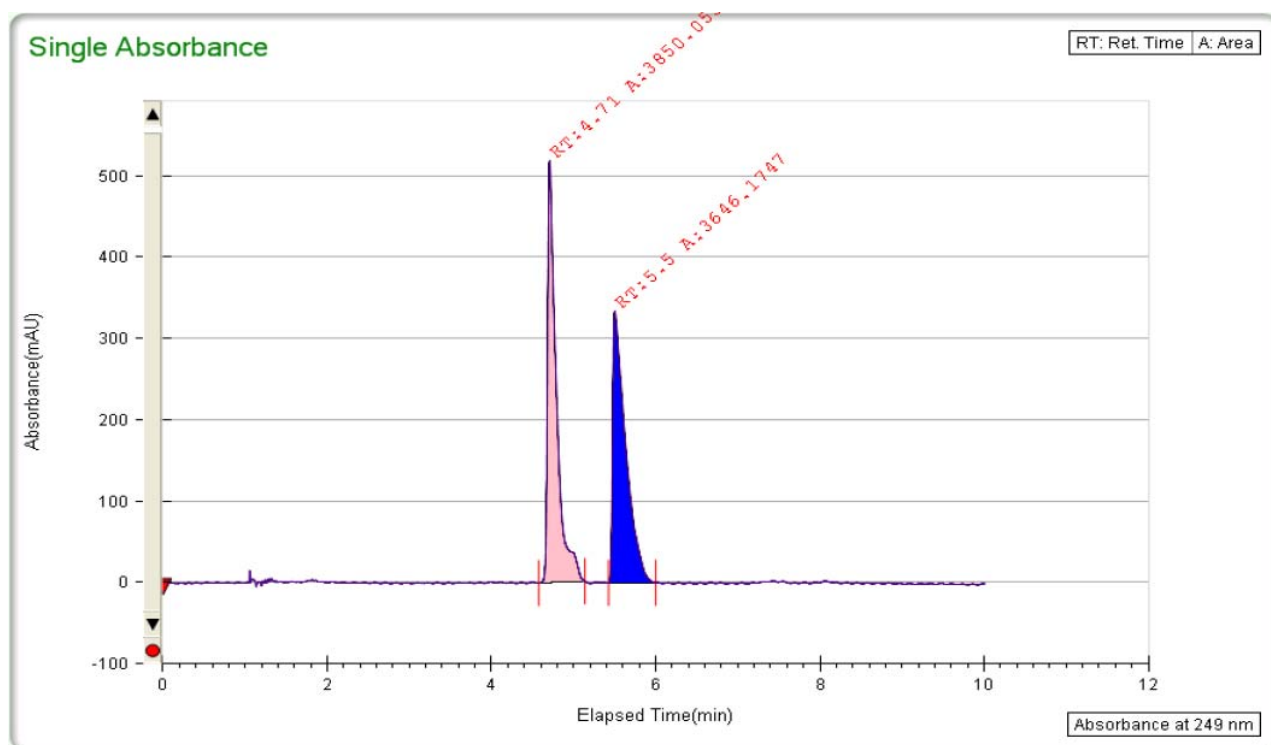
**Chiral SFC Data of compounds 4a-o, 7a and 3a.**



Peak Info					
Number	Area %	Area	RT (min)	St. (min)	End (min)
1	4.0778	796.5832	3.55	3.4666	3.6583
2	95.9222	18738.0703	3.84	3.7666	4.2133

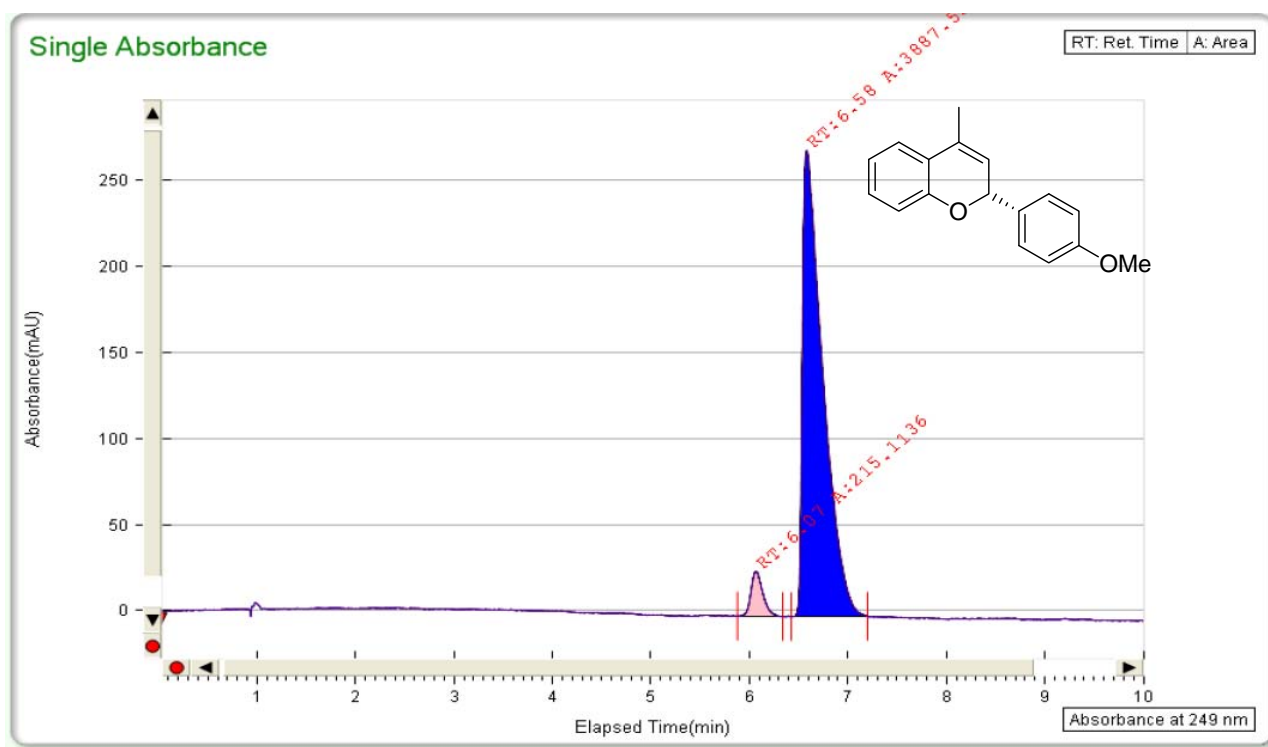
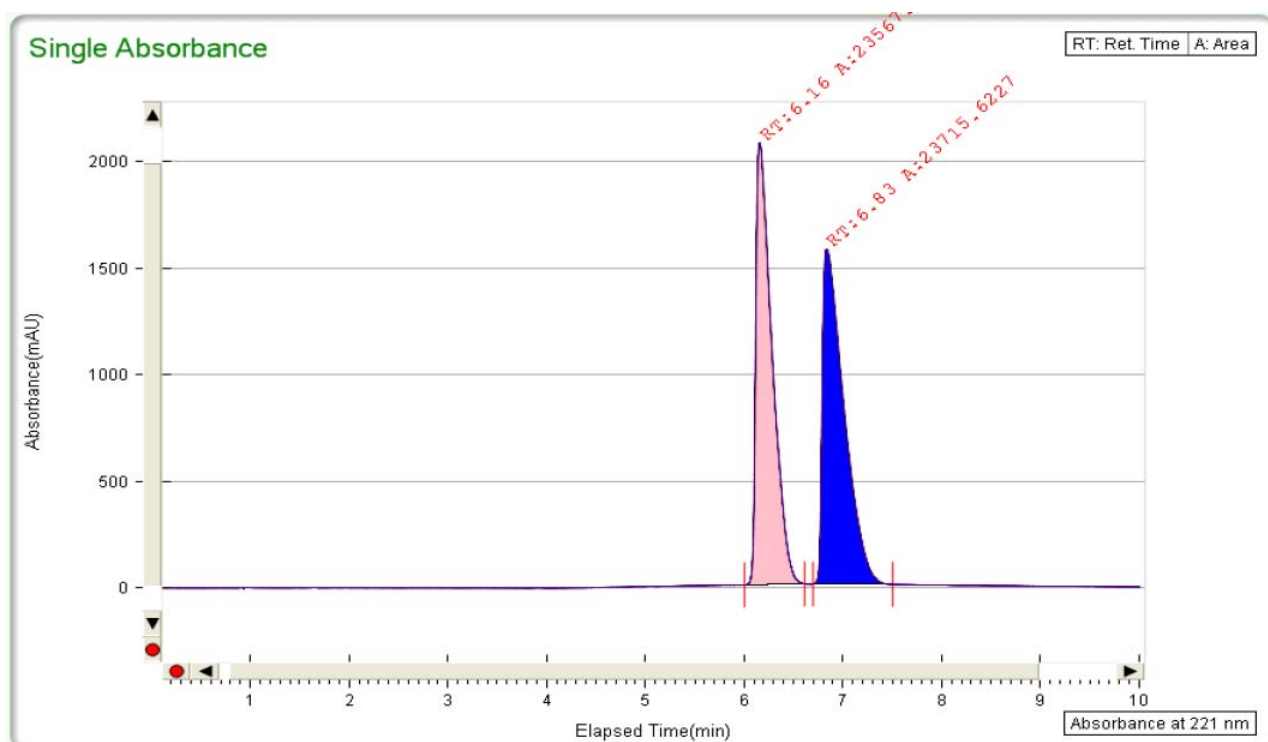
**Figure S20:** SFC chromatograms of compound **4a**.





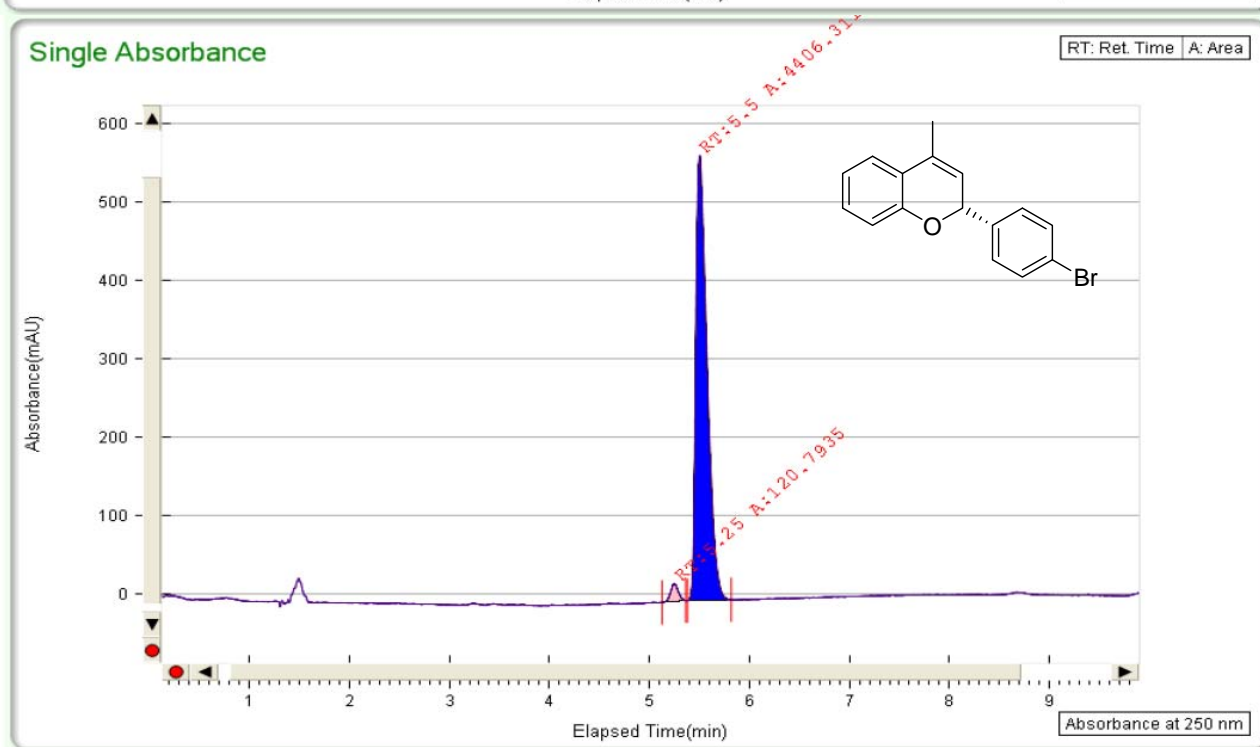
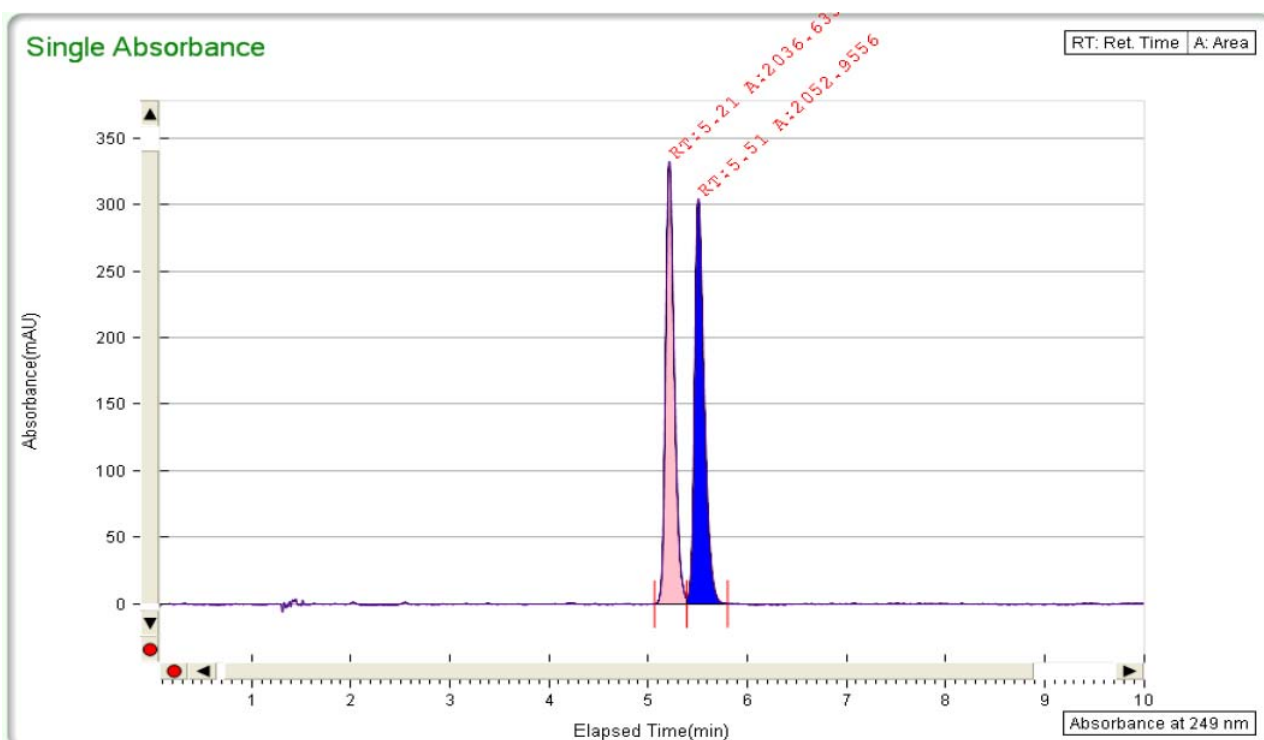
Peak Info					
Number	Area %	Area	RT (min)	St. (min)	End (min)
1	3.4503	212.9335	3.8	3.7083	3.9316
2	96.5497	5958.5841	4.32	4.2183	4.9016

Figure S21: SFC chromatograms of compound 4b.



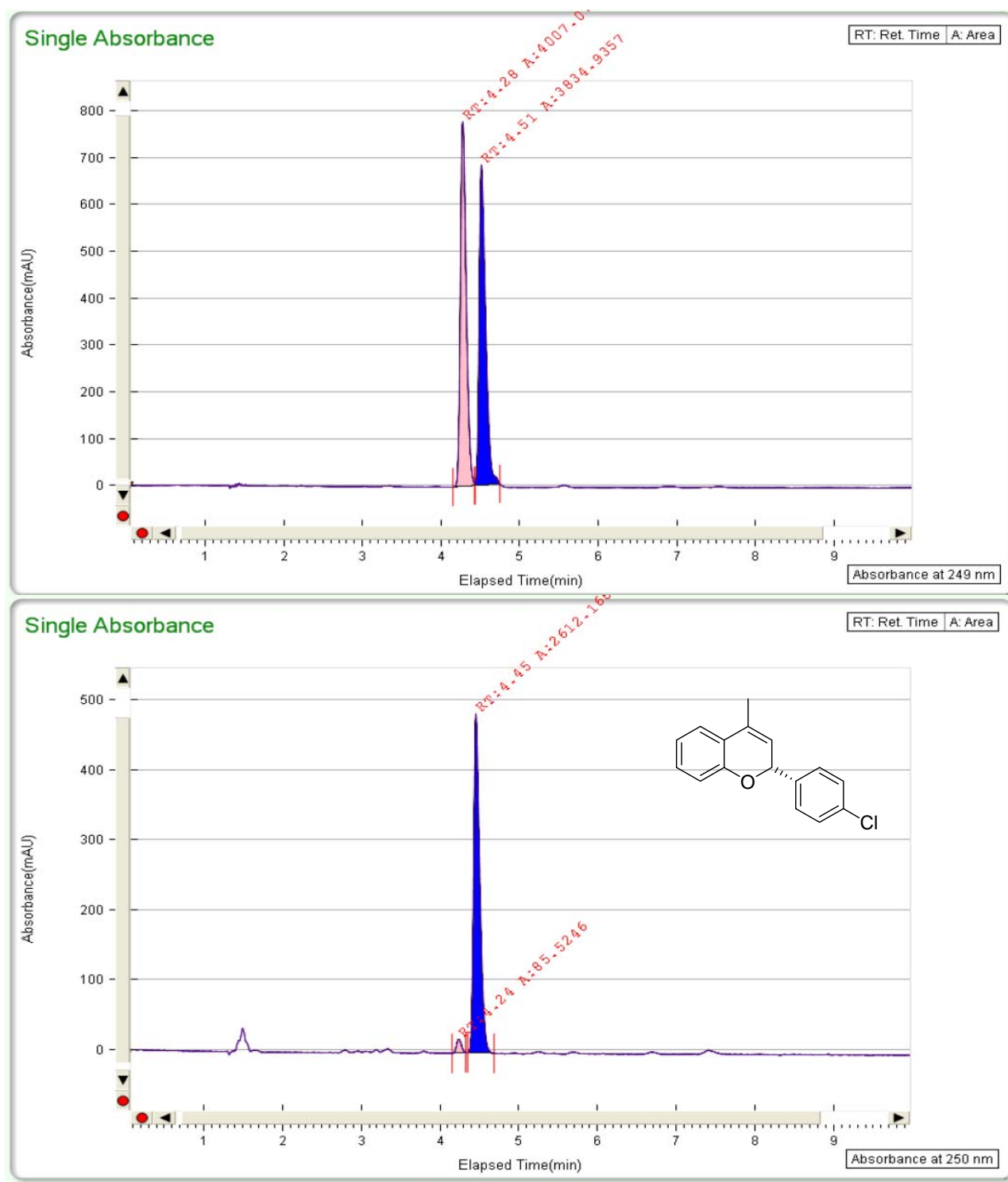
Peak Info					
Number	Area %	Area	RT (min)	St. (min)	End (min)
1	5.2432	215.1136	6.07	5.8779	6.3345
2	94.7568	3887.5982	6.58	6.4245	7.1978

Figure S22: SFC chromatograms of compound **4c**.



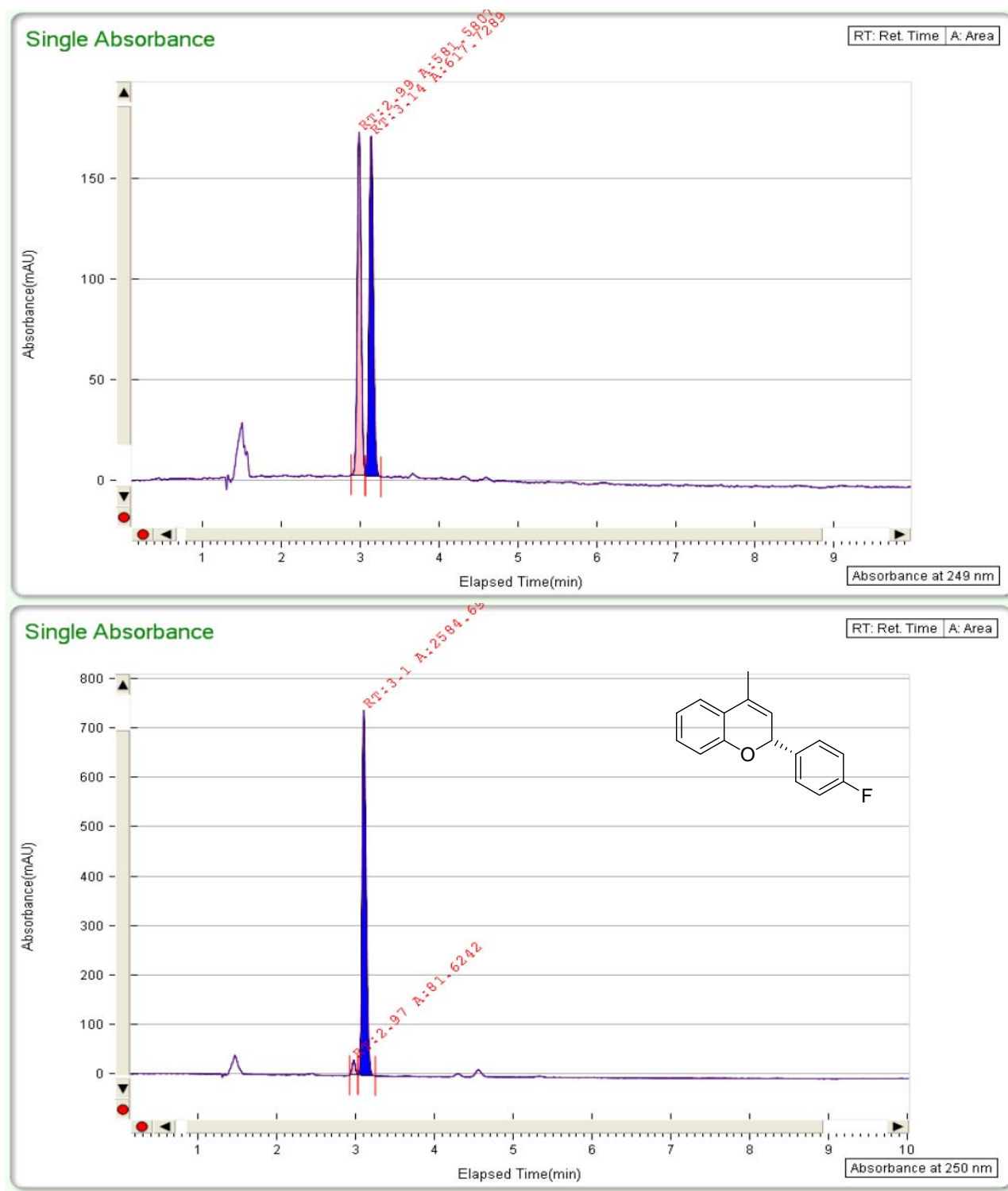
Peak Info					
Number	Area %	Area	RT (min)	St. (min)	End (min)
1	2.6682	120.7935	5.25	5.1266	5.3615
2	97.3318	4406.3118	5.5	5.3799	5.8165

Figure S23: SFC chromatograms of compound **4d**.



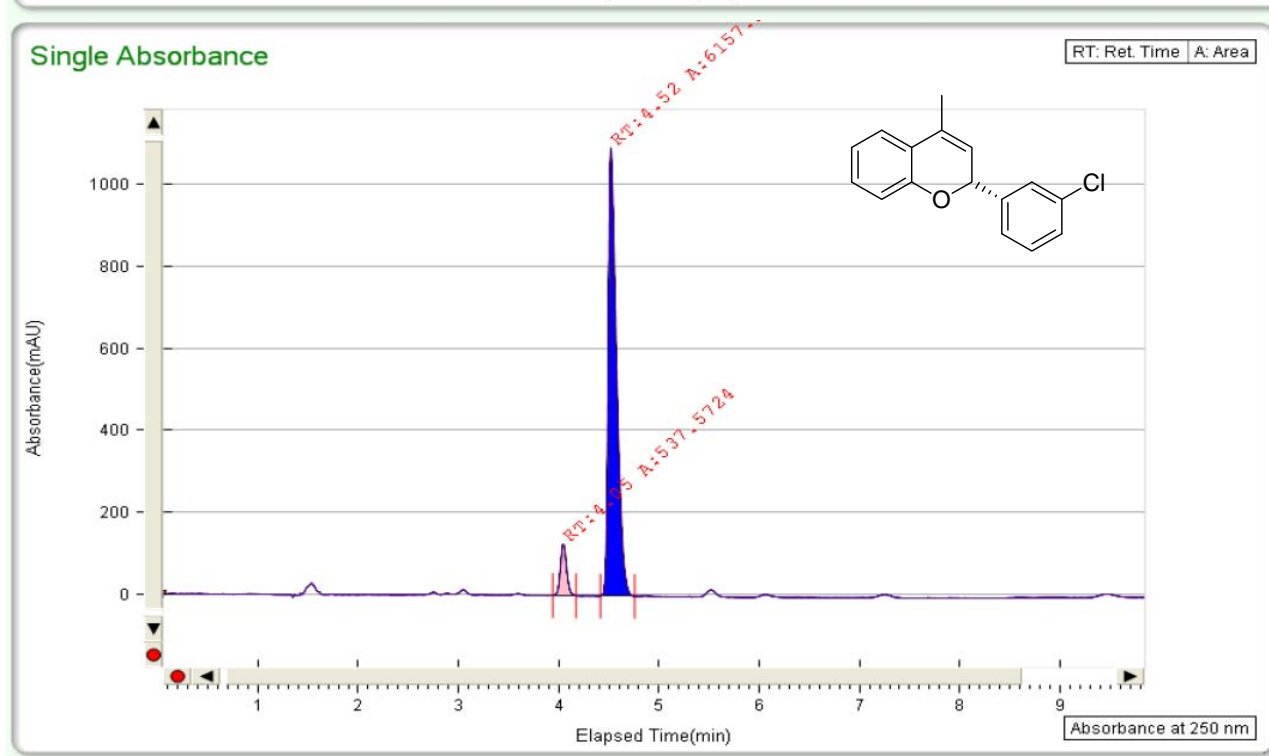
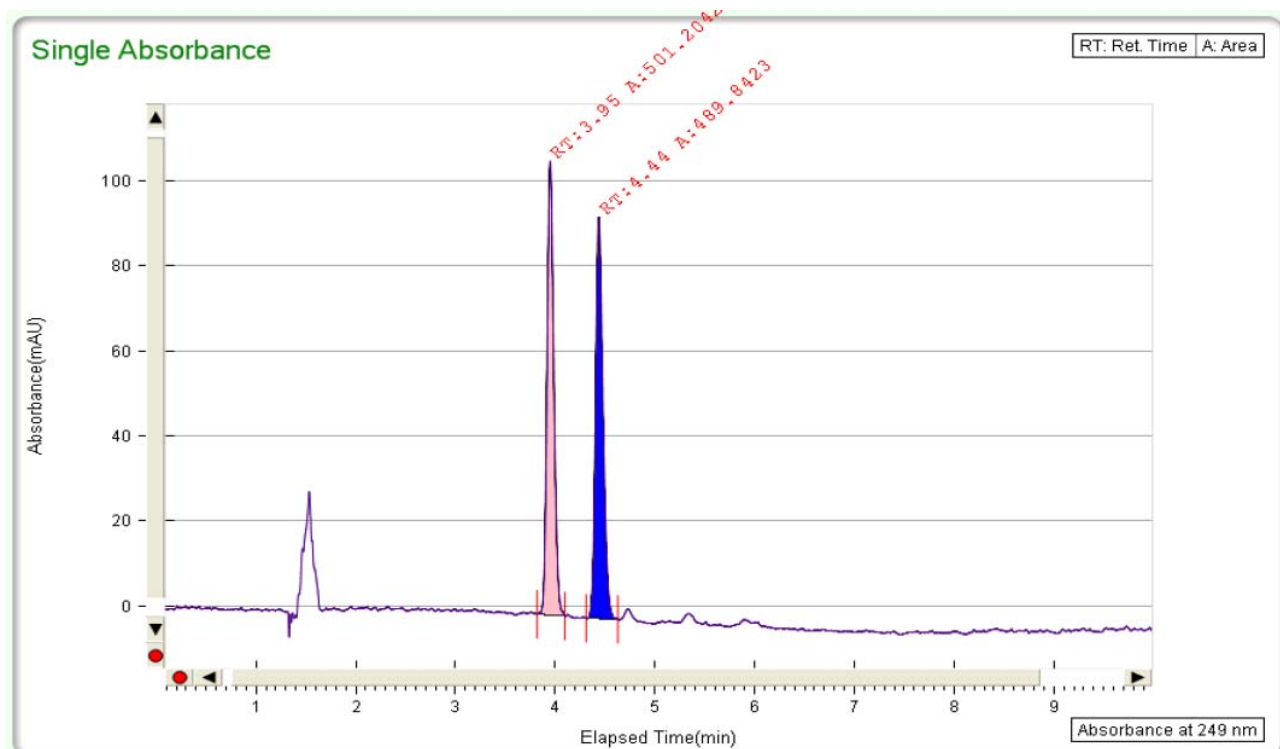
Peak Info					
Number	Area %	Area	RT (min)	St. (min)	End (min)
1	3.1703	85.5246	4.24	4.1532	4.3249
2	96.8297	2612.1687	4.45	4.3499	4.6832

Figure S24: SFC chromatograms of compound **4e**.



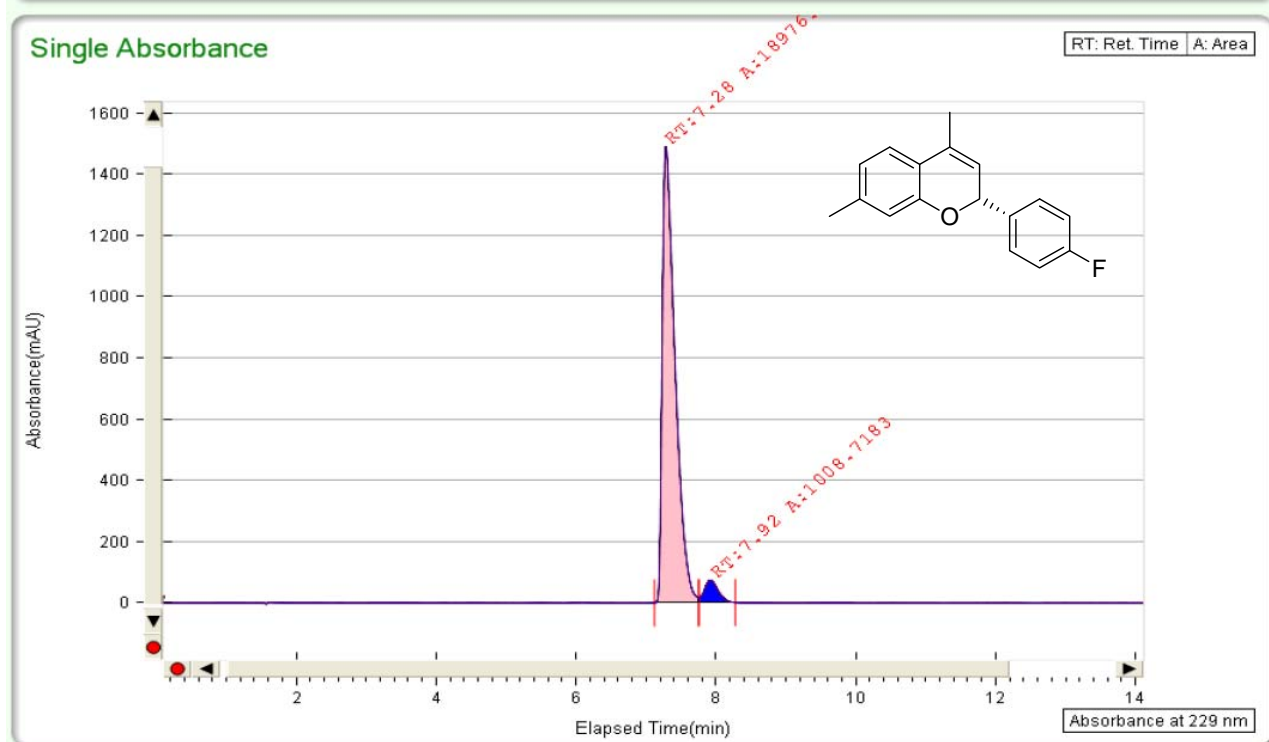
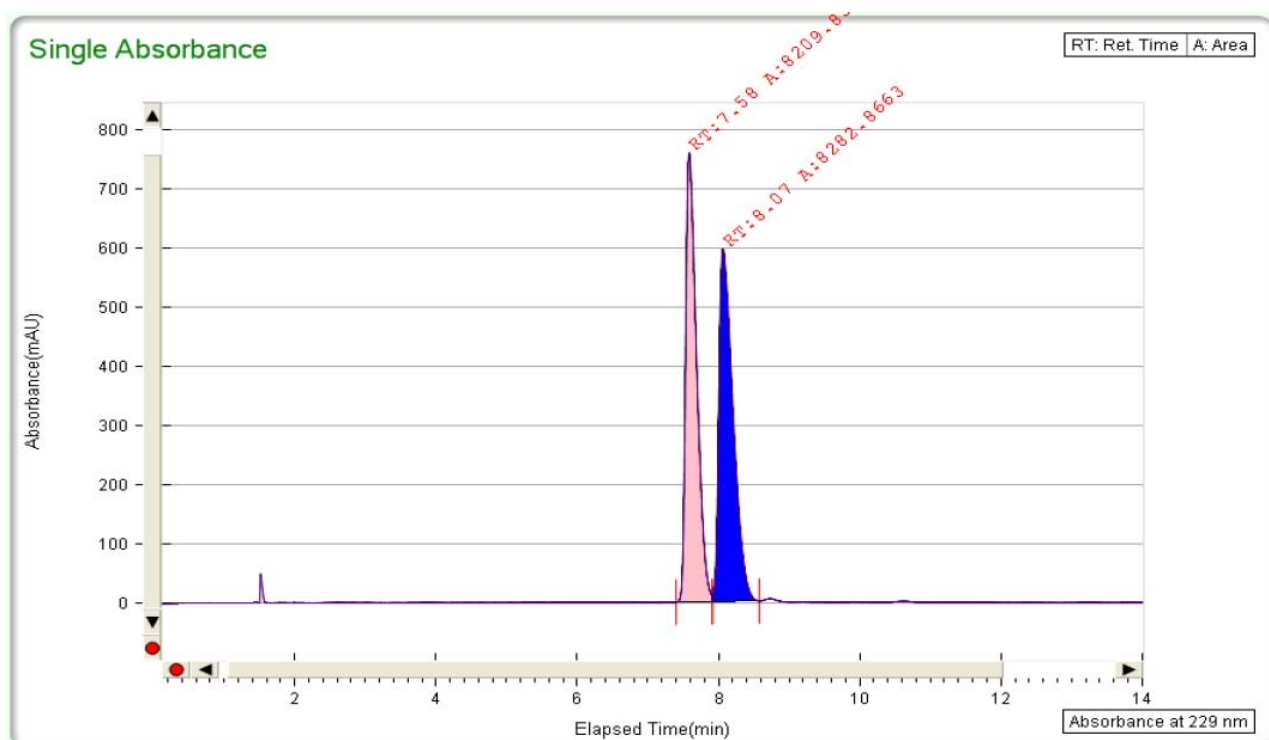
Peak Number	Area %	Area	RT (min)	St. (min)	End (min)
1	3.0613	81.6242	2.97	2.9199	3.0216
2	96.9387	2584.6924	3.1	3.0283	3.2466

**Figure S25:** SFC chromatograms of compound **4f**.



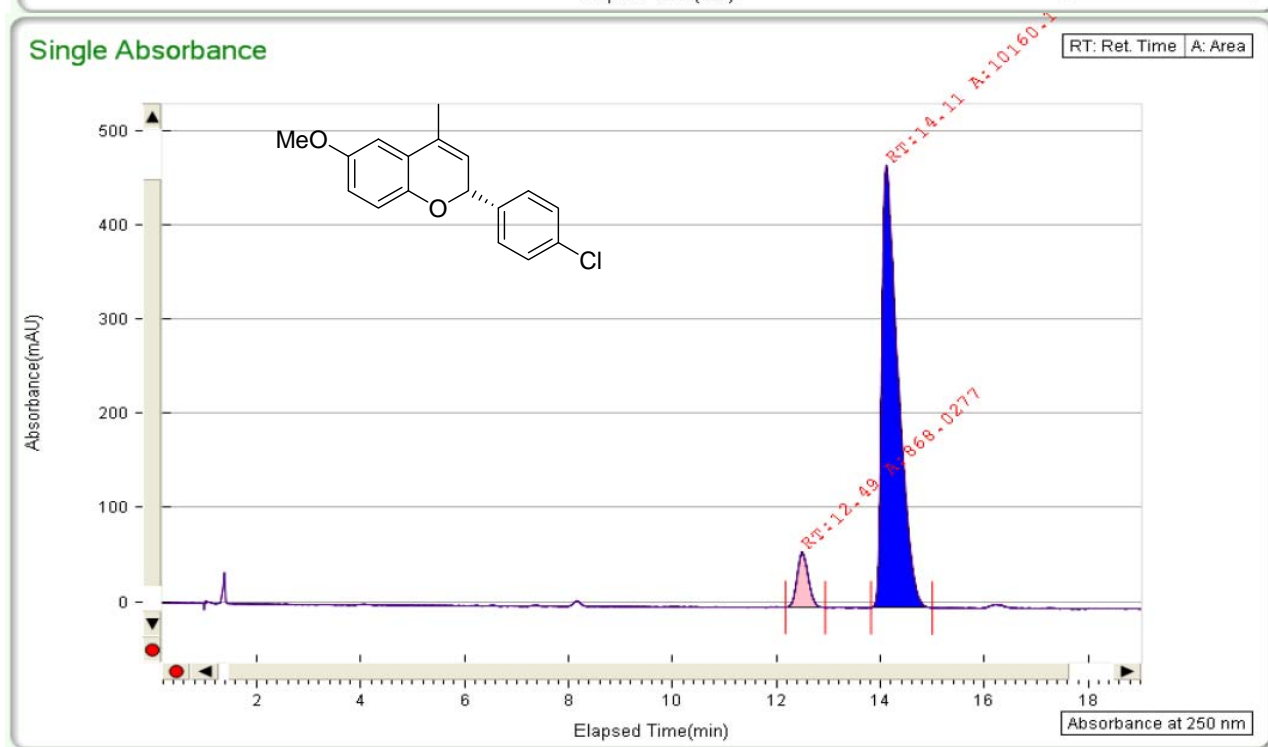
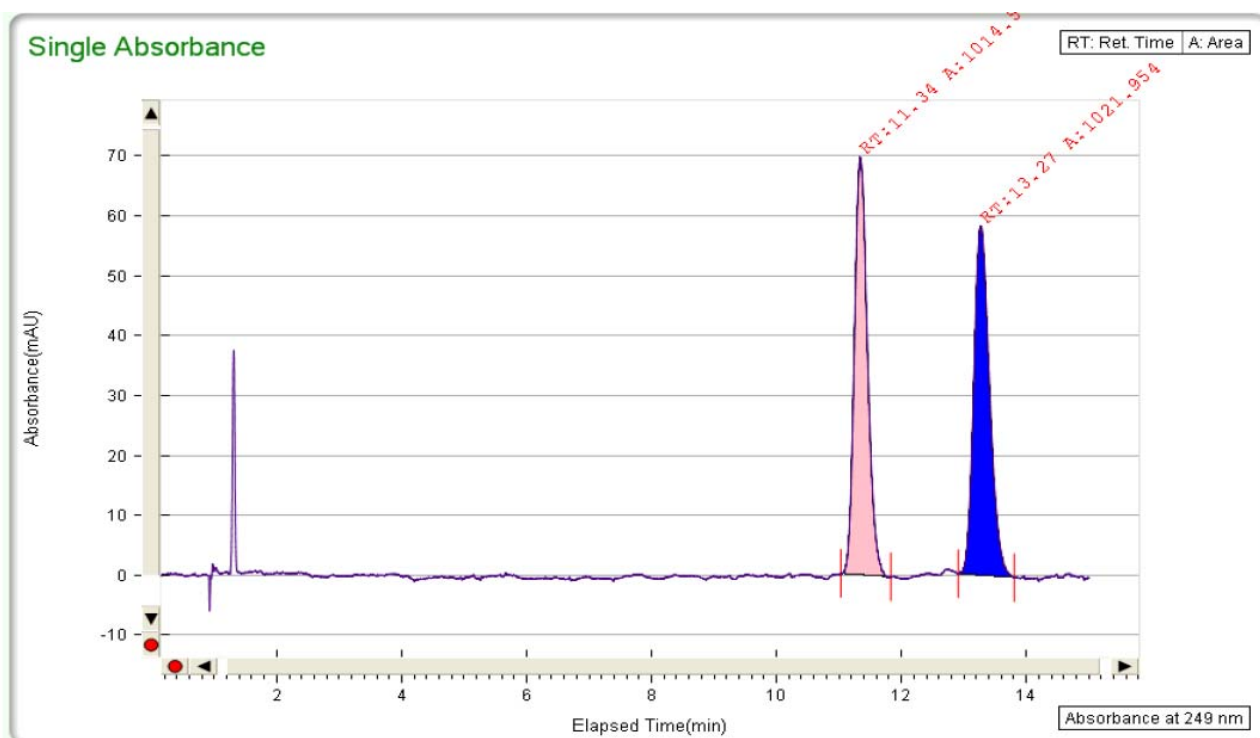
Peak Info					
Number	Area %	Area	RT (min)	St. (min)	End (min)
1	8.0288	537.5724	4.05	3.9408	4.1708
2	91.9712	6157.9695	4.52	4.4158	4.7557

**Figure S26:** SFC chromatograms of compound **4g**.



Peak Number	Area %	Area	RT (min)	St. (min)	End (min)
1	94.9527	18976.6028	7.28	7.1198	7.7514
2	5.0473	1008.7183	7.92	7.7531	8.2731

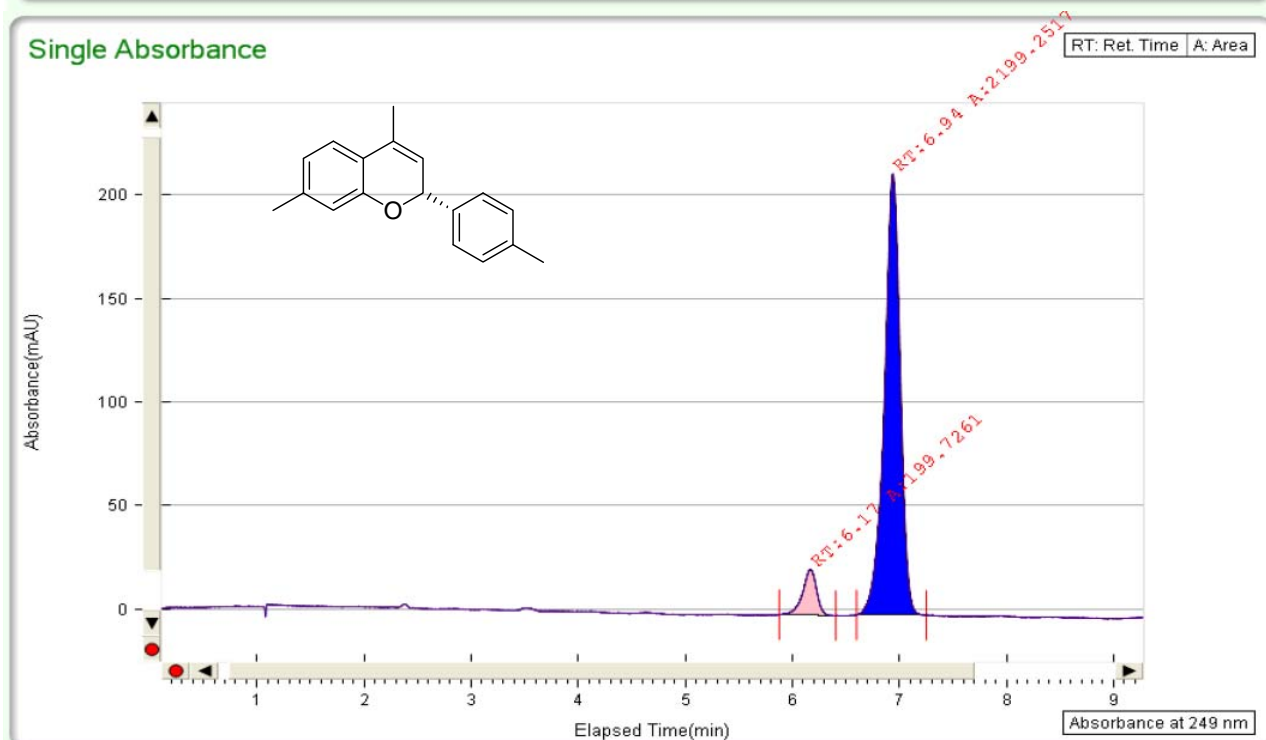
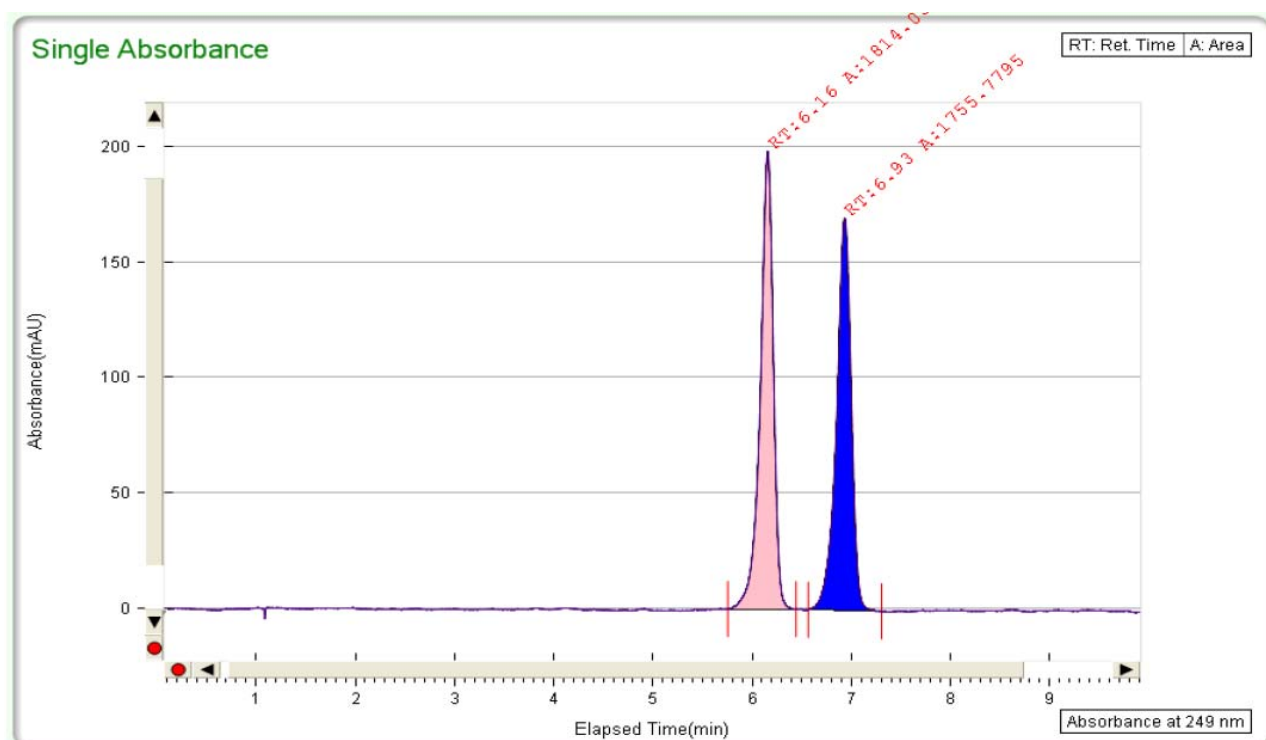
Figure S27: SFC chromatograms of compound **4h**.



Peak Info					
Number	Area %	Area	RT (min)	St. (min)	End (min)
1	7.871	868.0277	12.49	12.1737	12.9355
2	92.129	10160.149	14.11	13.819	14.9926

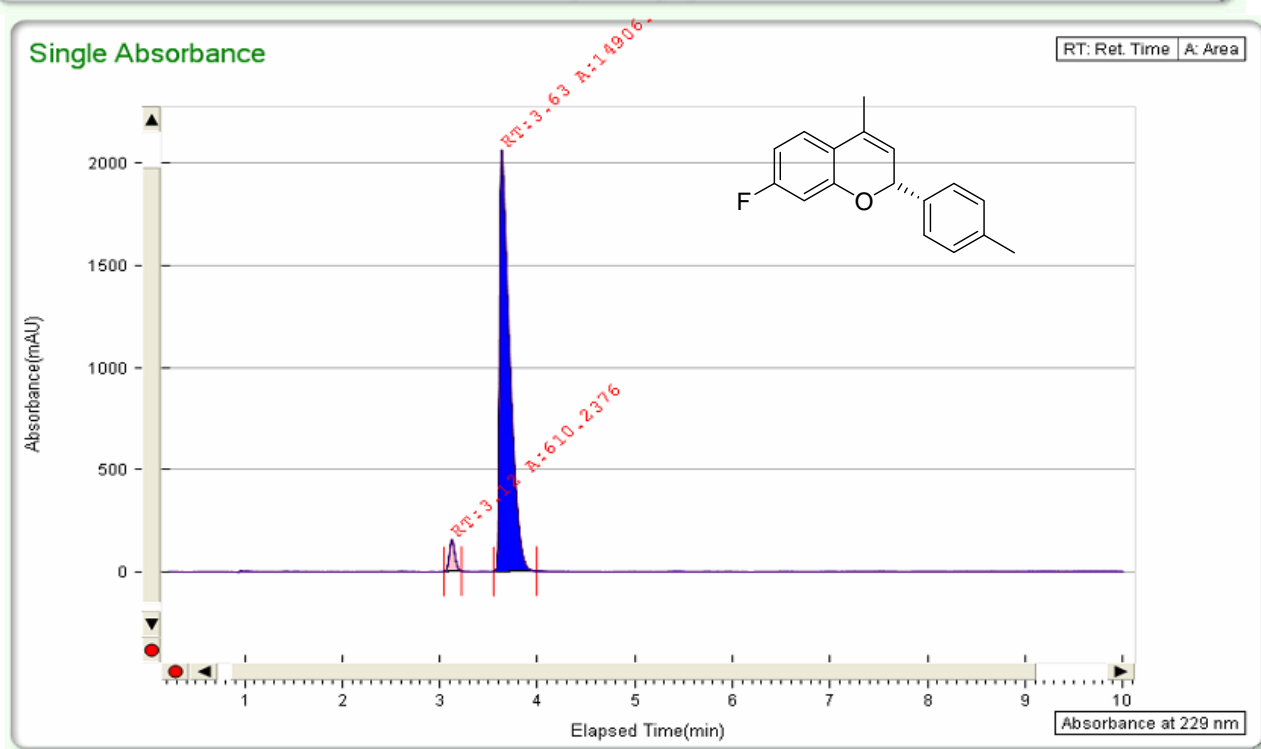
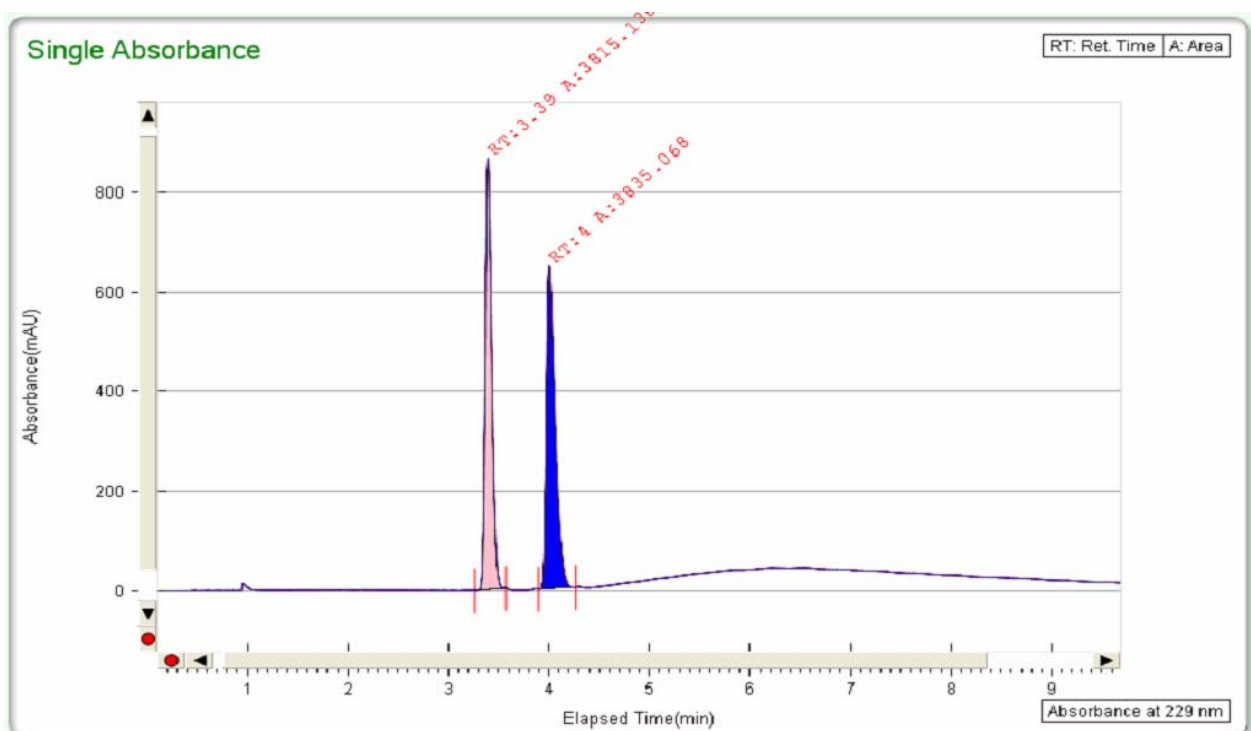
Figure S28: SFC chromatograms of compound 4i.





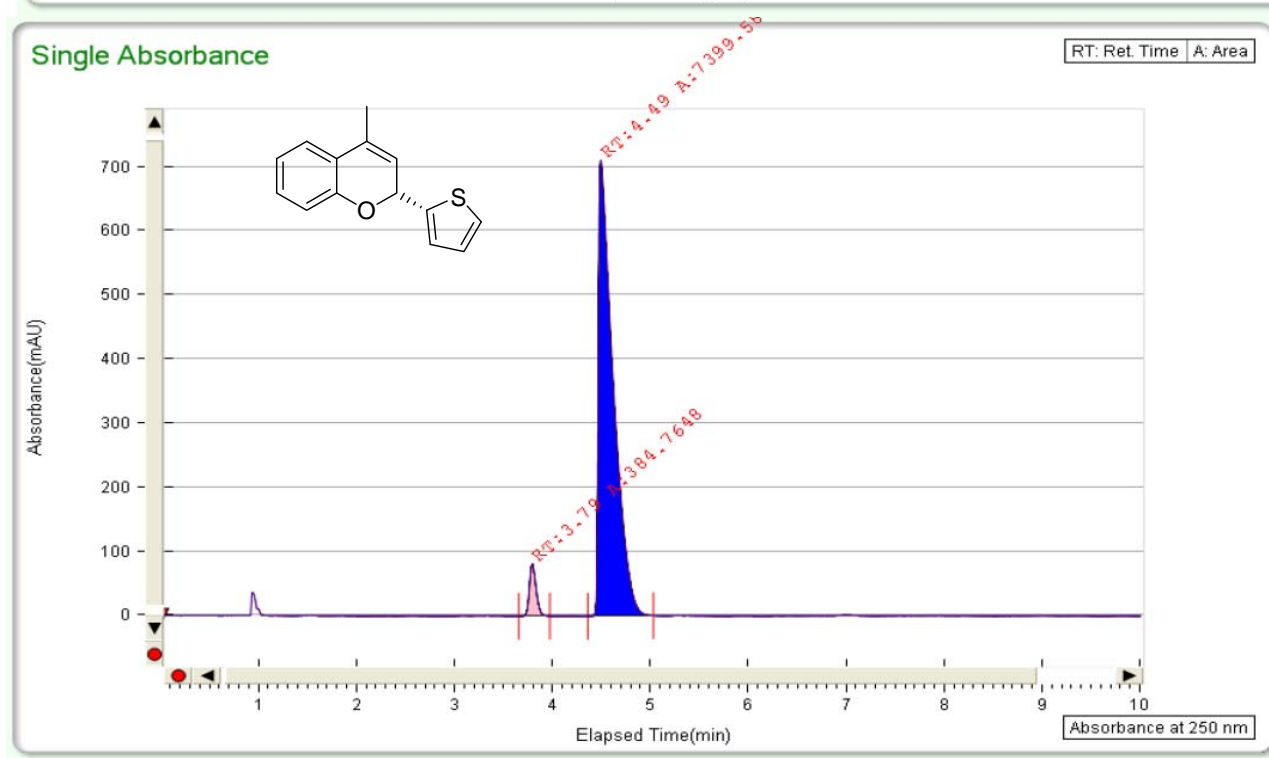
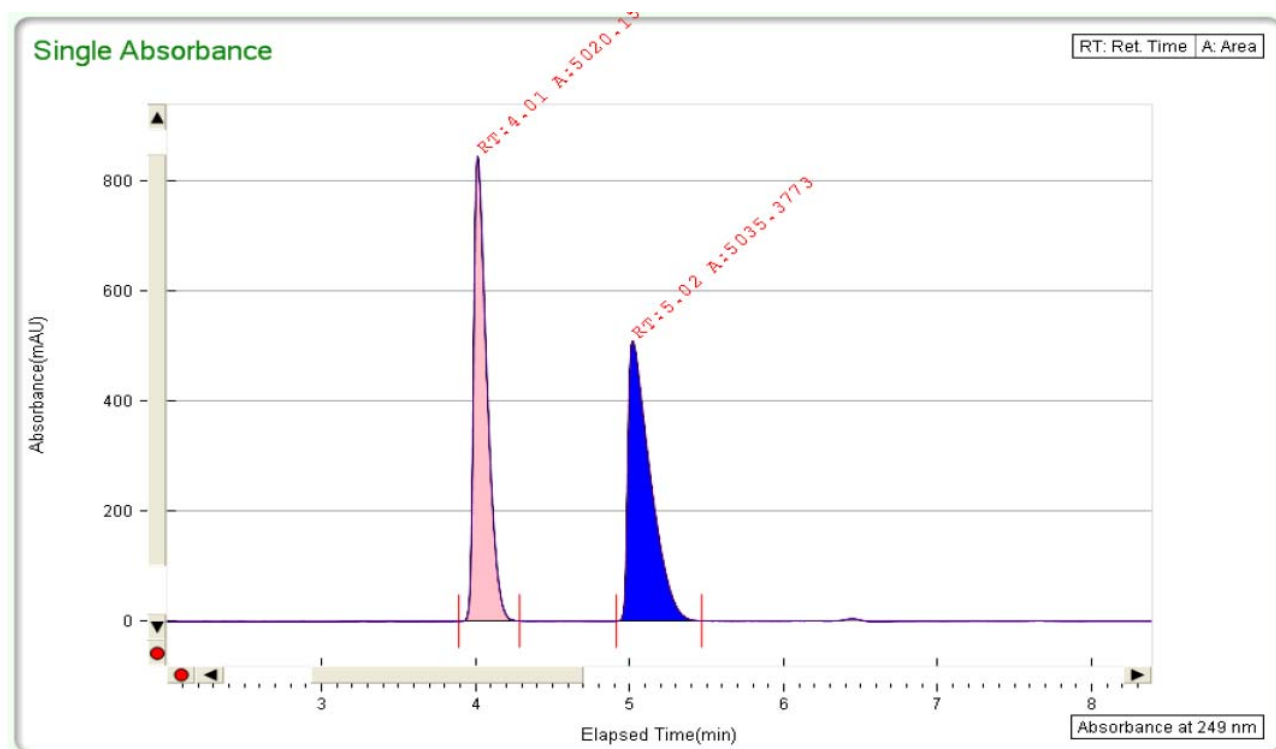
Peak Info					
Number	Area %	Area	RT (min)	St. (min)	End (min)
1	8.3255	199.7261	6.17	5.8782	6.4048
2	91.6745	2199.2517	6.94	6.5998	7.2497

Figure S29: SFC chromatograms of compound 4j.



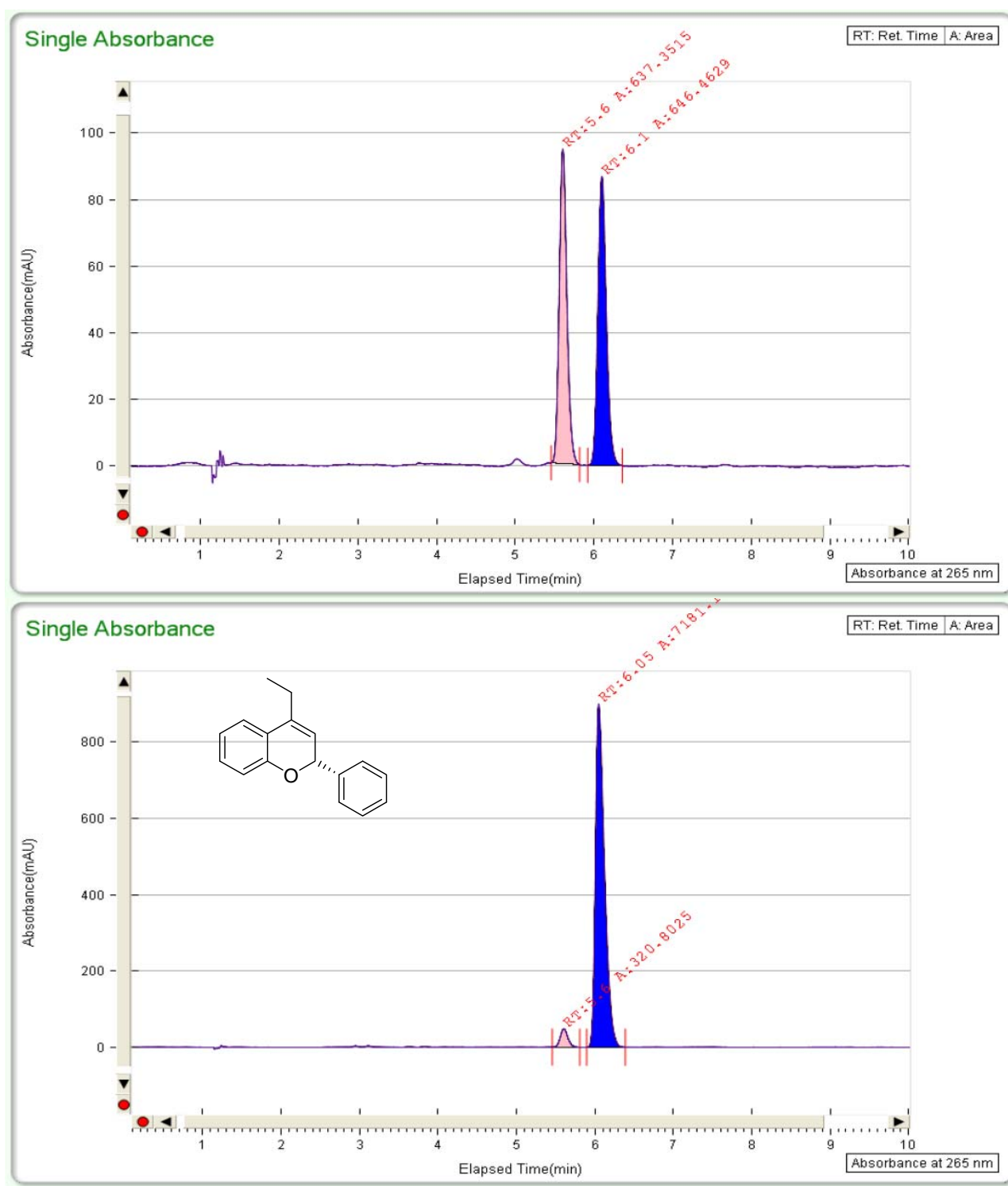
Peak Info					
Number	Area %	Area	RT (min)	St. (min)	End (min)
1	3.9328	610.2376	3.12	3.0433	3.2216
2	96.0672	14906.4811	3.63	3.5499	3.99

Figure S30: SFC chromatograms of compound **4k**.

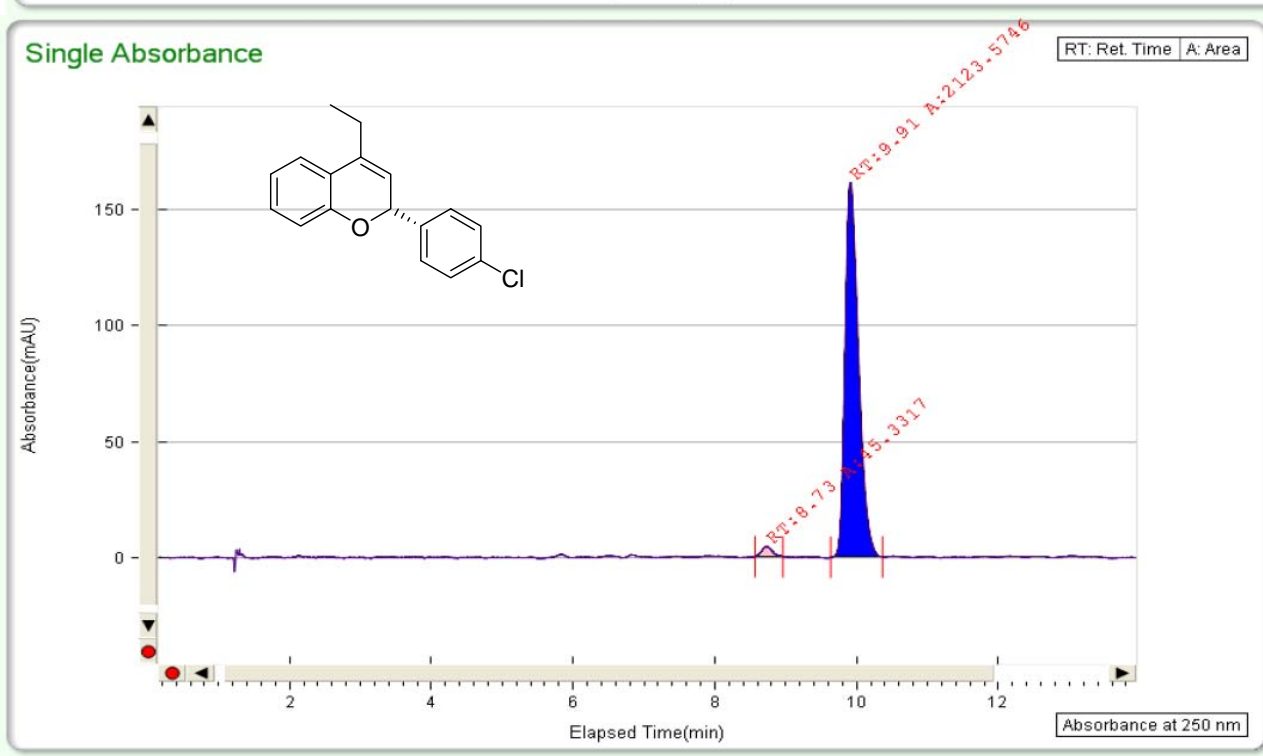
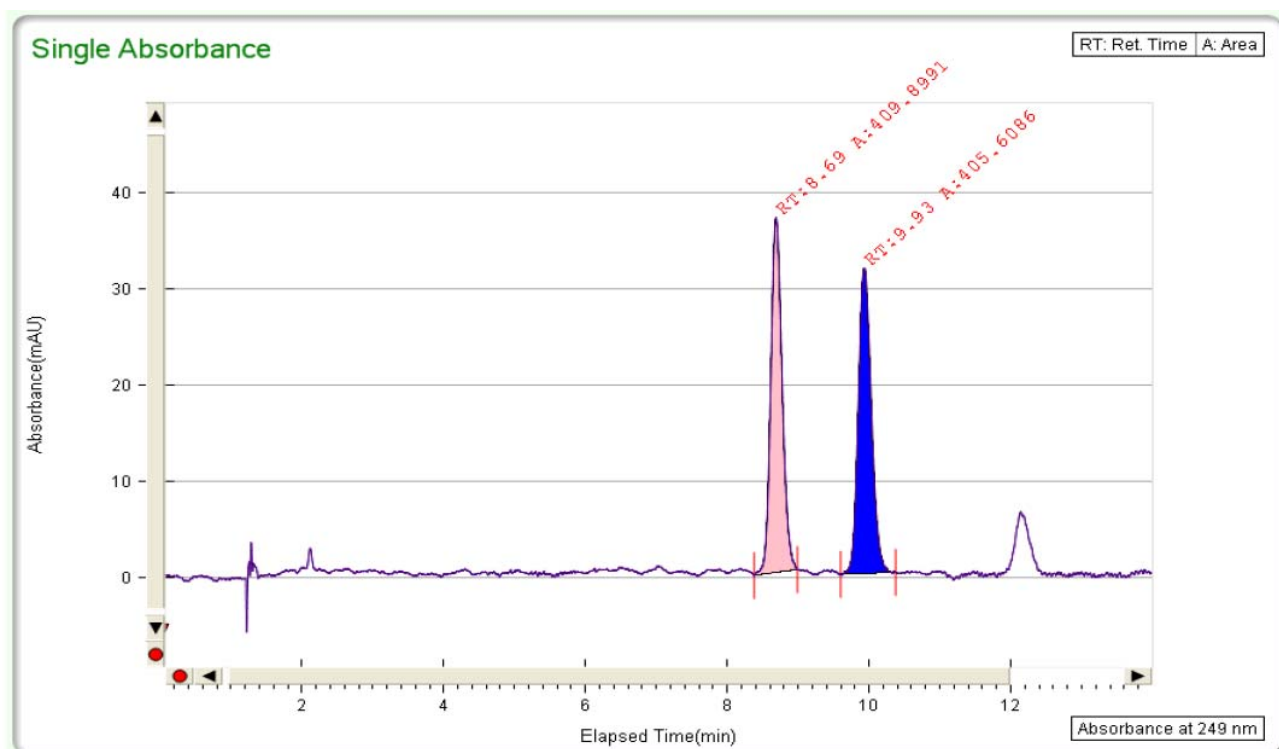


Peak Info					
Number	Area %	Area	RT (min)	St. (min)	End (min)
1	4.9428	384.7648	3.79	3.6566	3.9733
2	95.0572	7399.5867	4.49	4.3616	5.0299

**Figure S31:** SFC chromatograms of compound **4l**.

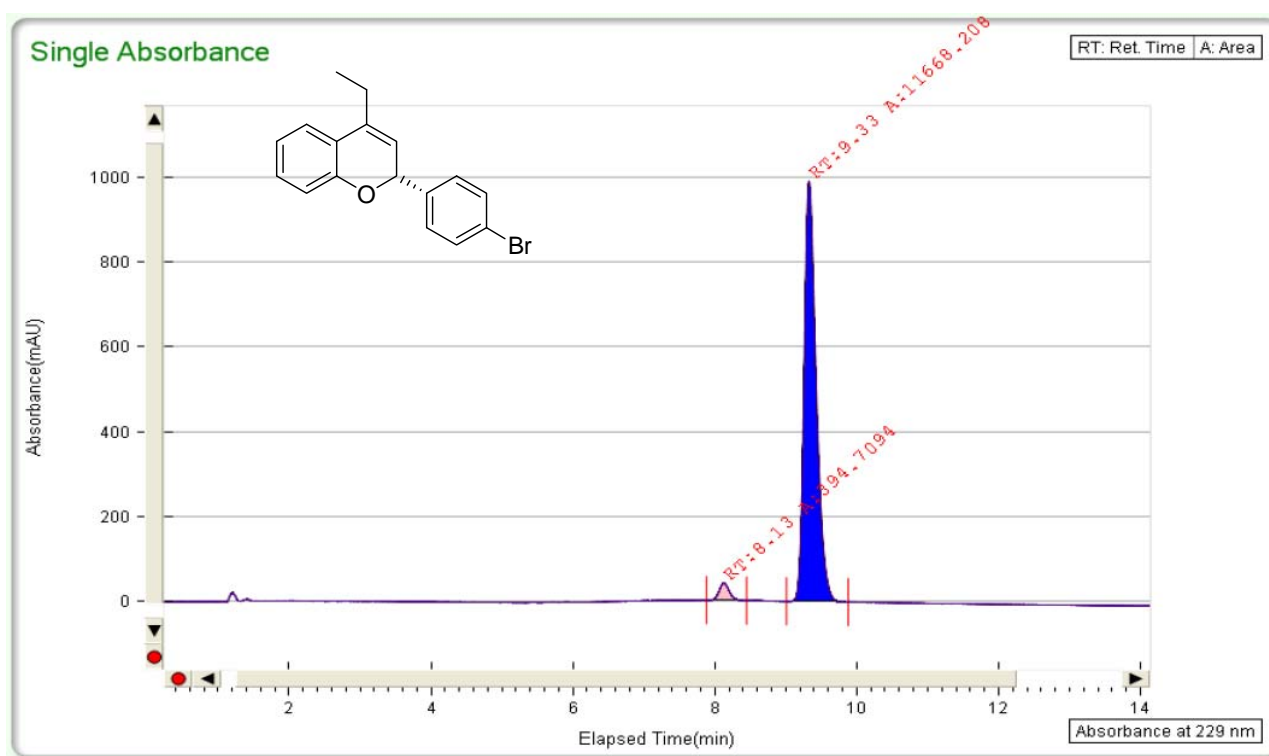
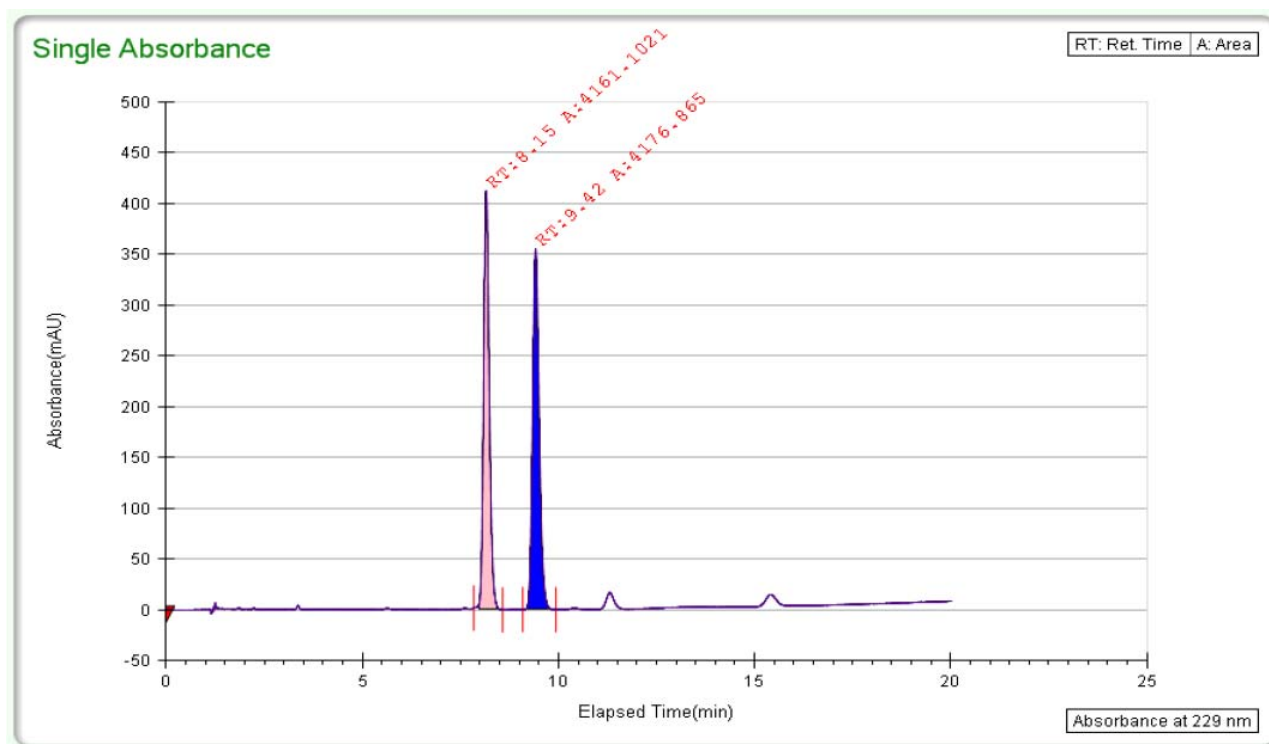


**Figure S32:** SFC chromatograms of compound **4m**.



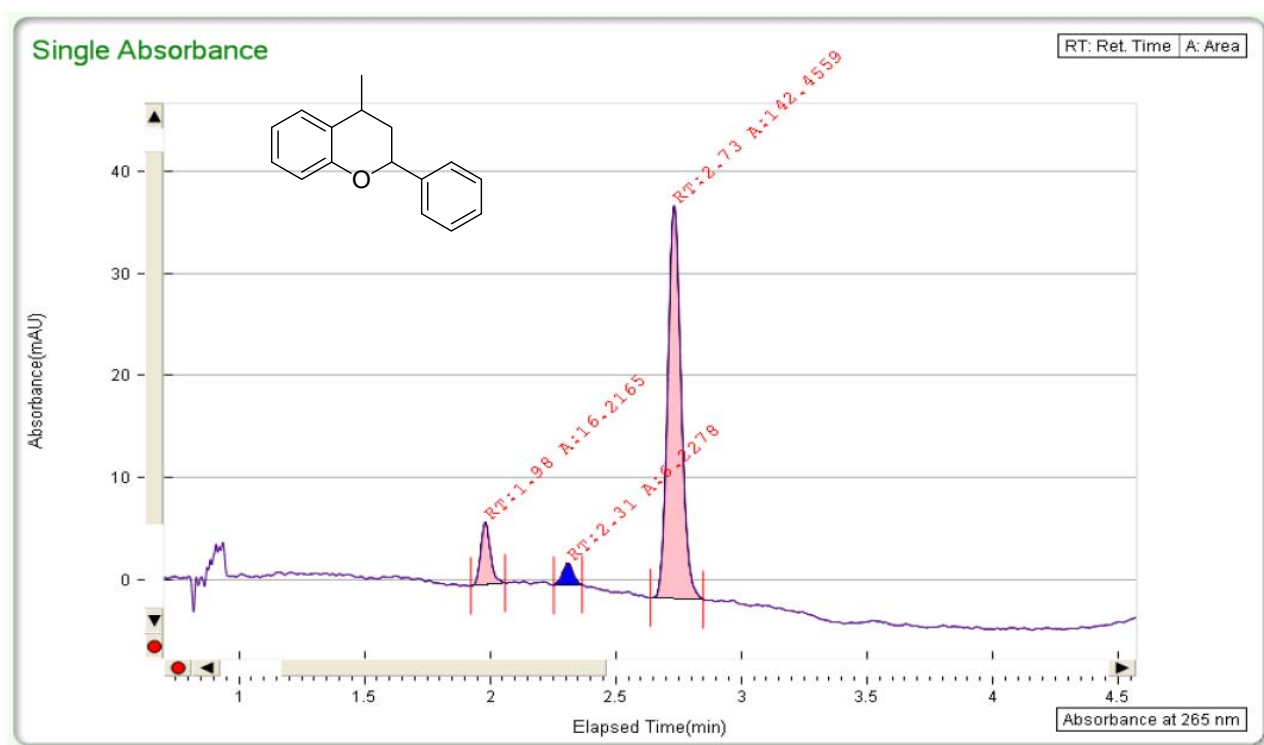
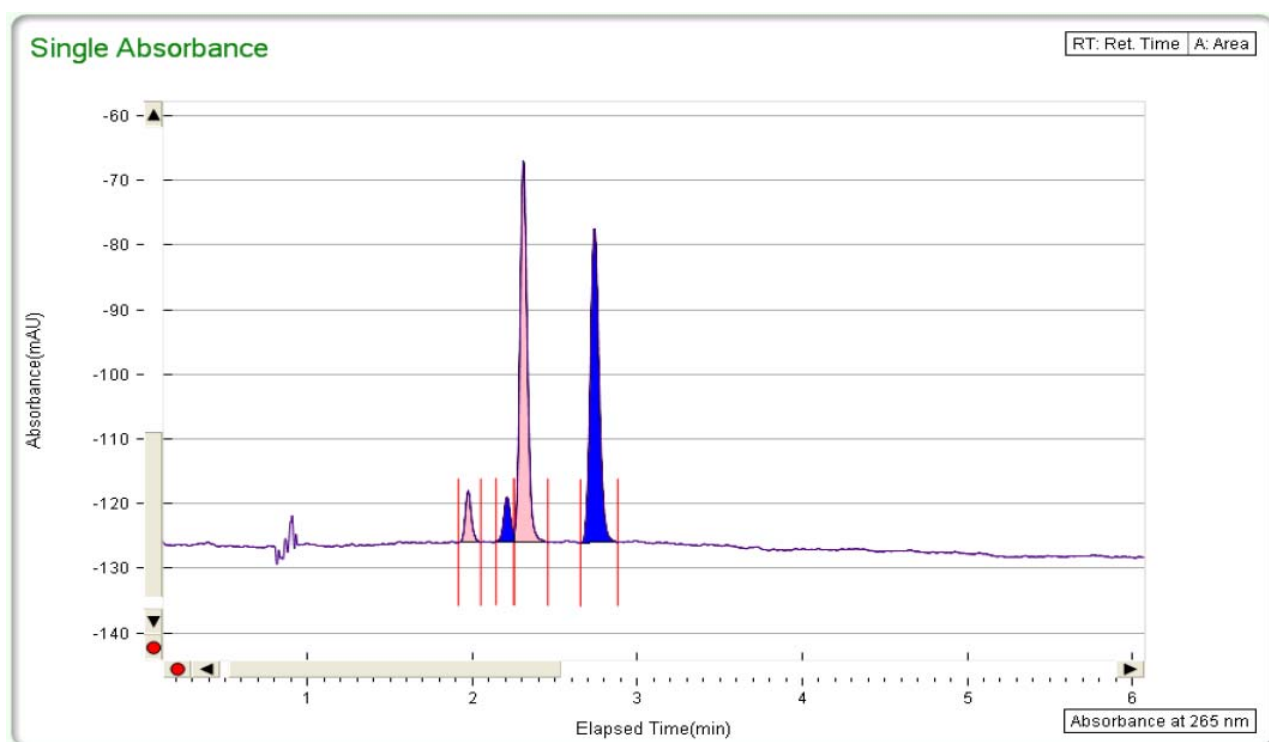
Peak Info					
Number	Area %	Area	RT (min)	St. (min)	End (min)
1	2.0901	45.3317	8.73	8.5658	8.9576
2	97.9099	2123.5746	9.91	9.6311	10.3612

Figure S33: SFC chromatograms of compound **4n**.



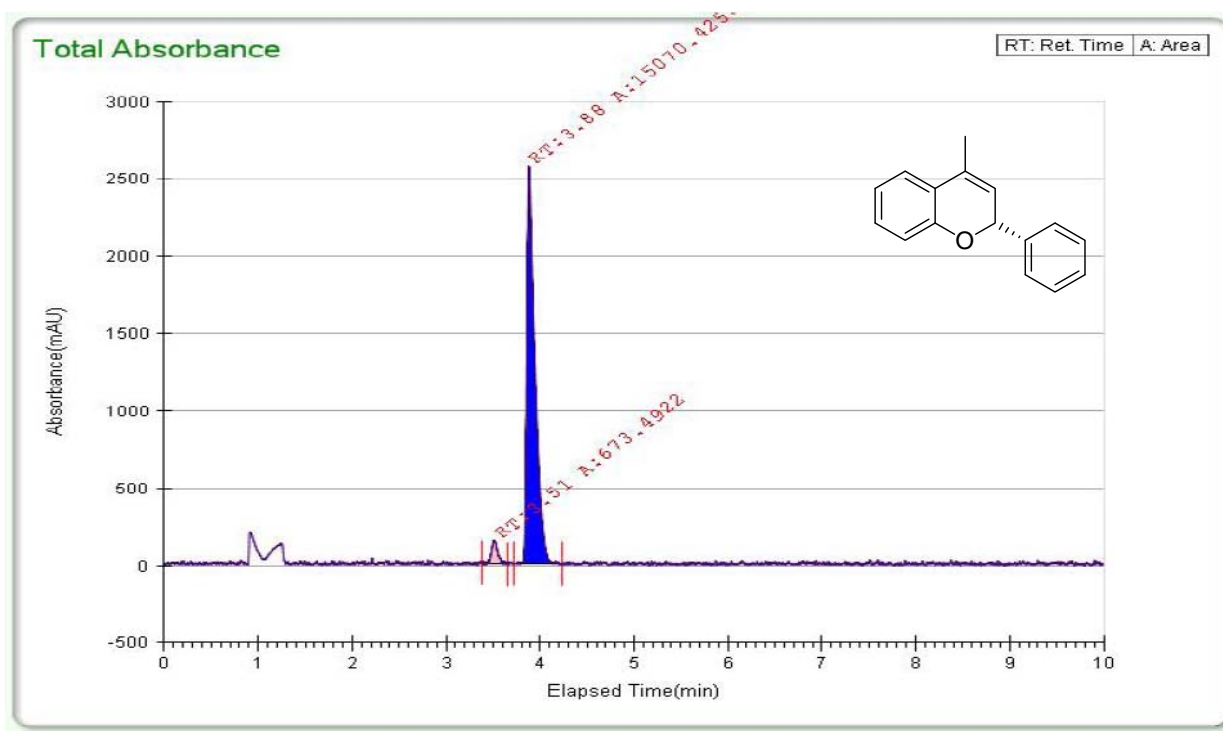
Peak Info					
Number	Area %	Area	RT (min)	St. (min)	End (min)
1	3.2721	394.7094	8.13	7.883	8.4448
2	96.7279	11668.208	9.33	9.0116	9.8784

Figure S34: SFC chromatograms of compound **4o**

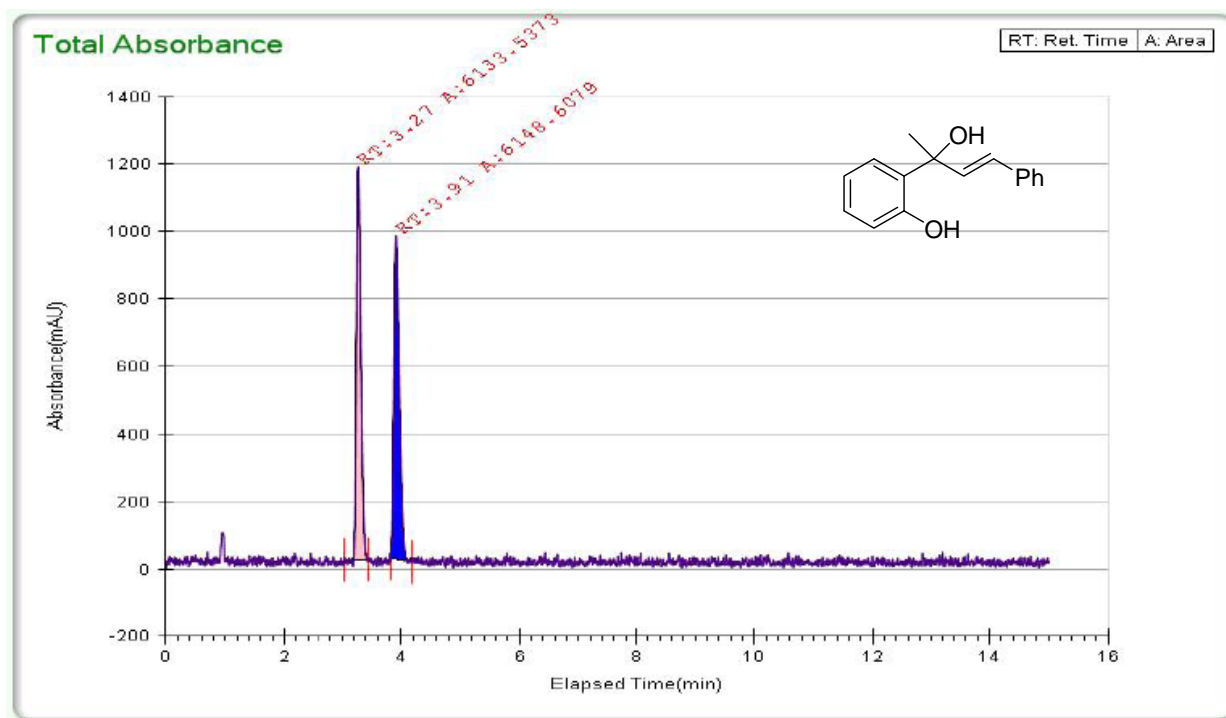


Peak Number	Area %	Area	RT (min)	St. (min)	End (min)
1	9.8341	16.2165	1.98	1.9232	2.0582
2	3.7767	6.2278	2.31	2.2532	2.3648
3	86.3892	142.4559	2.73	2.6382	2.8465

Figure S35: SFC chromatograms of compound 7a

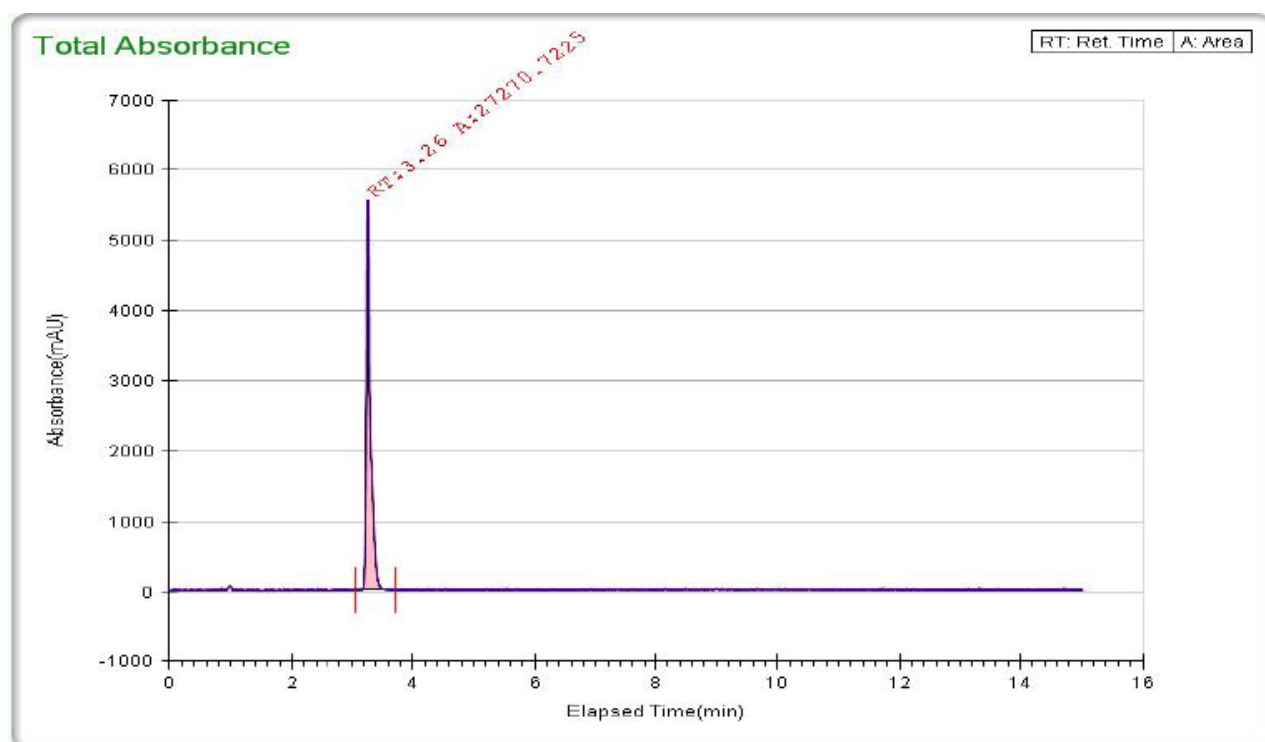


**Figure S36:** SFC chromatogram of **4a** (91% ee) obtained in the reaction starting from optically pure **3a** (ee > 99%) and chiral catalyst **5a**.

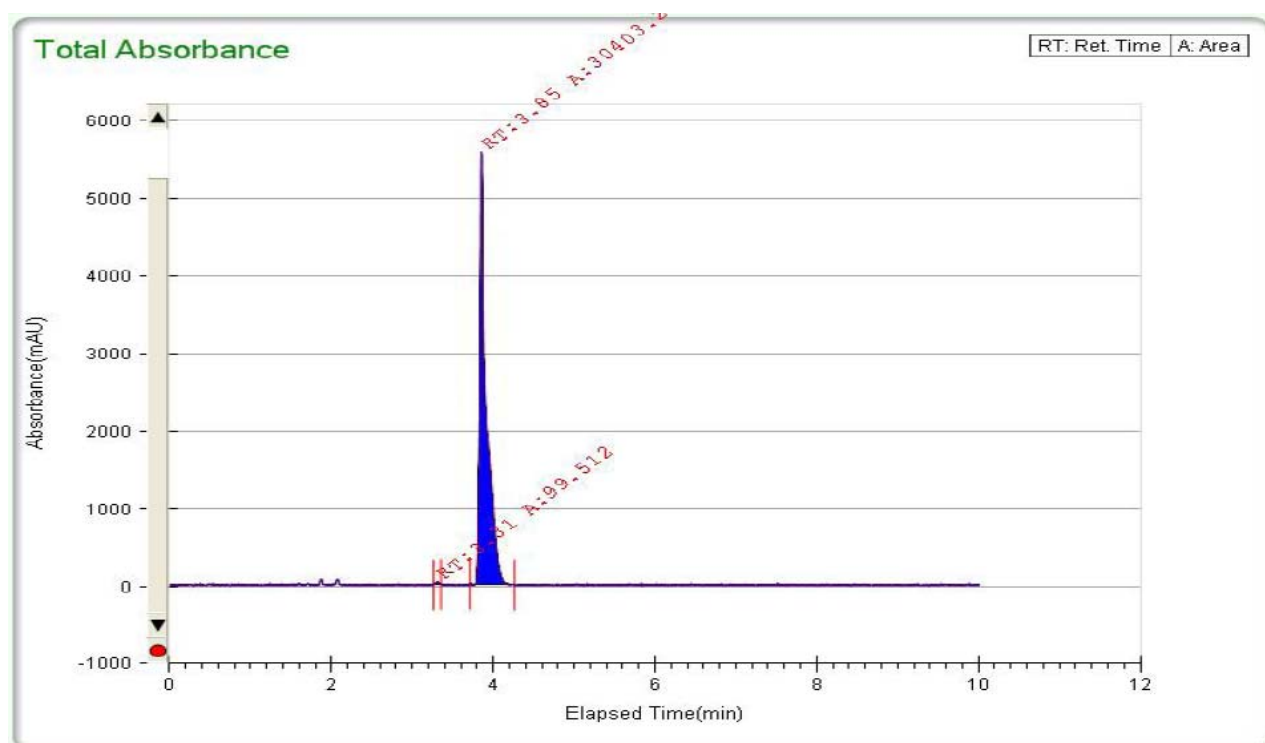


**Figure S37:** SFC chromatogram of racemic **3a**





Peak Info					
Number	Area %	Area	RT (min)	St. (min)	End (min)
1	100	27270.7225	3.26	3.0673	3.719



Peak Info					
Number	Area %	Area	RT (min)	St. (min)	End (min)
1	0.3262	99.512	3.31	3.2599	3.3533
2	99.6738	30403.2863	3.85	3.7116	4.2616

**Figure S38:** SFC chromatograms of the two enantiomers of **3a**.