Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Asymmetric Organocatalytic Double 1,6-Addition: Rapid Access to Chiral Chromans with Molecular Complexity

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Supporting Information

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Supporting Information

1. General Information:

All reactions were performed in flame-dried glassware under argon atmosphere unless otherwise stated. Liquids and solutions were transferred with syringes. Solvents used were dried and purified by following standard procedures.

Technical grade solvents for extraction or chromatography (ethyl acetate, and petroleum ether) were distilled prior to use. $CDCl_3$ was stored over 4A° molecular sieves. Used chemicals were purchased from Sigma-Aldrich, TCI, Alfa-Aesar and Sisco Research Laboratories (SRL) used without further purification. All the liquid chemicals distilled freshly prior to use.

Analytical thin-layer chromatography (TLC) was performed on using pre-coated aluminium-backed plates (Merck Kieselgel 60 F254) and visualized by UV radiation, basic aqueous potassium permangante ($KMnO_4$), *p*-anisaldehyde stains and heat as developing agents. Flash column chromatography was performed on silica gel 60 (40–63 μm, 230–400 mesh, ASTM) from Merck using the indicated solvents. Organic solutions were concentrated under reduced pressure on Heidolph rotary evaporator.

NMR spectra were acquired on a JEOL JNM ECS-400 instrument running at 400 MHz for ^{1}H, 101 MHz ^{13}C and 376 MHz for ^{19}F respectively. Chemical shifts (δ) are reported in ppm relative to residual solvent signals ($CHCl_3$, 7.26 ppm for ^{1}H NMR, $CDCl_3$, 77.0 ppm for ^{13}C NMR). Data are reported as follows: chemical shift, multiplicity (br = broad singlet, s = singlet, d = doublet, dd = doublet of doublets, t = triplet, q = quartet, ddd = doublet of doublet of doublet, td = triplet of doublet, m = multiplet), coupling constants (Hz), and integration.

1,2-Dibromomethane was used as an internal standard to calculate NMR yields & diastereomeric ratio (dr) of products by ^{1}H NMR analysis of the crude mixture.

Optical rotations were measured on a Anton Paar MCP 200, $[\alpha]_D$ values are given in $deg \cdot cm^3 \cdot g^{-1} \cdot dm^{-1}$; concentration (c) in g $(100\ mL)^{-1}$.

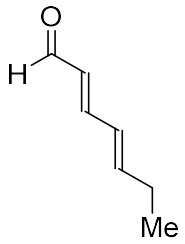
The enantiomeric excess (*ee*) of products was determined by High Performance liquid Chromatography (Waters modular system.) using Daicel Chiralpak IA, IB, IC, ODH, and ADH columns as chiral stationary phases. All the HRMS data were recorded on XEVO G2-XS QTOF. All the X-ray data were recorded on Bruker D8 venture instrument.

Dienals **1a, 1b, 1c** and amines **3a, 3b, 3g** has been obtained from commercial sources. Dienals **1d-1f** [S1], **1g-1i** [S2], *p*-QM's **2a-2k** [S3] and Amines **3c-3f** [S4-S7] were synthesized according to the procedure in the literature.

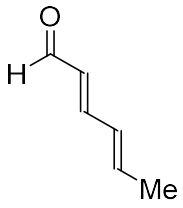
2. List of Substrates used.

The list of substrates for GP-1 and GP-2 are given bellow.

2.1. List of 2,4 dienals.



1a



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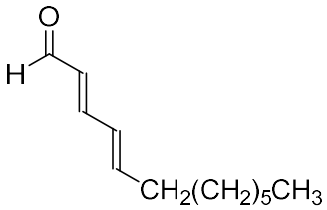
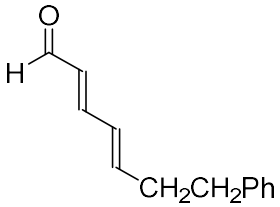
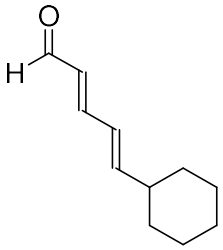


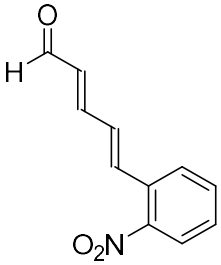
1c



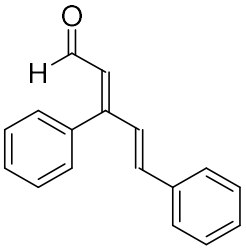
1d



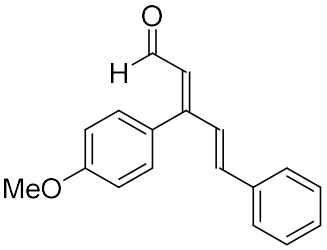
1e



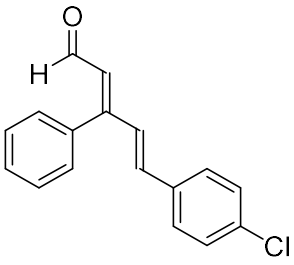
1f



1g

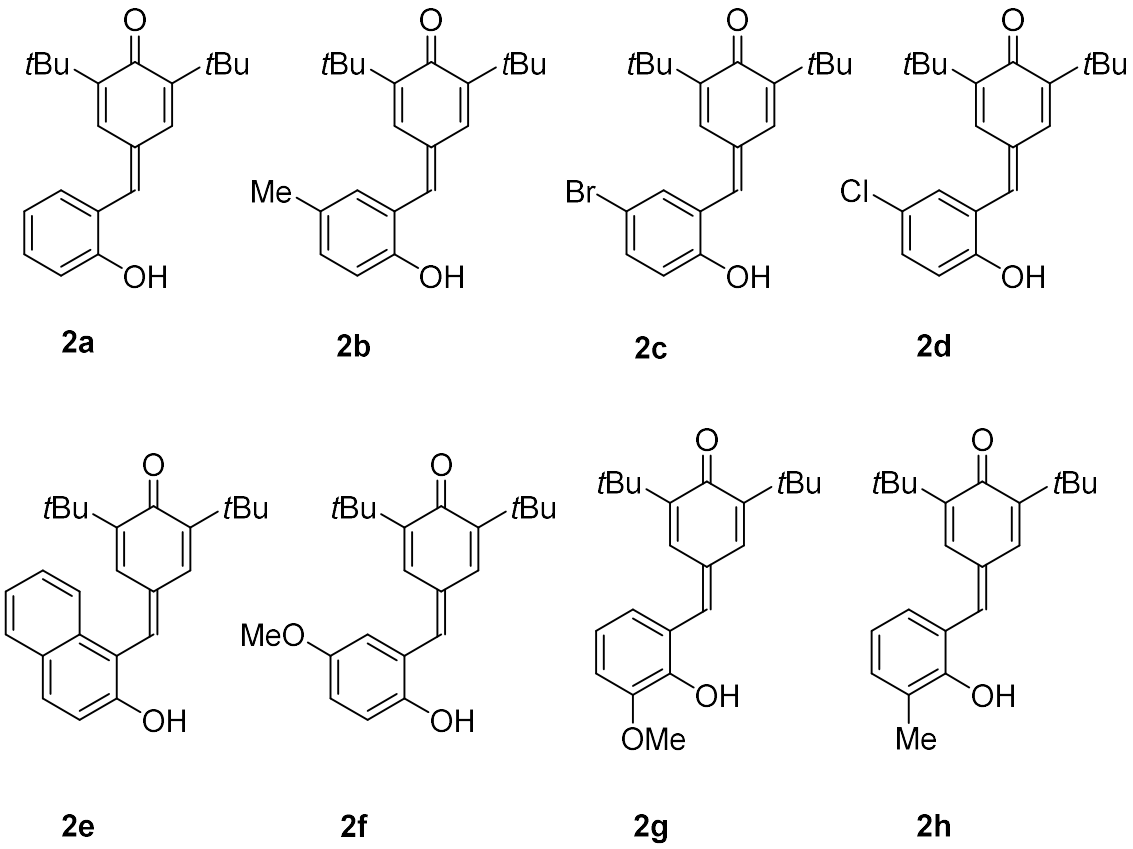


1h



1i

2.2 List of *p*-QM's.

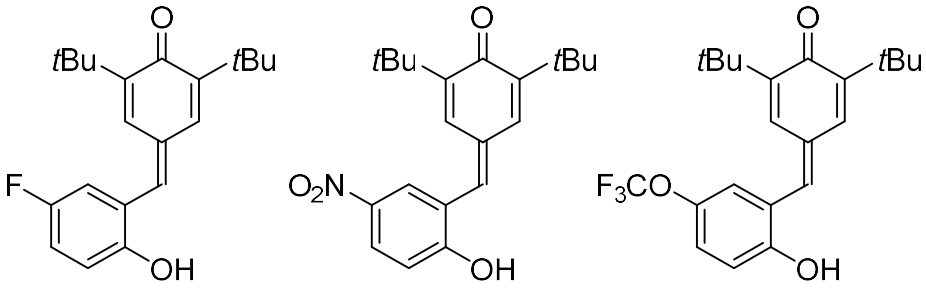


2a **2b** **2c** **2d**

2e **2f** **2g** **2h**

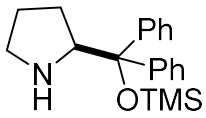
2.3 List of unreacted *p*-QM's.

Following substrates remains un-reacted according to GP-1 and GP-2.

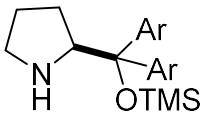


2i **2j** **2k**

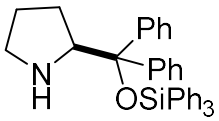
2.4 List of amines.



3a

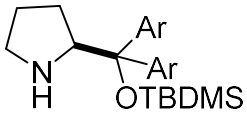


3b

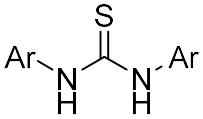


3c

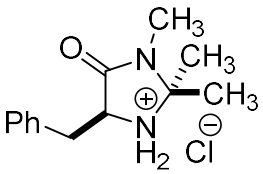
Ar = 3,5-$(CF_3)_2$-C_6H_3



3d

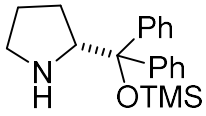


3e



3f

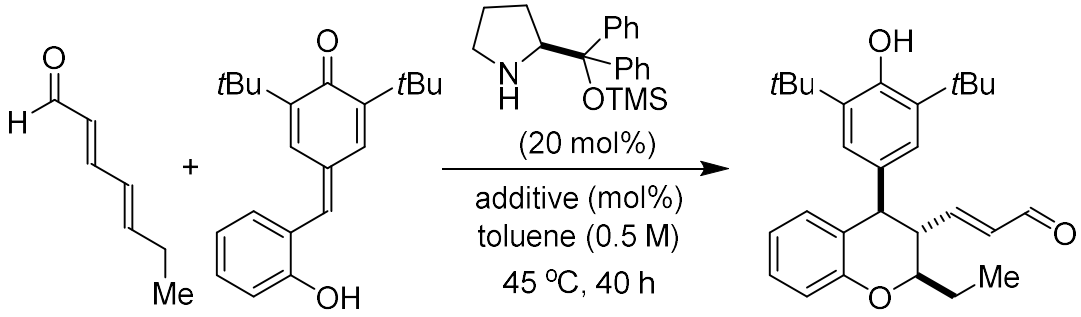
Ar = 3,5-$(CF_3)_2$-C_6H_3



3g

3. Optimization Table.

3.1. Table 1: Additive Screening.[a]

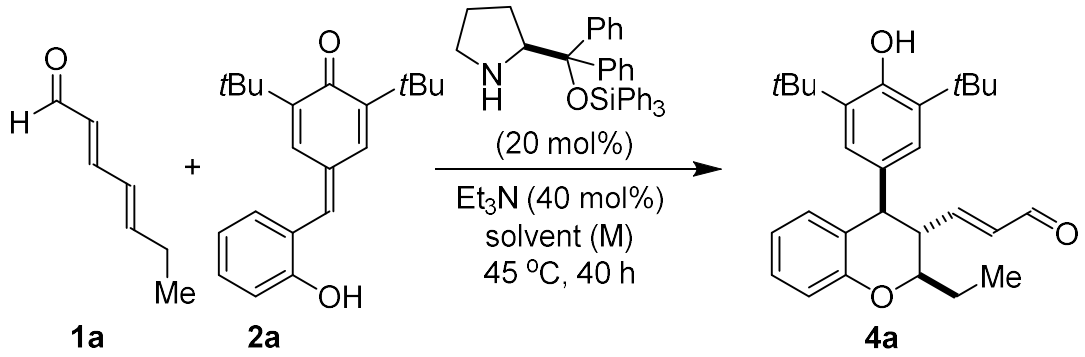


1a **2a** **4a**

Entry	1a/2a	Additive (mol%)	Yield (%)[b]	d.r.[c]	*ee* (%)[d]
1	1/2	$PhCO_2H$ (20)	42	2:1	-
2	1/1.2	$PhCO_2H$ (20)	23	2:1	71
3	2/1	$PhCO_2H$ (20)	28	2.5:1	67
4	2/1	4-NO_2-BA (20)	24	3:1	-
5	1/2	DABCO (20)	39	1.5:1	70
6	2/1	DABCO (20)	23	1.2:1	65
7	2/1	DABCO (40)	47	2:1	-
8	2/1	DIPEA (20)	58	1.2:1	71
9	1/1	DIPEA (40)	60	1:1	64
10	1/1.2	DIPEA (40)	53	1.1:1	61
11	1/1.5	DBU (20)	52	1.2:1	-
12	1/1.5	DBU (40)	60	1.5:1	62
13	1/1	DBU (40)	27	1.6:1	67
14	2/1	Et_3N (20)	44	1.4:1	60
15	1/1	Et_3N (40)	60	1.2:1	81
16	1/1	Et_3N (20)	68	1.2:1	-
17	1/1.5	Et_3N (40)	98	1:1:1	-
18	**2/1**	**Et_3N (40)**	**52**	**1.4:1**	**81**
19	1/1	Et_3N (100)	54	1:1	-

[a] unless untill mentioned all reactions were carried out in a 0.1 mmol scale by taking 1a (2.0 equiv) & 2a (1.0 equiv). [b] yield was measured by ^{1}H-NMR analysis of the crude reaction mixture. [c] diastereomeric mixture measured by ^{1}H-NMR analysis of the crude reaction mixture. [d] enantiomeric excess was measured by HPLC on a chiral stationary phase.

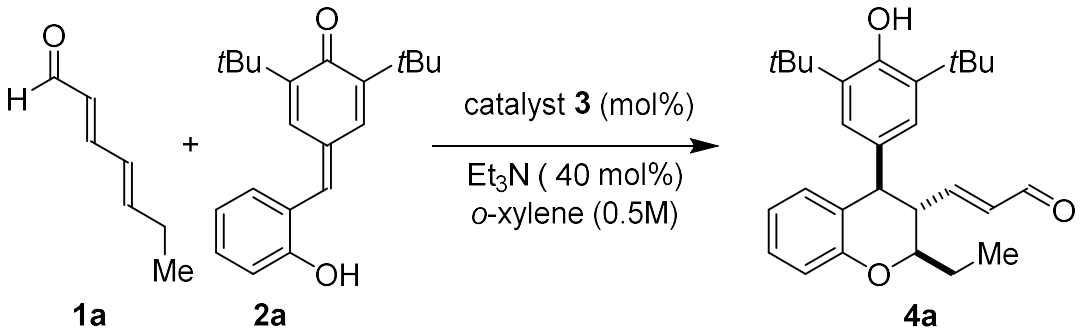
3.2. Table 2: Solvent Screening.[a]



Entry	Solvent (M)	Yield (%)[b]	d.r.[c]	*ee* (%)[d]
1	toluene (0.5)	69	3:1	85
2	CH_2Cl_2 (0.5)	54	3.5:1	94
3	$CHCl_3$ (0.5)	60	2.5:1	85
4	CH_3CN (0.5)	42	1.2:1	-
5	THF (0.5)	63	1.8:1	92
6	Et_2O (0.5)	23	2.2:1	92
7	IPA (0.5)	21	4:1	-
8	benzene (0.5)	68	3:1	94
9	*p*-xylene (0.5)	74	2.5:1	92
10	*m*-xylene (0.5)	71	2.4:1	-
11	mesitylene (0.5)	69	2.5:1	-
12	***o*-xylene (0.5)**	**63**	**4.5:1**	**94**
13	*o*-xylene (0.25)	69	3:1	85
14	*o*-xylene (0.1)	68	3:1	85
15	*o*-xylene (0.5) brine (3 equiv.)	67	3.5:1	90

[a] unless untill mentioned all reactions were carried out in a 0.1 mmol scale by taking 1a (2.0 equiv) & 2a (1.0 equiv). [b] yield was measured by ^{1}H-NMR analysis of the crude reaction mixture. [c] diastereomeric mixture measured by ^{1}H-NMR analysis of the crude reaction mixture. [d] enantiomeric excess was measured by HPLC on a chiral stationary phase.

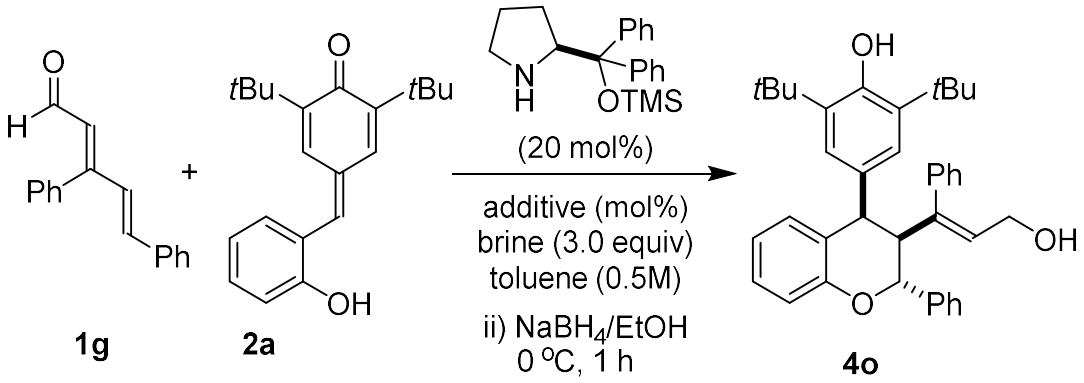
3.3. Table 3: Screening of Catalyst & Other Parameters.[a]



Entry	catalyst (mol%)	Temp. (°C)	Time (h)	Yield (%)[b]	d.r.[c]	ee (%)[d]
1	3c (20)	rt	40	67	2.5:1	88
2	3c (10)	10	40	68	2:1	93
3[e]	3c (10)	10	40	57	3.5:1	85
4	3c (20)	10	24	62	2.5:1	85
5	3c (20)	10	14	56	3:1	87
6	3a (20)	10	48	90	1.1:1	67
7[f]	3b (20)	10	48	36	-	-
8	**3c (20)**	**10**	**48**	**92(84)**	**8:1**	**98**
9	3d (20)	10	48	73	1.3:1	75
10	3e (20)	10	48	n.r	-	-
11	3f (20)	10	48	n.r	-	-
12	3c (20)	10	40	72	5:1	94
13	3c + 3e (20+30)	10	48	14	1:1	-

[a] unless untill mentioned all reactions were carried out in a 0.1 mmol scale by taking 1a (2.0 equiv) & 2a (1.0 equiv). [b] yield was measured by ^{1}H-NMR analysis of the crude reaction mixture, isolated yield in parentheses. [c] diastereomeric mixture measured by ^{1}H-NMR analysis of the crude reaction mixture. [d] enantiomeric excess was measured by HPLC on a chiral stationary phase. [e] 20 mol% Et_3N was used as an additive. [f] mixture of several isomers were found from ^{1}H NMR analysis of crude reaction mixture.

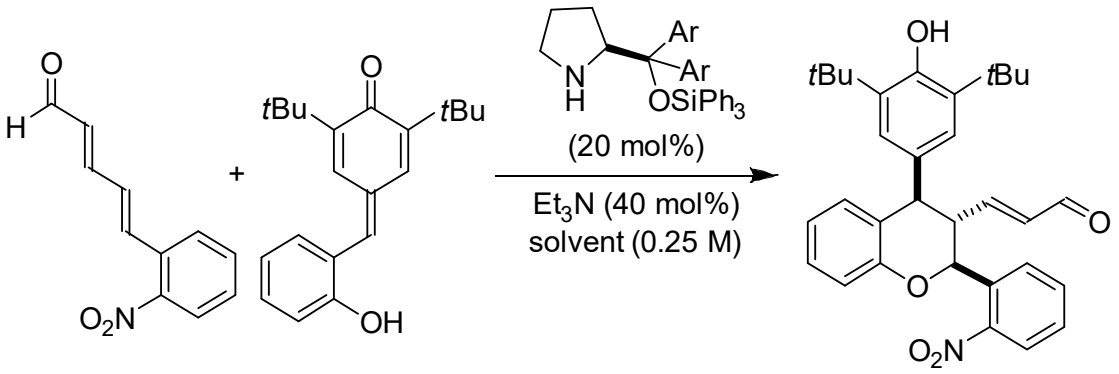
3.4. Table 4: Miscellaneous Optimization-1.[a]



Entry	1g/2a	Additive (mol%)	Temp. (°C)	Time (h)	Yield (%)[b]	d.r.[c]	*ee* (%)[d]
1[g]	2/1	Et_3N (20)	rt	12	64	5:1	82
2	2/1	$PhCO_2H$ (20)	rt	12	20	9:1	81
3	2/1	Et_3N (20)	rt	12	70	6:1	83
4	2/1	NaOAc (20)	rt	12	54	10:1	75
5	2/1	DIPEA (20)	rt	12	67	5:1	79
6	2/1	K_2CO_3 (20)	rt	12	40	5:1	55
7[h]	2/1	Et_3N (20)	rt	12	69	90:1	76
8	2/1	Et_3N (20)	rt	40	45	30:1	70
9	2/1	Et_3N (20)	80	12	37	10:1	33
10	1/1	Et_3N (20)	rt	12	47	46:1	-
11	1/1.5	Et_3N (20)	rt	12	44	20:1	-
12	4/1	Et_3N (20)	rt	12	71	10:1	63
13	**2/1**	**Et_3N (40)**	**rt**	**12**	**92(83)**	**45:1**	**90**

[a] unless untill mentioned all reactions were carried out in a 0.1 mmol scale by taking 1g (2.0 equiv) & 2a (1.0 equiv). [b] yield was measured by ^{1}H-NMR analysis of the crude reaction mixture, isolated yield in parentheses. [c] diastereomeric mixture measured by ^{1}H-NMR analysis of the crude reaction mixture. [d] enantiomeric excess was measured by HPLC on a chiral stationary phase. [g] reaction performed without brine. [h] reaction carried out by taking 3c instead of 3a.

3.5. Table 5: Miscellaneous Optimization-2.[a]



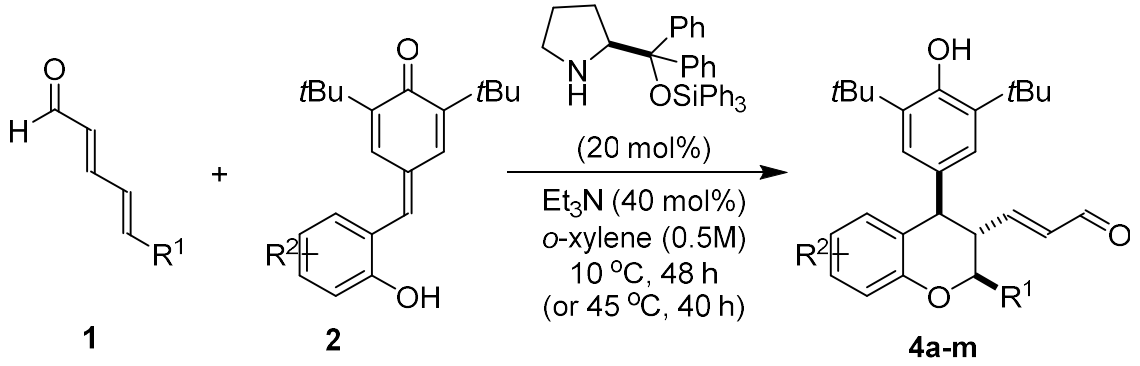
1f **2a** **4l**

Entry	1f/2a	Solvent (M)	Temp. (°C)	Time	Conv. (%)[b]	d.r.[c]	*ee* (%)[d]
1	2/1	*o*-xylene	10	48h	n.r	-	-
2	1/1	*o*-xylene	45	40h	n.r	-	-
3	1/1	$CHCl_3$	10	48h	15	5:1	-
4	1/1	CH_2Cl_2	45	40h	24	2:1	60
5	1/1	toluene	45	40h	7	-	-
6	1/2	$CHCl_3$	45	5d	40	2:1	-
7	1/2	$CHCl_3$ (0.5)	45	5d	27	2:1	-
8	1/2	$CHCl_3$	60	5d	47	2.5:1	-
9	1/1	$CHCl_3$/*o*-xylene (1:2)	60	5d	12	-	-
10	1/2	$CHCl_3$	80	4d	6	-	-
11	**1/4**	**$CHCl_3$ (0.1)**	**45**	**7d**	**54(36)**	**3:1**	**76**
12[i]	1/2	$CHCl_3$	10	4d	12	2:1	-
13[i]	1/2	$CHCl_3$	45	10d	41	3:1	-

[a] unless untill mentioned all reactions were carried out in a 0.1 mmol scale. [b] conversion was measured by ^{1}H-NMR analysis of the crude reaction mixture, isolated yield in parentheses. [c] diastereomeric mixture measured by ^{1}H-NMR analysis of the crude reaction mixture. [d] enantiomeric excess was measured by HPLC on a chiral stationary phase. [i] 1.0 equiv Et_3N was used as an additive.

4. Asymmetric Organocatalytic Double 1,6-Addition: Synthesis of Chiral Chromans.

4.1. General Procedure for formation of chroman derivatives from linear 2,4 dienals (GP-1)

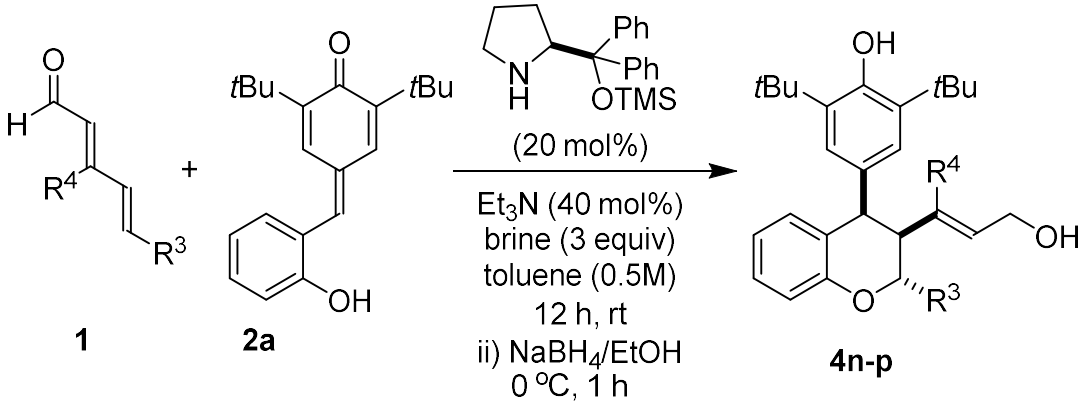


All the reactions were carried out in *o*-xylene (synthesis grade, >98%), without any precaution to exclude air and moisture (open air chemistry on the benchtop). An ordinary vial equipped with a Teflon-coated stir bar and a plastic screw cap was charged with amine **3c** (0.02 mmol, 10.2 mg, 0.2 equiv). Then *o*-xylene (0.2 mL, 0.5 M) and the additive triethylamine (0.04 mmol, 6.0 µL, 0.4 equiv) were sequentially added. The reaction mixture was stirred in a cooling bath maintained at 10 °C (or 45 °C) for 5 minutes to let the mixture reaching a uniform temperature. The reaction was started by the addition of α,β,γ,δ-unsaturated aldehyde (2.0 equiv, 0.2 mmol) and the reaction mixture was stirred at 10 °C (or 45 °C) for 15 min. After that, *p*-QM derivative (1.0 equiv, 0.1 mmol) was added and purged with argon then the vial was sealed and immerged in the cooling bath again maintained at 10 °C (or 45 °C). Stirring was continued over 48 h.

The progress of the reaction was monitored by TLC and by ^{1}H NMR analysis of the aliquot taken from the crude mixture using CH_2Br_2 as internal standard. The analytically pure product is obtained by column chromatography on silica gel using petroleum ether and ethyl acetate as eluent.

Racemic samples were prepared according to **GP-1** by using mixture of amine **3a** (0.010 mmol, 3.4 mg, 0.1 equiv) and amine **3g** (0.010 mmol, 3.4 mg, 0.1 equiv) instead of amine **3c.**

4.2. General Procedure for formation of chroman derivatives from branched 2,4 dienals (GP-2).

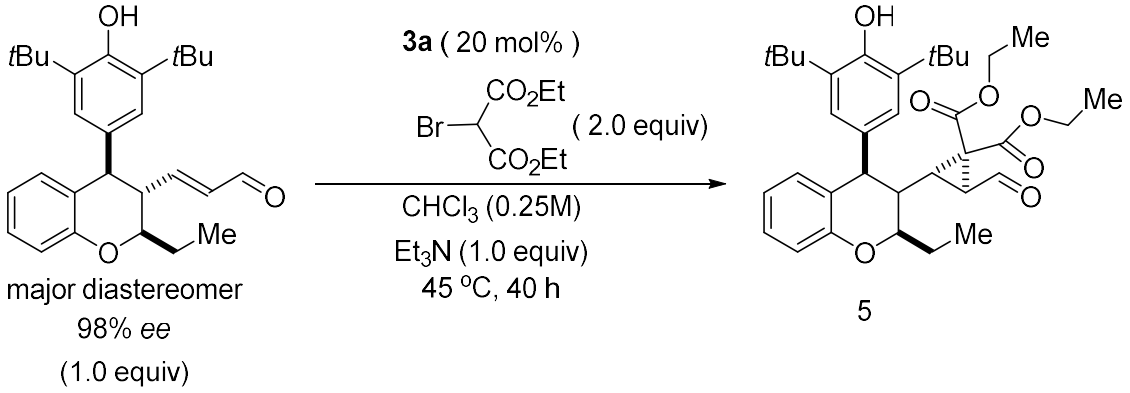


All the reactions were carried out in toluene (HPLC grade, >98%), without any precaution to exclude air and moisture (open air chemistry on the benchtop). An ordinary vial equipped with a Teflon-coated stir bar and a plastic screw cap was charged with amine **3a** (0.02 mmol, 6.5 mg, 0.2 equiv). Then toluene (0.2 mL, 0.5 M), the additive triethylamine (0.04 mmol, 6.0 µL, 0.4 equiv) and brine (0.6 mmol, 3.0 equiv) were sequentially added. The reaction mixture was stirred at room temperature for 5 minutes to let the mixture reaching a uniform temperature. The reaction was started by the addition of α,β,γ,δ-unsaturated aldehyde (2.0 equiv, 0.2 mmol) and the reaction mixture was stirred at room temperature for 15 min. After that, *p*-QM derivative (1.0 equiv, 0.1 mmol) was added and purged with argon then the vial was sealed and kept at room temperature. Stirring was continued over 12 h. Upon completion of the reaction the reaction mixture was diluted with 1.0 mL of ethanol and solid $NaBH_4$ (0.4 mmol, 4.0 equiv) were added and kept at 0 °C for 60 minutes. The reaction was quenched by adding few drops of water. Brine (5 mL) was added and resulted mixture was extracted with DCM (3 X 10 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*.

The progress of the reaction was monitored by TLC and by ^{1}H NMR analysis of the aliquot taken from the crude mixture using CH_2Br_2 as internal standard. The analytically pure product is obtained by column chromatography on silica gel using petroleum ether and ethyl acetate as eluent.

Racemic samples were prepared according to **GP-2** by using mixture of amine **3a** (0.010 mmol, 3.4 mg, 0.1 equiv) and amine **3g** (0.010 mmol, 3.4 mg, 0.1 equiv) instead of amine **3a.**

4.3. General Procedure for asymmetric synthesis of cyclopropane derivative from α,β-unsaturated Aldehyde (4a) (GP-3).[S8]

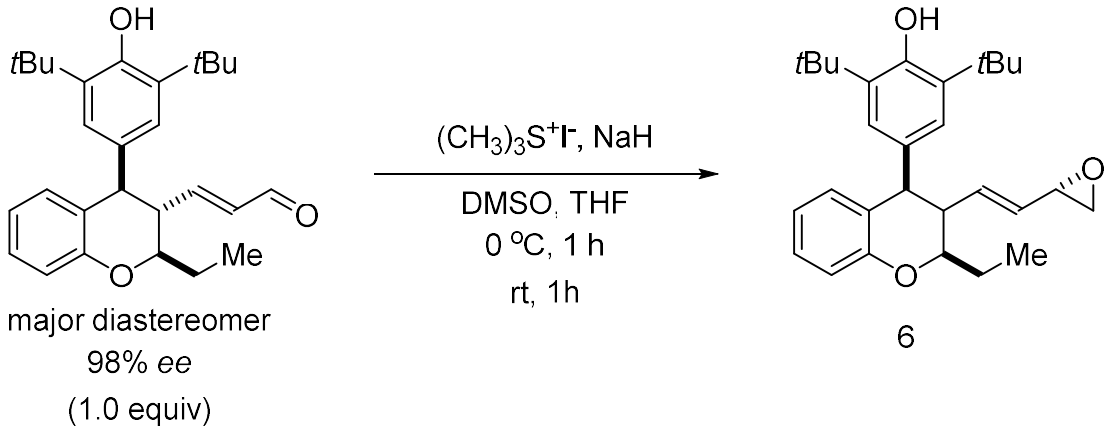


All the reactions were carried out in chloroform (HPLC grade, >98%), without any precaution to exclude air and moisture (open air chemistry on the benchtop). An ordinary vial equipped with a Teflon-coated stir bar and a plastic screw cap was charged with amine **3a** (0.02 mmol, 6.5 mg, 0.2 equiv). Then chloroform (0.4 mL, 0.25 M) and the additive triethylamine (0.1 mmol, 14.0 µL, 1.0 equiv) were sequentially added. The reaction mixture was stirred in a heating bath maintained at 45 °C for 5 minutes to let the mixture reaching a uniform temperature. The reaction was started by the addition of α,β-unsaturated aldehyde (0.1 mmol, 42.0 mg, 1.0 equiv) and the reaction mixture was stirred at 45 °C for 15 min. After that, diethyl bromomalonate (0.2 mmol, 35.0 µL, 2.0 equiv) was added and purged with argon then the vial was sealed and immerged in the heating bath again 45 °C. Stirring was continued over 40 h.

The progress of the reaction was monitored by TLC and by ^{1}H NMR analysis of the aliquot taken from the crude mixture using CH_2Br_2 as internal standard. The analytically pure product is obtained by column chromatography on silica gel using petroleum ether and ethyl acetate as eluent.

Racemic samples were prepared according to **GP-3** by using mixture of amine **3a** (0.010 mmol, 3.4 mg, 0.1equiv) and amine **3g** (0.010 mmol, 3.4 mg, 0.1 equiv) instead of amine **3a.**

4.4. General Procedure for Corey-Chaykovsky reaction of α,β-unsaturated Aldehyde (4a) (GP-4).[S9]

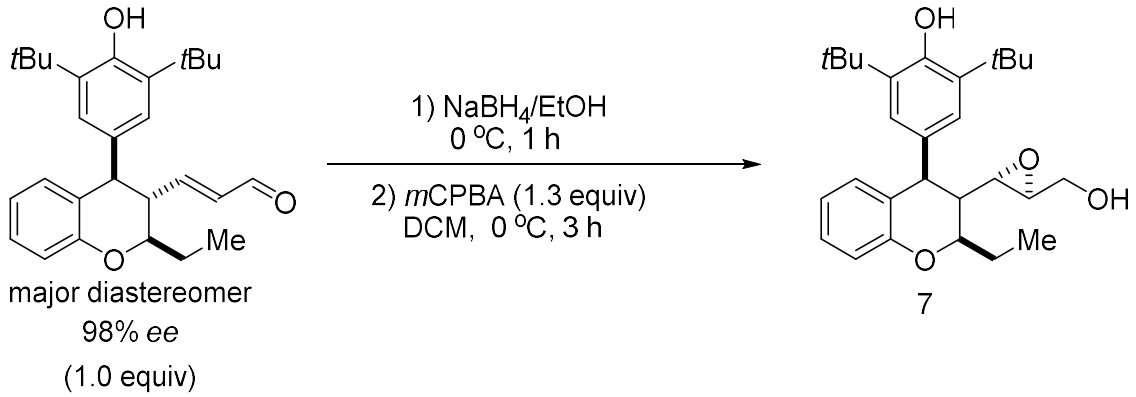


A 5 mL oven-dried Schlenk flask was charged with NaH (60 % dispersion in oil, washed hexanes (5 x 5 mL) and dried under vacuum, 12.0 mg, 0.31 mmol, 3.1 equiv). Dry THF (0.15 mL) and DMSO (0.15 mL) were added to the flask and the resulting slurry solution was cooled to 0 ºC. Trimethylsulfonium iodide (61.0 mg, 0.3 mmol, 3.0 equiv) and DMSO (0.25 mL) were added to a separate oven-dried Schlenk flask. The solution was transferred slowly to the NaH solution via cannula. After the transfer was complete, α,β-unsaturated aldehyde **4a** (0.1 mmol, 42.0 mg, 1.0 equiv) was then added to the reaction mixture in one portion. The resulting mixture was stirred at 0 °C for 1 h, then at room temperature for another 1 h and quenched with distilled water (1 mL). The resulting mixture was then diluted with diethyl ether (5 mL) and brine (10 mL). The two layers were separated, and the aqueous layer was back extracted with diethyl ether (2 X 20 mL). The combined organic layer was dried with $MgSO_4$, filtered, and concentrated *in vacuo*.

The progress of the reaction was monitored by TLC and by ^{1}H NMR analysis of the aliquot taken from the crude mixture using CH_2Br_2 as internal standard. The analytically pure product is obtained by column chromatography on silica gel using petroleum ether and ethyl acetate as eluent.

Racemic sample was prepared according to **GP-4** by taking *rac*-**4a** instead of **4a.**

4.5. General Procedure for formation of epoxide ring from α,β-unsaturated aldehyde (GP-5).[S2]



In an oven dried ordinary vial equipped with a Teflon-coated stir bar and a plastic screw cap α,β-unsaturated aldehyde **4a** (0.1 mmol, 42.0 mg, 1.0 equiv) was taken and diluted with 1.0 mL of ethanol. Then to this mixture solid $NaBH_4$ (0.4 mmol, 4.0 equiv) were added and kept at 0 °C for 60 minutes. The reaction was quenched by adding few drops of water. Brine (5 mL) was added and resulted mixture was extracted with DCM (3 X 10 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*.

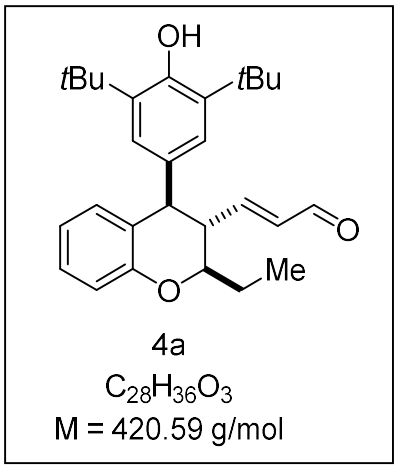
The analytically pure product was obtained by column chromatography on silica gel using petroleum ether and ethyl acetate as eluent.

Allyllic alcohol (36.0 mg, 0.085 mmol) obtained from above procedure was placed in a round bottom flask and dissolved in DCM (0.2 mL) at 0 °C. *meta*-Chloroperoxybenzoic acid (*m*CPBA, 1.3 equiv, 0.11 mmol) was added and the reaction mixture stirred for 3 h. Then the reaction was diluted with 10 mL of DCM and washed with $NaHCO_3$ solution (2 times) and brine. The organic phase was dried over Na_2SO_4 and filtered. Solvent was evaporated in vacuo and the crude reaction mixture purified by column chromatography on silica gel using petroleum ether and ethyl acetate as eluent.

Racemic sample was prepared according to **GP-5** by taking *rac*-**4a** instead of **4a.**

5. Results & Characterization.

5.1. (*E*)-3-((2R,3S,4R)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-ethylchroman-3-yl)acrylaldehyde (4a).



According to **GP-1** compound **(4a)** was prepared by using **1a** (22.0 µL, 0.2 mmol, 2.0 equiv) **2a** (31.0 mg, 0.1 mmol, 1.0 equiv), triethylamine (6.0 µL, 0.04 mmol, 0.4 equiv) and **Amine 3c** (10.2 mg, 0.02 mmol) in *o*-xylene for 48 h at 10 ºC.

Column chromatographic purification (petroleum ether/EtOAc 99:1 to 97:3) afforded **4a** (major diastereomer) as pale yellow solid (35.5 mg, 84%).

Melting Point: 108-110 ºC

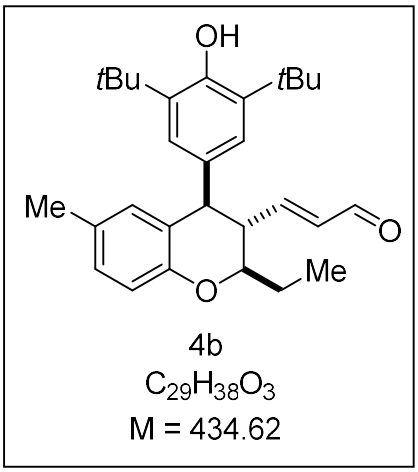
$[\alpha]_D^{20}$ = +16.0 (c = 0.4, CH_2Cl_2).

HPLC: Daicel CHIRALPAK IC column; *n*-hexane/*i*PrOH = 200/1; flow rate = 0.2 mL/min; T = 25 ºC; retention time: 46.24 min (major), 52.66 min (minor), *ee*: 98 %.

HRMS (ESI): *m/z* $[M-H]^+$ Calculated for **$C_{28}H_{35}O_3^+$:** 419.2586; Found 419.2588.

^{1}H NMR (400 MHz, $CDCl_3$) : δ 9.41 (d, *J* = 7.8 Hz, 1H), 7.13-70.9 (m, 1H), 6.88 (d, *J* = 8.2 Hz, 1H), 6.77 (d, *J* = 4.0 Hz, 2H), 6.74 (s, 2H), 6.52 (dd, *J* = 15.7, 9.8 Hz, 1H), 5.69 (dd, *J* = 15.7, 7.8 Hz, 1H), 5.08 (s, 1H), 4.03 (ddd, *J* = 10.6, 8.0, 2.9 Hz, 1H), 3.92 (d, *J* = 10.8 Hz, 1H), 2.76 (q, *J* = 10.1 Hz, 1H), 1.77 ((dqd, *J* = 14.4, 7.5, 7.0, 3.2 Hz, 1H), 1.64-1.60 (m, 1H), 1.34 (s, 18H), 1.08 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 193.1, 155.7, 154.7, 152.7, 135.9, 135.2, 132.4, 130.2, 127.8, 125.6, 125.0, 120.7, 116.5, 78.7, 50.1, 48.6, 34.4, 30.5, 27.2, 9.2. **^{13}C NMR DEPT-135 (101 MHz, $CDCl_3$) :** δ 193.1, 155.8, 135.2, 130.2, 127.8, 125.6, 120.7, 116.5, 78.7, 50.1, 48.6, 30.5, 27.2, 9.2.

5.2. (*E*)-3-((2R,3S,4R)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-ethyl-6-methylchroman-3-yl)acrylaldehyde (4b).



4b

$C_{29}H_{38}O_3$

M = 434.62

According to **GP-1** compound **(4b)** was prepared by using **1a** (22.0 µL, 0.2 mmol, 2.0 equiv) **2b** (32.5 mg, 0.1 mmol, 1.0 equiv), triethylamine (6.0 µL, 0.04 mmol, 0.4equiv) and **Amine 3c** (10.2 mg, 0.02 mmol) in *o*-xylene for 48 h at 10 °C.

Column chromatographic purification (petroleum ether/EtOAc 99:1 to 97:3) afforded **4b** (major diastereomer) as pale yellow solid (35.0 mg, 80 %).

Melting Point: 128-130 °C

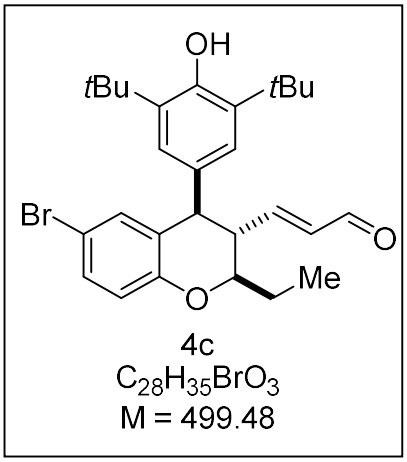
$[\alpha]_D^{20}$ = + 60.1. (c = 0.2, EtOH).

HPLC: Daicel CHIRALPAK ODH column; *n*-hexane/ *i*PrOH = 400/1; flow rate = 1.0 mL/min; T = 25 °C; retention time: 12.73 min (major), 17.58 min (minor) *ee*: > 99 %.

HRMS (ESI): *m/z* $[M+H]^+$ Calculated for **$C_{29}H_{39}O_3^+$:** 435.2899; Found 435.2882

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.41 (d, *J* = 7.8 Hz, 1H), 6.91 (d, *J* = 8.2 Hz, 1H), 6.78 (d, *J* = 8.2 Hz, 1H), 6.73 (s, 2H), 6.58 (s, 1H), 6.51 (dd, *J* = 15.6, 9.8 Hz, 1H), 5.66 (dd, *J* = 15.5, 7.9 Hz, 1H), 5.08 (s, 1H), 3.97 (ddd, *J* = 10.2, 8.7, 2.7 Hz, 1H). , 3.87 (d, *J* = 10.8 Hz, 1H), 2.72 (q, *J* = 10.1 Hz, 1H), 2.13 (s, 3H), 1.74 (dqd, *J* = 14.7, 7.5, 2.9 Hz, 1H), 1.63-1.59 (m, 1H), 1.34 (s, 18H), 1.06 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 193.1, 156.0, 152.7, 152.6, 135.8, 135.1, 132.5, 130.3, 129.9, 128.5, 125.6, 124.6, 116.2, 78.7, 50.6, 48.5, 34.4, 30.5, 27.2, 20.7, 9.2. **^{13}C NMR DEPT-135 (101 MHz, $CDCl_3$):** δ 193.1, 156.0, 135.1, 130.3, 128.5, 125.6, 116.2, 78.7, 50.6, 48.5, 30.5, 27.2, 20.7, 9.2.

5.3. (*E*)-3-((2R,3S,4R)-6-bromo-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-ethylchroman-3-yl)acrylaldehyde (4c).



According to **GP-1** compound **(4c)** was prepared by using **1a** (22.0 µL, 0.2 mmol, 2.0 equiv) **2c** (39.0 mg, 0.1 mmol, 1.0 equiv) triethylamine (6.0 µL, 0.04 mmol, 0.4 equiv) and **Amine 3c** (10.2 mg, 0.02 mmol) in *o*-xylene for 48 h at 10 °C.

Column chromatographic purification (petroleum ether/EtOAc 99:1 to 97:3) afforded **4c** (major diastereomer) as yellow solid (33.0 mg, 66%).

Melting Point: 156-158 °C

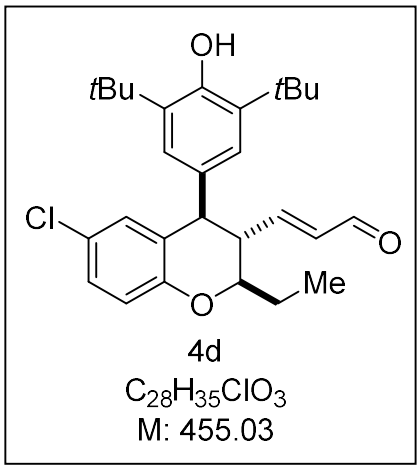
$[\alpha]_D^{20}$ = + 25.4. (c = 0.6, EtOH).

HPLC: Daicel CHIRALPAK ODH column; *n*-hexane/ *i*PrOH = 1000/1; flow rate = 1.0 mL/min; T = 25 °C; retention time: 16.57 min (major), 21.21 min (minor), *ee*: 96%.

HRMS (ESI): *m/z* $[M-H]^+$ Calculated for **$C_{28}H_{34}BrO_3^+$:** 497.1691; Found 497.1687.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.40 (d, *J* = 7.7 Hz, 1H), 7.22-7.19 (m, 1H), 6.90 (dd, *J* = 2.4, 1.1 Hz, 1H), 6.77 (d, *J* = 8.7 Hz, 1H), 6.71 (s, 2H), 6.47 (dd, *J* = 15.7, 9.8 Hz, 1H), 5.67 (dd, *J* = 15.5, 7.5 Hz, 1H), 5.11 (s, 1H), 3.99 (ddd, *J* = 10.1, 8.0, 3.0 Hz, 1H), 3.86 (d, *J* = 10.8 Hz, 1H), 2.71 (q, *J* = 10.1 Hz, 1H), 1.76 (dqd, *J* = 14.9, 7.5, 3.0 Hz, 1H), 1.64-1.60 (m, 1H), 1.35 (s, 18H), 1.06 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 192.9, 155.0, 154.0, 152.9, 136.1, 135.4, 132.6, 131.5, 130.8, 127.3, 125.5, 118.5, 112.8, 79.0, 49.8, 48.4, 34.4, 30.4, 27.1, 9.1. **^{13}C NMR DEPT-135 (101 MHz, $CDCl_3$):** δ 192.9, 155.0, 135.4, 132.6, 130.8, 125.5, 118.5, 79.0, 49.8, 48.4, 30.4, 27.1, 9.1.

5.4. (*E*)-3-((2R,3S,4R)-6-chloro-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-ethylchroman-3-yl)acrylaldehyde (4d).



According to **GP-1** compound **(4d)** was prepared by using **1a** (22.0 µL, 0.2 mmol, 2 equiv) **2d** (34.5 mg, 0.1 mmol, 1equiv) triethylamine (6.0 µL, 0.04 mmol, 0.4 equiv) and **Amine 3c** (10.2 mg, 0.02 mmol) in *o*-xylene for 48 h at 10 ºC.

Column chromatographic purification (petroleum ether/EtOAc 99:1 to 97:3) afforded **4d** (major diastereomer) as yellow solid (18.0 mg, 40 %).

Melting Point: 150-152 ºC

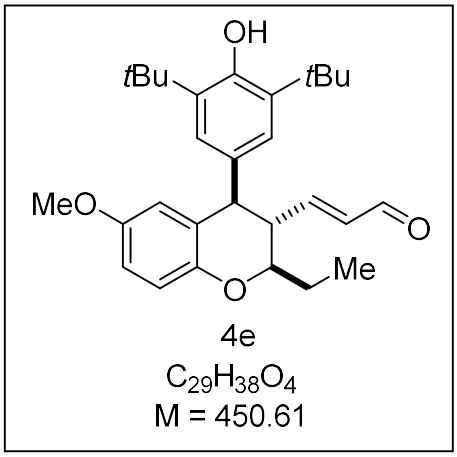
$[\alpha]_D^{20}$ = + 53.7. (c = 0.6., EtOH).

HPLC: Daicel Chiralpak ODH column; *n*-hexane/ *i*PrOH = 1000/1; flow rate = 1 mL/min; T = 25 ºC; retention time: 13.80 min (major), 19.63 min (minor), *ee*: 98%.

HRMS (ESI): *m/z* $[M-H]^+$ Calculated for **$C_{28}H_{34}ClO_3^+$:** 453.2196; Found 453.2194.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.40 (d, *J* = 7.7 Hz, 1H), 7.06 (dd, *J* = 8.6, 2.7 Hz, 1H), 6.82 (d, *J* = 9.0 Hz, 1H), 6.75 (d, *J* = 2.5 Hz, 1H), 6.72 (s, 2H), 6.47 (dd, *J* = 15.7, 9.8 Hz, 1H), 5.67 (dd, *J* = 15.7, 7.7 Hz, 1H), 5.11 (s, 1H), 3.99 (ddd, *J* = 10.7, 8.0, 2.9 Hz, 1H), 3.85 (d, *J* = 10.8 Hz, 1H), 2.72 (q, *J* = 10.1 Hz, 1H), 1.76 (dqd, *J* = 14.7, 7.3, 3.1 Hz, 1H), 1.64-1.57 (m, 1H), 1.35 (s, 18H), 1.07 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 192.9, 155.0, 153.4, 152.9, 136.1, 135.4, 131.5, 129.6, 127.9, 126.7, 125.5 (2C), 118.0, 79.1, 49.9, 48.5, 34.4, 30.5, 27.2, 9.2. **^{13}C NMR DEPT-135 (101 MHz, $CDCl_3$):** δ 192.9, 155.0, 135.4, 129.6, 127.9, 125.5, 118.0, 79.1, 49.9, 48.5, 30.5, 27.2, 9.2.

5.5. (*E*)-3-((2R,3S,4R)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-ethyl-6-methoxychroman-3-yl)acrylaldehyde (4e).



According to **GP-1** compound **(4e)** was prepared by using **1a** (22.0 µL, 0.2 mmol, 2.0 equiv) **2f** (34.0 mg, 0.1 mmol, 1.0 equiv) triethylamine (6.0 µL, 0.04 mmol, 0.4 equiv) and **Amine 3c** (10.2 mg, 0.02 mmol) in *o*-xylene for 48 h. at 10 ºC.

Column Chromatographic purification (petroleum ether/EtOAc 99:1 to 95:5) afforded **4e** (major diastereomer) as light yellow gummy liquid (32.5 mg, 72%).

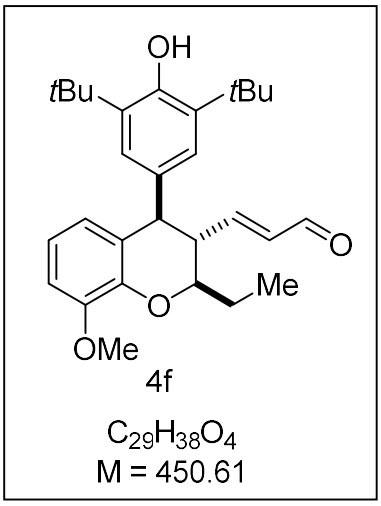
$[\alpha]_D^{20}$ = + 82.1 (c = 2.0, EtOH).

HPLC: Daicel CHIRALPAK IC column; *n*-hexane/ *i*PrOH = 95/5; flow rate = 1.0 mL/min; T = 25 ºC; retention time: 26.77 min (major), 35.84 min (minor), *ee*: > 99%.

HRMS (ESI): *m/z* $[M-H]^+$ Calculated for **$C_{29}H_{37}O_4^+$:** 449.2692; Found 449.2705.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.41 (d, *J* = 7.8 Hz, 1H), 6.81 (d, *J* = 8.8 Hz, 1H), 6.73 (s, 2H), 6.69 (d, *J* = 8.0 Hz, 1H), 6.52 (dd, *J* = 15.6, 9.8 Hz, 1H), 6.29 (s, 1H), 5.70 (dd, *J* = 15.7, 7.8 Hz, 1H), 5.07 (s, 1H), 3.98-3.94 (m, 1H), 3.88 (d, *J* = 10.6 Hz, 1H), 3.60 (s, 3H), 2.75 (q, *J* = 9.9 Hz, 1H), 1.79-1.70 (m, 1H), 1.56-1.54 (m, 1H), 1.34 (s, 18H), 1.06 (t, *J* = 7.3 Hz, 3H).**^{13}C NMR (101 MHz, $CDCl_3$):** δ 193.1, 155.9, 153.5, 152.7, 149.0, 135.9, 135.2, 132.1, 125.8, 125.5, 117.1, 115.0, 113.8, 78.8, 55.9, 50.2, 48.8, 34.4, 30.5, 27.2, 9.2. **^{13}C NMR DEPT-135 (101 MHz, $CDCl_3$):** δ 193.1, 155.9, 135.2, 125.5, 117.1, 115.0, 113.8, 78.8, 55.9, 50.2, 48.8, 30.5, 27.2, 9.2.

5.6. (*E*)-3-((2R,3S,4R)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-ethyl-8-methoxychroman-3-yl)acrylaldehyde (4f).



According to **GP-1**compound **(4f)** was prepared by using **1a** (22.0 µL, 0.2 mmol, 2.0 equiv) **2g** (34.0 mg, 0.1 mmol, 1.0 equiv) triethylamine (6.0 µL, 0.04 mmol, 0.4 equiv) and **Amine 3c** (10.2 mg, 0.02 mmol) in *o*-xylene for 48 h at 10 °C.

Column Chromatographic purification (petroleum ether/EtOAc 99:1 to 90:10) afforded **4f** (d.r. 5:1) as light yellow gummy liquid (32.0 mg, 71 %).

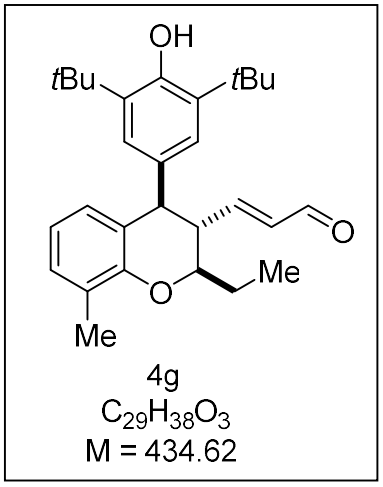
$[\alpha]_D^{20}$ = + 14.8 (c = 1.0, EtOH).

HPLC: Daicel CHIRALPAK IC column; *n*-hexane/ *i*PrOH = 95/5; flow rate = 0.5 mL/min; T = 25 °C; retention time: 13.71 min (major), 18.24 min (minor), *ee*: 92%.

HRMS (ESI): *m/z* $[M-H]^+$ Calculated for **$C_{29}H_{37}O_4^+$:** 449.2692; Found 449.2683.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.42 (d, *J* = 7.8 Hz, 1H), 6.81-6.76 (m, 1H), 6.72-6.71 (m, 3H), 6.53 (dd, *J* = 15.7, 9.9 Hz, 1H), 6.38 (dd, *J* = 6.3, 3.2 Hz, 1H), 5.69 (dd, *J* = 15.6, 7.8 Hz, 1H), 5.07 (s, 1H), 4.03 (ddd, *J* = 10.6, 7.9, 3.1 Hz, 1H), 3.90 (d, *J* = 3.6 Hz, 1H), 3.88 (s, 3H), 2.78 (q, *J* = 10.1 Hz, 1H), 1.82 (dtd, *J* = 14.8, 7.3, 3.0 Hz, 1H), 1.69 (dq, *J* = 14.7, 7.4 Hz, 1H), 1.33 (s, 18H), 1.11 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 193.1, 155.7, 152.6, 148.2, 144.5, 135.8, 135.2, 132.5, 125.9, 125.5, 122.1, 120.1, 109.7, 79.1, 56.2, 50.2, 48.5, 34.4, 30.5, 27.2, 9.4. **^{13}C NMR DEPT-135 (101 MHz, $CDCl_3$):** δ 193.1, 155.7, 135.2, 125.5, 122.1, 120.1, 109.7, 79.1, 56.2, 50.2, 48.5, 30.4, 27.2, 9.4.

5.7. (*E*)-3-((2R,3S,4R)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-ethyl-8-methylchroman-3-yl)acrylaldehyde (4g).



According to **GP-1**compound **(4g)** was prepared by using **1a** (22.0 µL, 0.2 mmol, 2.0 equiv), **2h** (33.5 mg, 0.1 mmol, 1.0 equiv), triethylamine (6.0 µL, 0.04 mmol, 0.4 equiv) and **Amine 3c** (10.2 mg, 0.02 mmol) in *o*-xylene for 48 h at 10 °C.

Column Chromatographic purification (petroleum ether/EtOAc 99:1 to 97:3) afforded **4g** (major diastereomer) as pale yellow solid (28.0 mg, 64 %).

Melting Point: 134-136 °C

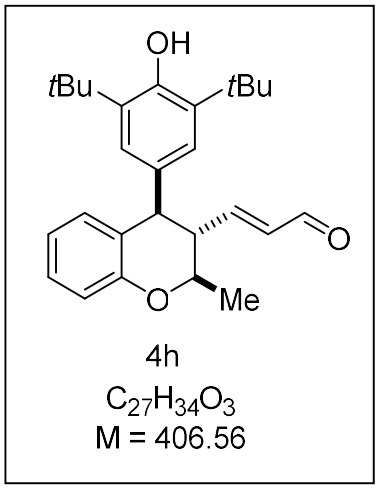
$[\alpha]_D^{20}$ = + 10.6 (c = 0.8, EtOH).

HPLC: Daicel CHIRALPAK IC column; *n*-hexane/ *i*PrOH = 400/1; flow rate = 0.2 mL/min; T = 25 °C; retention time: 64.66 min (major), 69.78 min (minor), *ee*: >99 %.

HRMS (ESI): *m/z* $[M-H]^+$ Calculated for **$C_{29}H_{37}O_3^+$:** 433.2743; Found 433.2729.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.41 (d, *J* = 7.8 Hz, 1H), 6.97 (d, *J* = 7.4 Hz, 1H), 6.74 (s, 2H), 6.67 (t, *J* = 7.0 Hz, 1H), 6.60 (d, *J* = 7.5 Hz, 1H), 6.52 (dd, *J* = 15.7, 9.8 Hz, 1H), 5.70 (dd, *J* = 15.6, 7.8 Hz, 1H), 5.07 (s, 1H), 3.99 (td, *J* = 8.9, 2.3 Hz, 1H), 3.92 (d, *J* = 10.8 Hz, 1H), 2.75 (q, *J* = 10.2 Hz, 1H), 2.25 (s, 3H), 1.80-1.71 (m, 1H), 1.67-1.59 (m, 1H), 1.34 (s, 18H), 1.11 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 193.2, 156.1, 152.8, 152.6, 135.8, 135.1, 132.6, 128.8, 127.7, 125.7, 125.6, 124.5, 120.0, 78.7, 50.5, 48.8, 34.4, 30.5, 27.5, 16.1, 9.6. **^{13}C NMR DEPT-135 (101 MHz, $CDCl_3$):** δ 193.2, 156.1, 135.1, 128.8, 127.7, 125.6, 120.0, 78.7, 50.5, 48.8, 30.5, 27.5, 16.1, 9.6.

5.8. (*E*)-3-((2R,3S,4R)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-methylchroman-3-yl)acrylaldehyde (4h).



According to **GP-1** compound **(4h)** was prepared by using **1b** (22.0 µL, 0.2 mmol, 2.0 equiv) **2a** (31.0 mg, 0.1 mmol, 1.0 equiv) triethylamine (6.0 µL, 0.04 mmol, 0.4 equiv) and **Amine 3c** (10.2 mg, 0.02 mmol) in *o*-xylene for 40 h. at 45 ºC.

Column Chromatographic purification (petroleum ether/EtOAc 99:1 to 97:3) afforded **4h** (major diastereomer) as light yellow gummy liquid (27.5 mg, 68 %).

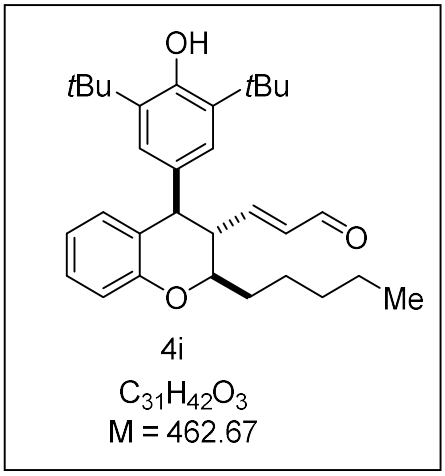
$[\alpha]_D^{20}$ = + 52.1 (c = 0.2, EtOH).

HPLC: Daicel Chiralpak IC column; *n*-hexane/ *i*PrOH = 400/1; flow rate = 1.0 mL/min; T = 25 ºC; retention time: 17.56 min (major), 23.38 min (minor), *ee*: 82 %.

HRMS (ESI): *m/z* $[M-H]^+$ Calculated for **$C_{27}H_{33}O_3^+$:** 405.2430; Found 405.2425.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.42 (d, *J* = 7.8 Hz, 1H), 7.13-7.09 (m, 1H), 6.86 (d, *J* = 8.1 Hz, 1H), 6.78-6.77 (m, 2H), 6.74 (s, 2H), 6.51 (dd, *J* = 15.6, 9.7 Hz, 1H), 5.72 (dd, *J* = 15.7, 7.8 Hz, 1H), 5.08 (s, 1H), 4.23-4.16 (m, 1H), 3.92 (d, *J* = 10.9 Hz, 1H), 2.70 (q, *J* = 10.0 Hz, 1H), 1.38 (d, *J* = 6.3 Hz, 3H), 1.34 (s, 18H).**^{13}C NMR (101 MHz, $CDCl_3$):** δ 193.1, 155.7, 154.5, 152.7, 135.9, 135.3, 132.3, 130.3, 127.8, 125.6, 125.0, 120.8, 116.4, 74.2, 52.1, 48.4, 34.4, 30.5, 20.6. **^{13}C NMR DEPT-135 (101 MHz, $CDCl_3$):** δ 193.1, 155.7, 135.3, 130.3, 127.8, 125.6, 120.8, 116.4, 74.2, 52.1, 48.4, 20.6.

5.9. (*E*)-3-((2R,3S,4R)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-pentylchroman-3-yl)acrylaldehyde (4i).



According to **GP-1** compound **(4i)** was prepared by using **1c** (35.0 µL, 0.2 mmol, 2.0 equiv), **2a** (31.0 mg, 0.1 mmol, 1 equiv), triethylamine (6.0 µL, 0.04 mmol, 0.4 equiv) and **Amine 3c** (10.2 mg, 0.02 mmol) in *o*-xylene for 40 h at 45 °C.

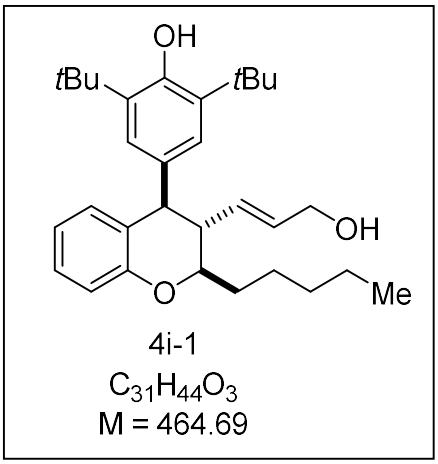
Column Chromatographic purification (petroleum ether/EtOAc 99:1 to 98:2) afforded **4i** (major diastereomer) as light yellow gummy liquid (30.5 mg, 66 %).

$[\alpha]_D^{20}$ = + 20.0 (c = 1.0, EtOH).

HRMS (ESI): *m/z* $[M-H]^+$ Calculated for **$C_{31}H_{41}O_3^+$:** 461.3056; Found 461.3050.

^{1}H NMR (400 MHz, $CDCl_3$) : δ 9.42 (d, *J* = 7.8 Hz, 1H), 7.13-7.09 (m, 1H), 6.87 (d, *J* = 8.1 Hz, 1H), 6.77 (d, *J* = 4.2 Hz, 2H), 6.73 (s, 2H), 6.51 (dd, *J* = 15.6, 9.8 Hz, 1H), 5.68 (dd, *J* = 15.7, 7.8 Hz, 1H), 5.08 (s, 1H), 4.09-4.06 (m, 1H), 3.91 (d, *J* = 10.8 Hz, 1H), 2.75 (q, *J* = 10.1 Hz, 1H), 1.67-1.59 (m, 3H), 1.49-1.41 (m, 5H), 1.34 (s, 18H), 0.89 (t, *J* = 6.2 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 193.1, 155.9, 154.7, 152.7, 135.9, 135.2, 132.4, 130.3, 127.7, 125.6, 125.0, 120.7, 116.5, 77.7, 50.6, 48.6, 34.4, 34.3, 31.8, 30.5, 24.5, 22.7, 14.2. **^{13}C NMR DEPT-135 (101 MHz, $CDCl_3$):** δ 193.1, 155.9, 135.2, 130.3, 127.7, 125.6, 120.7, 116.5, 77.7, 50.6, 48.6, 34.3, 31.8, 30.5, 24.5, 22.7, 14.2.

5.10. 2,6-di-*tert*-butyl-4-((2R,3S,4R)-3-((*E*)-3-hydroxyprop-1-en-1-yl)-2-pentylchroman-4-yl)phenol (4i-1).



Compound **(4i-1)** was prepared by the reduction of **4i** (30.5 mg, 0.066 mmol, 1 equiv) using $NaBH_4$/EtOH at 0 °C for 1 h.

Column Chromatographic purification (petroleum ether/EtOAc 99:1 to 90:10) afforded **4j** as colourless gummy liquid (24.0 mg, 78 %).

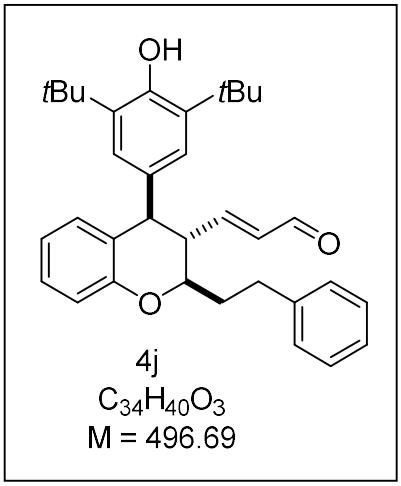
$[\alpha]_D^{20}$ = –14.0 (c = 0.2, EtOH).

HPLC: Daicel Chiralpak IC column; *n*-hexane/ *i*PrOH = 200/1; flow rate = 1.0 mL/min; T = 25 °C; retention time: 9.55 min (major), 10.49 min (minor), *ee*: 92 %.

HRMS (ESI): *m/z* $[M-H]^+$ Calculated for **$C_{31}H_{43}O_3$:** 463.3212; Found 463.3250.

^{1}H NMR (400 MHz, $CDCl_3$) : δ 7.09-7.05 (m, 1H), 6.84 (d, *J* = 8.0 Hz, 1H), 6.77-6.71 (m, 4H), 5.33 (dd, *J* = 15.7, 9.1 Hz, 1H), 5.23-5.16 (m, 1H), 5.04 (s, 1H), 3.97-3.91 (m, 3H), 3.75 (d, *J* = 10.7 Hz, 1H), 2.42 (q, *J* = 10.1 Hz, 1H), 1.75-1.68 (m, 1H), 1.62-1.57 (m, 1H), 1.44-1.40 (m, 1H), 1.36 (s, 18H), 1.35-1.28 (m, 5H), 0.89 (t, *J* = 6.8 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 155.0, 152.2, 135.5, 133.7, 132.3, 131.1, 130.4, 127.4, 126.1, 126.0, 120.3, 116.3, 78.7, 63.5, 49.8, 49.0, 34.4, 34.1, 32.0, 30.5, 24.6, 22.8, 14.2. **^{13}C NMR DEPT-135 (101 MHz, $CDCl_3$):** δ 132.3, 131.1, 130.4, 127.4, 126.0, 120.3, 116.3, 78.7, 63.5, 49.8, 49.0, 34.1, 32.0, 24.6, 22.8, 14.2.

5.11. (*E*)-3-((2R,3S,4R)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-phenethylchroman-3-yl)acrylaldehyde (4j).



According to **GP-1** compound **(4j)** was prepared by using **1d** (37.0 mg, 0.2 mmol, 2.0 equiv) **2a** (31.0 mg, 0.1 mmol, 1.0 equiv) triethylamine (6.0 µL, 0.04 mmol, 0.4 equiv) and **Amine 3c** (10.2 mg, 0.02 mmol) in *o*-xylene for 40 h. at 45 ºC.

Column Chromatographic purification (petroleum ether/EtOAc 99:1 to 97:3) afforded **4j** (major diastereomer) as pale yellow gummy liquid (35.5 mg, 71 %).

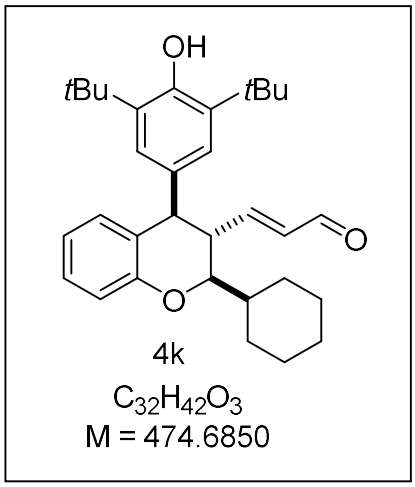
$[\alpha]_D^{20}$ = + 15.5 (c = 0.8, EtOH).

HPLC: Daicel CHIRALPAK IC column; *n*-hexane/ *i*PrOH = 200/1; flow rate = 1.0 mL/min; T = 25 ºC; retention time: 16.55 min (major), 18.26 min (minor), *ee*: > 99%.

HRMS (ESI): *m/z* $[M-H]^+$ Calculated for **$C_{34}H_{39}O_3^+$:** 495.2899; Found 495.2887.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.38 (d, *J* = 7.8 Hz, 1H), 7.29-7.27 (m, 1H), 7.20-7.19 (m, 3H), 7.16-7.12 (m, 2H), 6.94 (d, *J* = 8.1 Hz, 1H), 6.79-6.78 (m, 2H), 6.72 (s, 2H), 6.44 (dd, *J* = 15.6, 9.9 Hz, 1H), 5.64 (dd, *J* = 15.6, 7.8 Hz, 1H), 5.08 (s, 1H), 4.07-4.02 (m, 1H), 3.88 (d, *J* = 10.8 Hz, 1H), 3.02-2.95 (m, 1H), 2.88-2.81 (m, 1H), 2.80-2.74 (m, 1H), 1.95-1.90 (m, 2H), 1.33 (s, 18H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 193.0, 155.4, 154.5, 152.7, 141.6, 135.9, 135.3, 132.3, 130.3, 128.7, 128.6, 127.8, 126.1, 125.6, 125.1, 120.9, 116.5, 76.5, 50.7, 48.5, 36.2, 34.4, 31.1, 30.4. **^{13}C NMR DEPT-135 (101 MHz, $CDCl_3$):** δ 193.0, 155.4, 135.3, 130.3, 128.7, 128.6, 127.8, 126.1, 125.6, 125.1, 120.9, 116.5, 76.5, 50.7, 48.5, 36.2, 31.1, 30.4.

5.12. (*E*)-3-((2R,3S,4R)-2-cyclohexyl-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)chroman-3-yl)acrylaldehyde (4k).



According to **GP-1** compound **(4k)** was prepared by using **1e** (33.0 mg, 0.2 mmol, 2.0 equiv) **2a** (31.0 mg, 0.1 mmol, 1.0 equiv) triethylamine (6.0 µL, 0.04 mmol, 0.4 equiv) and **Amine 3c** (10.2 mg, 0.02 mmol) in *o*-xylene for 40 h. at 45 ºC.

Column Chromatographic purification (petroleum ether/EtOAc 99:1 to 97:3) afforded **4k** (major diastereomer) as orange solid (28.5 mg, 60%).

Melting Point: 106-108 ºC

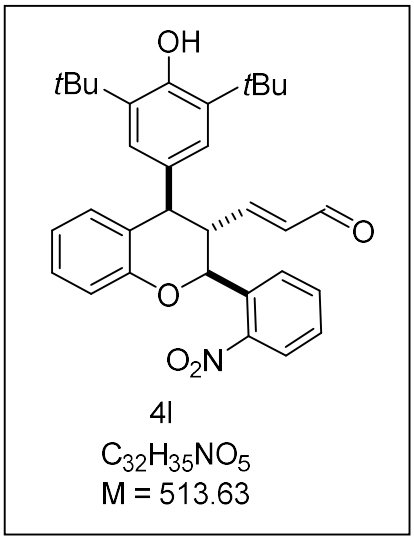
$[\alpha]_D^{20}$ = + 15.0 (c = 0.8, EtOH).

HPLC: Daicel CHIRALPAK IC column; *n*-hexane/ *i*PrOH = 200/1; flow rate = 1 mL/min; T = 25 ºC; retention time: 8.60 min (minor), 10.15 min (major), *ee*: 92%.

HRMS (ESI): *m/z* $[M+H]^+$ Calculated for $C_{32}H_{43}O_3^+$**:** 475.3212; Found 475.3188.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.42 (d, *J* = 7.7 Hz, 1H), 7.12-7.08 (m, 1H), 6.86 (d, *J* = 8.3 Hz, 1H), 6.76 (d, *J* = 4.3 Hz, 2H), 6.73 (s, 2H), 6.53 (dd, *J* = 15.6, 10.0 Hz, 1H), 5.68 (dd, *J* = 15.6, 7.8 Hz, 1H), 5.07 (s, 1H), 3.97-3.91 (m, 2H), 2.91 (q, *J* = 10.1 Hz, 1H), 1.77-1.73 (m, 3H), 1.69-1.63 (m, 3H), 1.42-1.38 (m, 2H), 1.34 (s, 18H), 1.14-1.08 (m, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 193.2, 156.0, 155.0, 135.8, 134.8, 132.3, 130.2, 127.7, 125.6, 124.9, 120.5, 116.5, 81.8, 48.8, 47.6, 40.6, 34.4, 30.5, 30.2, 26.7, 26.4, 26.2, 24.7. **^{13}C NMR DEPT-135 (101 MHz, $CDCl_3$):** δ 193.2, 156.0, 134.8, 130.2, 127.7, 125.6, 120.5, 116.5, 81.8, 48.8, 47.6, 40.6, 30.5, 30.2, 26.7, 26.4, 26.2, 24.7.

5.13. (*E*)-3-((2S,3S,4R)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-(2-nitrophenyl)chroman-3-yl)acrylaldehyde (4l).



According to **GP-1** compound **(4l)** was prepared by using **1f** (21.0 mg, 0.1 mmol, 1.0 equiv) **2a** (124.0 mg, 0.4 mmol, 4.0 equiv) triethylamine (6.0 µL, 0.04 mmol, 0.4 equiv) and **Amine 3c** (10.2 mg, 0.02 mmol) in chloroform (0.1 M) for 7 d. at 45 °C.

Column Chromatographic purification (petroleum ether/EtOAc 99:1 to 90:10) afforded **4l** (major diastereomer) as yellow gummy liquid (18.0 mg, 35 %).

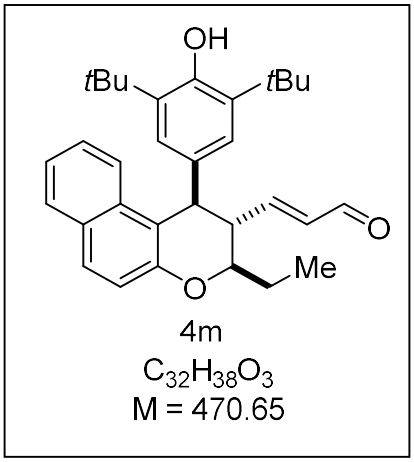
$[\alpha]_D^{20}$ = + 34.1 (c = 0.6, EtOH).

HPLC: Daicel CHIRALPAK IC column; *n*-hexane/ *i*PrOH = 95/5; flow rate = 1.0 mL/min; T = 25 °C; retention time: 7.53min (major), 9.91min (minor), *ee*: 76 %.

HRMS (ESI): *m/z* $[M+H]^+$ Calculated for $C_{32}H_{36}NO_5^+$ **:** 514.2593; Found 514.2564.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.28 (d, *J* = 7.9 Hz, 1H), 8.11 (d, *J* = 7.6 Hz, 1H), 7.80 (d, *J* = 7.8 Hz, 1H), 7.67-7.63 (m, 1H), 7.49-7.45 (m, 1H), 7.22 (d, *J* = 7.7 Hz, 1H), 7.03 (dd, *J* = 12.9, 7.8 Hz, 2H), 6.95-6.91 (m, 1H), 6.88-6.81 (m, 3H), 6.15 (d, *J* = 8.0 Hz, 1H), 5.27 (dd, *J* = 15.7, 7.8 Hz, 1H), 5.11 (s, 1H), 4.89 (d, *J* = 5.3 Hz, 1H), 3.35 (dd, *J* = 10.9, 5.4 Hz, 1H), 1.34 (s, 18H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 192.8, 154.6, 152.9, 152.5, 137.4, 135.7, 135.0, 133.7, 130.7, 130.5, 128.9, 128.7, 128.3, 126.2, 125.2, 123.7, 121.8, 117.0, 76.8, 49.1, 48.3, 34.4, 30.4. **^{13}C NMR DEPT-135 (101 MHz, $CDCl_3$):** δ 192.8, 152.5, 137.4, 133.7, 130.7, 128.9, 128.7, 128.3, 126.2, 125.2, 121.8, 117.0, 76.8, 49.1, 48.3, 30.4.

5.14. (*E*)-3-((1R,2S,3R)-1-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-3-ethyl-2,3-dihydro-1*H*-benzo[*f*]chromen-2-yl)acrylaldehyde (4m).



According to **GP-1** compound **(4m)** was prepared by using **1a** (22.0 µL, 0.2 mmol, 2.0 equiv) **2e** (36.0 mg, 0.1 mmol, 1.0 equiv) triethylamine (3.0 µL, 0.02 mmol, 0.2 equiv) and **Amine 3c** (10.2 mg, 0.02 mmol) in *o*-xylene for 48 h at 10 °C.

Column Chromatographic purification (petroleum ether/EtOAc 99:1 to 97:3) afforded **4m** as light yellow gummy liquid (23.0 mg, 49 %).

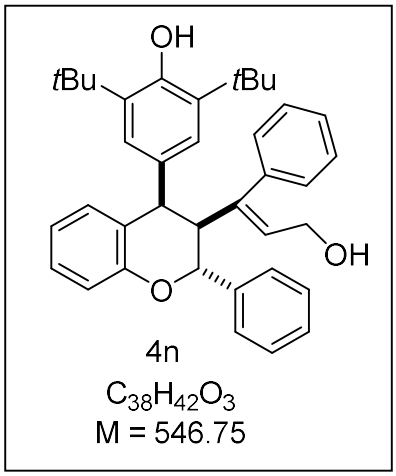
$[\alpha]_D^{20}$ = – 32.1 (c = 0.6, EtOH).

HPLC: Daicel Chiralpak IC column; *n*-hexane/ *i*PrOH = 95/5; flow rate = 1.0 mL/min; T = 25 °C; retention time: 7.15 min (minor), 10.53 min (major), *ee*: 58 %.

HRMS (ESI): HRMS (ESI): *m/z* $[M-H]^+$ Calculated for **$C_{28}H_{37}O_3^+$:** 469.2743; Found 469.2739.

^{1}H NMR (400 MHz, $CDCl_3$) :δ 9.41 (d, *J* = 7.9 Hz, 1H), 7.76-7.68 (m, 2H), 7.44-7.42 (m, 1H), 7.30-7.26 (m, 2H), 7.16 (d, *J* = 9.0 Hz, 1H), 6.86 (s, 2H), 6.79 (dd, *J* = 15.7, 9.8 Hz, 1H), 6.30 (dd, *J* = 15.7, 7.9 Hz, 1H), 5.09 (s, 1H), 4.48-4.46 (m, 1H), 4.08 (ddd, *J* = 8.8, 4.9, 1.8 Hz, 1H), 2.88 (d, *J* = 9.7 Hz, 1H), 1.80-1.69 (m, 1H), 1.51-1.43 (m, 1H), 1.31 (s, 18H), 1.01 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 194.0, 156.0, 152.5, 135.9, 134.9, 134.9, 133.3, 129.6, 129.3, 128.5, 126.6, 125.1, 123.4, 123.4, 118.7, 112.5, 77.3, 73.5, 48.2, 44.2, 34.4, 30.3, 26.7, 10.1. **^{13}C NMR DEPT-135 (101 MHz, $CDCl_3$):** δ 194.0, 156.0, 134.9, 129.3, 128.5, 126.6, 125.1, 123.4, 118.7, 77.3, 73.5, 48.2, 44.2, 30.3, 26.7, 10.1.

5.15. 2,6-di-*tert*-butyl-4-((2R,3S,4R)-3-((*Z*)-3-hydroxy-1-phenylprop-1-en-1-yl)-2-phenylchroman-4-yl)phenol (4n).



According to **GP-2** compound **(4n)** was prepared by using **1g** (46.0 mg, 0.2 mmol, 2.0 equiv) **2a** (31.0 mg, 0.1 mmol, 1.0 equiv) triethylamine (6.0 µL, 0.04 mmol, 0.4 equiv), brine (3.0 equiv) and **Amine 3a** (6.7 mg, 0.02 mmol) in toluene for 12 h. at room temperature.

Column Chromatographic purification (petroleum ether/EtOAc 99:1 to 85:15) afforded **4n** (major diastereomer) as white solid (45.0 mg, 83 %).

Melting Point: 166-168 ºC

$[\alpha]_D^{20}$ = – 76.9 (c = 1.0, EtOH).

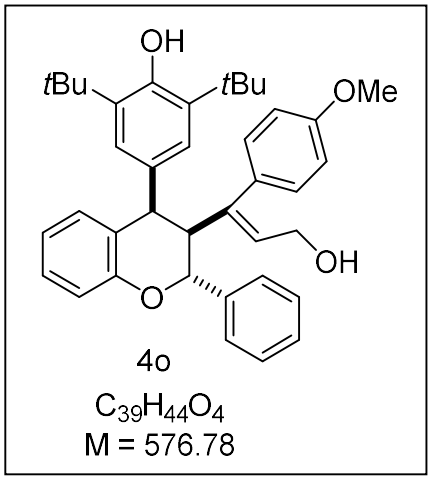
HPLC: Daicel CHIRALPAK IC column; *n*-hexane/ *i*PrOH = 200/1; flow rate = 1.0 mL/min; T = 25 ºC; retention time: 13.42 min (major), 15.84 min (minor), *ee*: 90%.

HRMS (ESI): *m/z* $[M+H]^+$ Calculated for **$C_{38}H_{43}O_3^+$:** 547.3212; Found 547.3239

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39-7.28 (m, 5H), 7.23-7.20 (m, 3H), 7.17-7.12 (m, 1H), 7.00-6.96 (m, 2H), 6.90 (s, 2H), 6.81 (td, *J* = 7.5, 1.2 Hz, 1H), 6.76-6.74 (m, 2H), 5.31 (d, *J* = 11.1 Hz, 1H), 5.15 (s, 1H), 4.57 (dd, *J* = 7.7, 6.0 Hz, 1H), 4.10 (d, *J* = 4.6 Hz, 1H), 3.73-3.62 (m, 2H), 3.39 (dd, *J* = 11.1, 4.7 Hz, 1H), 1.41 (s, 18H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 154.4, 152.6, 140.8, 140.3, 139.4, 135.0, 132.2, 131.1, 130.5, 128.4, 128.4, 128.3, 128.2, 128.1, 128.0, 127.4, 127.3, 125.6, 120.5, 116.5, 77.9, 60.3, 50.8, 45.6, 34.4, 30.5. **^{13}C NMR DEPT-135 (101 MHz, $CDCl_3$):** δ 131.1, 130.5, 128.4, 128.4, 128.3, 128.2, 128.1, 128.0, 127.4, 127.3, 120.5, 116.5, 77.9, 60.3, 50.8, 45.6, 30.5.

5.16. 2,6-di-*tert*-butyl-4-((2R,3S,4R)-3-((*Z*)-3-hydroxy-1-(4-methoxyphenyl)prop-1-en-1-yl)-2-phenylchroman-4-yl)phenol (4o).



According to **GP-2** compound **(4o)** was prepared by using **1h** (52.0 mg, 0.2 mmol, 2.0 equiv) **2a** (31.0 mg, 0.1 mmol, 1.0 equiv) triethylamine (6.0 µL, 0.04 mmol, 0.4 equiv), brine (3.0 equiv) and **Amine 3a** (6.7 mg, 0.02 mmol) in toluene for 12 h. at room temperature.

Column Chromatographic purification (petroleum ether/EtOAc 0199:1 to 85:15) afforded **4o** (major diastereomer) as colourless gummy liquid (55.0 mg, 96 %).

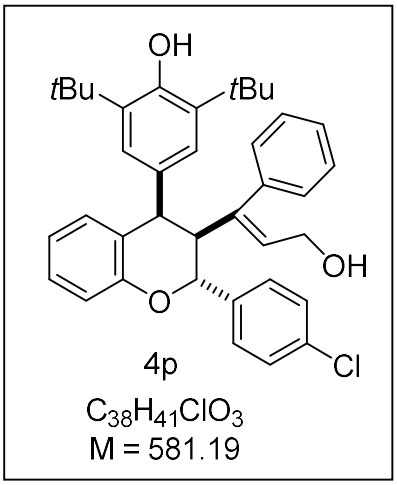
$[\alpha]_D^{20}$ = – 127.8 (c = 1.0, EtOH).

HPLC: Daicel Chiralpak IC column; *n*-hexane/ *i*PrOH = 200/1; flow rate = 1.0 mL/min; T = 25 ºC; retention time: 22.78. min (major), 25.69 min (minor), *ee*: 92 %.

HRMS (ESI): *m/z* $[M+H]^+$ Calculated for **$C_{39}H_{45}O_4^+$:** 577.3318; Found 577.3289

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38-7.36 (m, 2H), 7.34-7.27 (m, 3H), 7.14 (ddd, *J* = 8.6, 7.4, 1.8 Hz, 1H), 6.98 (td, *J* = 7.3, 6.8, 1.1 Hz, 2H), 6.87 (s, 2H), 6.81 (td, *J* = 7.3, 1.1 Hz, 1H), 6.78-6.69 (m, 4H), 5.30 (d, *J* = 11.1 Hz, 1H), 5.14 (s, 1H), 4.54 (dd, *J* = 7.8, 5.9 Hz, 1H), 4.08 (d, *J* = 4.6 Hz, 1H), 3.76 (s, 3H), 3.69 (m, 2H), 3.39 (dd, *J* = 11.1, 4.7 Hz, 1H), 1.41 (s, 18H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 158.9, 154.4, 152.6, 140.4, 139.0, 135.0, 133.0, 132.3, 130.6, 130.5, 129.3, 128.4, 128.3, 128.0, 127.2, 125.6, 120.5, 116.5, 113.5, 77.9, 60.3, 55.4, 50.8, 45.7, 34.4, 30.5. **^{13}C NMR DEPT-135 (101 MHz, $CDCl_3$):** δ 130.6, 130.5, 129.3, 128.4, 128.3, 128.0, 127.2, 120.5, 116.5, 113.5, 77.9, 60.3, 55.4, 50.8, 45.7, 30.5.

5.17. 2,6-di-*tert*-butyl-4-((2R,3S,4R)-2-(4-chlorophenyl)-3-((*Z*)-3-hydroxy-1-phenylprop-1-en-1-yl)chroman-4-yl)phenol (4p).



According to **GP-2** compound **(4p)** was prepared by using **1i** (53.0 mg, 0.2 mmol, 2.0 equiv) **2a** (31.0 mg, 0.1 mmol, 1.0 equiv) triethylamine (6.0 µL, 0.04 mmol, 0.4 equiv), brine (3.0 equiv) and **Amine 3a** (6.7 mg, 0.02 mmol) in toluene for 12 h. at room temperature.

Column Chromatographic purification (petroleum ether/EtOAc 99:1 to 85:15) afforded **4p** (major diastereomer) as white solid (54.0 mg, 93 %).

Melting Point: 160-162 ºC

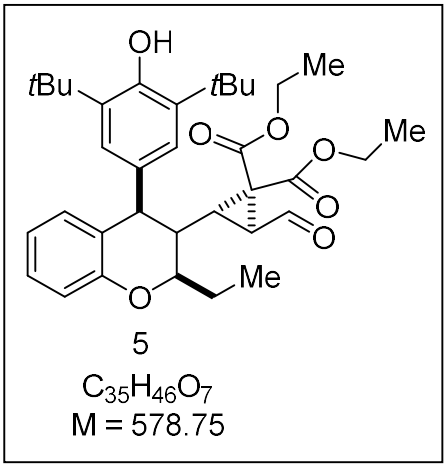
$[\alpha]_D^{20}$ = – 127.8 (c = 1.0, EtOH).

HPLC: Daicel Chiralpak IC column; *n*-hexane/ *i*PrOH = 200/1; flow rate = 1.0 mL/min; T = 25 ºC; retention time: 11.69. min (minor), 13.36 min (major), *ee*: 92 %.

HRMS (ESI): *m/z* $[M-H]^+$ Calculated for **$C_{38}H_{40}ClO_3^+$:** 579.2666; Found 579.2660

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31-7.30 (m, 4H), 7.24-7.21 (m, 3H), 7.17-7.12 (m, 1H), 6.97 (dd, *J* = 15.5, 7.7 Hz, 2H), 6.88 (s, 2H), 6.82 (td, *J* = 7.5, 1.0 Hz, 1H), 6.74-6.72 (m, 2H), 5.28 (d, *J* = 11.2 Hz, 1H), 5.16 (s, 1H), 4.57 (dd, *J* = 7.5, 6.2 Hz, 1H), 4.10 (d, *J* = 4.5 Hz, 1H). 3.76-3.64 (m, 2H), 3.34 (dd, *J* = 11.2, 4.7 Hz, 1H), 1.41 (s, 18H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 154.1, 152.7, 140.6, 139.1, 139.0, 135.1, 134.0, 132.0, 131.2, 130.5, 129.7, 128.5, 128.3, 128.1, 128.0, 127.5, 127.2, 125.5, 120.7, 116.4, 77.2, 60.2, 50.8, 45.7, 34.4, 30.5. **^{13}C NMR DEPT-135 (101 MHz, $CDCl_3$):** δ 131.2, 130.5, 129.7, 128.5, 128.3, 128.1, 128.0, 127.5, 127.2, 120.7, 116.4, 77.2, 60.2, 50.8, 45.7, 30.5.

5.18. (2S,3S)-diethyl 2-((2R,4R)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-ethylchroman-3-yl)-3-formylcyclopropane-1,1-dicarboxylate (5).



5

$C_{35}H_{46}O_7$

M = 578.75

According to **GP-3** compound **(5)** was prepared by using **4a** (42.0 mg, 0.1 mmol, 1.0 equiv) **diethyl bromomalonate** (34 .0 µL, 0.2 mmol, 2.0 equiv) triethylamine (14.0 µL, 0.1 mmol, 1 equiv) and **Amine 3a** (6.7 mg, 0.02 mmol) in chloroform for 40 h. at 45 °C.

Column Chromatographic purification (petroleum ether/EtOAc 99:1 to 90:10) afforded **1a** as colourless gummy liquid (31.0 mg, 54 %).

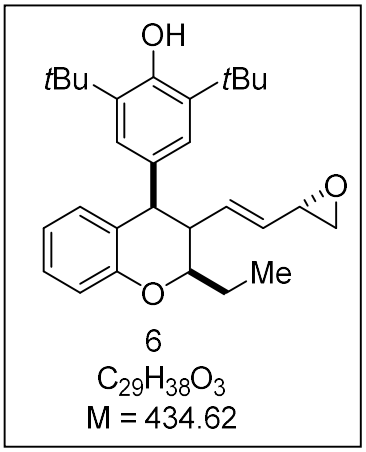
$[\alpha]_D^{20}$ = – 38.1 (c = 1.0, EtOH).

HPLC: Daicel CHIRALPAK IC column; *n*-hexane/*i*PrOH = 95/5; flow rate = 1.0 mL/min; T = 25 °C; retention time: 10.88 min (major), 11.79 min (minor), *ee*: > 99%.

HRMS (ESI): *m/z* $[M+H]^+$ Calculated for **$C_{35}H_{47}O_7^+$:** 579.3322; Found 579.3317

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.18 (d, *J* = 4.8 Hz, 1H), 7.09-7.04 (m, 1H), 6.85 (d, *J* = 9.0 Hz, 1H), 6.83 (s, 2H), 6.79-6.74 (m, 1H), 6.70 (d, *J* = 6.7 Hz, 1H), 5.04 (s, 1H), 4.22-4.09 (m, 2H), 4.03-3.98 (m, 2H), 3.89 (q, *J* = 6.4 Hz, 1H), 3.66-3.58 (m, 1H), 2.81 (dd, *J* = 7.1, 4.8 Hz, 1H), 2.42-2.30 (m, 2H), 1.62-1.58 (m, 2H), 1.33 (s, 18H), 1.20 (t, *J* = 7.2 Hz, 3H), 1.09 (t, *J* = 7.1 Hz, 3H), 0.95 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 196.4, 166.0, 165.8, 154.4, 152.3, 135.2, 133.9, 131.1, 127.4, 126.4, 125.5, 120.7, 116.7, 80.3, 77.3, 62.2, 62.0, 47.9, 42.2, 40.7, 40.2, 35.8, 34.4, 30.4, 26.4, 14.1, 9.7. **^{13}C NMR DEPT-135 (101 MHz, $CDCl_3$):** δ 196.4, 131.1, 127.4, 126.4, 120.7, 116.7, 80.3, 62.2, 62.0, 47.9, 40.7, 40.2, 35.8, 30.4, 26.4, 14.1, 9.7.

5.19. 2,6-di-*tert*-butyl-4-((2R,4R)-2-ethyl-3-((*E*)-2-((S)-oxiran-2-yl)vinyl)chroman-4-yl)phenol (6).



According to **GP-4** compound **(6)** was prepared by using **4a** (42.0 mg, 0.1 mmol, 1.0 equiv), NaH (60 % dispersion in oil, 12.0 mg, 0.31 mmol, 3.1 equiv), Trimethylsulfonium iodide (61.0 mg, 0.3 mmol, 3.0 equiv) in a mixture of dry THF & dry DMSO at 0 °C for 1 h, then at room temperature for another 1 h.

Column Chromatographic purification (petroleum ether/EtOAc 99:1 to 95:5) afforded **6** (major diastereomer) as pale yellow solid (29.0 mg, 66 %).

Melting Point: 95-97 °C

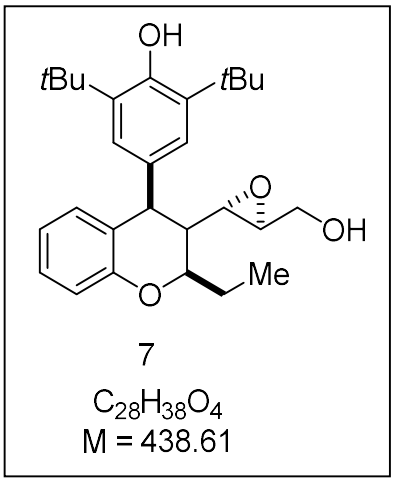
$[\alpha]_D^{20}$ = + 39.7 (c = 1.0, EtOH).

HPLC: Daicel CHIRALPAK ODH column; *n*-hexane/ *i*PrOH = 1000/1; flow rate = 1.0 mL/min; T = 25 °C; retention time: 7.46 min (minor), 9.25 min (major), *ee*: 98%.

HRMS (ESI): *m/z* $[M+H]^+$ Calculated for **$C_{29}H_{39}O_3^+$:** 435.2899; Found 435.2881

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.10-7.06 (m, 1H), 6.85 (d, *J* = 8.1 Hz, 1H), 6.78-6.75 (m, 2H), 6.74 (s, 2H), 5.57 (dd, *J* = 15.5, 9.6 Hz, 1H), 5.03 (s, 1H), 4.66 (dd, *J* = 15.5, 8.1 Hz, 1H), 3.91 (ddd, *J* = 10.5, 8.0, 3.0 Hz, 1H), 3.75 (d, *J* = 10.9 Hz, 1H), 3.21-3.17 (m, 1H), 2.82-2.80 (m, 1H), 2.44 (q, *J* = 10.1 Hz, 1H), 2.30 (dd, *J* = 5.3, 2.6 Hz, 1H), 1.84 (dqd, *J* = 14.9, 7.4, 2.8 Hz, 1H), 1.64-1.59 (m, 1H), 1.36 (s, 18H), 1.06 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 155.1, 152.2, 135.4, 134.2, 133.5, 131.1, 130.4, 127.4, 126.0, 125.9, 120.3, 116.3, 79.5, 52.1, 49.7, 48.9, 48.6, 34.3, 30.5, 27.0, 9.3. **^{13}C NMR DEPT-135 (101 MHz, $CDCl_3$):** δ 134.2, 133.5, 131.1, 130.4, 127.4, 125.9, 120.3, 116.3, 79.5, 52.1, 49.7, 48.9, 48.6, 30.5, 27.0, 9.3.

5.20. 2,6-di-*tert*-butyl-4-((2R,4R)-2-ethyl-3-((2S,3S)-3-(hydroxymethyl)oxiran-2-yl)chroman-4-yl)phenol (7).



According to **GP-4** compound **(7)** was prepared by the reduction of **4a** (42.0 mg, 0.1 mmol, 1.0 equiv) using $NaBH_4$/EtOH at 0 °C for 1 h.

Allyllic alcohol obtained from above procedure dissolved in DCM (0.2 mL) at 0 °C. *meta*-Chloroperoxybenzoic acid (*m*CPBA, 1.3 equiv, 0.11 mmol) was added and the reaction mixture stirred for 3 h

Column Chromatographic purification (petroleum ether/EtOAc 90:10 to 70:30) afforded **7** (major diastereomer) as colourless gummy liquid (26.0 mg, 60 %).

$[\alpha]_D^{20}$ = – 16.5 (c = 0.8, EtOH).

HPLC: Daicel CHIRALPAK IC column; *n*-hexane/iPrOH = 95/5; flow rate = 0.2 mL/min; T = 25 °C; retention time: 7.46 min (minor), 9.25 min (major), *ee*: >99%.

HRMS (ESI): *m/z* $[M-H]^+$ Calculated for **$C_{28}H_{37}O_4^+$:** 437.2692; Found 437.2679

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.10-7.06 (m, 1H), 6.88 (s, 2H), 6.85 (d, *J* = 8.7 Hz, 1H), 6.78-6.77 (m, 2H), 5.07 (s, 1H), 3.99 (d, *J* = 8.4 Hz, 1H), 3.92 (td, *J* = 8.2, 3.7 Hz, 1H), 3.82 (dd, *J* = 12.7, 2.2 Hz, 1H), 3.55 (dd, *J* = 12.7, 3.8 Hz, 1H), 3.03-3.02 (m, 1H), 2.96 (dd, *J* = 7.2, 2.0 Hz, 1H), 2.09 (q, *J* = 7.8 Hz, 1H), 1.79-1.73 (m, 1H), 1.71-1.64 (m, 1H), 1.37 (s, 18H), 1.01 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 154.3, 152.3, 135.7, 134.3, 130.5, 127.5, 125.8, 125.6, 120.7, 116.6, 78.2, 61.3, 57.0, 56.8, 45.3, 45.2, 34.4, 30.5, 26.7, 9.8.

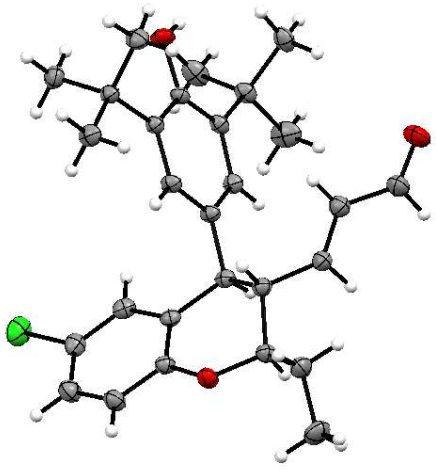
^{13}C NMR DEPT-135 (101 MHz, $CDCl_3$): δ 130.5, 127.5, 125.6, 120.7, 116.6, 78.2, 61.3, 57.0, 56.8, 45.3, 45.2, 30.5, 26.7, 9.8.

6. X-ray data of 4d & 4p.

1. X-Ray data of 4d and 4p:

For the determination of X-ray crystal structures of **4d** and **4p** a single crystal was selected and mounted with paratone oil on a glass fiber using gum. The data was collected at 298K on a CMOS based Bruker D8 Venture PHOTON 100 diffractometer equipped with a INCOATEC micro-focus source with graphite monochromatic Mo Kα radiation (λ = 0.71073 Å) operation at 50 kV and 30 mA. For the integration of diffraction profiles SAINT program[S10] was used. Absorption correction was done applying SADABS program.[S11] The crystal structure was solved by SIR 92[S12] and refined by full matrix least square method using SHELXL-97[S13] WinGX system, Ver 1.70.01.[S14] All the non-hydrogen atoms in the structure were located the Fourier map and refined anisotropically. The hydrogen atoms were fixed by HFIX in their ideal positions and refined using riding model with isotropic thermal parameters. The crystal structure (excluding structure factor) has been deposited to Cambridge Crystallographic Data Centre and allocated deposition number: **4d: CCDC 1982963** and **4p: CCDC 1982953**.[S15]

Crystal Data and Structure Refinement for Complex 4d (CCDC 1982963)

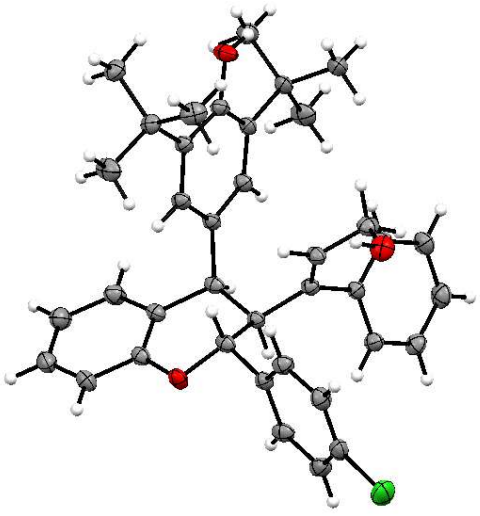


Atom color code: grey = carbon atom, white = hydrogen atom, green = chlorine atom and red = oxygen atom.

CCDC No.	CCDC 1982963
Formula	C28 H35 Cl O3
Formula weight	455.01
Crystal System	triclinic
Space group	P -1

a, b, c (Å)	10.335(3), 10.973(2), 14.104(3)
α, β, γ (°)	92.007(7), 109.843(8), 117.445(7)
V ($Å^3$)	1299.6(5)
Z	2
Calculated Density (g/cm^3)	1.163
Absorption coefficient (mm^{-1})	0.172
F(000)	488.0
Crystal Size (mm)	0.16 x 0.19 x 0.20
Theta range for data collection:	2.3° to 26.4°
Data set	-12: 12 ; -13: 13 ; -17: 17
R indices [I>=2σ (I)] (all data)	R1 = 0.0548, wR2 = 0.1583
Reflection	19227
Independent refl.	5299, [R(int) = 0.072]
S	1.035
Min. and Max. Resd. Dens. ($e/Å^3$)	-0.20 and 0.19
Npar	289

Crystal Data and Structure Refinement for Complex 4p (CCDC 1982953)



Atom color code: grey = carbon atom, white = hydrogen atom, green = chlorine atom and red = oxygen atom.

CCDC No.	CCDC 1982953
Formula	C38 H41 Cl O3
Formula weight	581.16
Crystal System	Orthorhombic
Space group	P212121
a, b, c (Å)	10.561(2), 16.603(3), 18.352(4)
α, β, γ (°)	90, 90, 90
V ($Å^3$)	3217.9(11)
Z	4
Calculated Density (g/cm^3)	1.200
Absorption coefficient (mm^{-1})	0.154
Crystal Size (mm)	0.26 x 0.30 x 0.31
F(000)	1240
Theta range for data collection:	2.2^o to 26.5^o
Data set	-13: 13 ; -20: 20 ; -22: 22
R indexes [I>=2σ (I)] (all data)	R1 = 0.0561, wR2 = 0.1641
Reflection	24944
Independent refl.	4189, [R(int) = 0.070]
S	1.04
Min. and Max. Resd. Dens. ($e/Å^3$)	-0.31 and 0.17
Npar	379

7. References:

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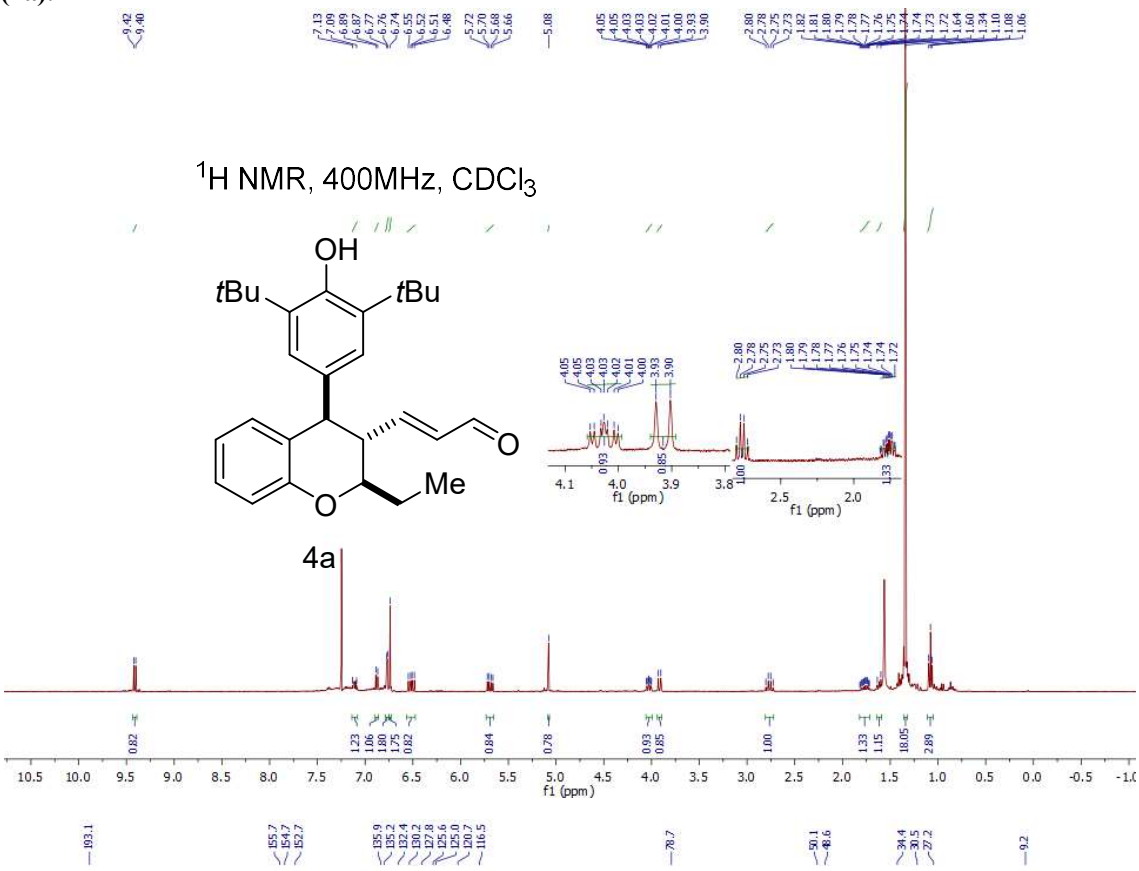
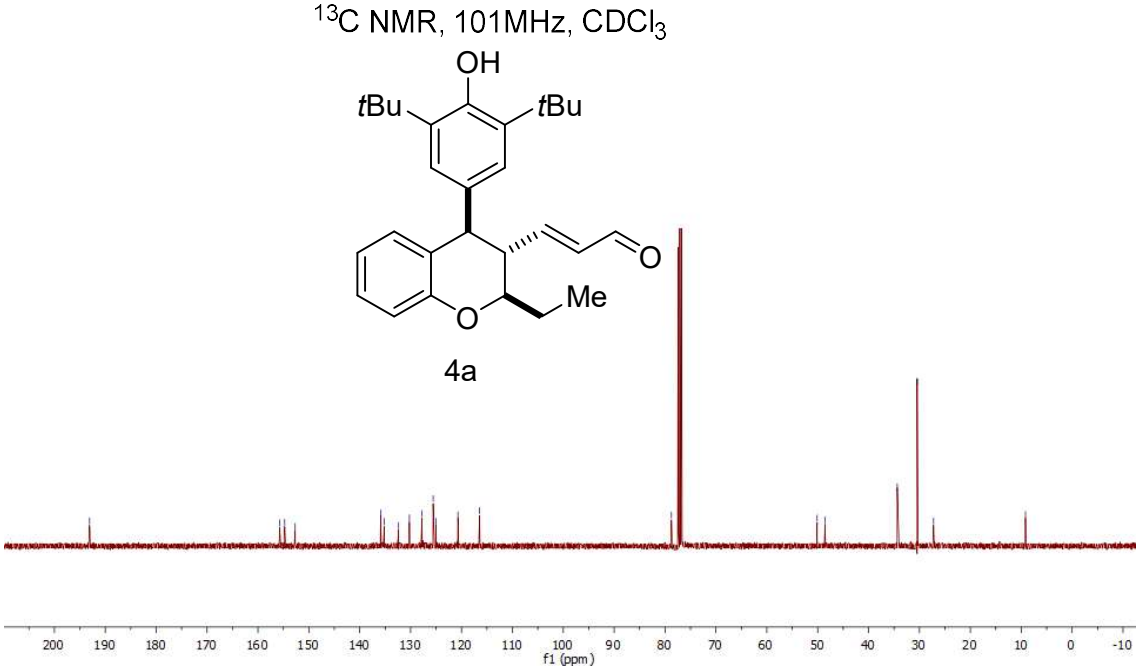
[S14] L. J. Farrugia, WinGX-A Windows Program for Crystal Structure Analysis, *J. Appl. Cryst*., 1999, **32**, 837–838.

[S15] CCDC **1982963** & CCDC **1982953** contain supplementary crystallographic data for the compound **4d** & **4p** respectively.

8. Experimental NMR Spectra:

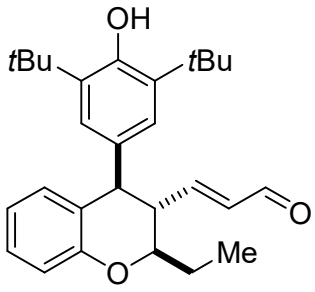
8.1. (*E*)-3-((2R,3S,4R)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-ethylchroman-3-yl)acrylaldehyde (4a).



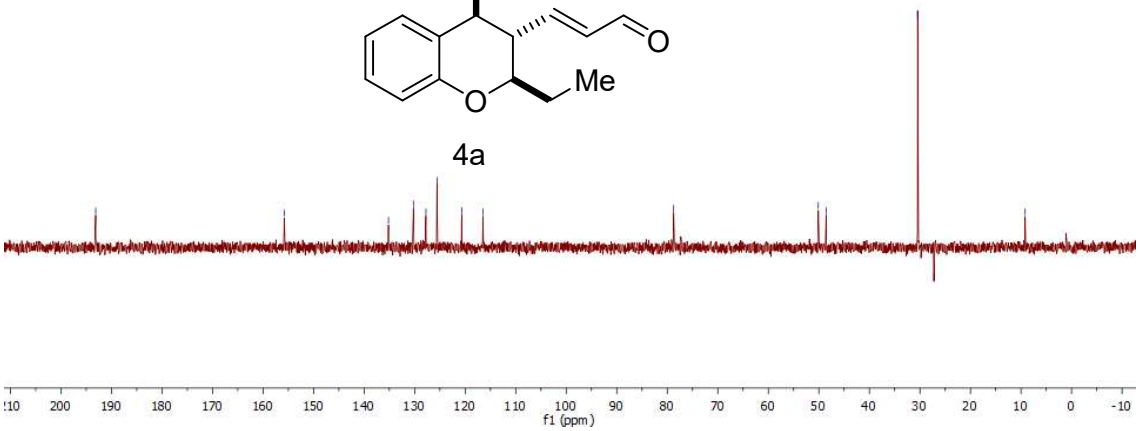


193.1
155.8
135.2
130.2
127.8
125.6
120.7
116.5
78.7
50.1
48.6
30.5
27.2
9.2

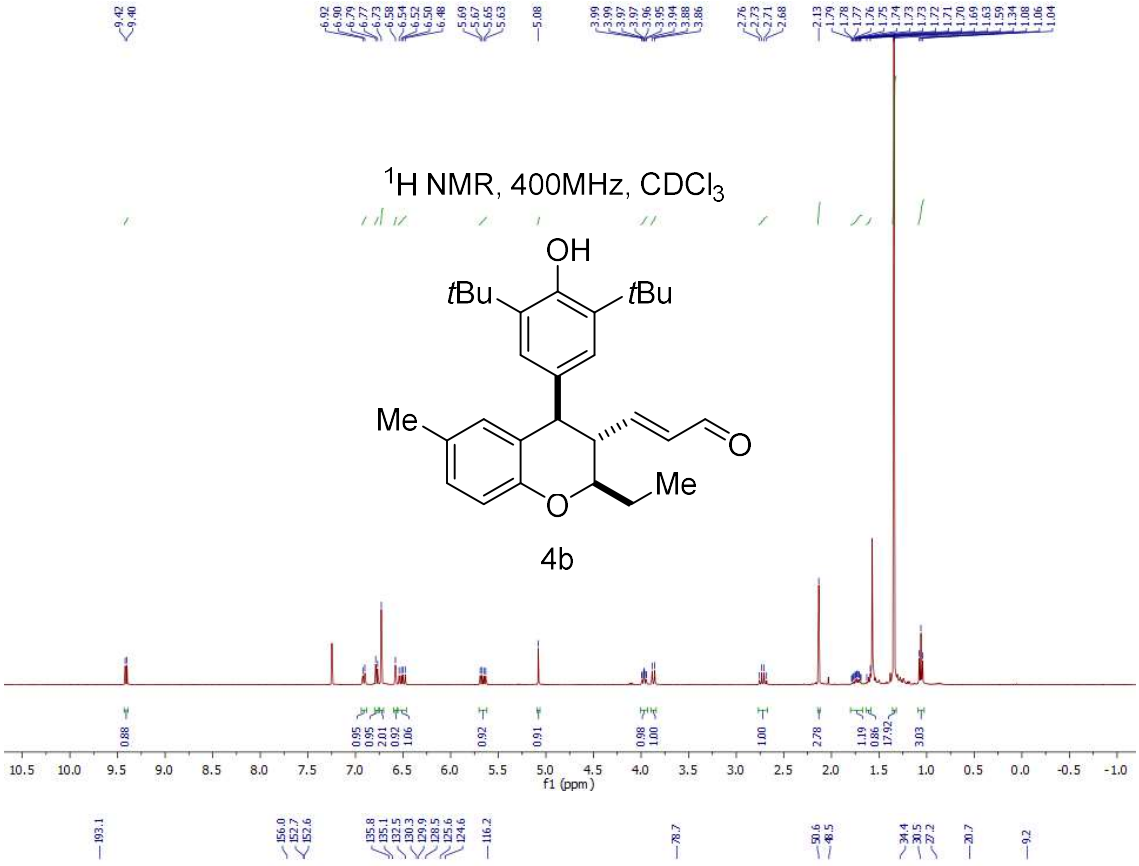
^{13}C NMR, 101MHz, DEPT-135, $CDCl_3$

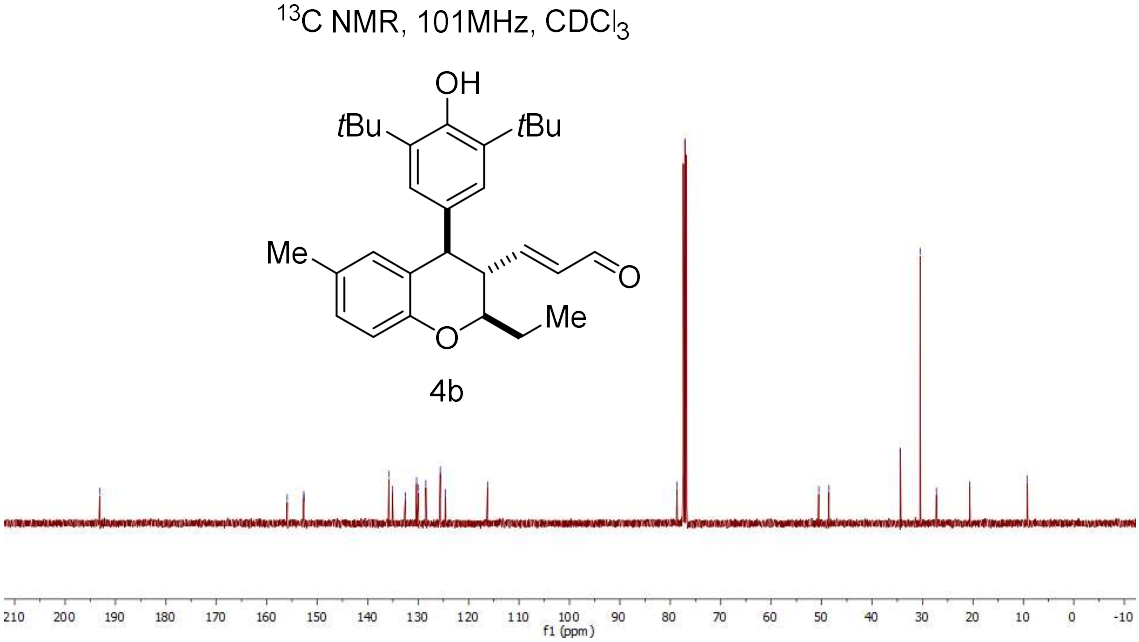


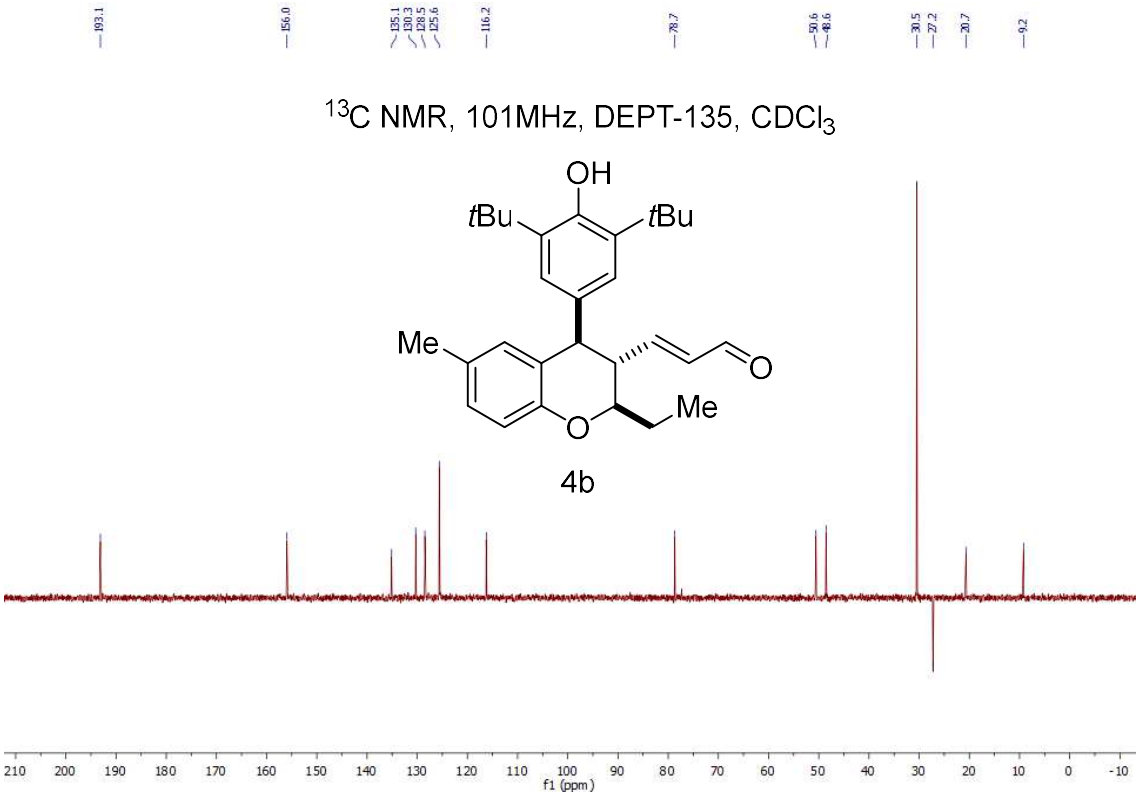
4a



8.2. (*E*)-3-((2R,3S,4R)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-ethyl-6-methylchroman-3-yl)acrylaldehyde (4b).

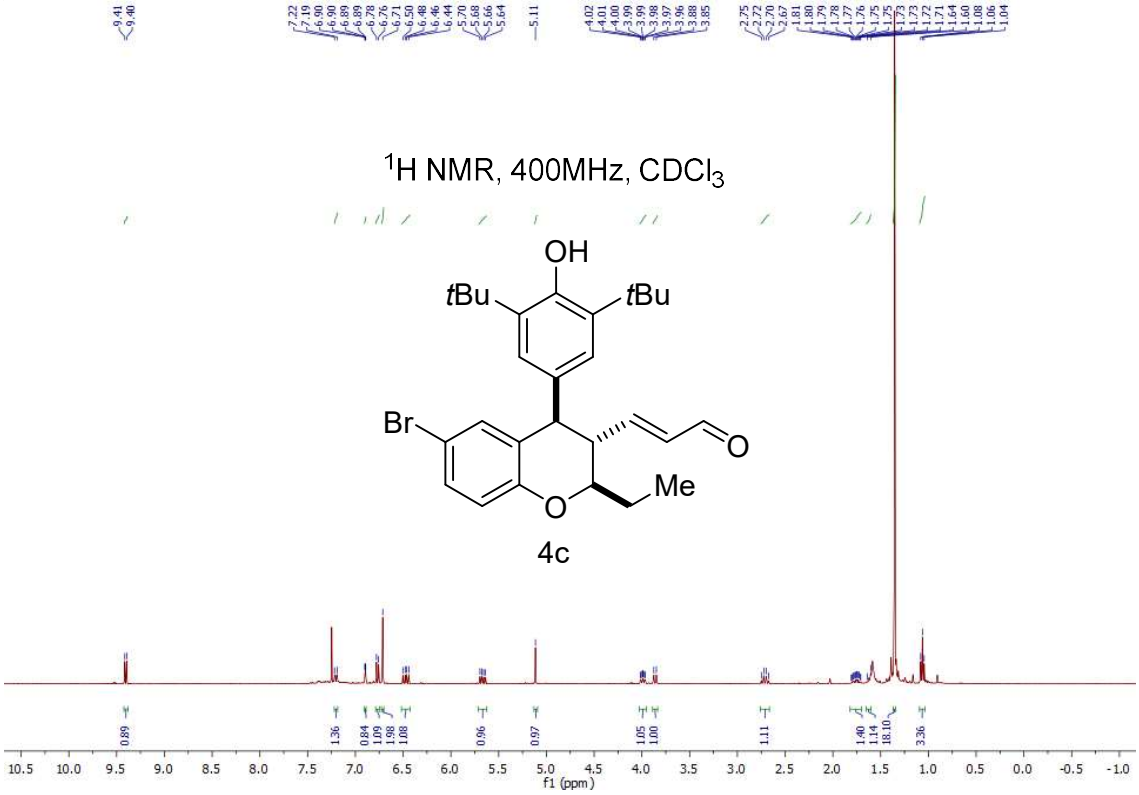




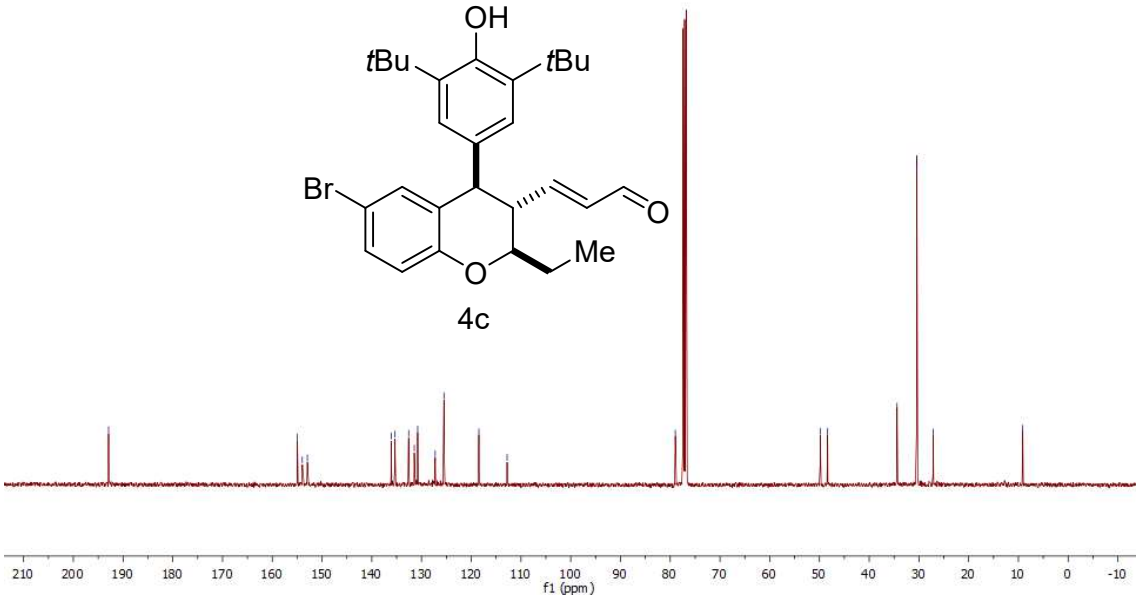

193.1
156.0
135.1
130.3
128.5
125.6
116.2
78.7
50.6
48.6
30.5
27.2
20.7
9.2
^{13}C NMR, 101MHz, DEPT-135, $CDCl_3$
OH
*t*Bu
*t*Bu
Me
O
Me
O
4b
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

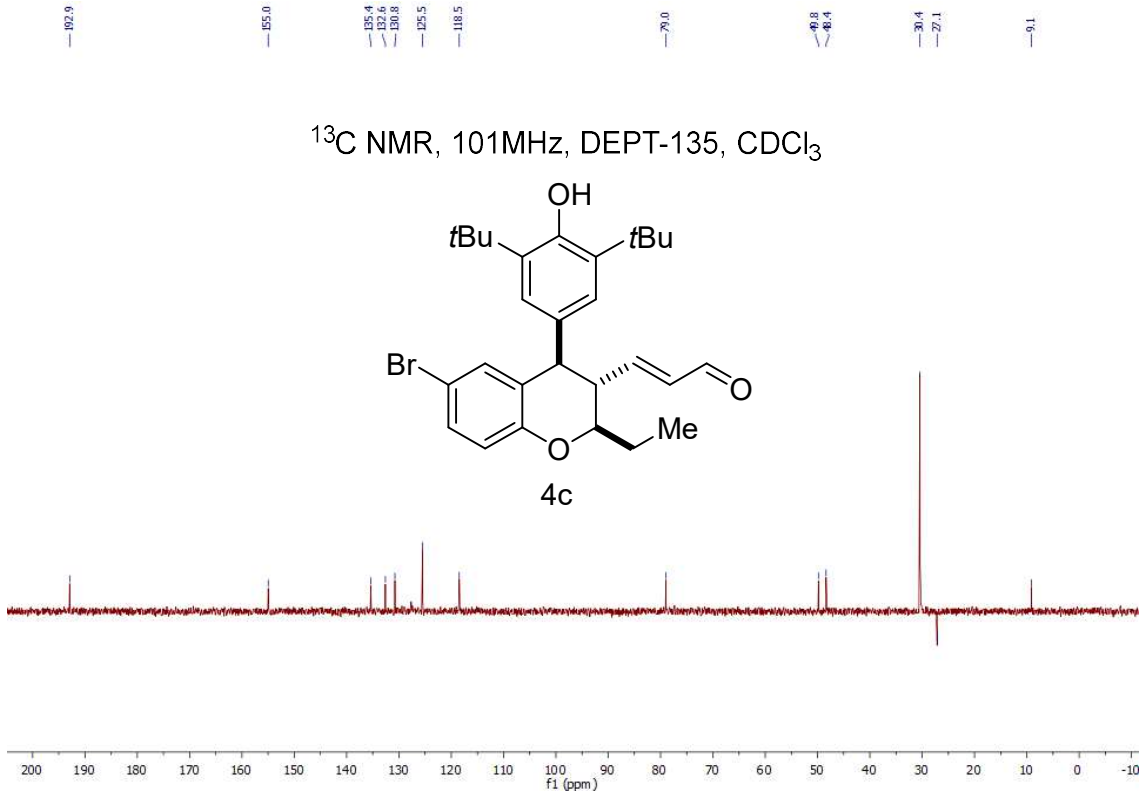
8.3. (*E*)-3-((2R,3S,4R)-6-bromo-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-ethylchroman-3-yl)acrylaldehyde (4c).

^{1}H NMR, 400MHz, $CDCl_3$

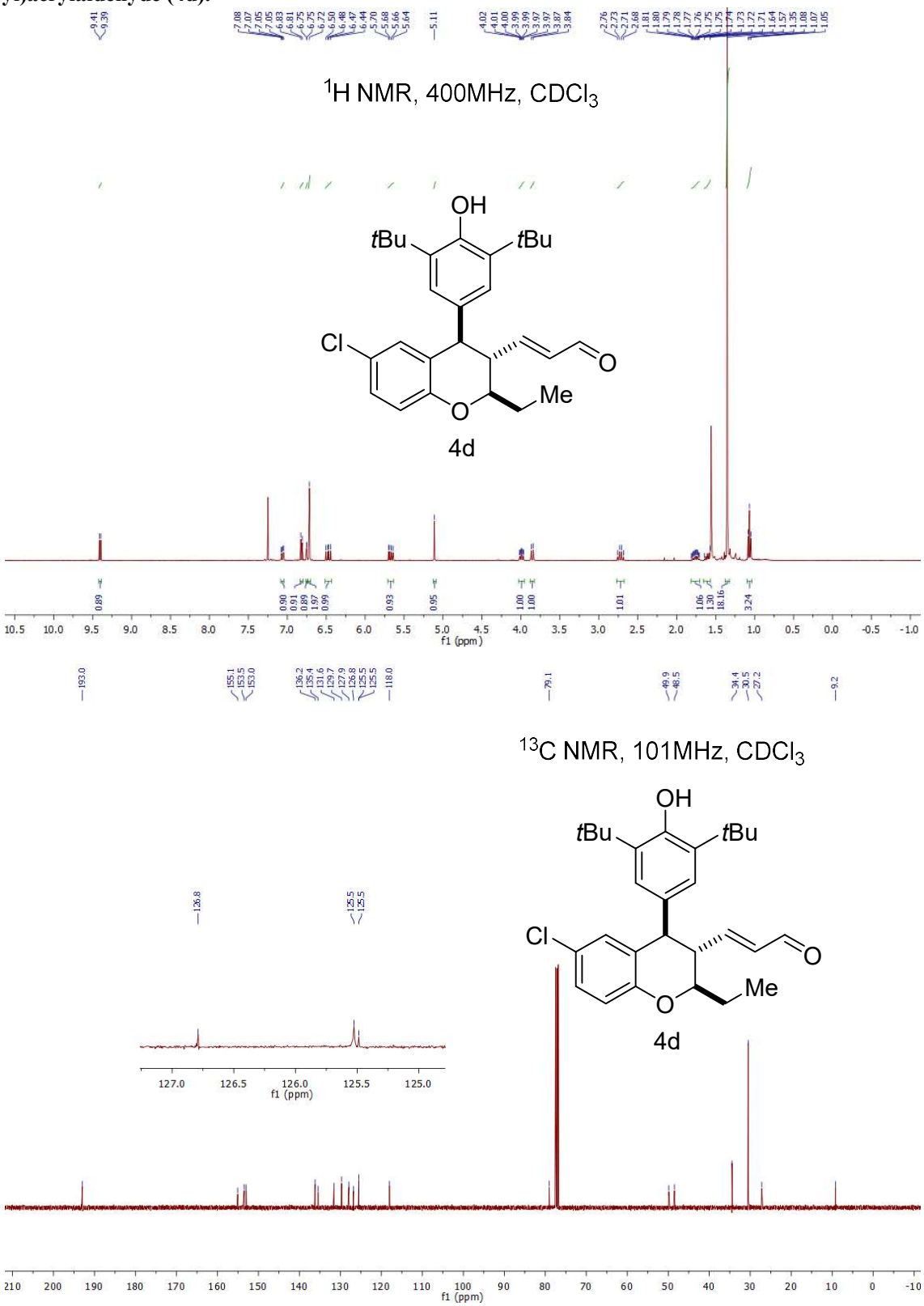


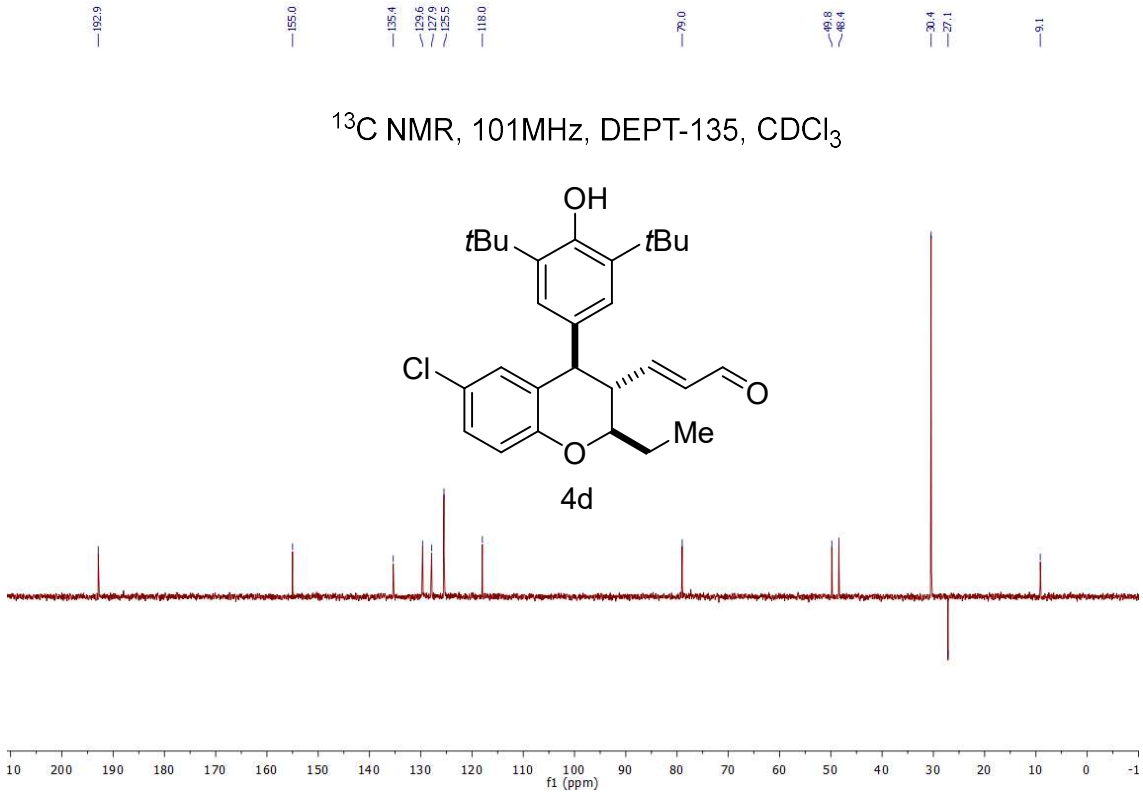
^{13}C NMR, 101MHz, $CDCl_3$



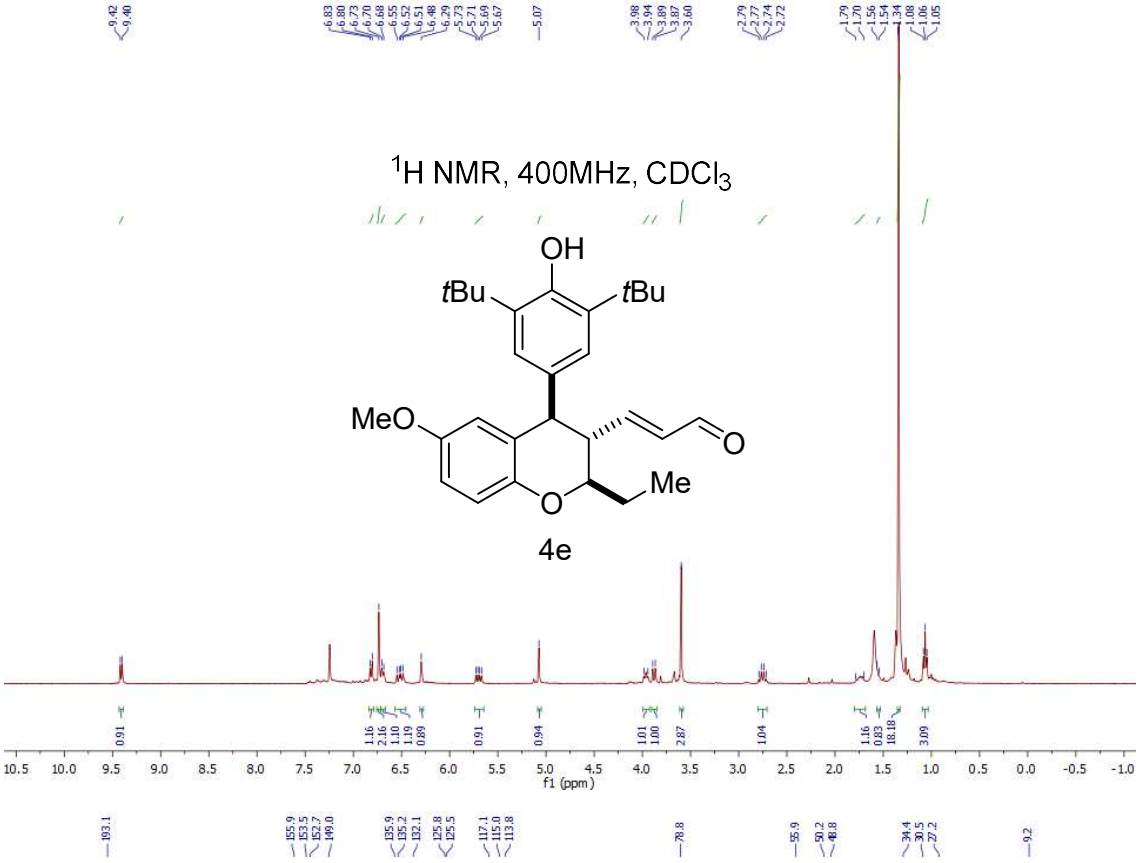

192.9
155.0
135.4
132.6
130.8
125.5
118.5
79.0
49.8
48.4
30.4
27.1
9.1
^{13}C NMR, 101MHz, DEPT-135, $CDCl_3$
OH
*t*Bu
*t*Bu
Br
O
Me
O
4c
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

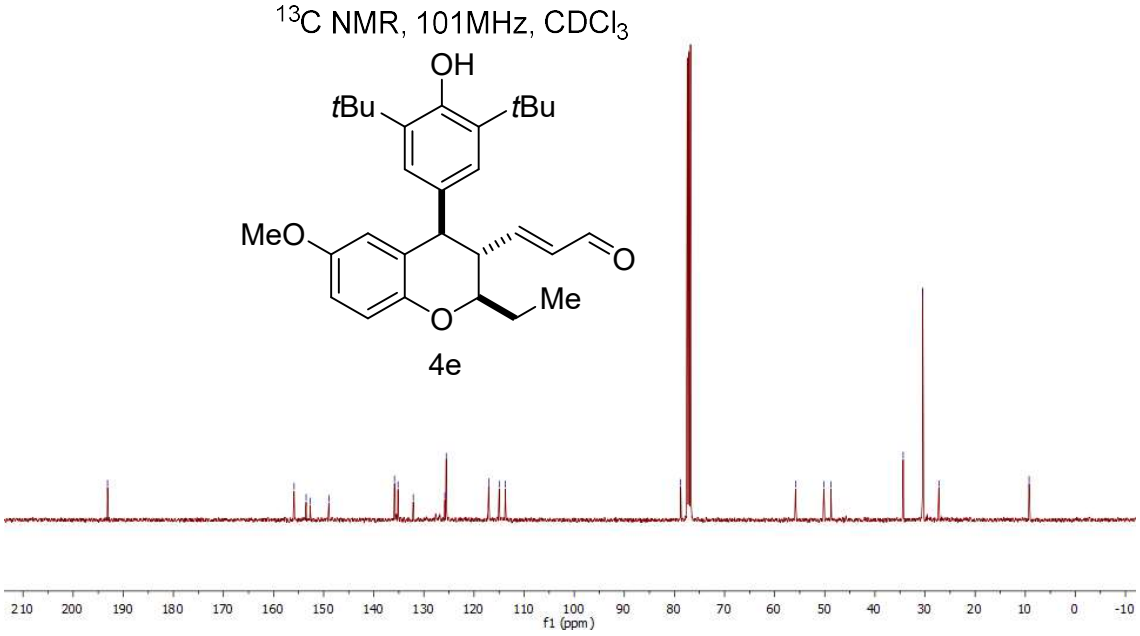
8.4. (*E*)-3-((2R,3S,4R)-6-chloro-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-ethylchroman-3-yl)acrylaldehyde (4d).

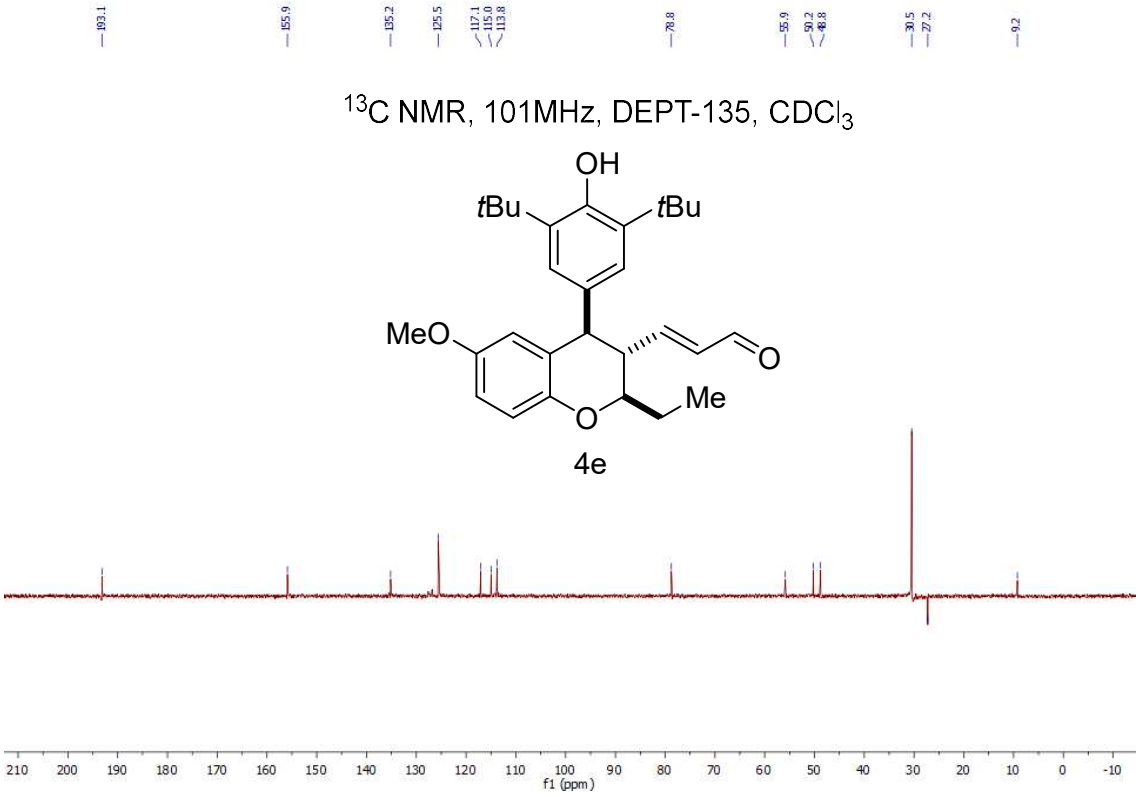



192.9
155.0
135.4
129.6
127.9
125.5
118.0
79.0
49.8
48.4
30.4
27.1
9.1
^{13}C NMR, 101MHz, DEPT-135, $CDCl_3$
OH
*t*Bu
*t*Bu
Cl
O
Me
O
4d
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

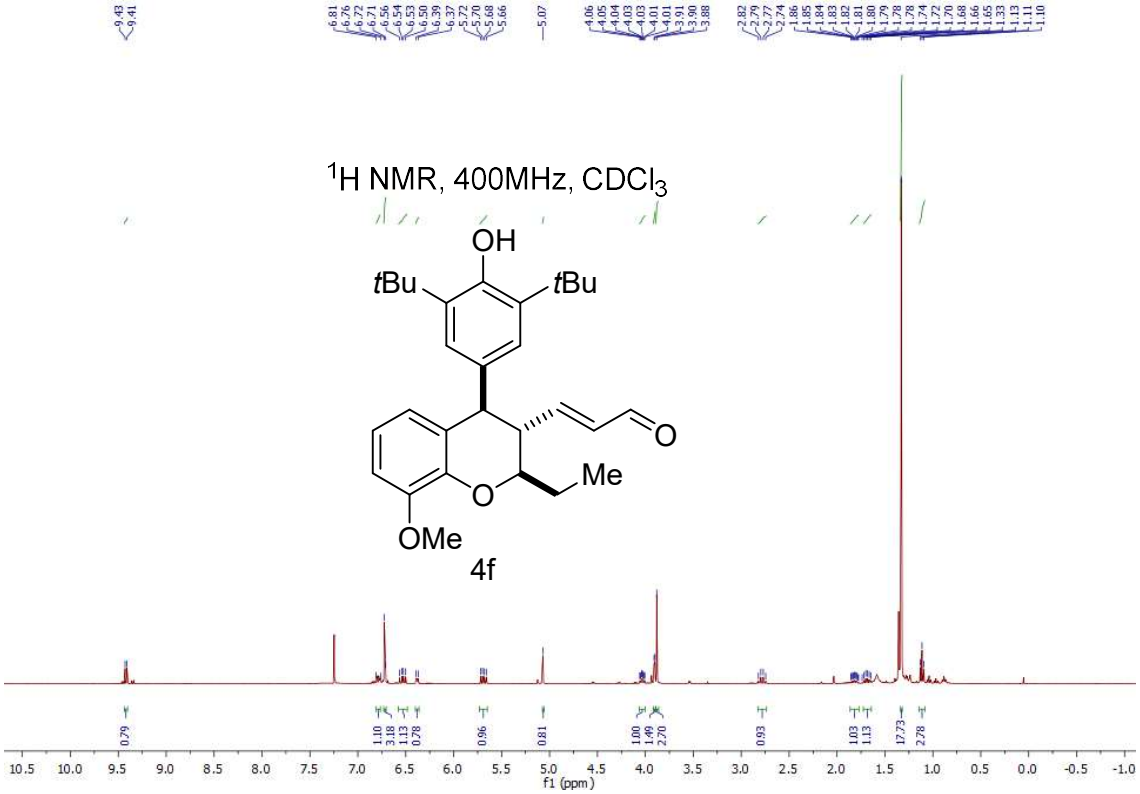
8.5. (*E*)-3-((2R,3S,4R)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-ethyl-6-methoxychroman-3-yl)acrylaldehyde (4e).

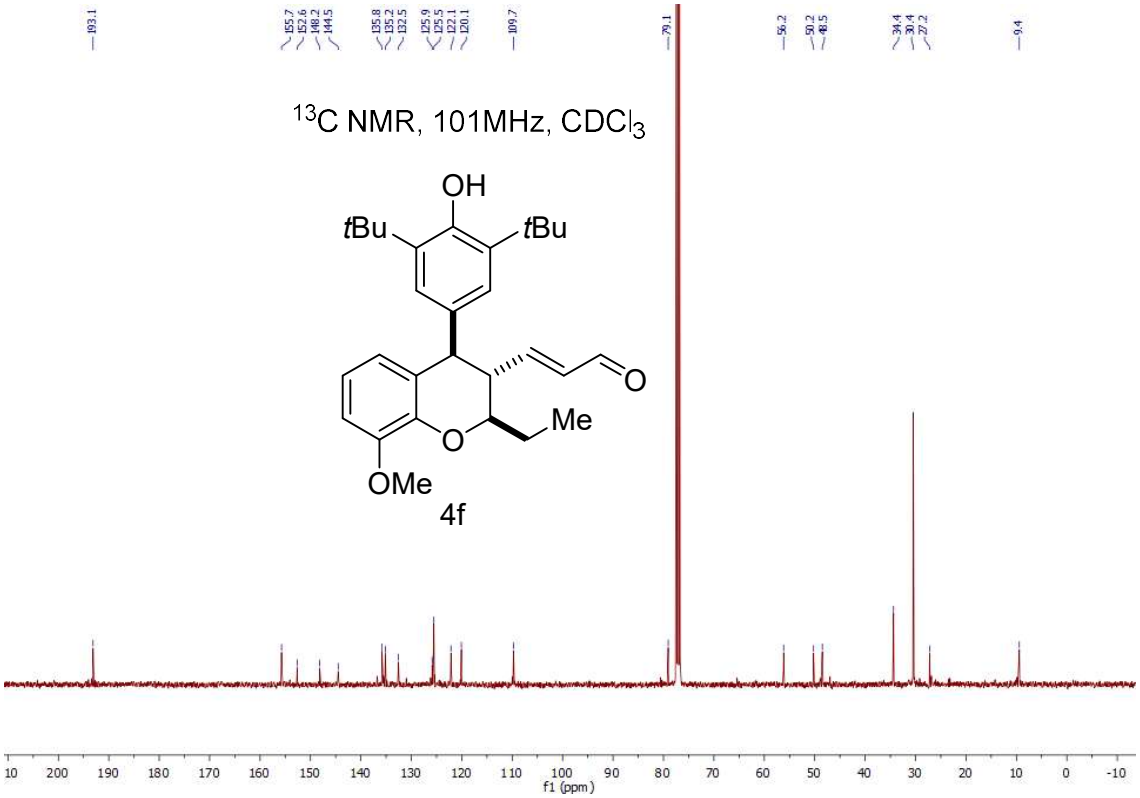


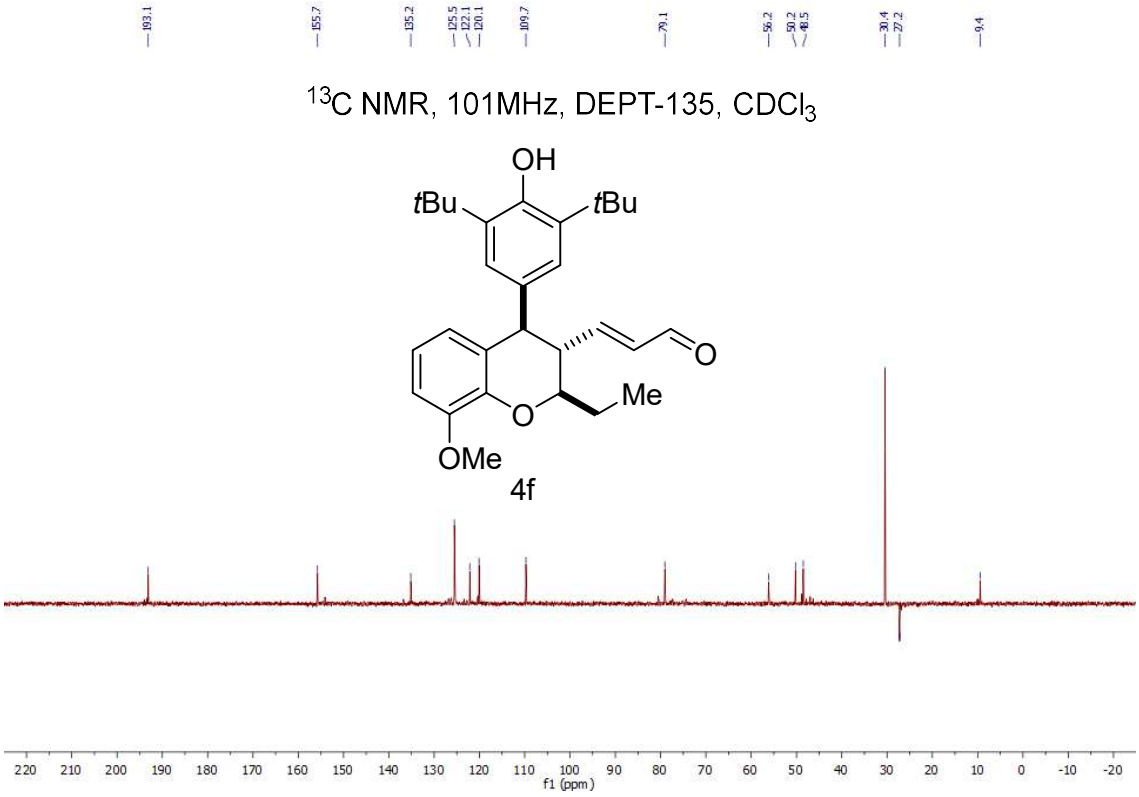



193.1
155.9
135.2
125.5
117.1
115.0
113.8
78.8
55.9
50.2
48.8
30.5
27.2
9.2
^{13}C NMR, 101MHz, DEPT-135, $CDCl_3$
OH
*t*Bu
*t*Bu
MeO
O
Me
O
4e
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

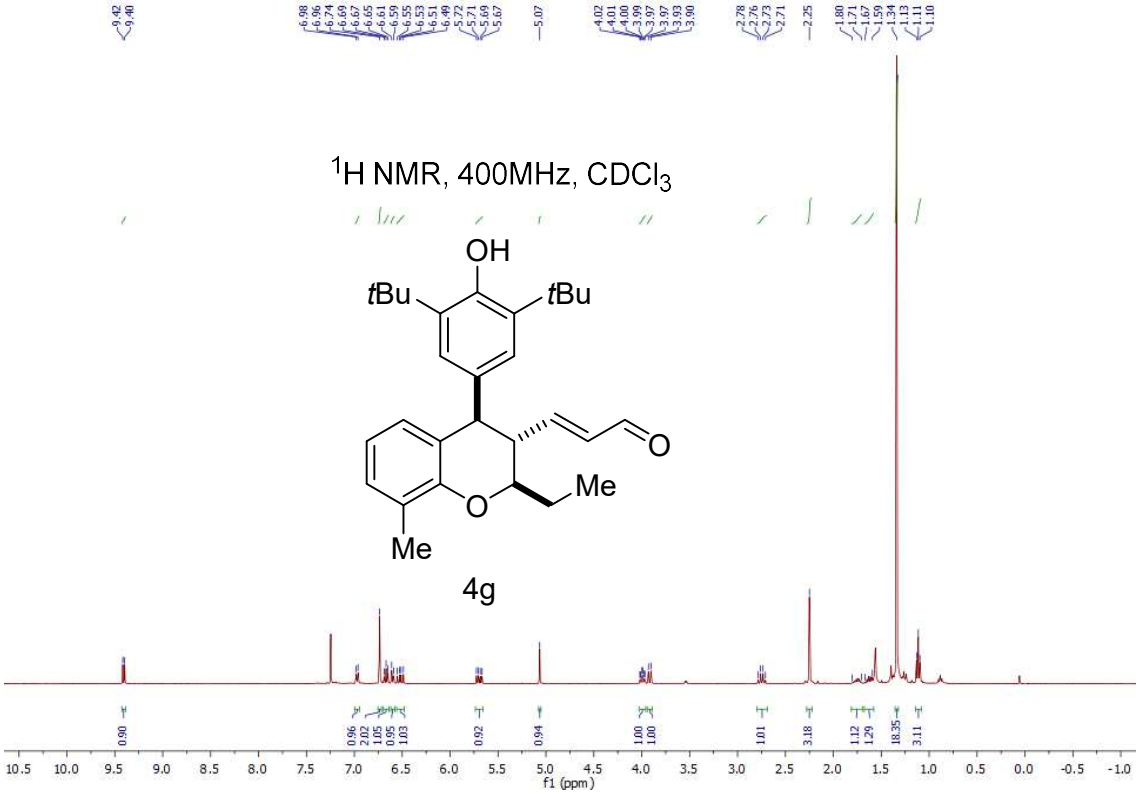
8.6. (*E*)-3-((2R,3S,4R)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-ethyl-8-methoxychroman-3-yl)acrylaldehyde (4f).

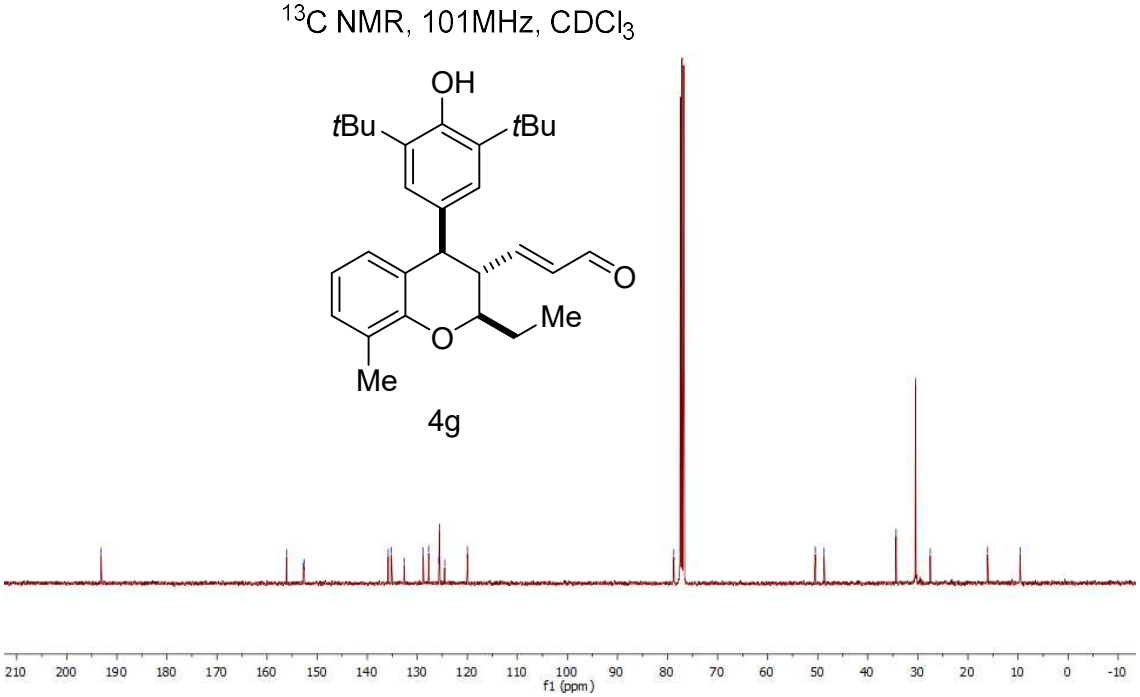


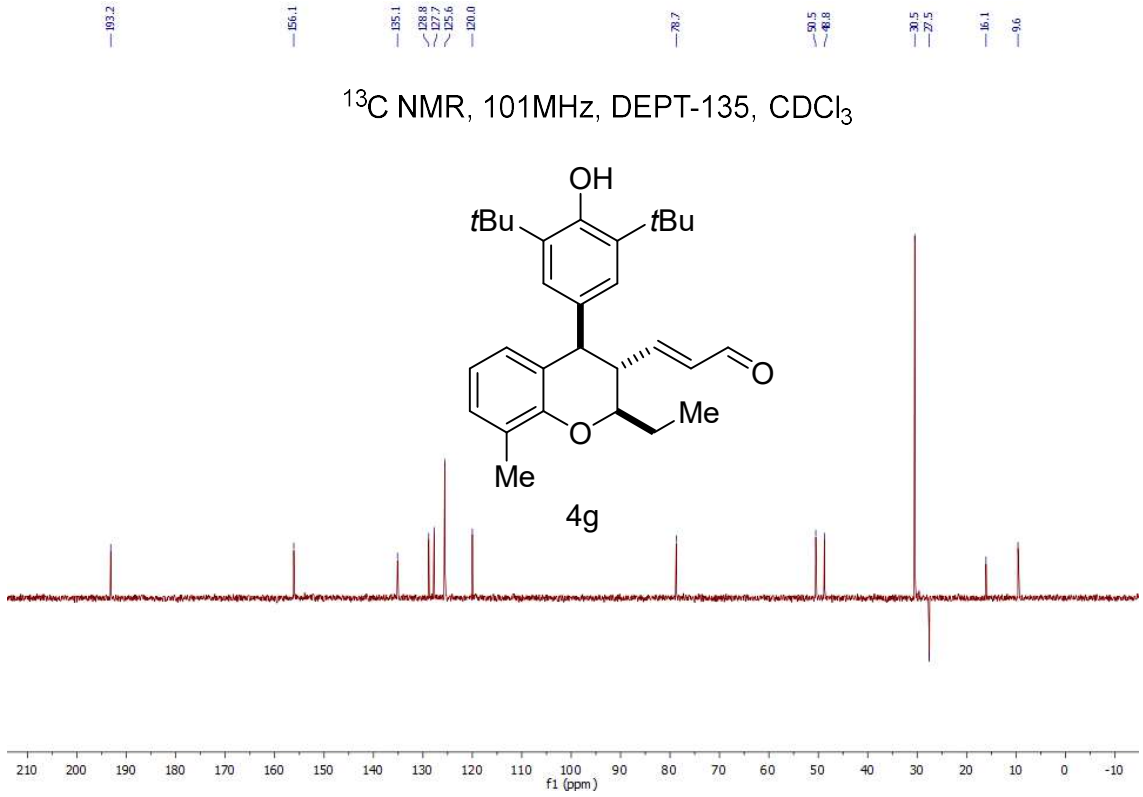



193.1
155.7
135.2
125.5
122.1
120.1
109.7
79.1
56.2
50.2
48.5
30.4
27.2
9.4
13C NMR, 101MHz, DEPT-135, CDCl3
OH
tBu
tBu
O
Me
O
OMe
4f
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

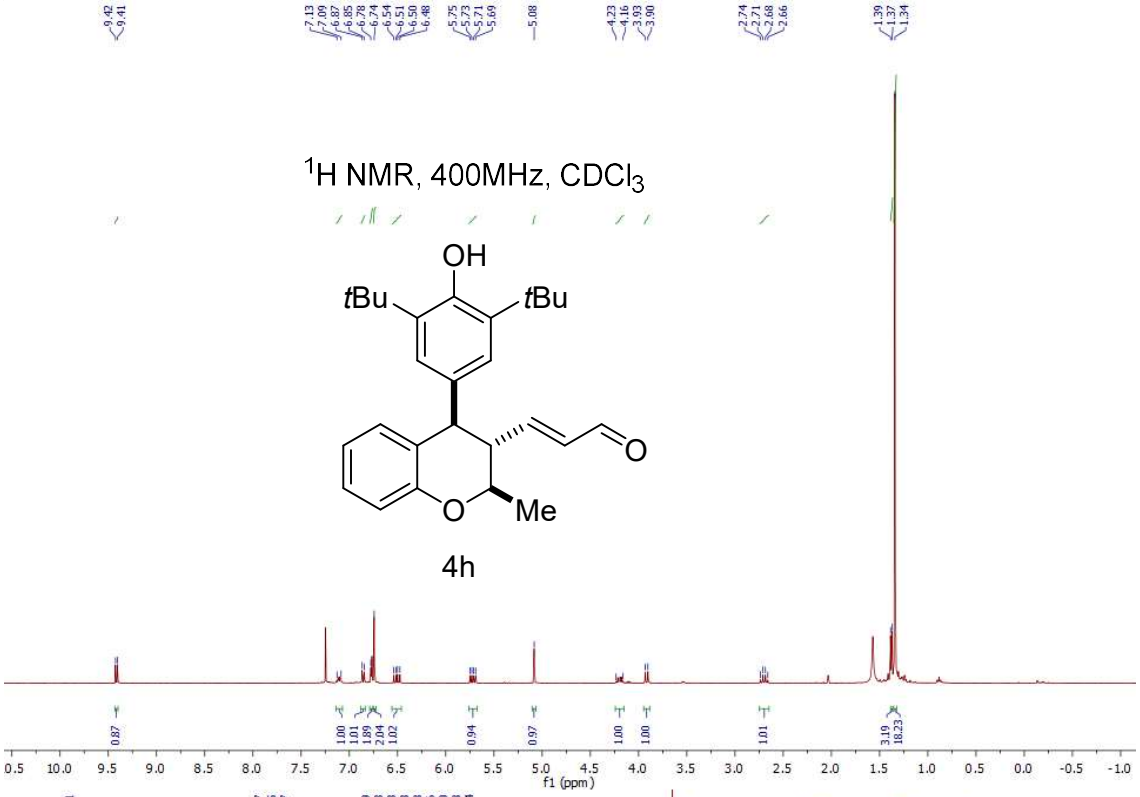
8.7. (*E*)-3-((2R,3S,4R)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-ethyl-8-methylchroman-3-yl)acrylaldehyde (4g).

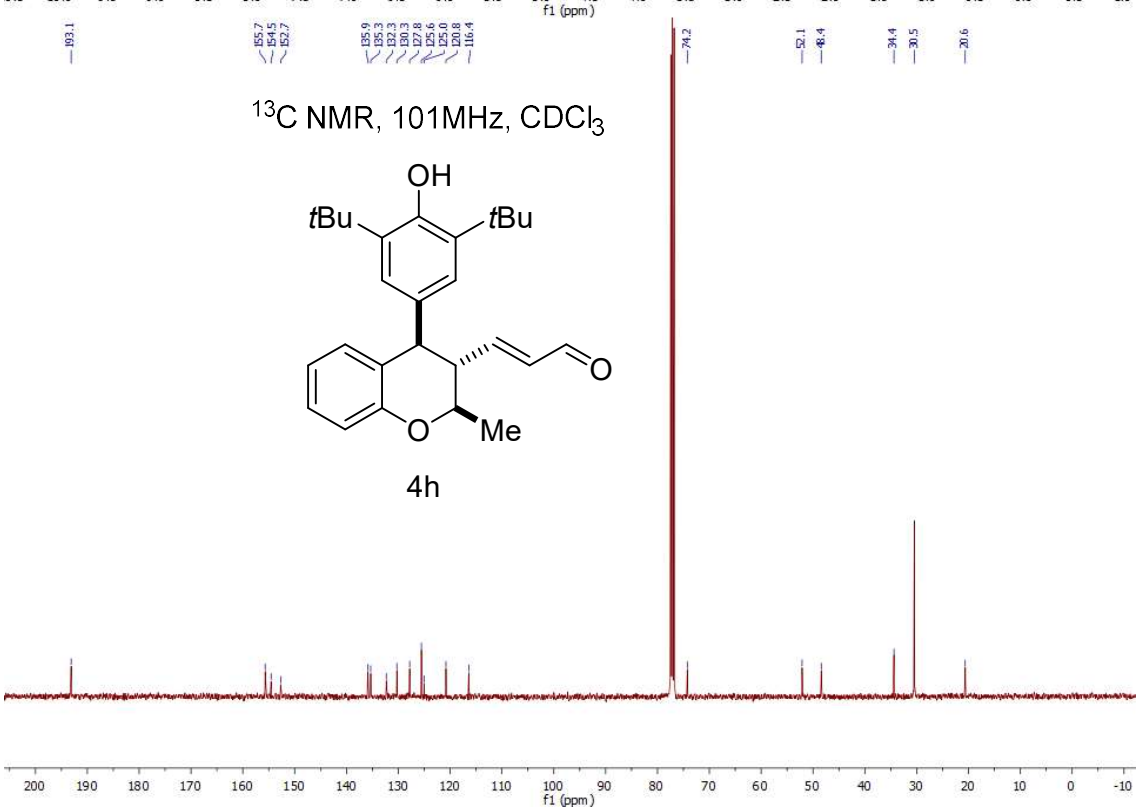





193.2
156.1
135.1
128.8
127.7
125.6
120.0
78.7
50.5
48.8
30.5
27.5
16.1
9.6
^{13}C NMR, 101MHz, DEPT-135, $CDCl_3$
OH
*t*Bu
*t*Bu
O
Me
O
Me
4g
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

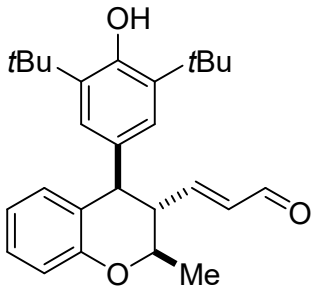
8.8. (*E*)-3-((2R,3S,4R)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-methylchroman-3-yl)acrylaldehyde (4h).



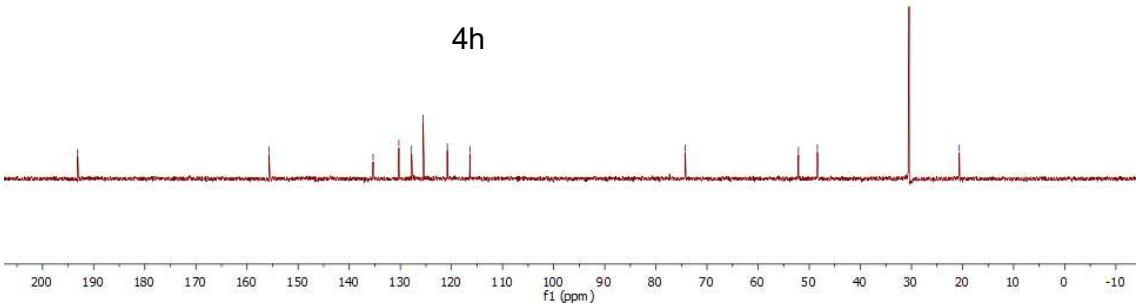


193.1 155.7 135.3 130.3 127.8 125.5 120.8 116.4 74.2 52.1 48.4 20.6

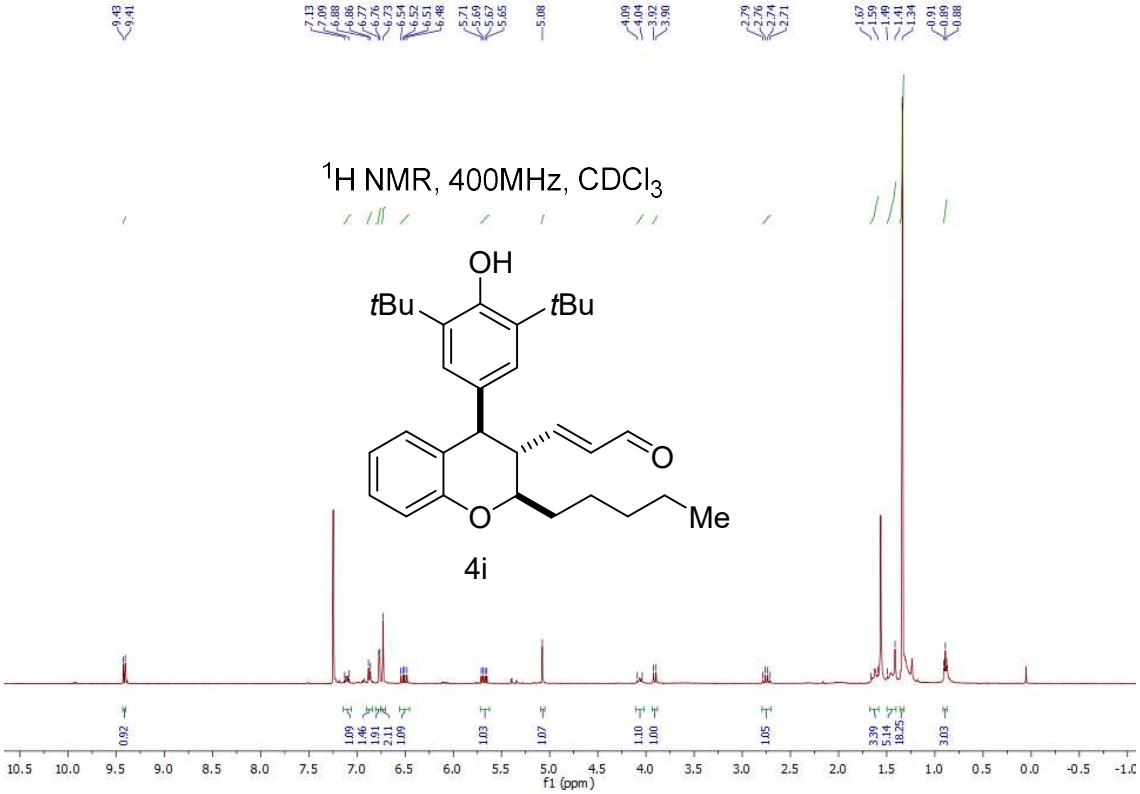
^{13}C NMR, 101MHz, DEPT-135, $CDCl_3$

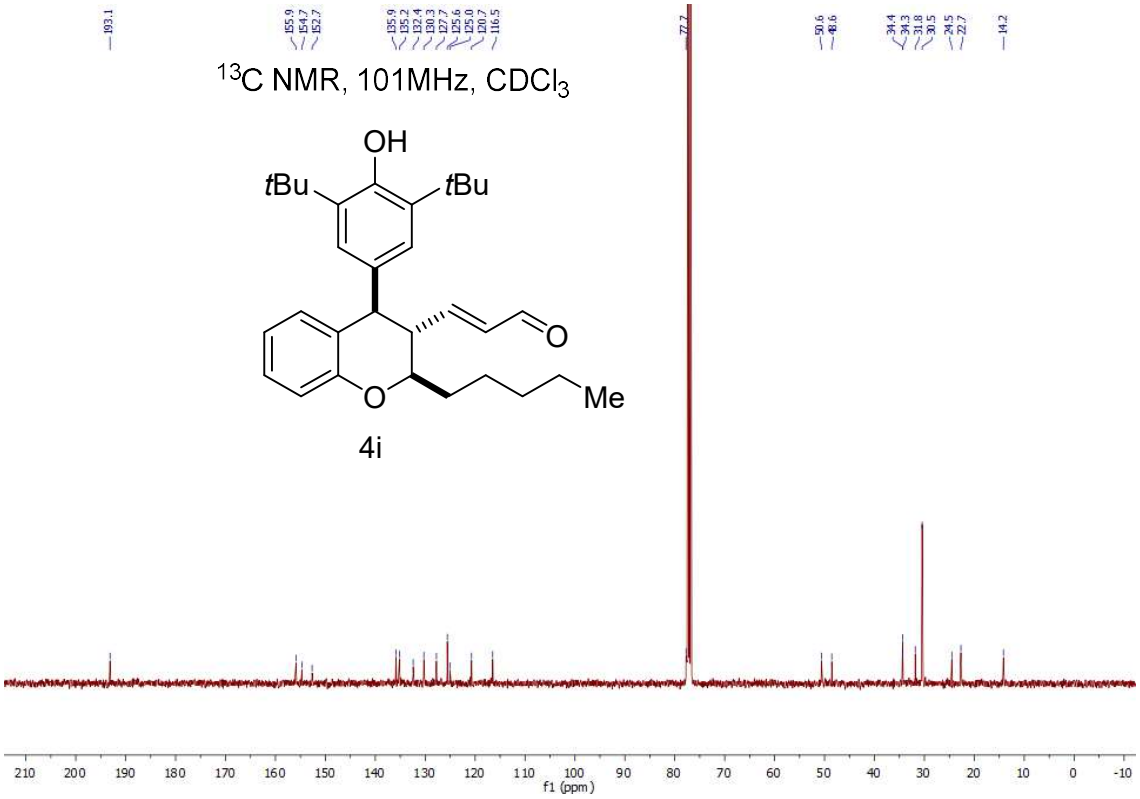


4h



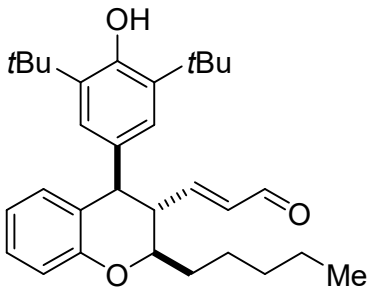
8.9. (*E*)-3-((2R,3S,4R)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-pentylchroman-3-yl)acrylaldehyde (4i).



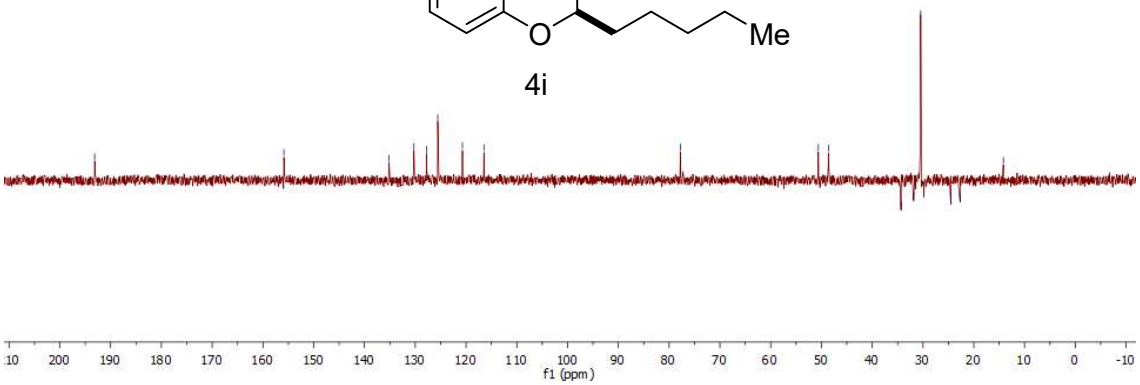


193.1 155.9 135.2 130.3 127.7 125.6 120.7 116.5 77.7 50.6 46.6 34.3 31.8 30.5 24.5 22.7 14.2

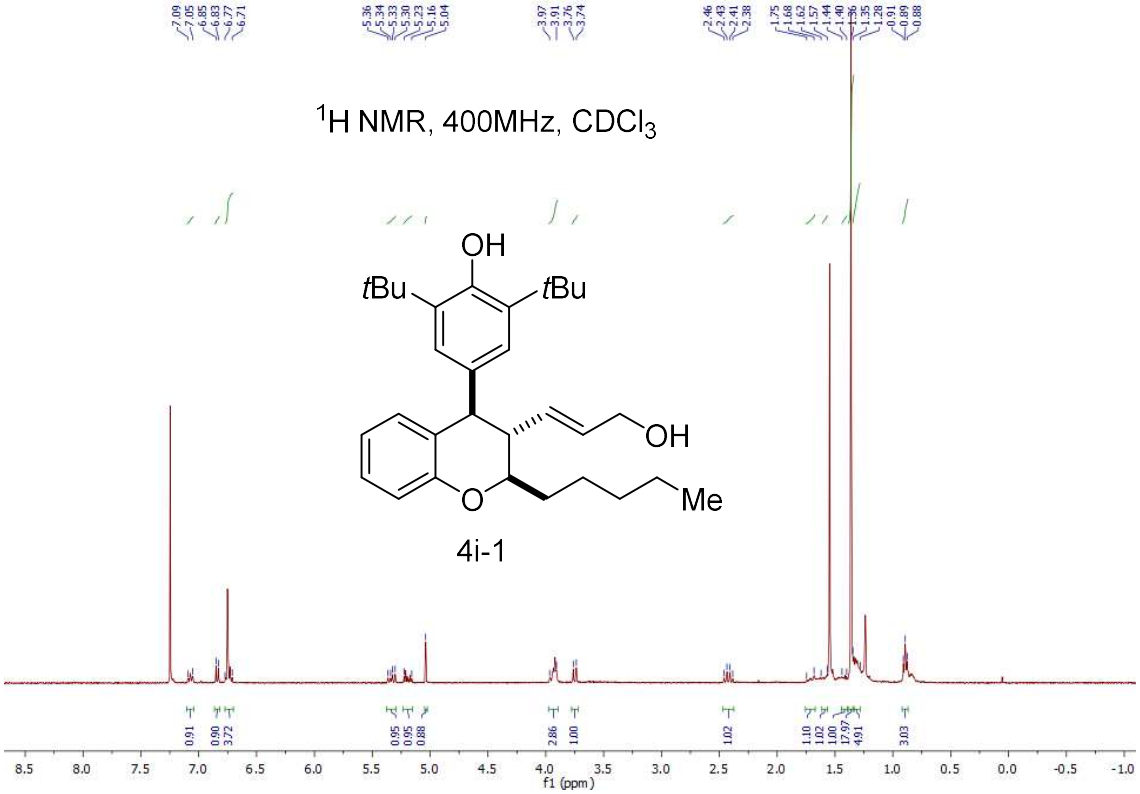
^{13}C NMR, 101MHz, DEPT-135, $CDCl_3$

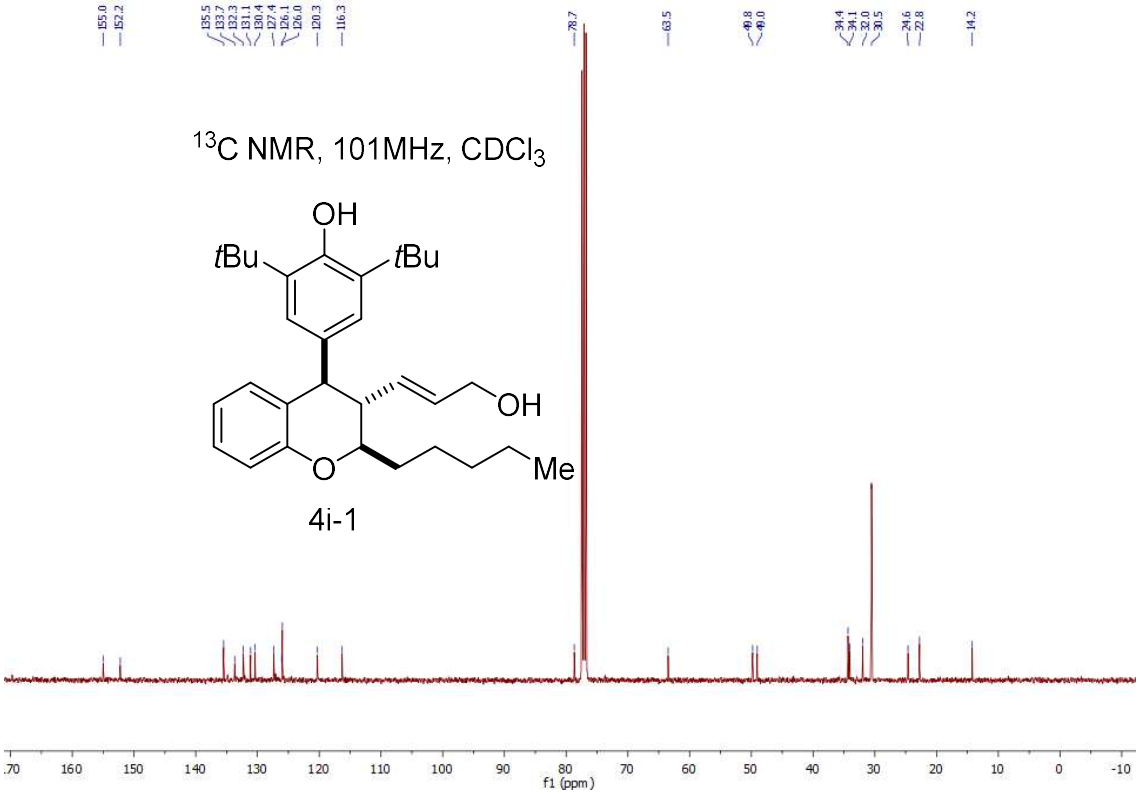


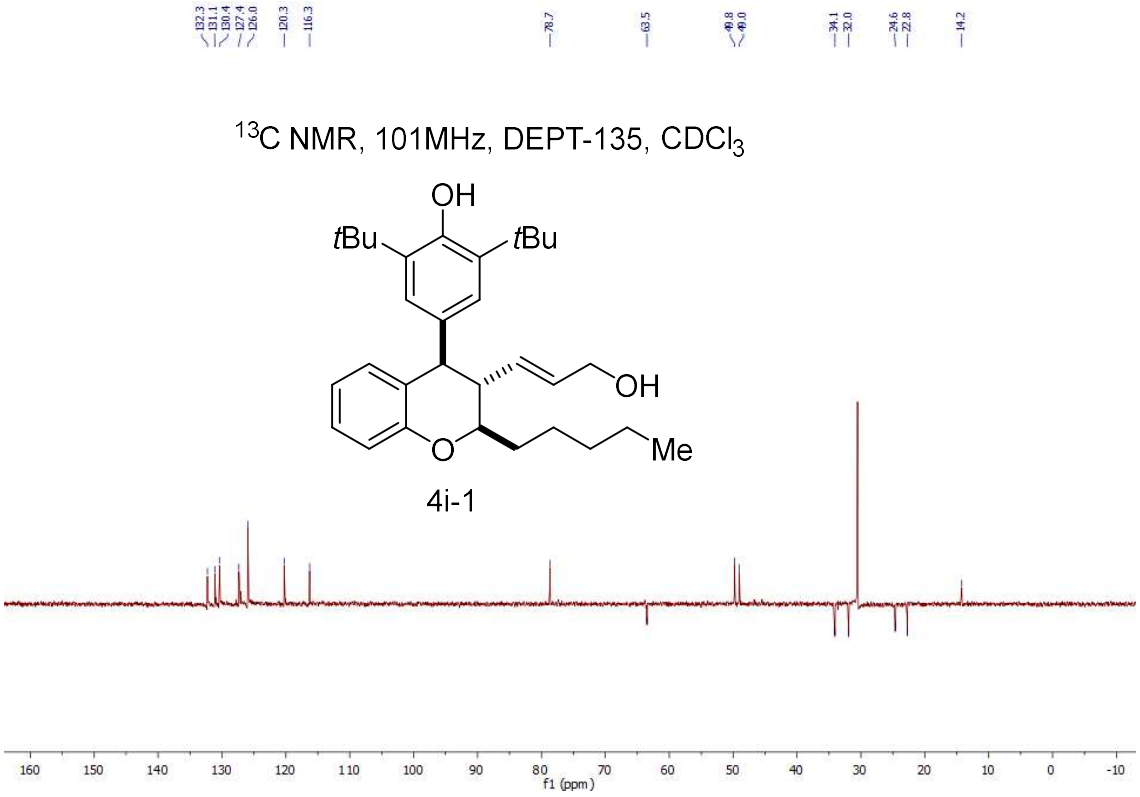
4i



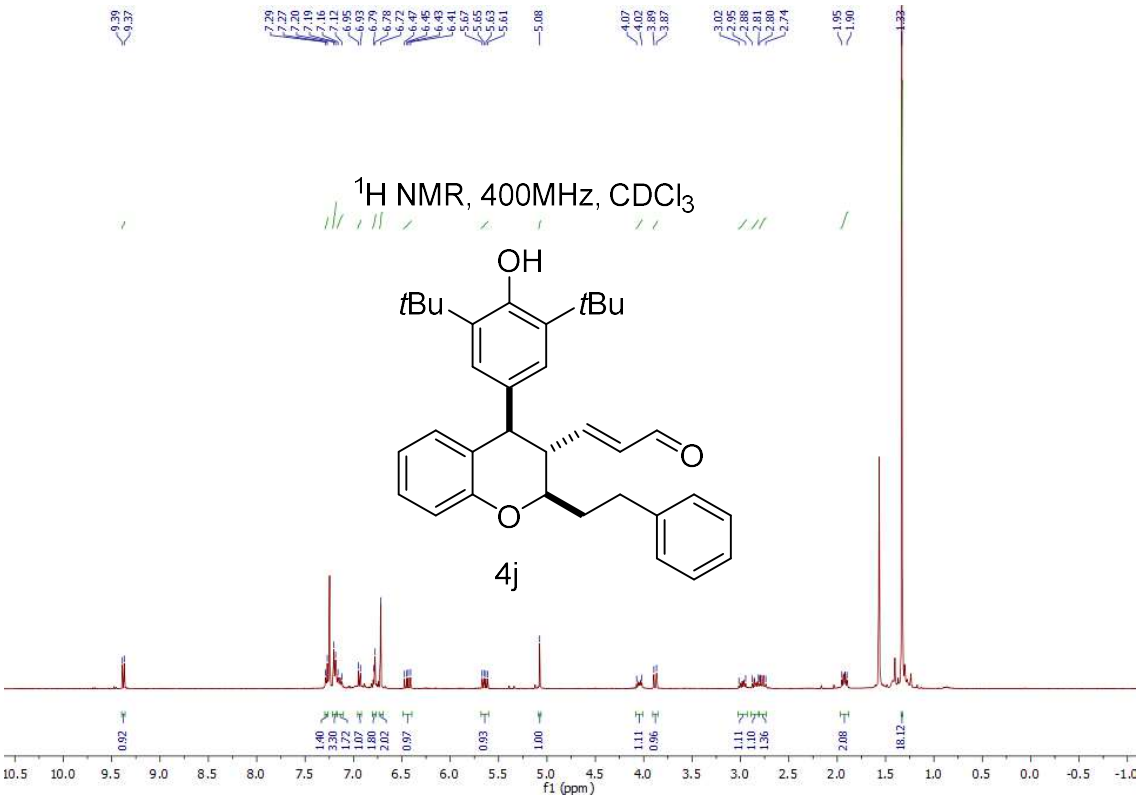
8.10. 2,6-di-*tert*-butyl-4-((2R,3S,4R)-3-((*E*)-3-hydroxyprop-1-en-1-yl)-2-pentylchroman-4-yl)phenol (4i-1).

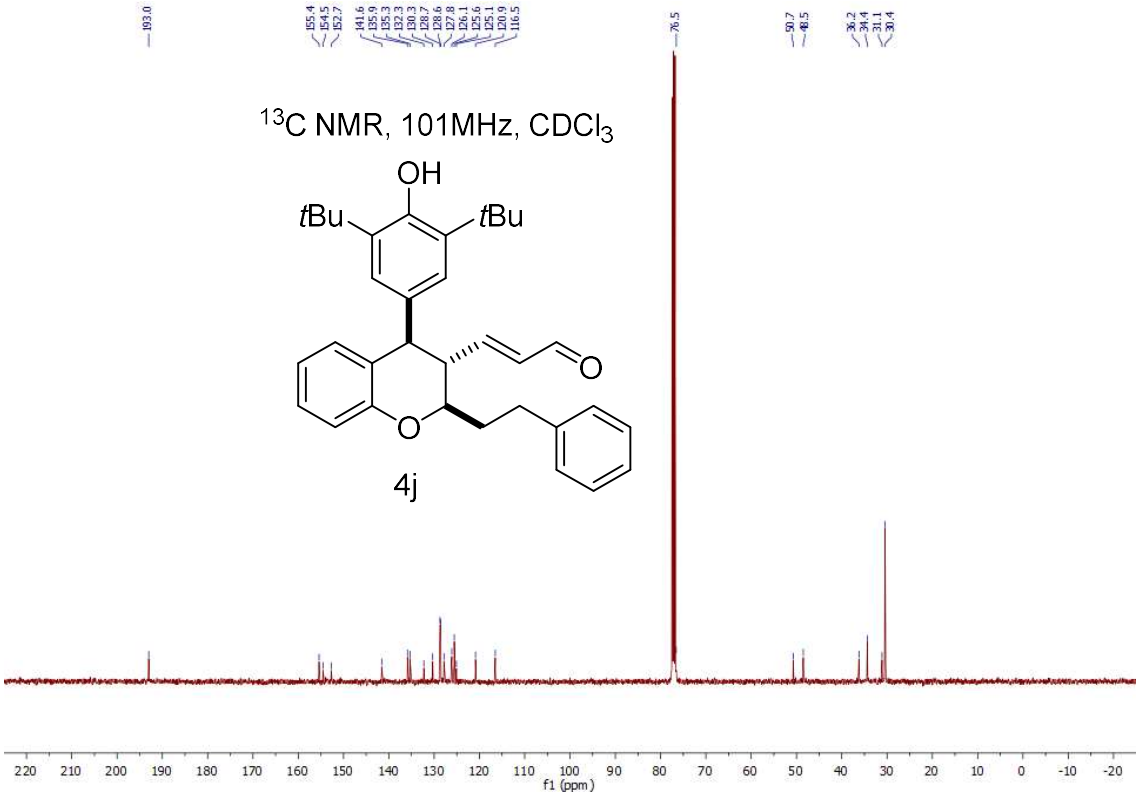


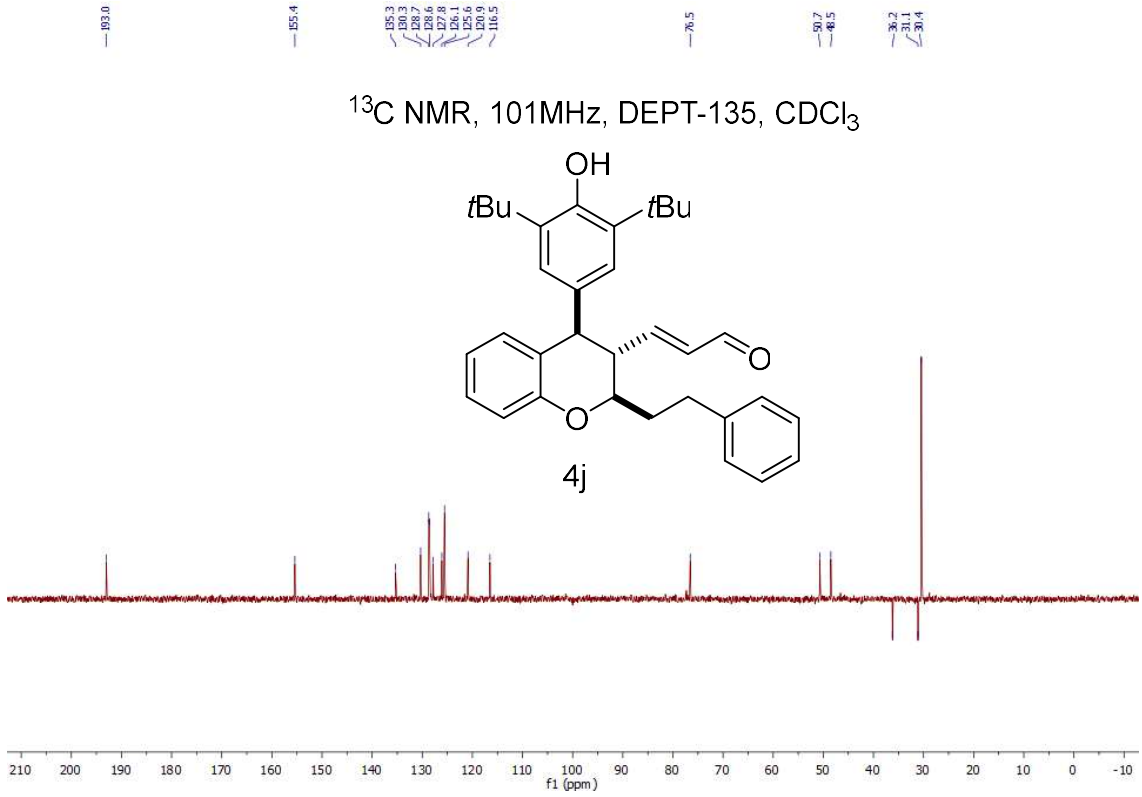



123.3
121.1
130.4
127.4
126.0
120.3
116.3
78.7
63.5
49.8
49.0
34.1
32.0
24.6
22.8
14.2
^{13}C NMR, 101MHz, DEPT-135, CDCl$_3$
OH
*t*Bu
*t*Bu
OH
O
Me
4i-1
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

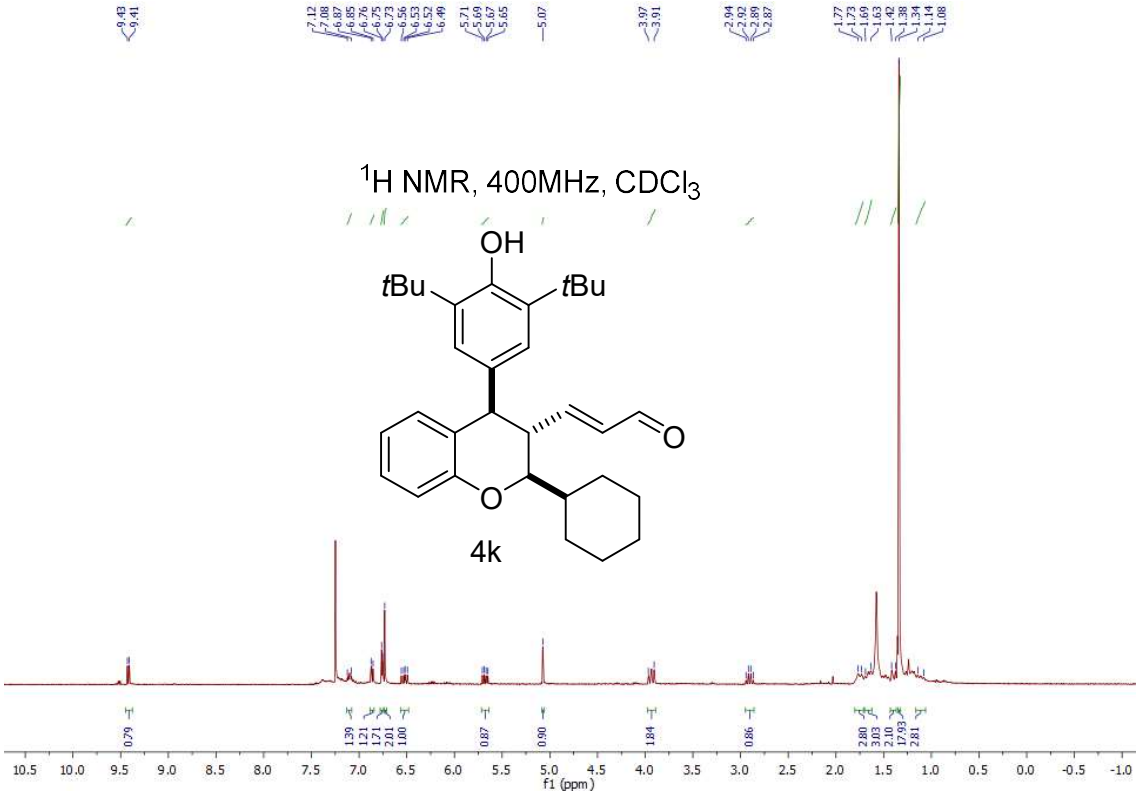
8.11. (*E*)-3-((2R,3S,4R)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-phenethylchroman-3-yl)acrylaldehyde (4j).

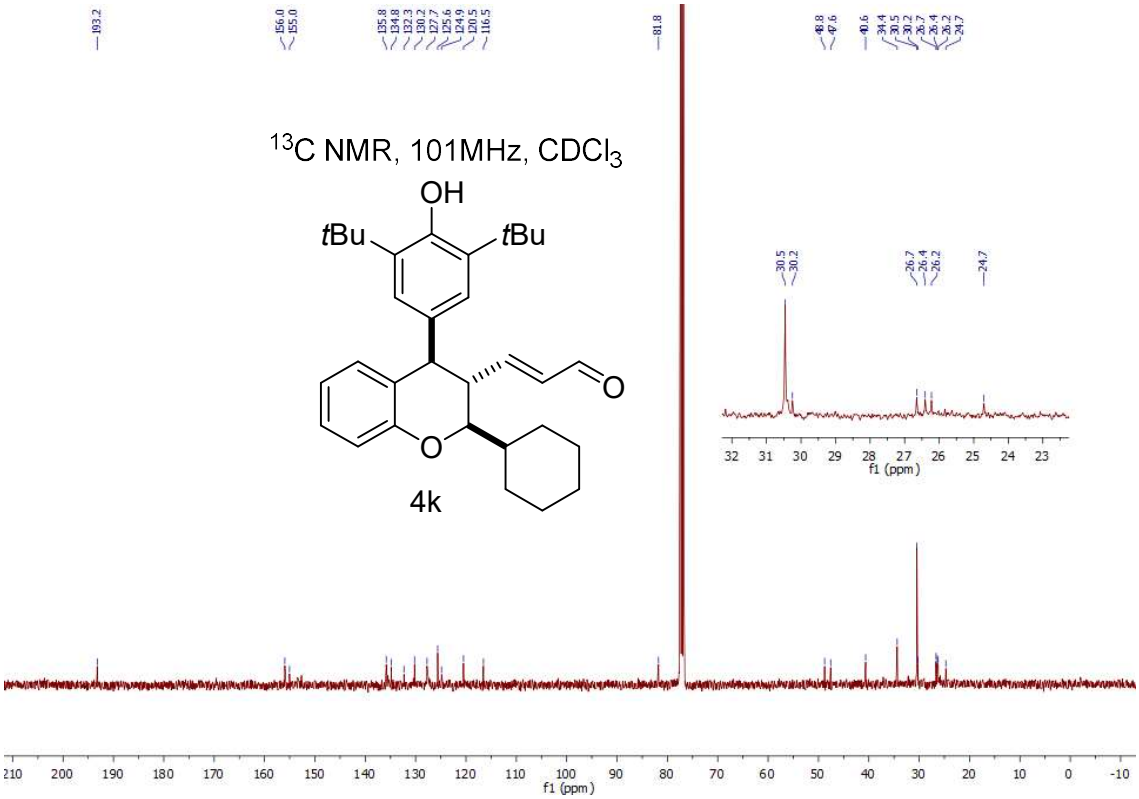


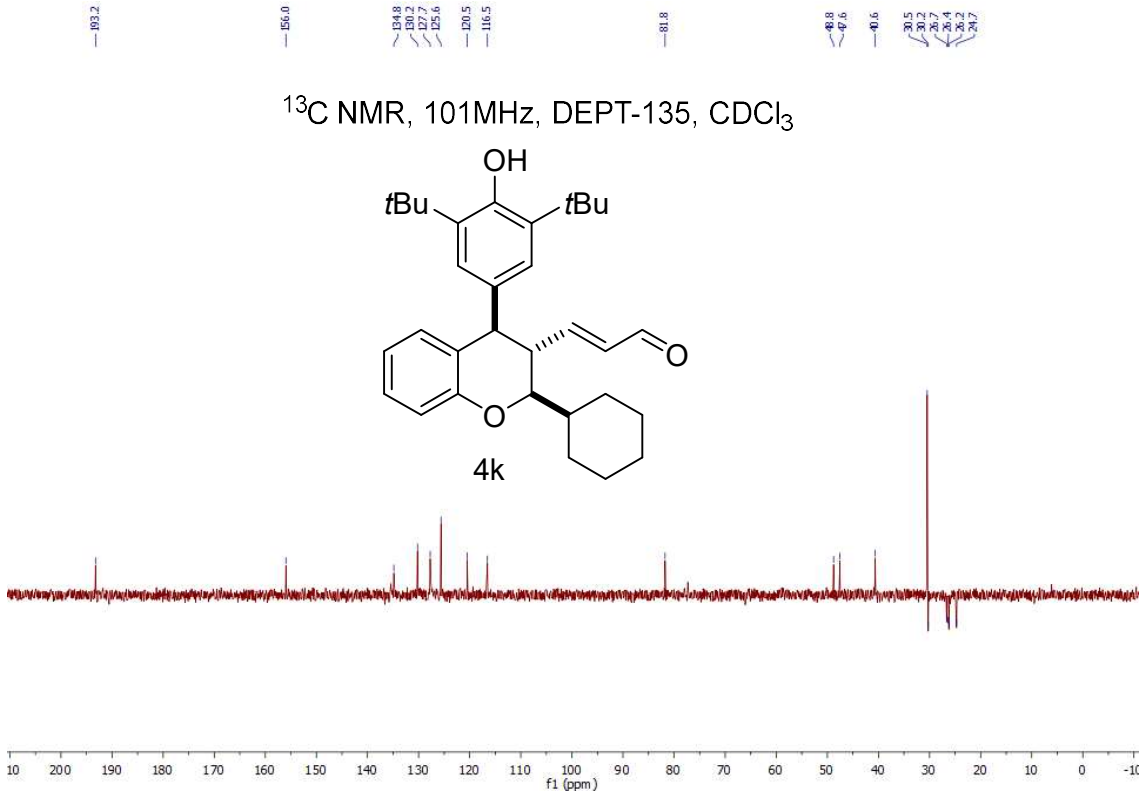



193.0
155.4
135.3
130.3
128.7
128.6
127.8
126.1
125.6
120.9
116.5
76.5
50.7
48.5
36.2
31.1
30.4
13C NMR, 101MHz, DEPT-135, CDCl3
OH
tBu
tBu
O
O
4j
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

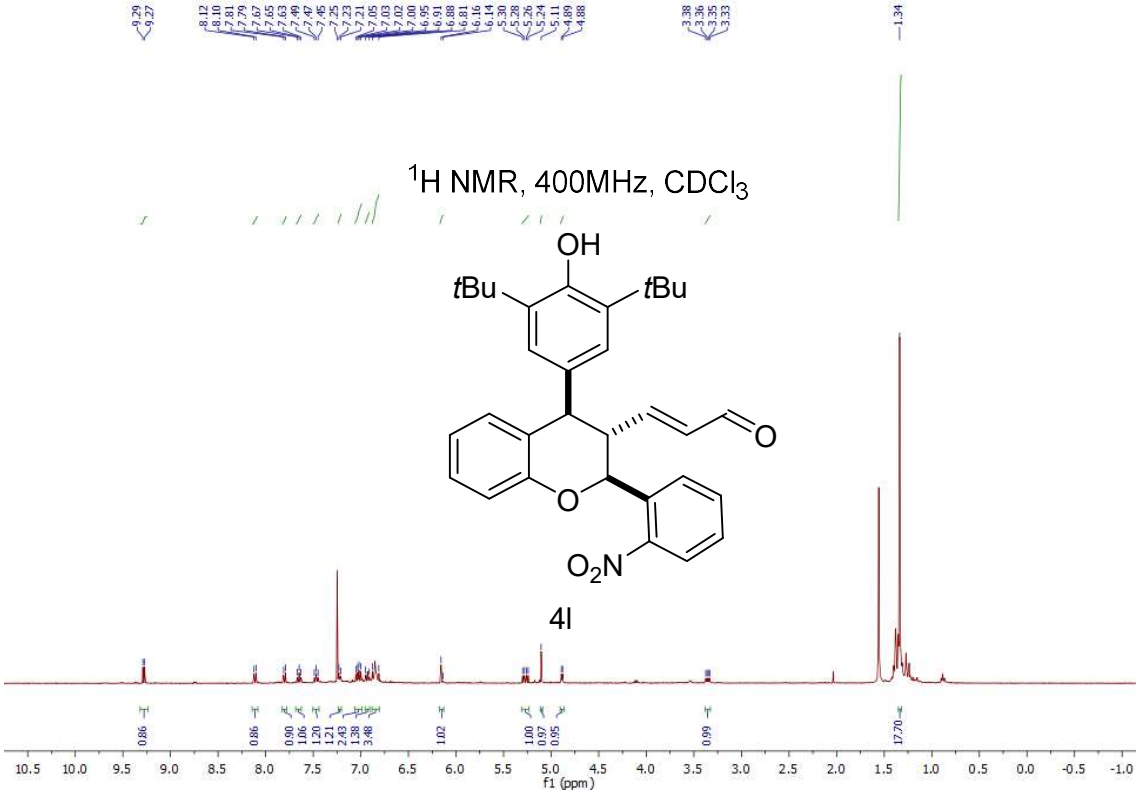
8.12. (*E*)-3-((2R,3S,4R)-2-cyclohexyl-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)chroman-3-yl)acrylaldehyde (4k).

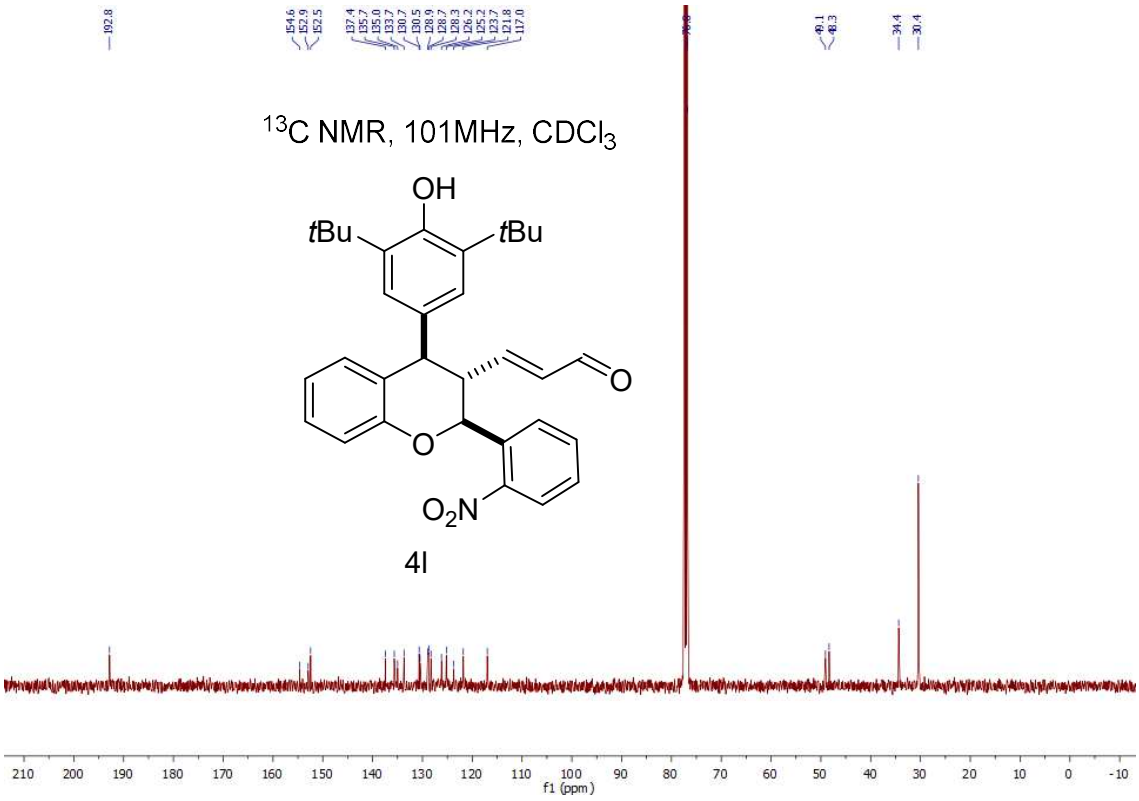


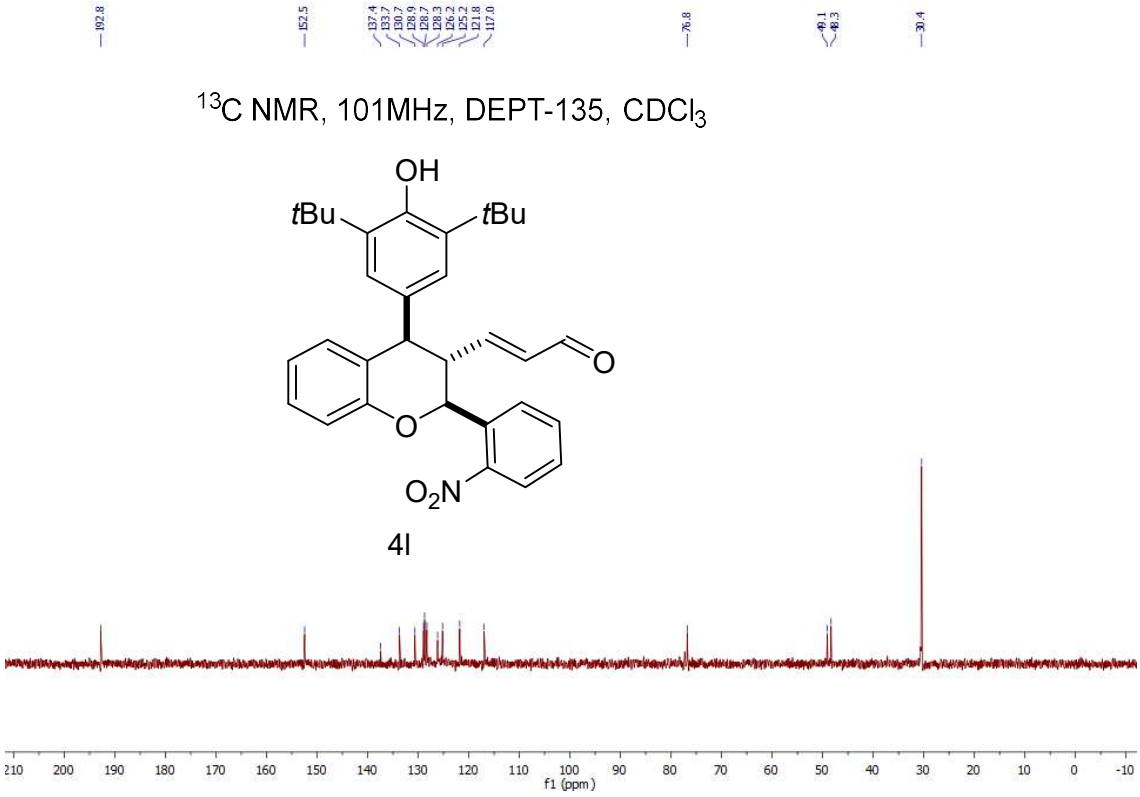



193.2
156.0
134.8
130.2
127.7
125.6
120.5
116.5
81.8
48.8
47.6
40.6
30.5
30.2
26.7
26.4
26.2
24.7
^{13}C NMR, 101MHz, DEPT-135, CDCl$_3$
OH
tBu
tBu
O
O
4k
f1 (ppm)

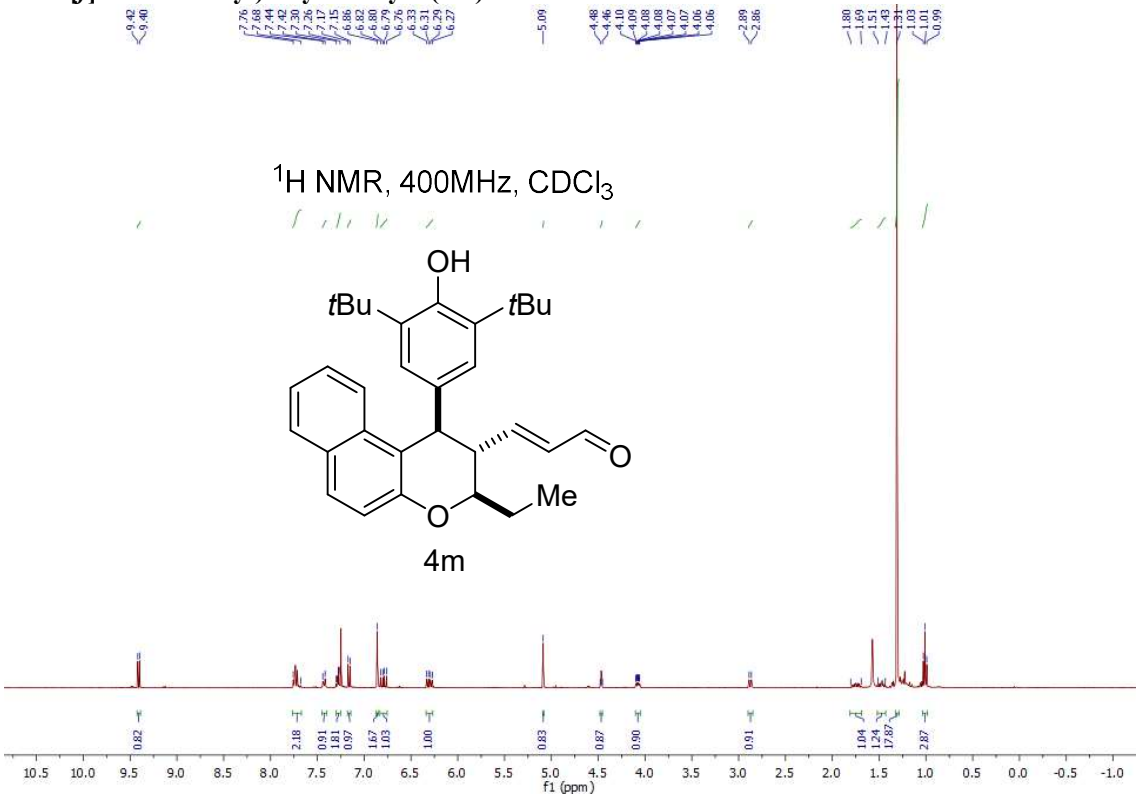
8.13. (*E*)-3-((2S,3S,4R)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-(2-nitrophenyl)chroman-3-yl)acrylaldehyde (4l).

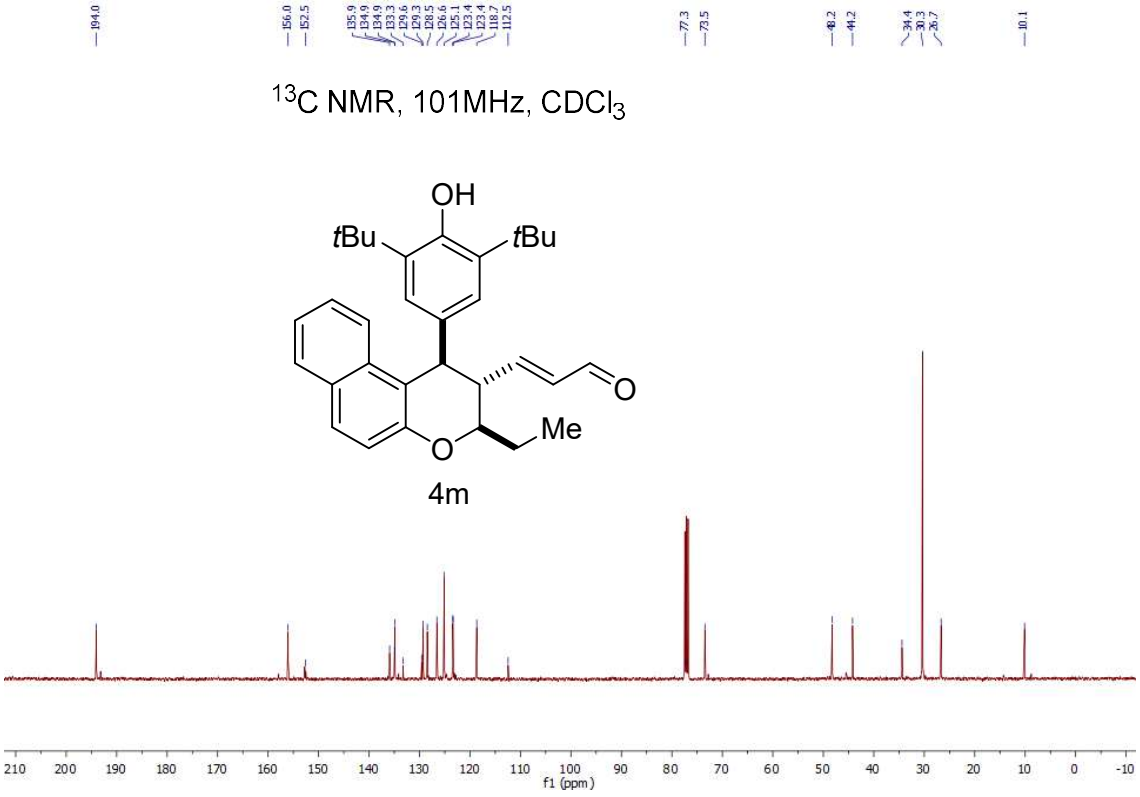


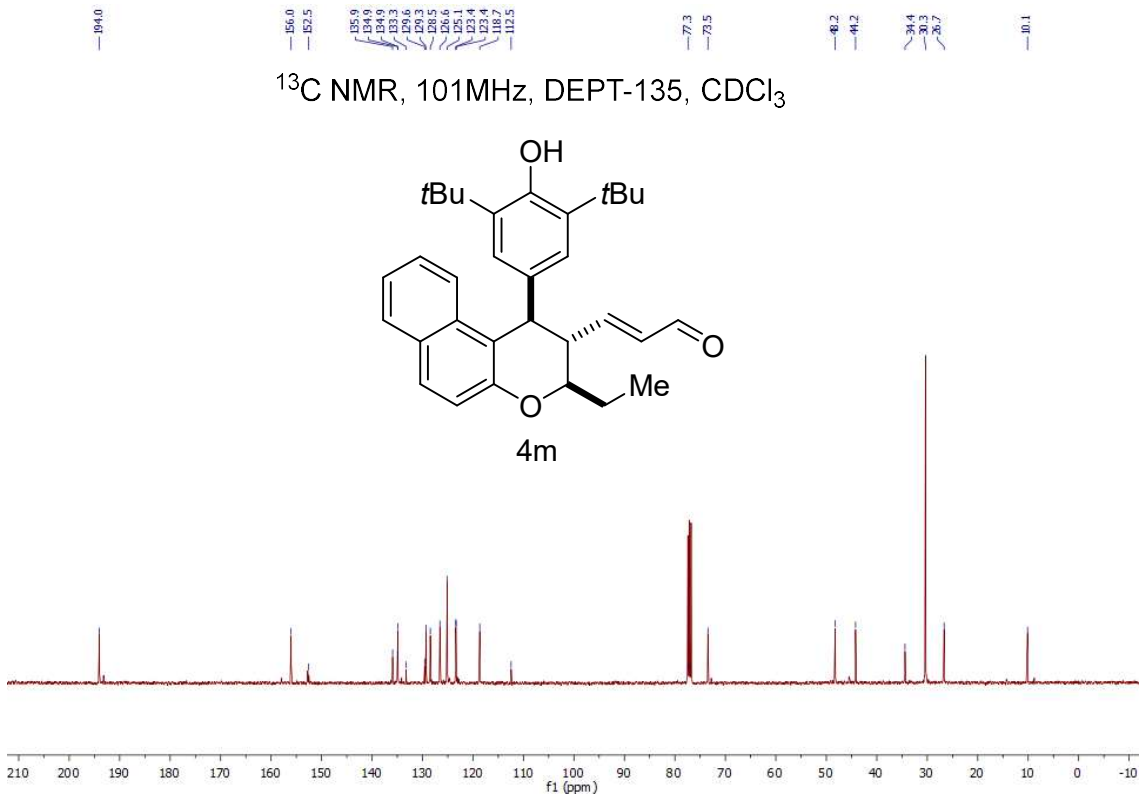



192.8
152.5
137.4
133.7
130.7
128.9
128.7
128.3
126.2
125.2
121.8
117.0
76.8
49.1
48.3
30.4
^{13}C NMR, 101MHz, DEPT-135, $CDCl_3$
OH
*t*Bu
*t*Bu
O
O
O_2N
4l
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

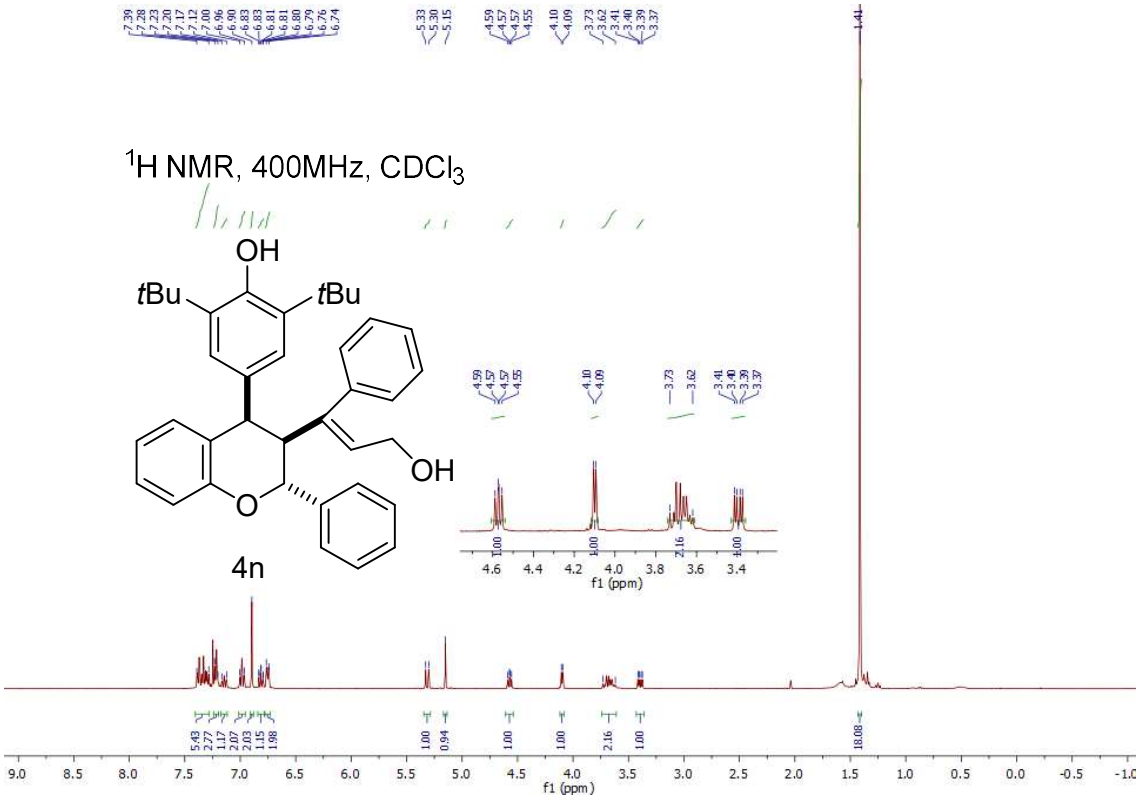
8.14. (*E*)-3-((1R,2S,3R)-1-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-3-ethyl-2,3-dihydro-1*H*-benzo[*f*]chromen-2-yl)acrylaldehyde(4m).

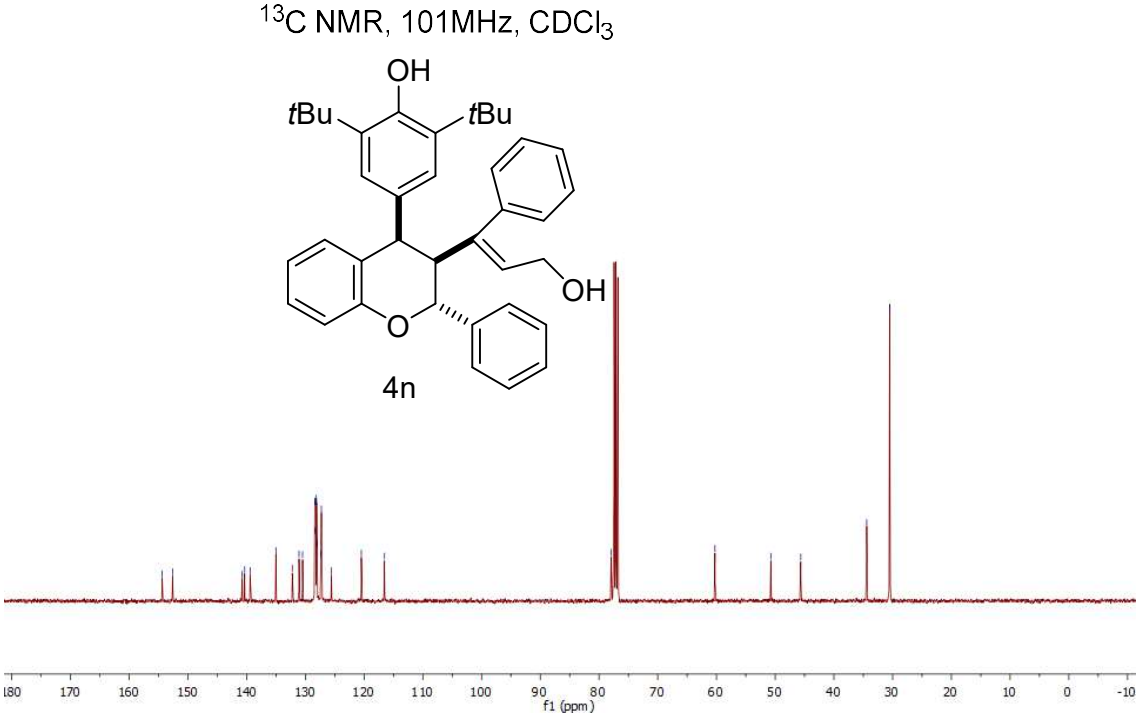


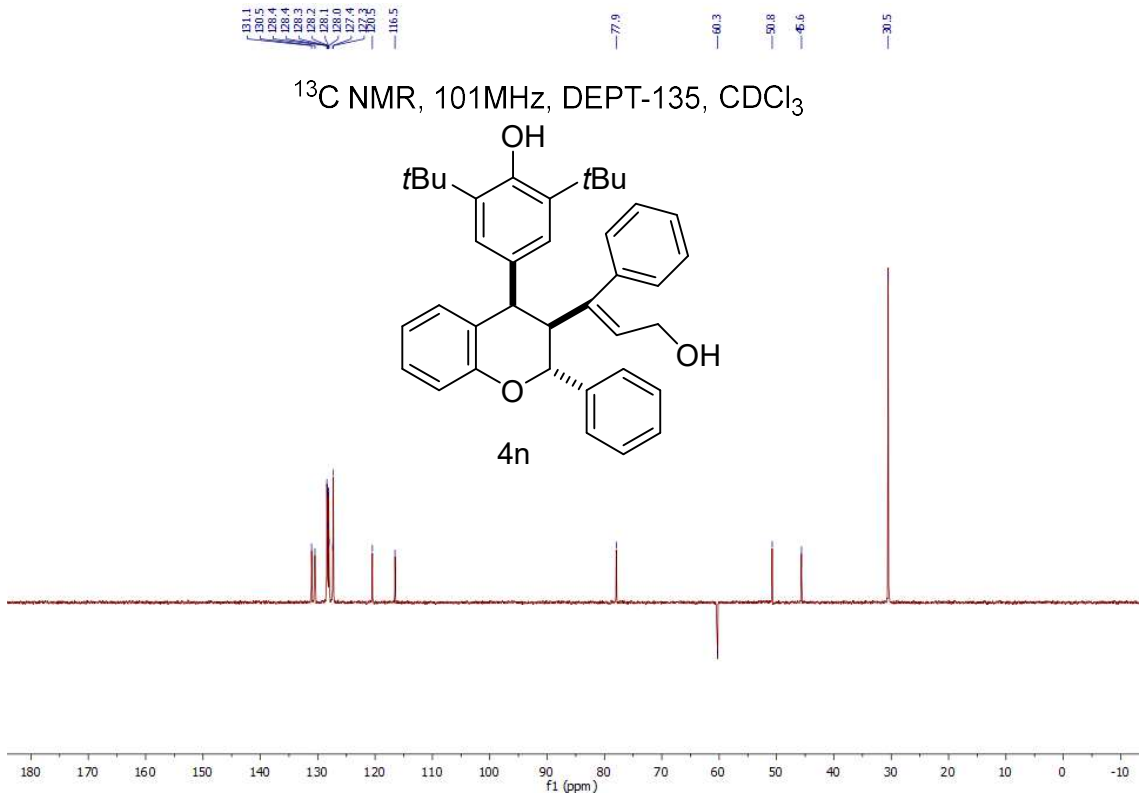



194.0
156.0
152.5
135.9
134.9
134.9
133.3
129.6
129.3
128.5
126.6
125.1
123.4
123.4
118.7
112.5
77.3
73.5
41.2
34.4
30.3
26.7
10.1
^{13}C NMR, 101MHz, DEPT-135, $CDCl_3$
OH
*t*Bu
*t*Bu
O
Me
O
4m
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

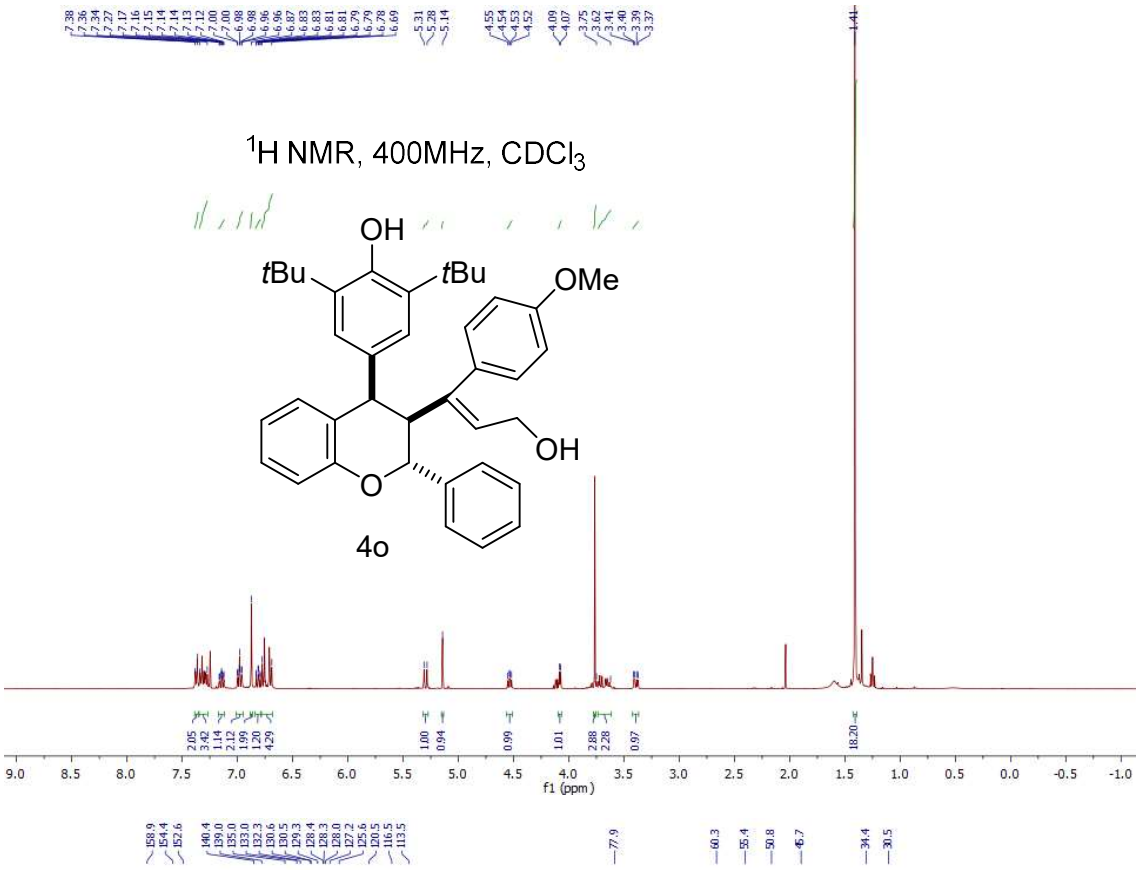
8.15. 2,6-di-*tert*-butyl-4-((2R,3S,4R)-3-((*Z*)-3-hydroxy-1-phenylprop-1-en-1-yl)-2-phenylchroman-4-yl)phenol (4n).

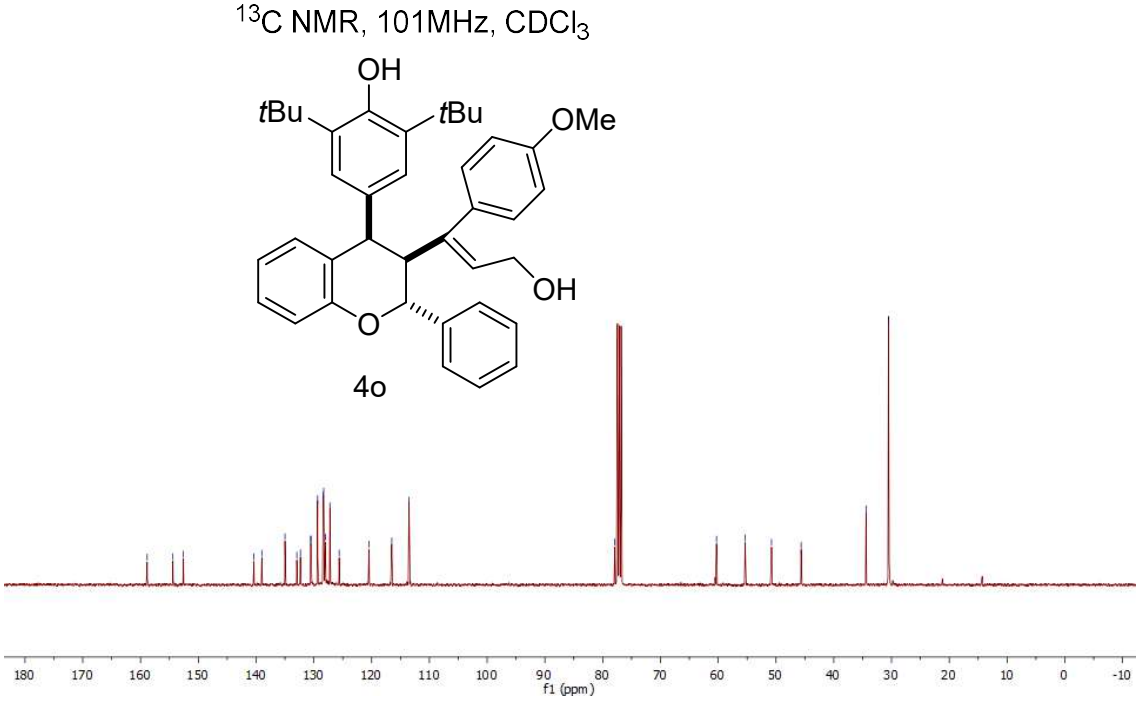


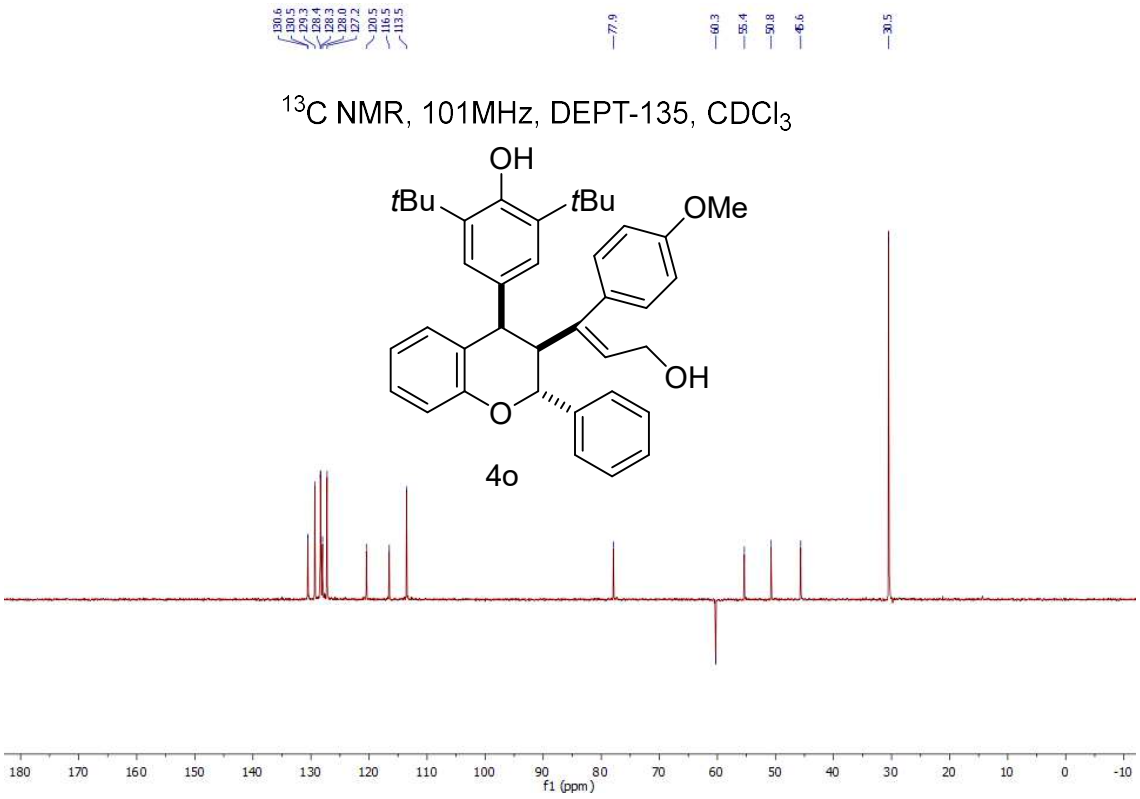



131.1
130.5
128.4
128.3
128.2
128.1
128.0
127.4
126.5
116.5
77.9
60.3
50.8
45.6
30.5
^{13}C NMR, 101MHz, DEPT-135, CDCl$_3$
OH
*t*Bu
*t*Bu
OH
O
4n
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

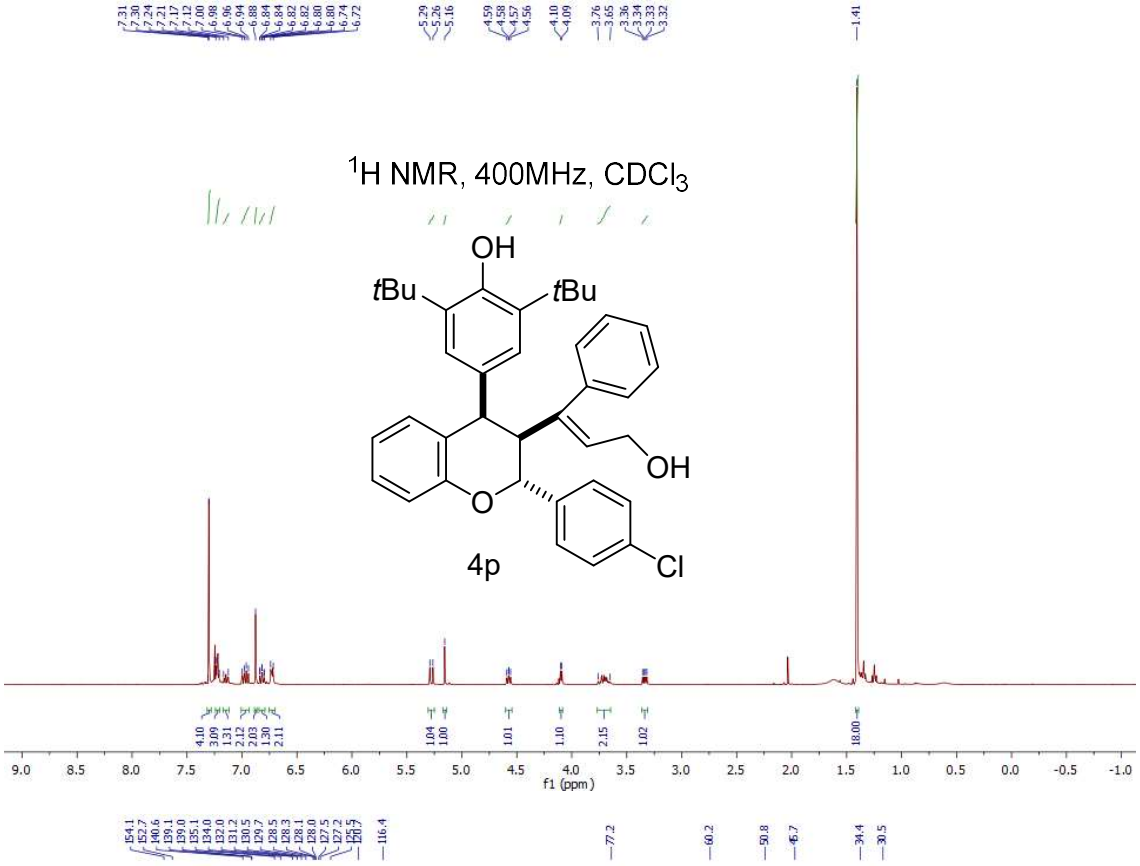
8.16. 2,6-di-*tert*-butyl-4-((2R,3S,4R)-3-((*Z*)-3-hydroxy-1-(4-methoxyphenyl)prop-1-en-1-yl)-2-phenylchroman-4-yl)phenol (4o).

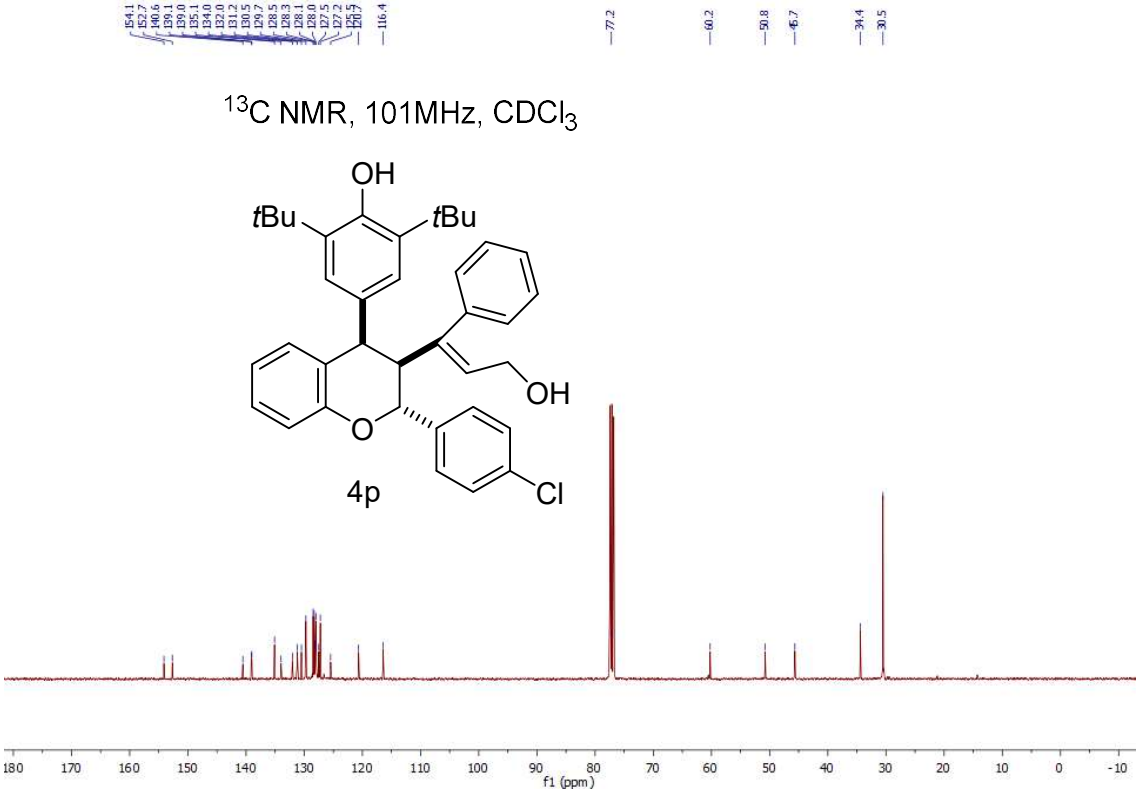




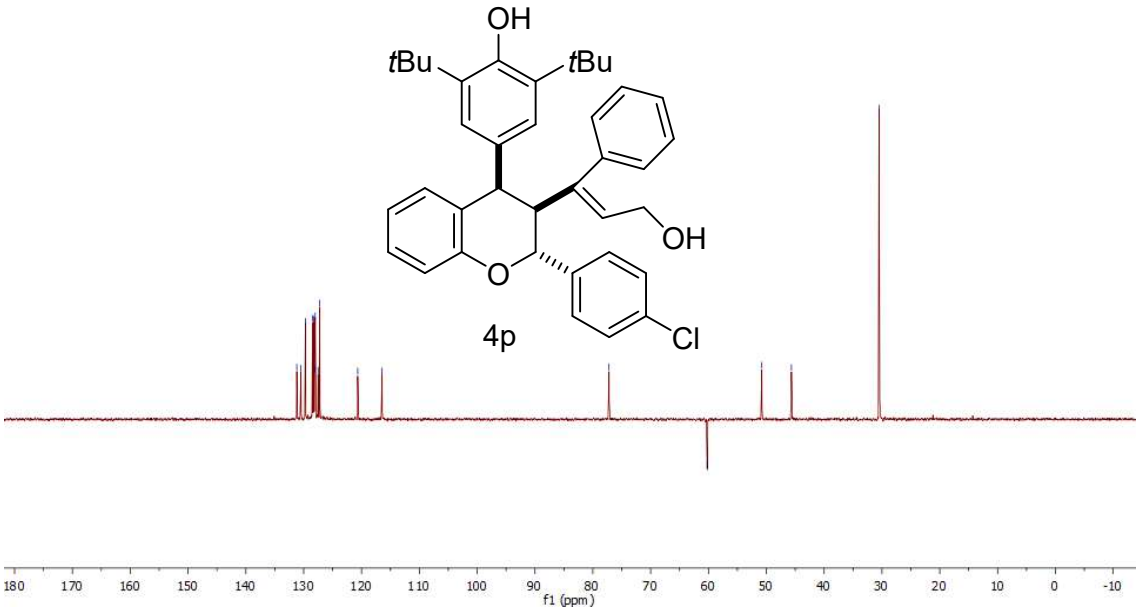

130.6
130.5
129.3
128.4
128.3
128.0
127.2
120.5
116.5
113.5
77.9
60.3
55.4
50.8
45.6
30.5
13C NMR, 101MHz, DEPT-135, CDCl3
OH
tBu
tBu
OMe
OH
O
4o
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

8.17. 2,6-di-*tert*-butyl-4-((2R,3S,4R)-2-(4-chlorophenyl)-3-((*Z*)-3-hydroxy-1-phenylprop-1-en-1-yl)chroman-4-yl)phenol (4p).

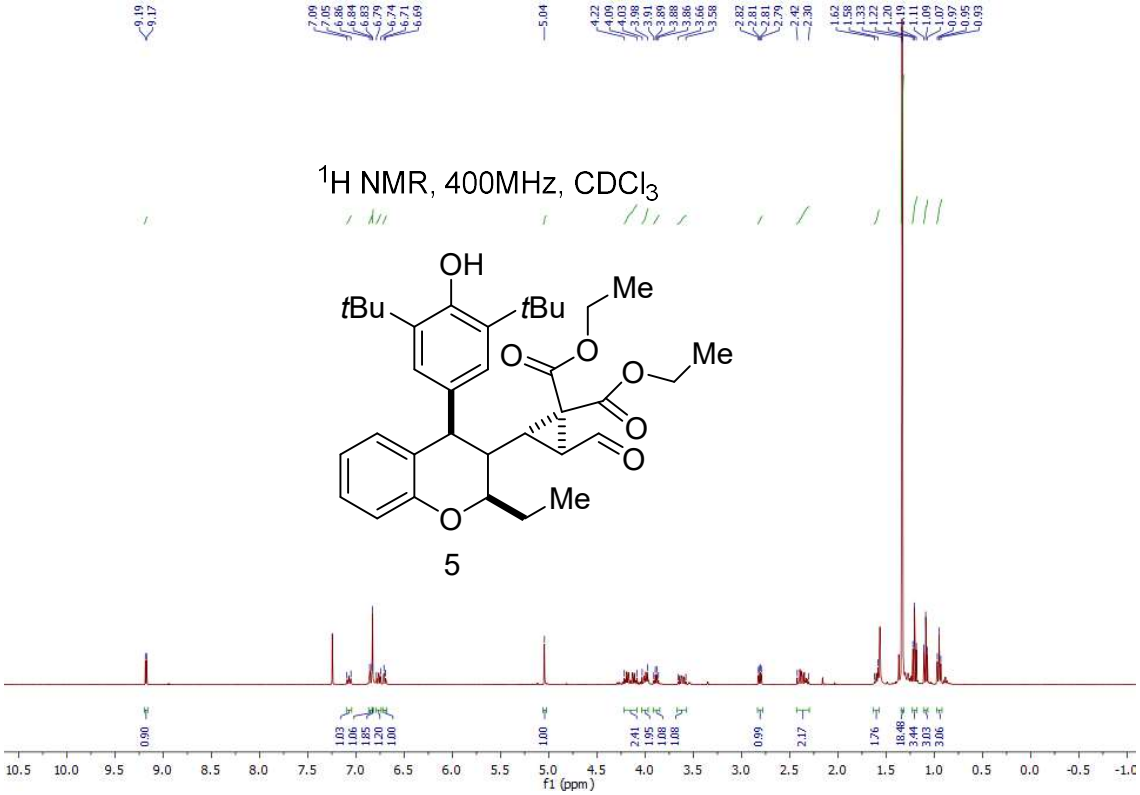


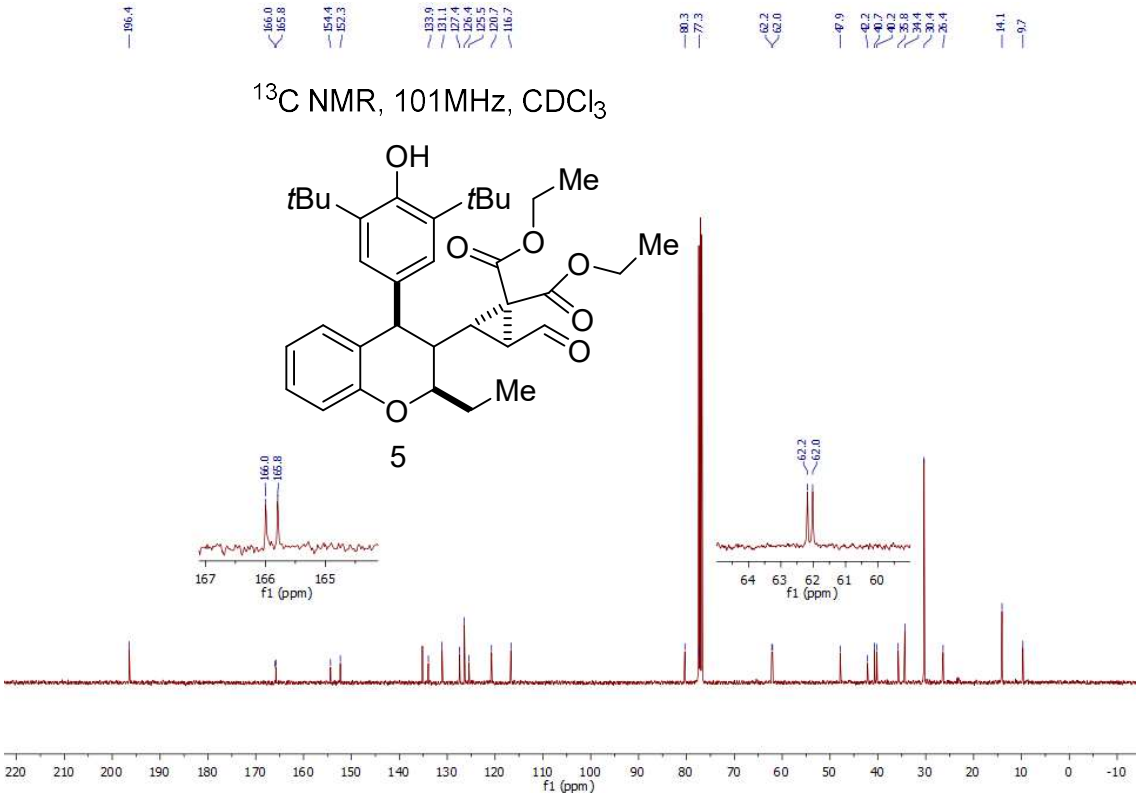


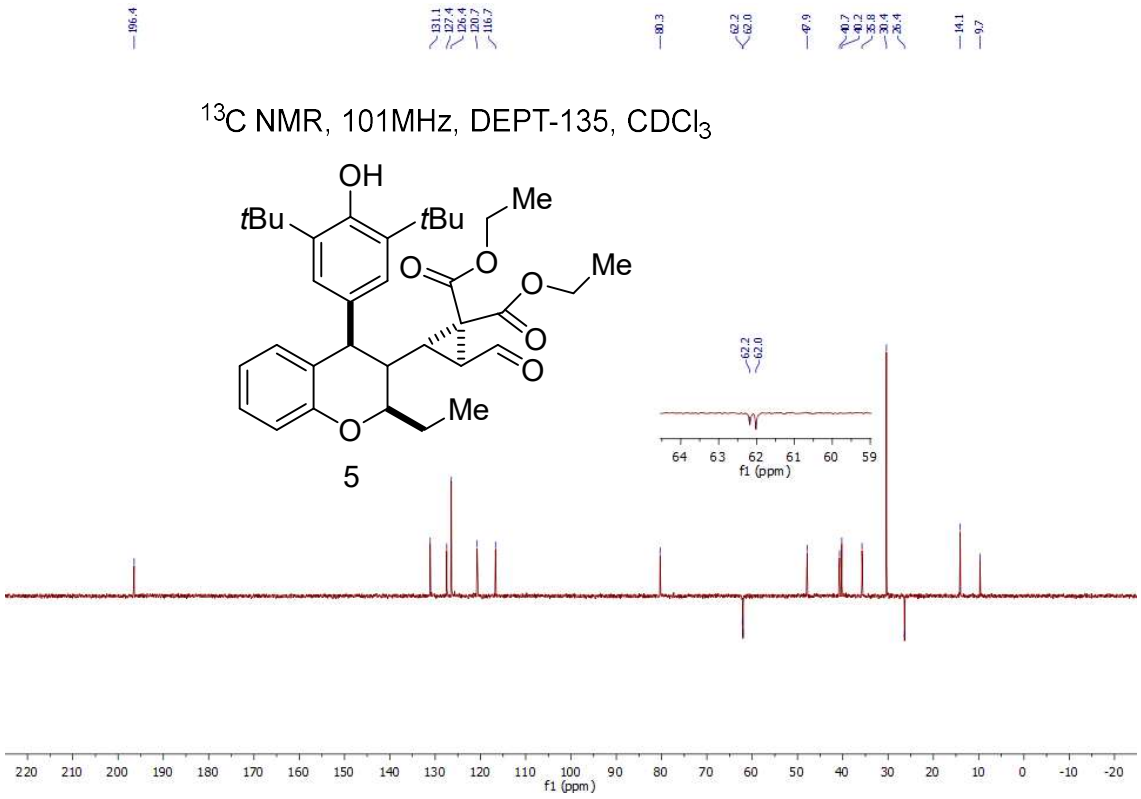
^{13}C NMR, 101MHz, DEPT-135, $CDCl_3$



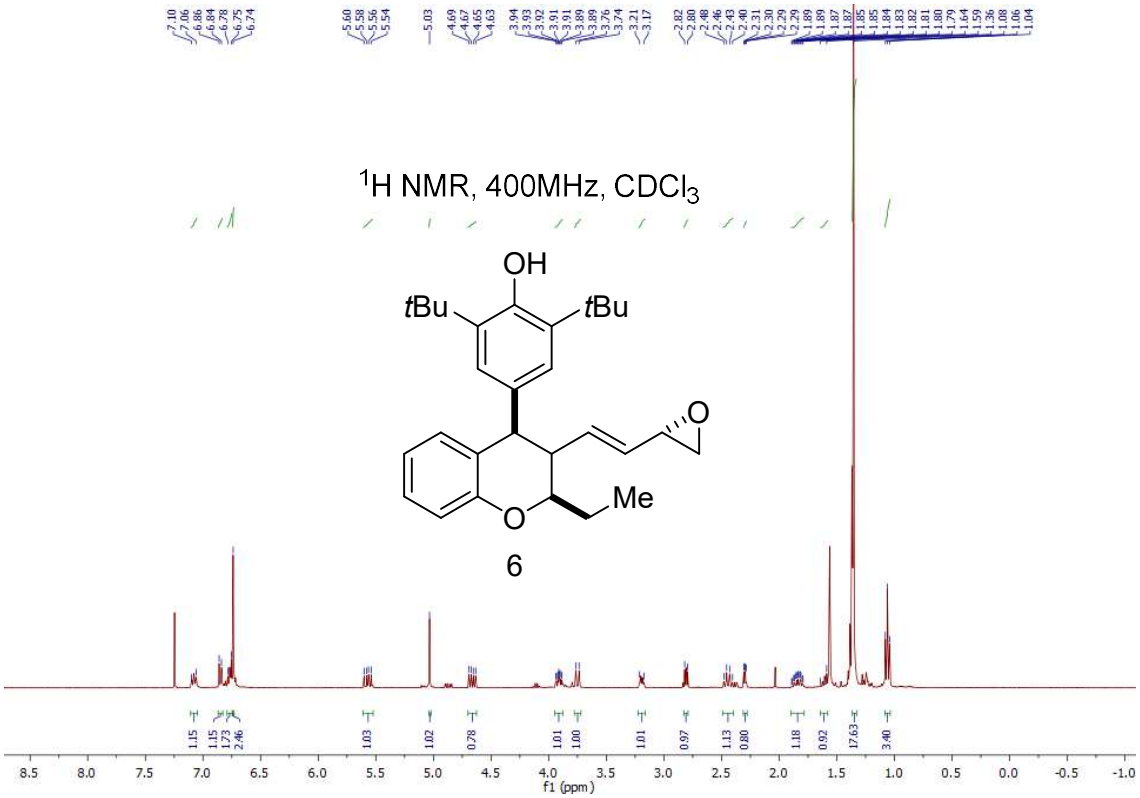
8.18. (2S,3S)-diethyl 2-((2R,4R)-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-ethylchroman-3-yl)-3-formylcyclopropane-1,1-dicarboxylate (5).

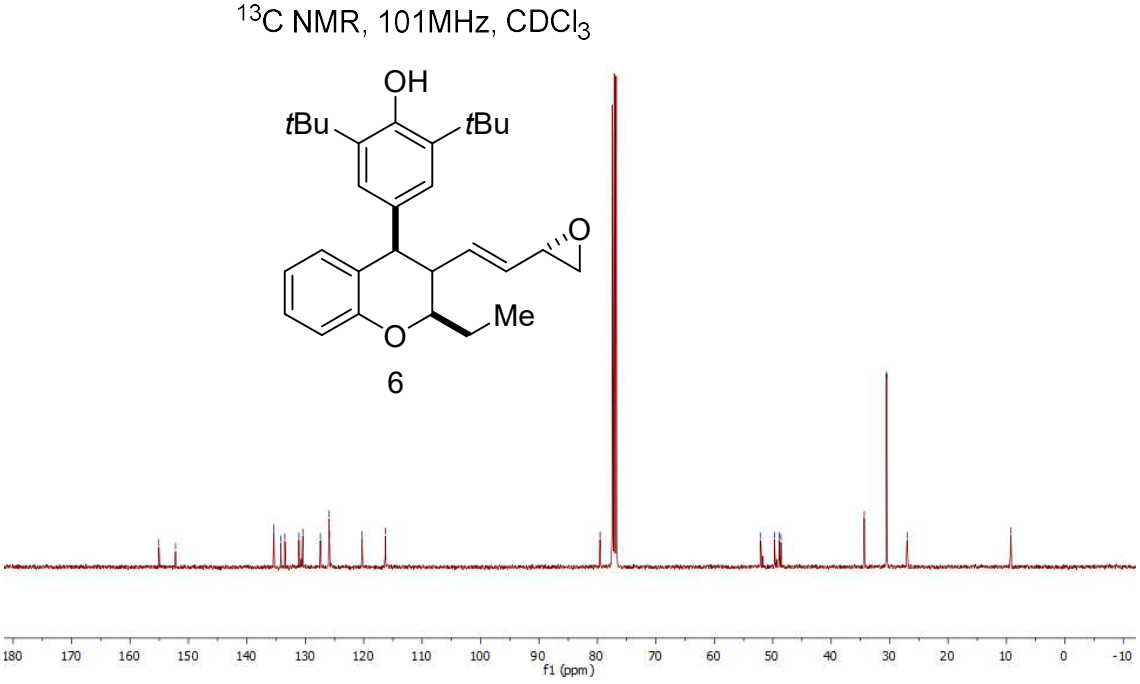


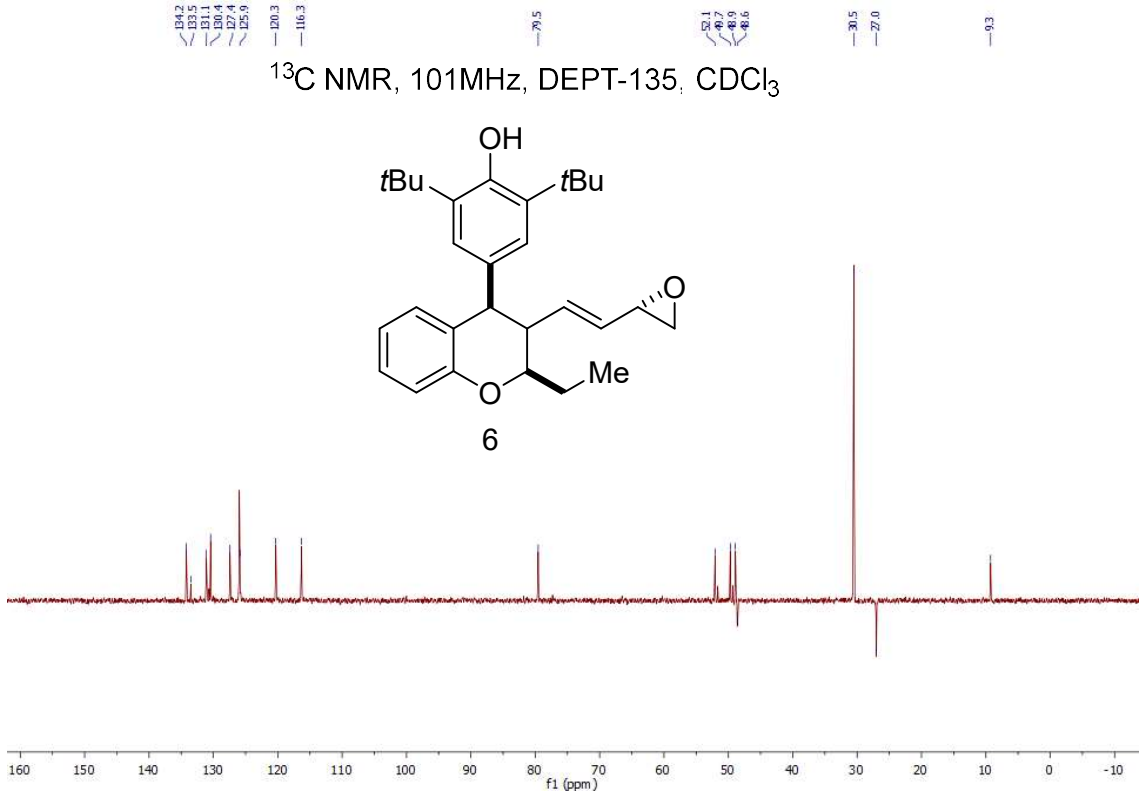



196.4
131.1
127.4
126.4
120.7
116.7
80.3
62.2
62.0
40.9
40.7
40.2
35.8
30.4
26.4
14.1
9.7
13C NMR, 101MHz, DEPT-135, CDCl3
OH
tBu
tBu
Me
O
O
O
Me
O
O
Me
O
5
62.2
62.0
64 63 62 61 60 59
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

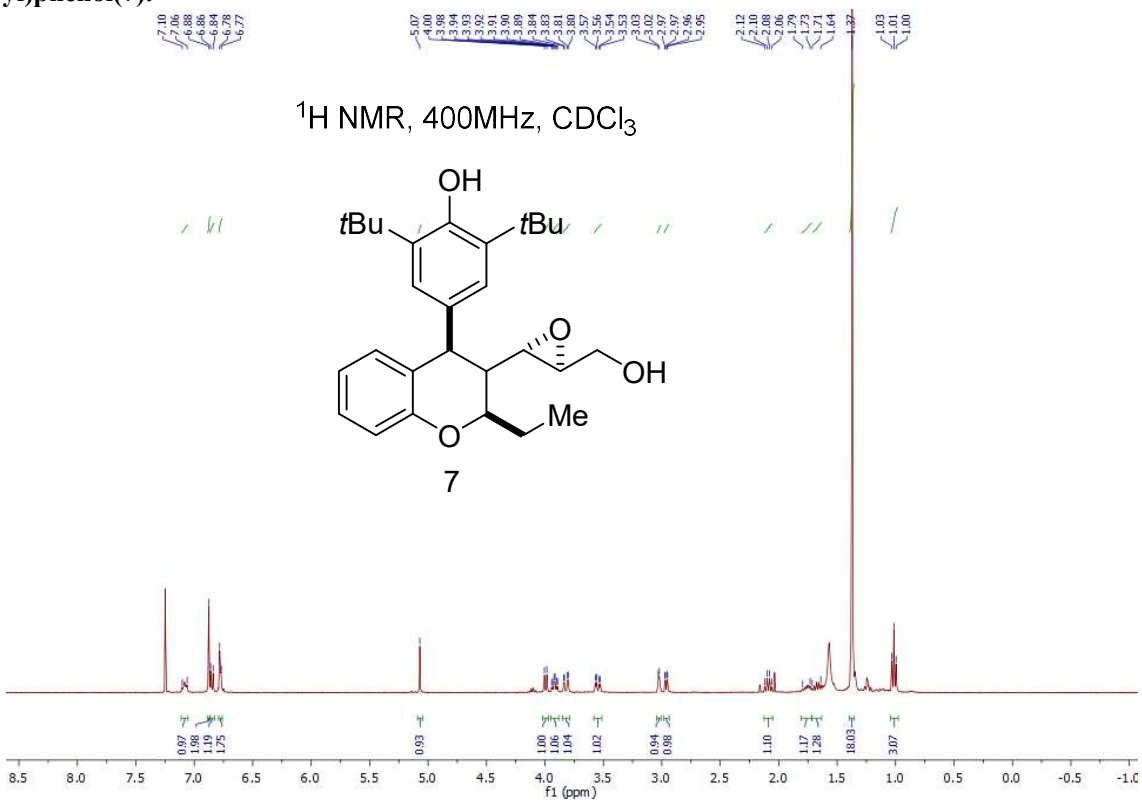
8.19. 2,6-di-*tert*-butyl-4-((2R,4R)-2-ethyl-3-((*E*)-2-((S)-oxiran-2-yl)vinyl)chroman-4-yl)phenol (6).

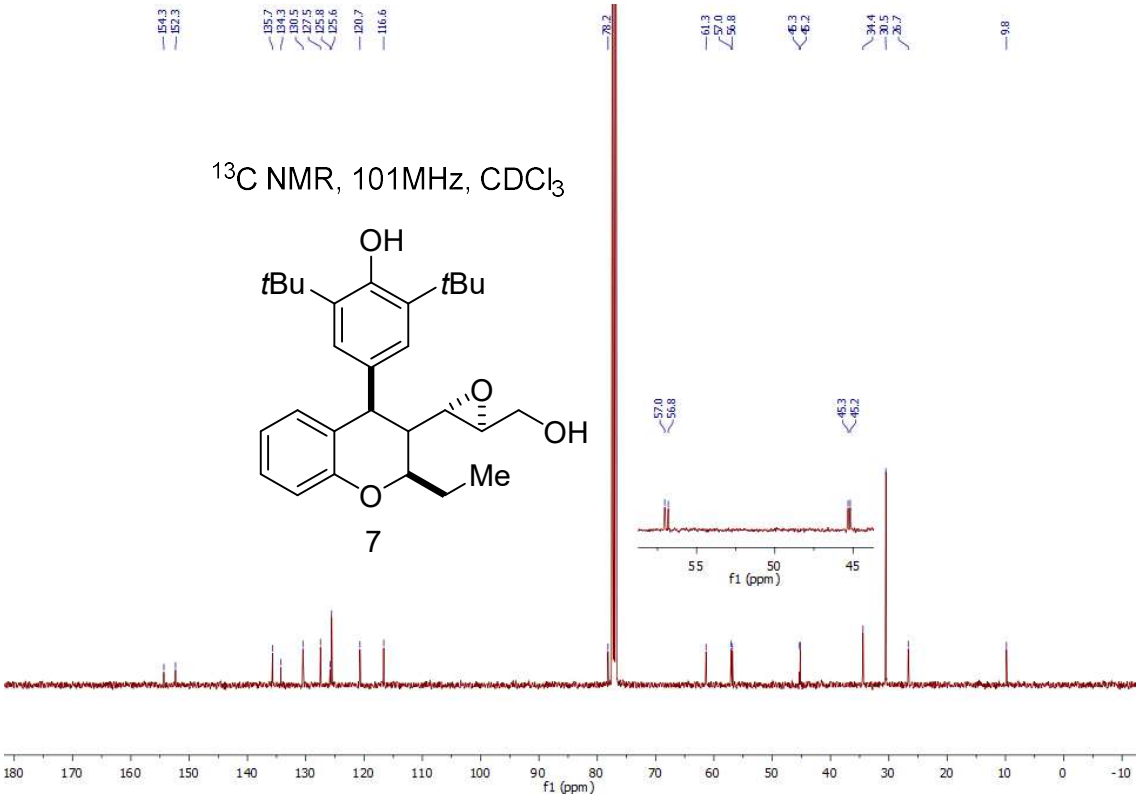


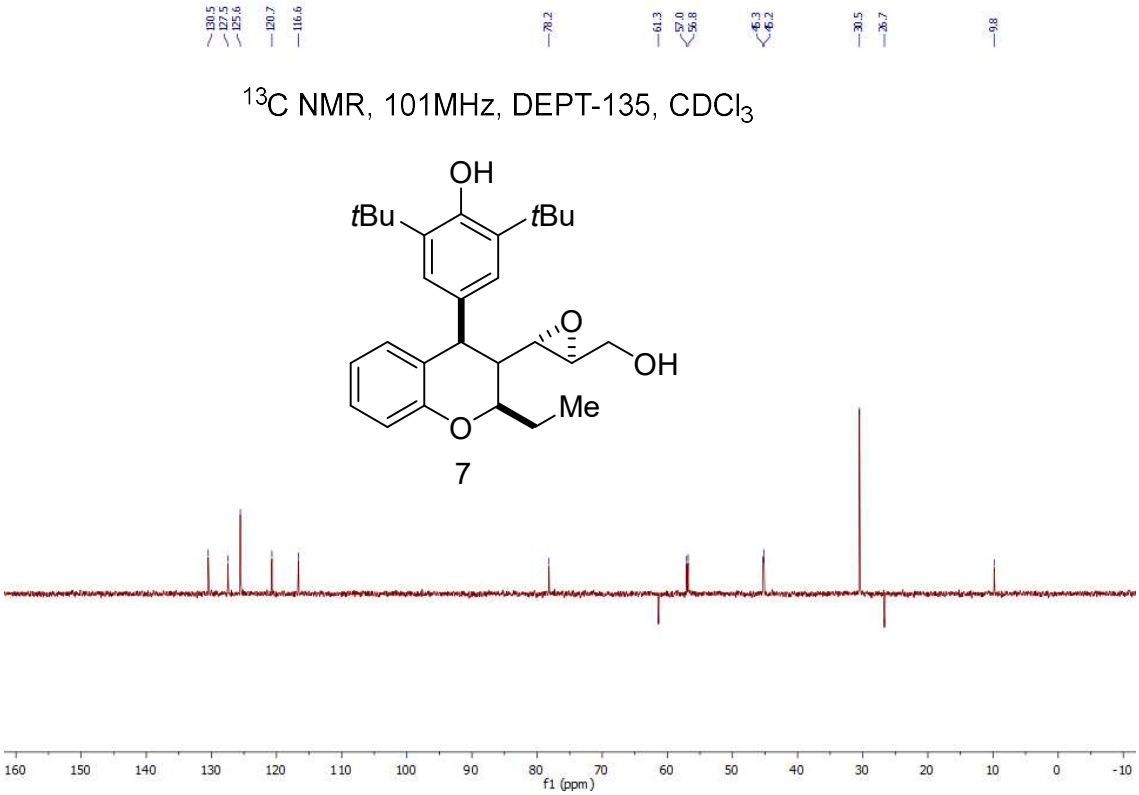



134.2
133.5
131.1
130.4
127.4
125.9
120.3
116.3
79.5
52.1
49.7
48.9
48.6
30.5
27.0
9.3
^{13}C NMR, 101MHz, DEPT-135, $CDCl_3$
OH
*t*Bu
*t*Bu
O
Me
O
6
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

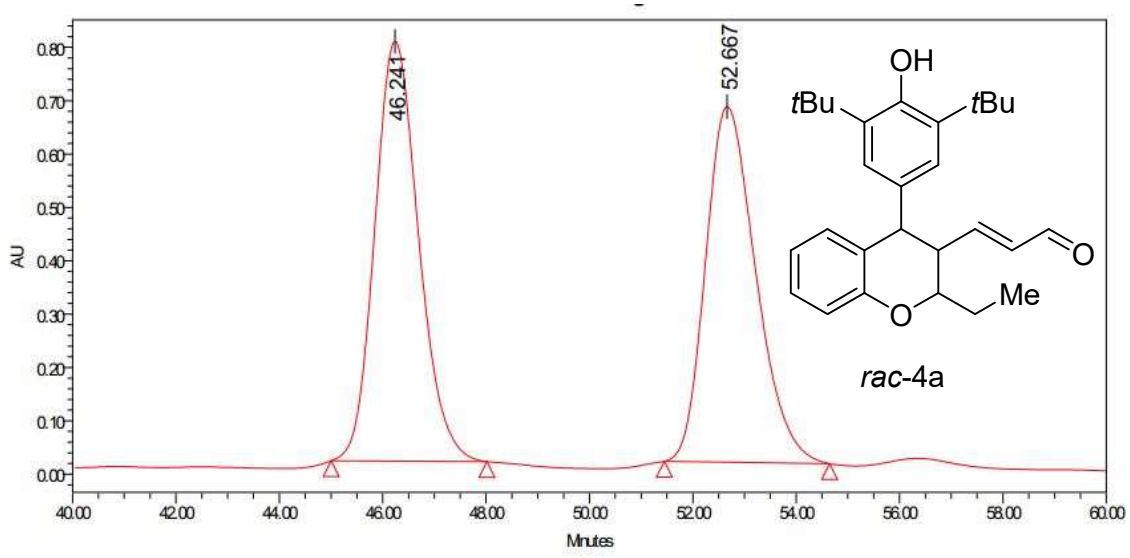
8.20. 2,6-di-*tert*-butyl-4-((2R,4R)-2-ethyl-3-((2S,3S)-3-(hydroxymethyl)oxiran-2-yl)chroman-4-yl)phenol(7).





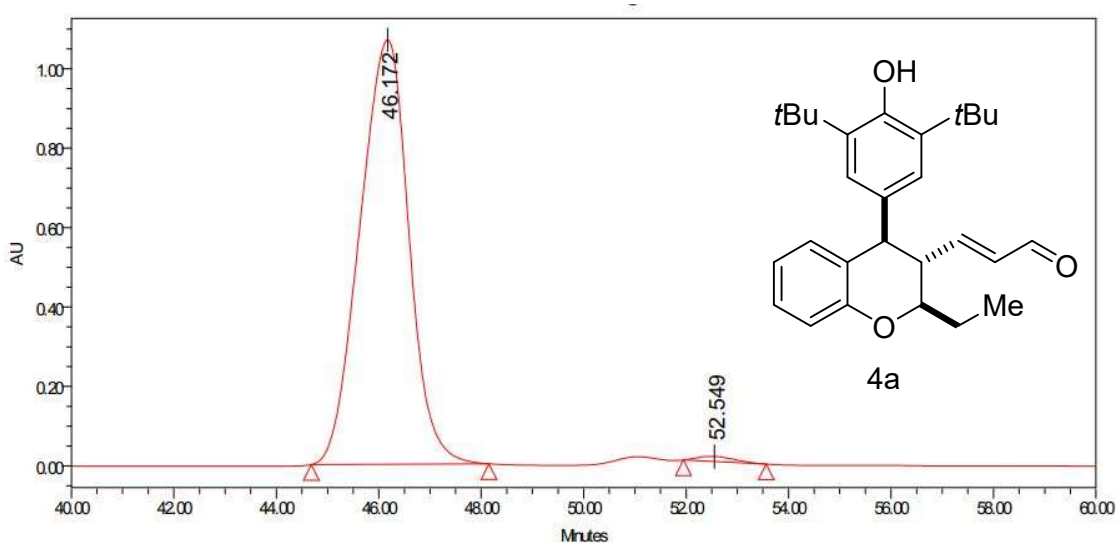

130.5
127.5
125.6
120.7
116.6
78.2
61.3
57.0
56.8
45.3
45.2
30.5
26.7
9.8
^{13}C NMR, 101MHz, DEPT-135, $CDCl_3$
OH
*t*Bu
*t*Bu
O
OH
Me
O
7
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

9. HPLC Traces:



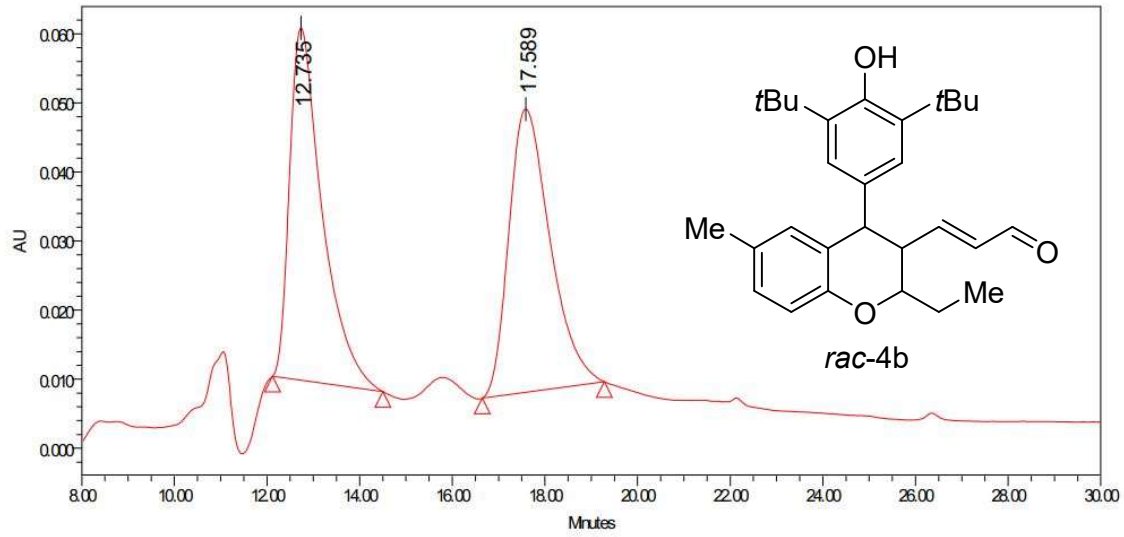
Peak Results

	RT	Area	%Area	Height
1	46.241	46411428	50.80	786866
2	52.667	44968609	49.20	666352



Peak Results

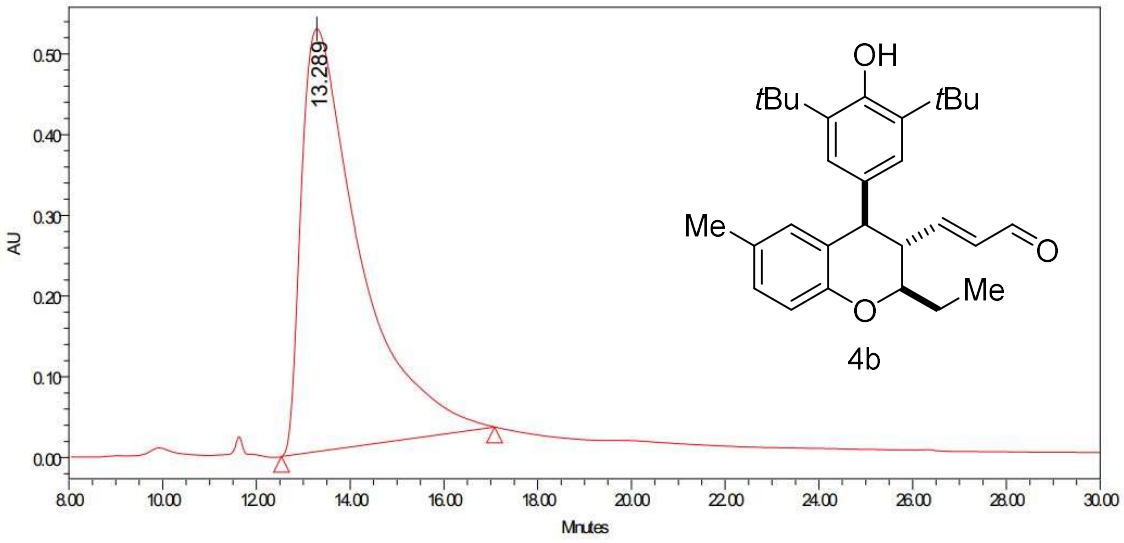
	RT	Area	%Area	Height
1	46.172	70964734	99.11	1068996
2	52.549	640833	0.89	12915



rac-4b

Peak Results

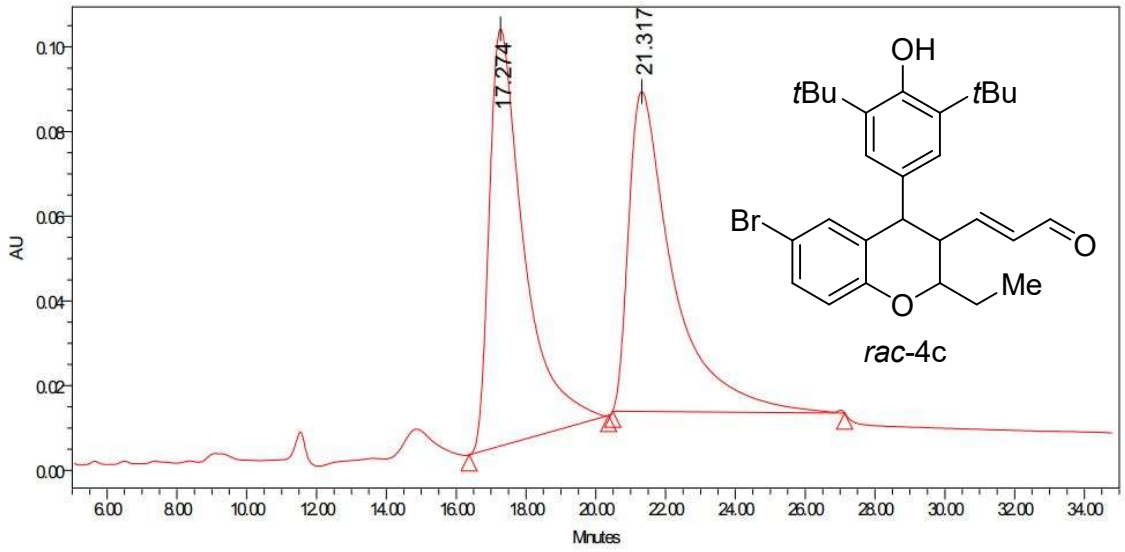
	RT	Area	%Area	Height
1	12.735	2487487	49.52	51000
2	17.589	2535264	50.48	41017



4b

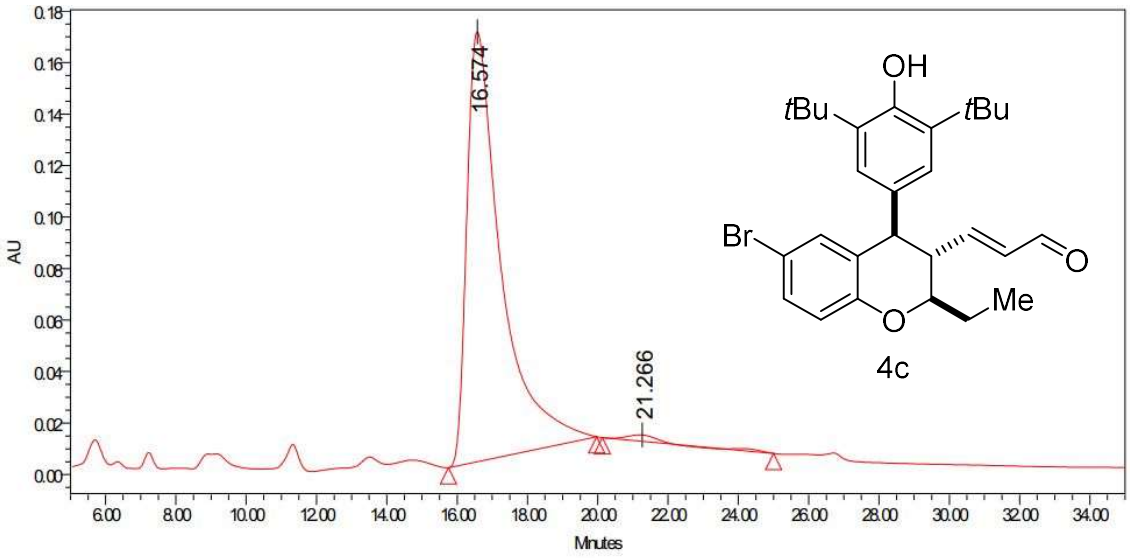
Peak Results

	RT	Area	%Area	Height
1	13.289	45311099	100.00	523829



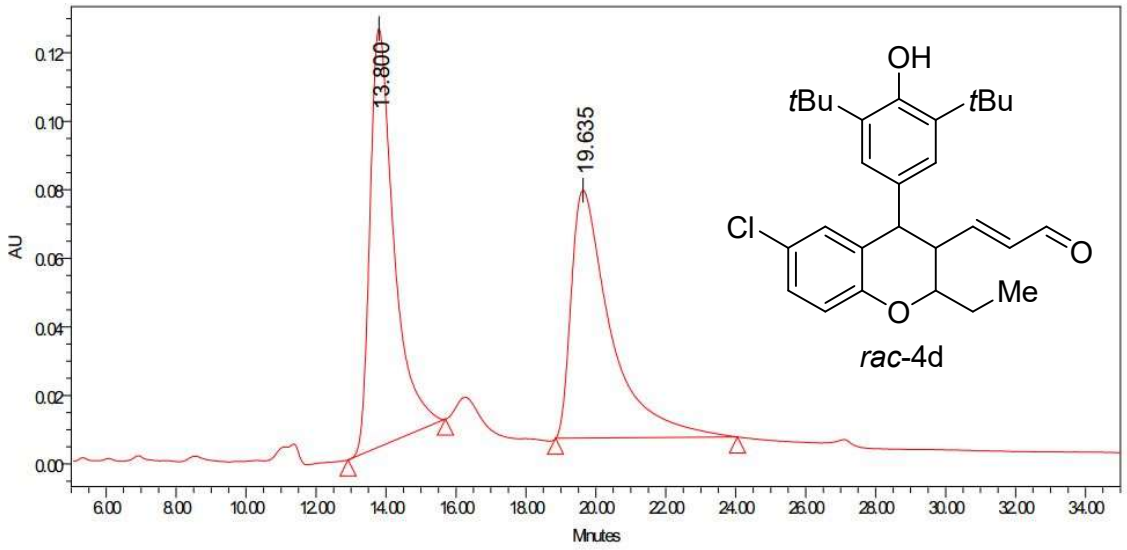
Peak Results

	RT	Area	%Area	Height
1	17.274	6841682	50.65	98554
2	21.317	6665945	49.35	75523



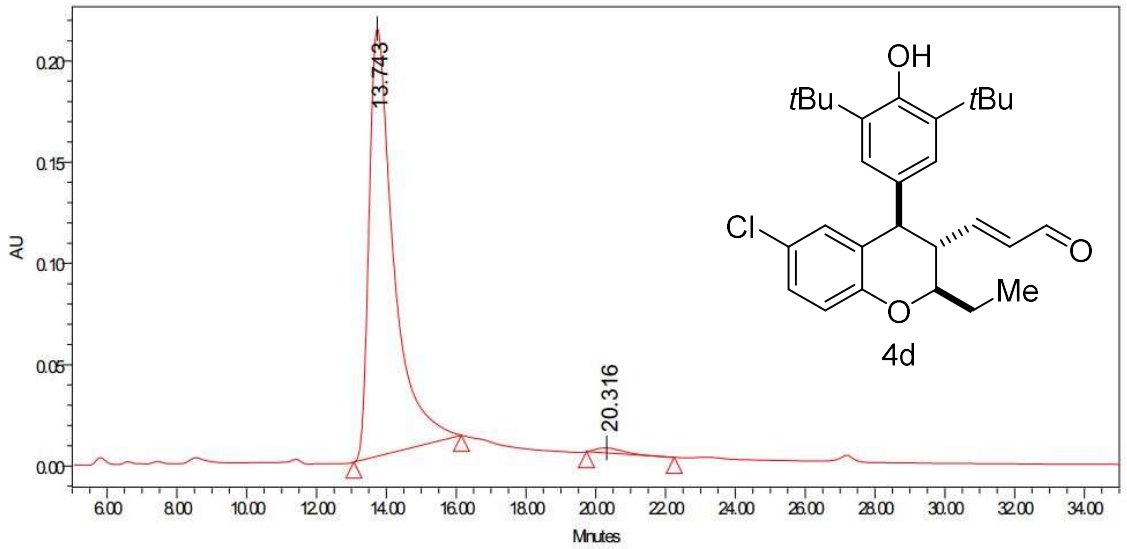
Peak Results

	RT	Area	%Area	Height
1	16.574	11361230	98.24	166951
2	21.266	203891	1.76	2504



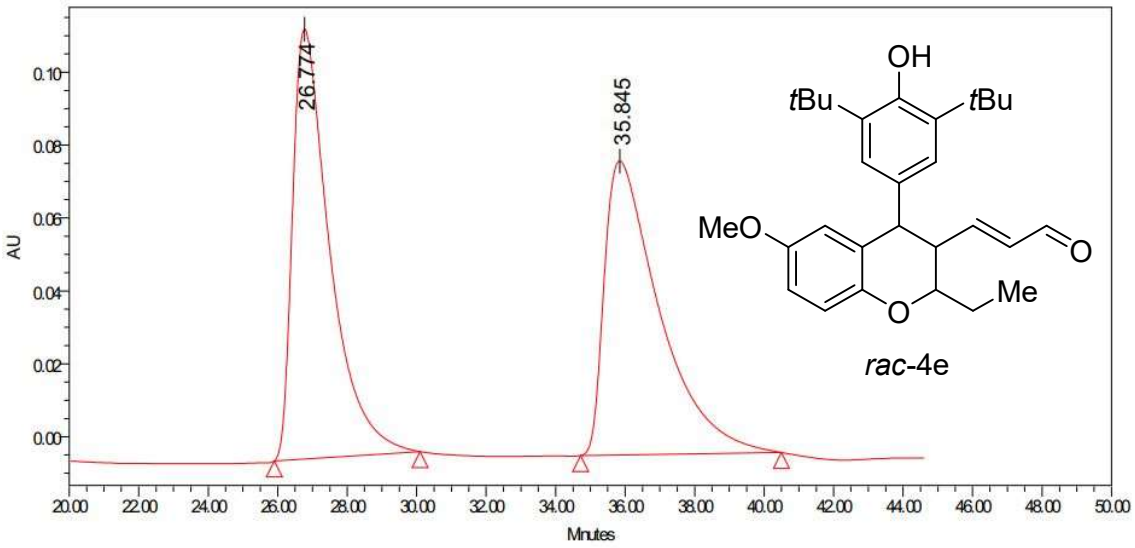
Peak Results

	RT	Area	%Area	Height
1	13.800	5816663	50.59	122158
2	19.635	5681789	49.41	72372



Peak Results

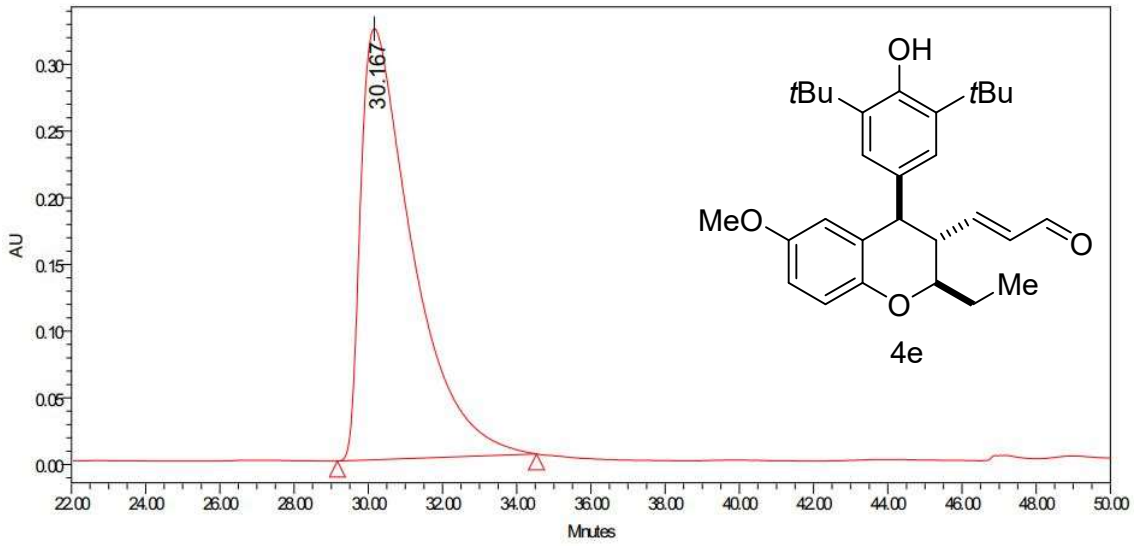
	RT	Area	%Area	Height
1	13.743	10338205	98.69	211233
2	20.316	136776	1.31	2517



rac-4e

Peak Results

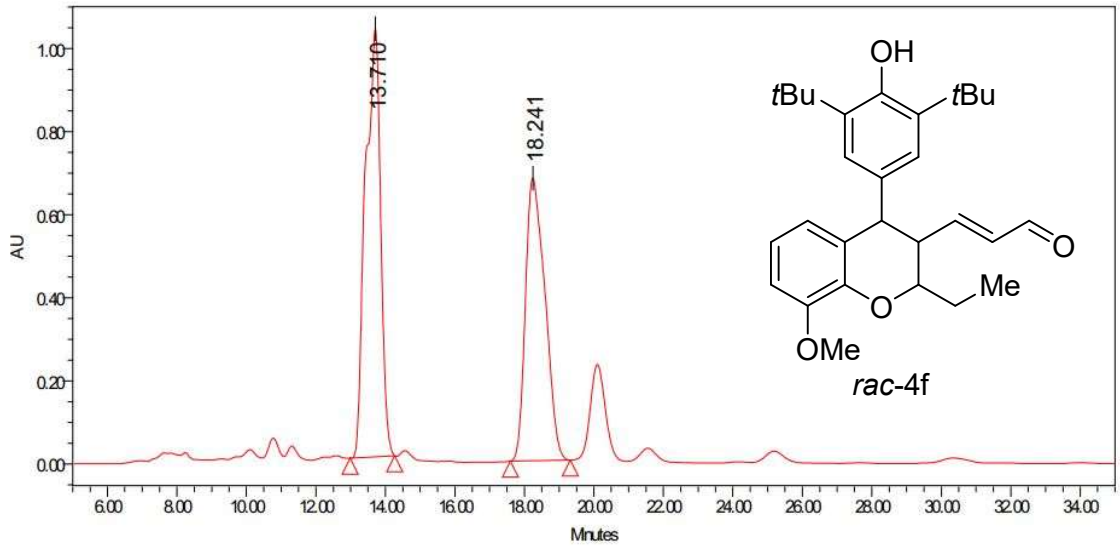
	RT	Area	%Area	Height
1	26.774	8775427	49.70	117932
2	35.845	8881871	50.30	80628



4e

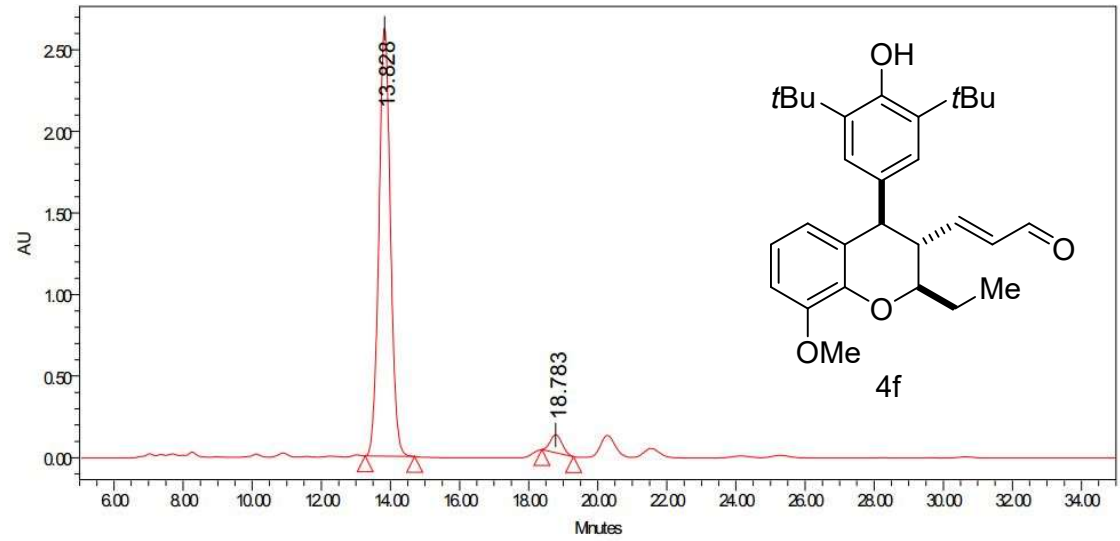
Peak Results

	RT	Area	%Area	Height
1	30.167	31254293	100.00	323255



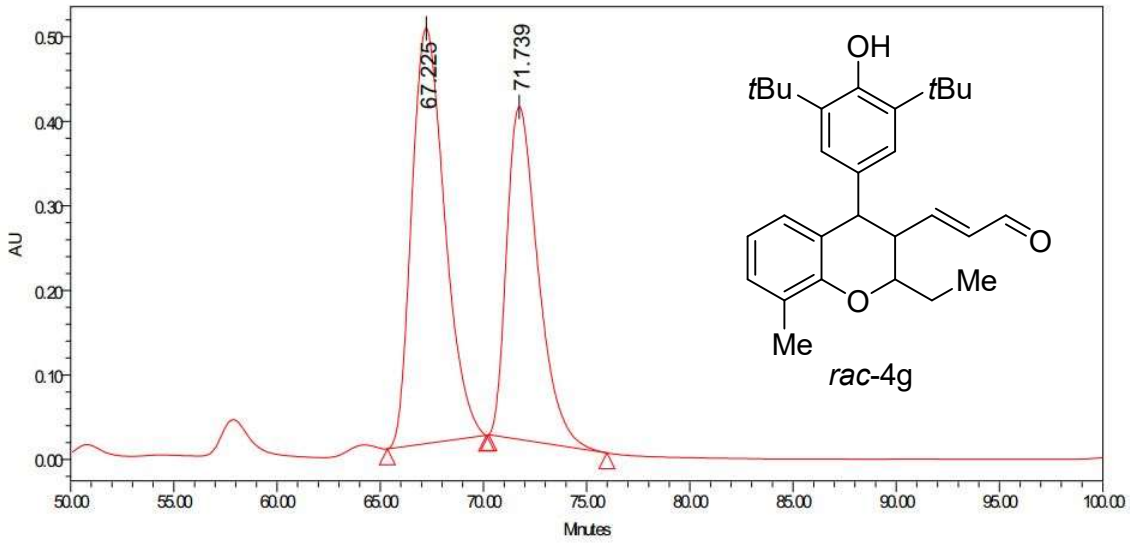
Peak Results

	RT	Area	%Area	Height
1	13.710	31338942	54.11	1032136
2	18.241	26582538	45.89	680307



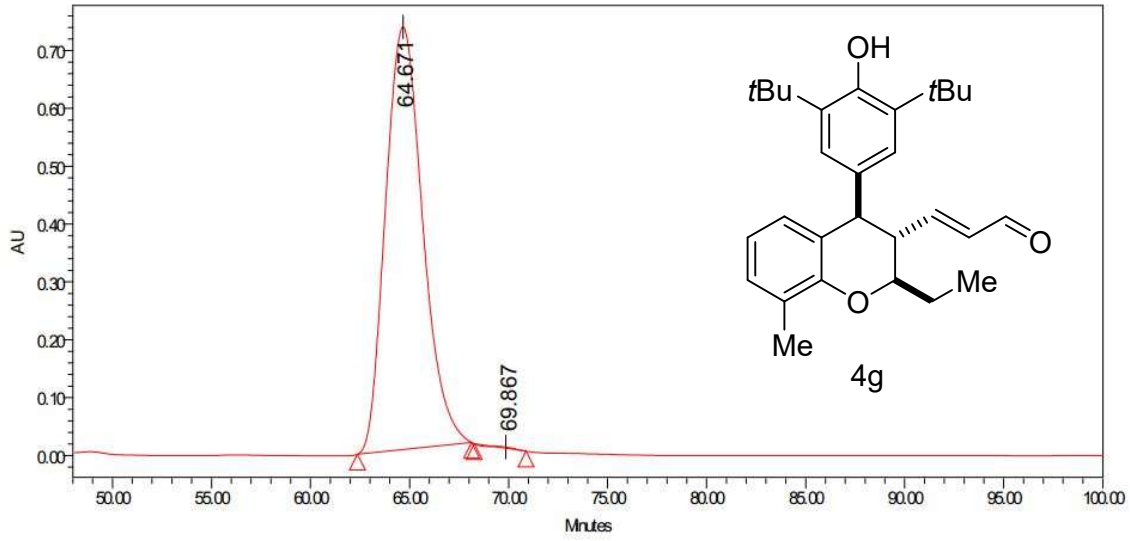
Peak Results

	RT	Area	%Area	Height
1	13.828	60807232	95.82	2625809
2	18.783	2651487	4.18	109872



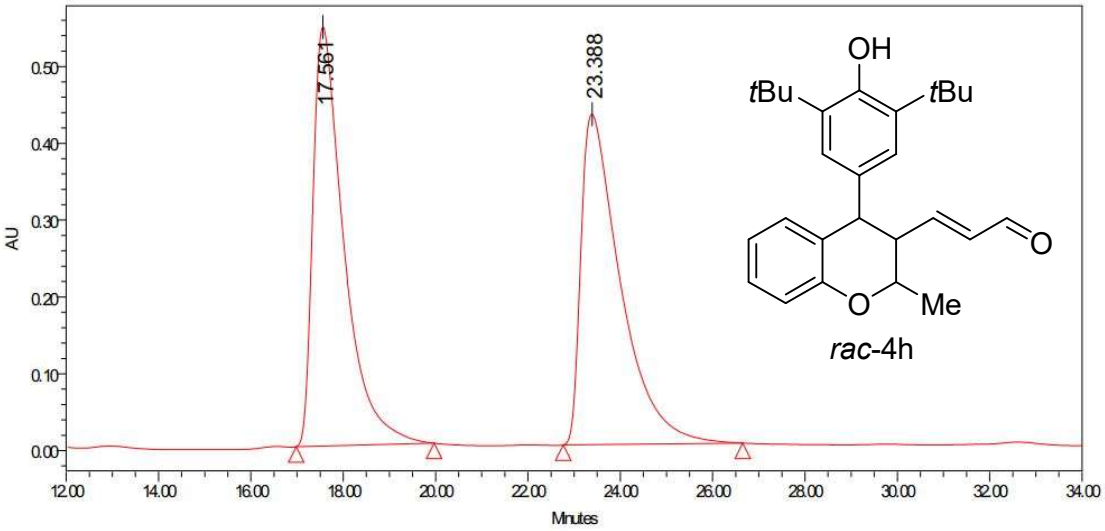
Peak Results

	RT	Area	%Area	Height
1	67.225	54627881	56.74	49111
2	71.739	41642560	43.26	393414



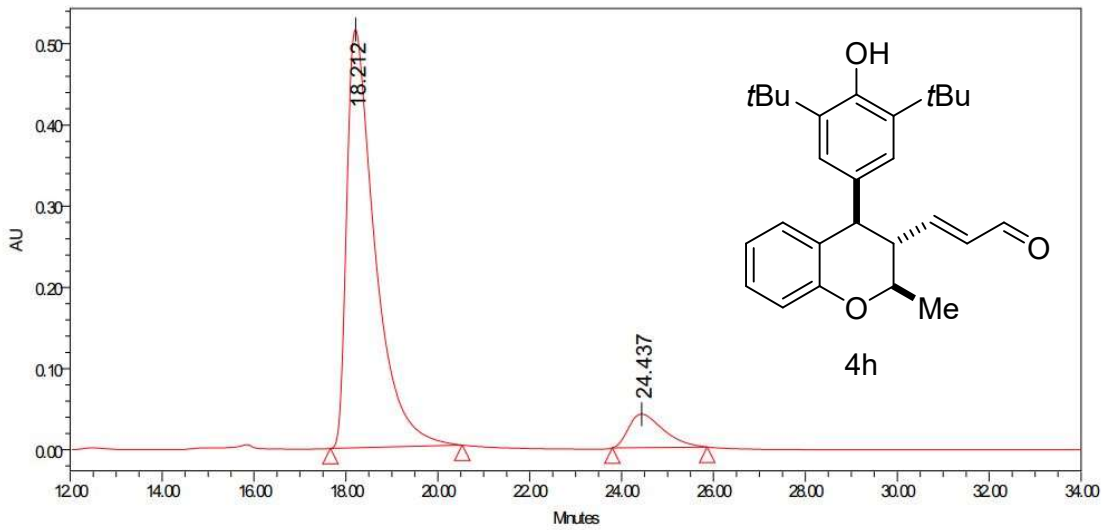
Peak Results

	RT	Area	%Area	Height
1	64.671	95373401	99.79	730588
2	69.867	198113	0.21	2138



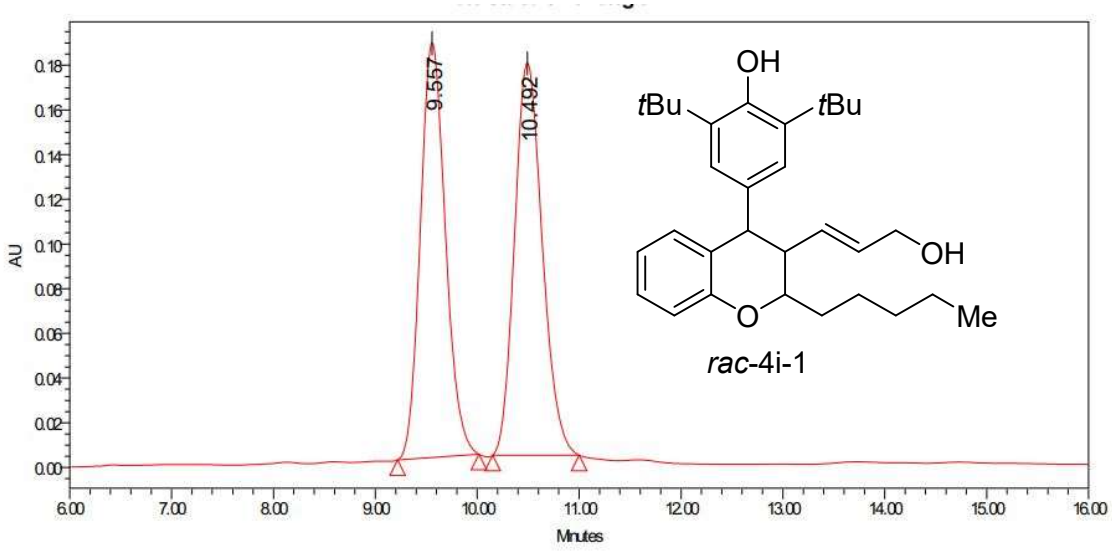
Peak Results

	RT	Area	%Area	Height
1	17.561	25436583	49.88	545363
2	23.388	25657150	50.12	429987



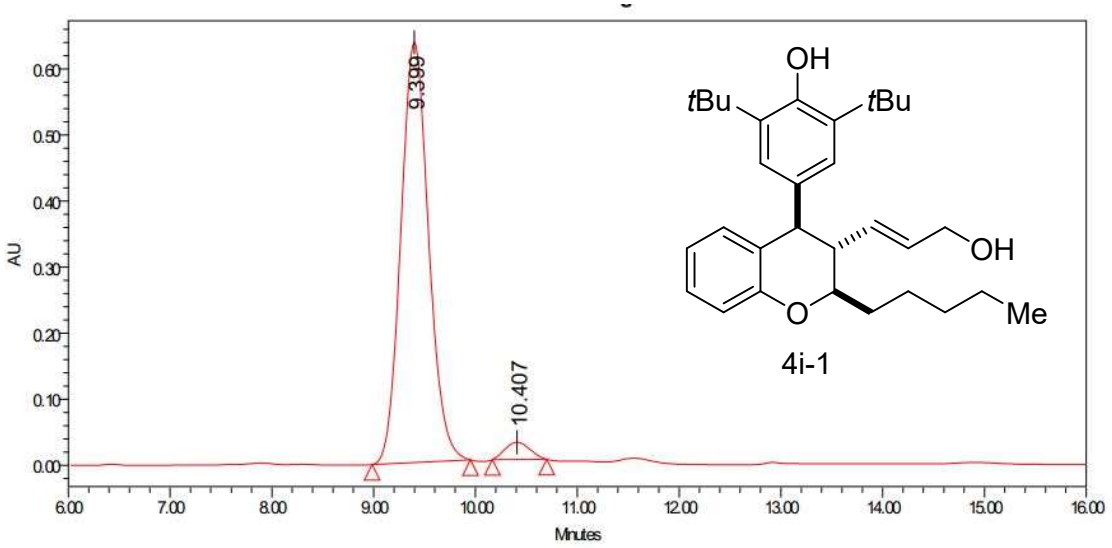
Peak Results

	RT	Area	%Area	Height
1	18.212	21997846	91.00	515188
2	24.437	2175667	9.00	41339



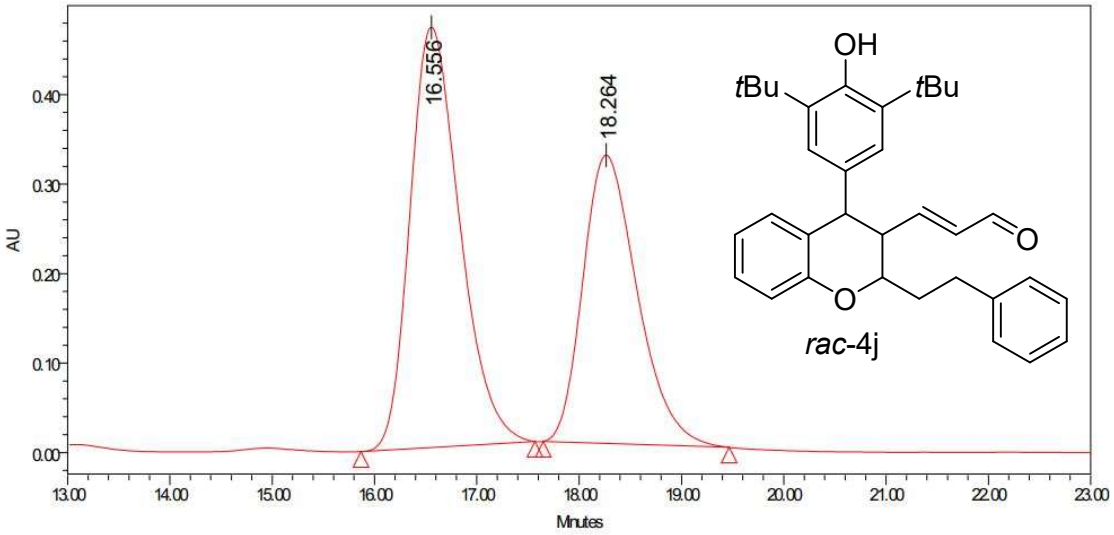
Peak Results

	RT	%Area	Area	Height
1	9.557	48.85	3175080	185903
2	10.492	51.15	3325226	175817



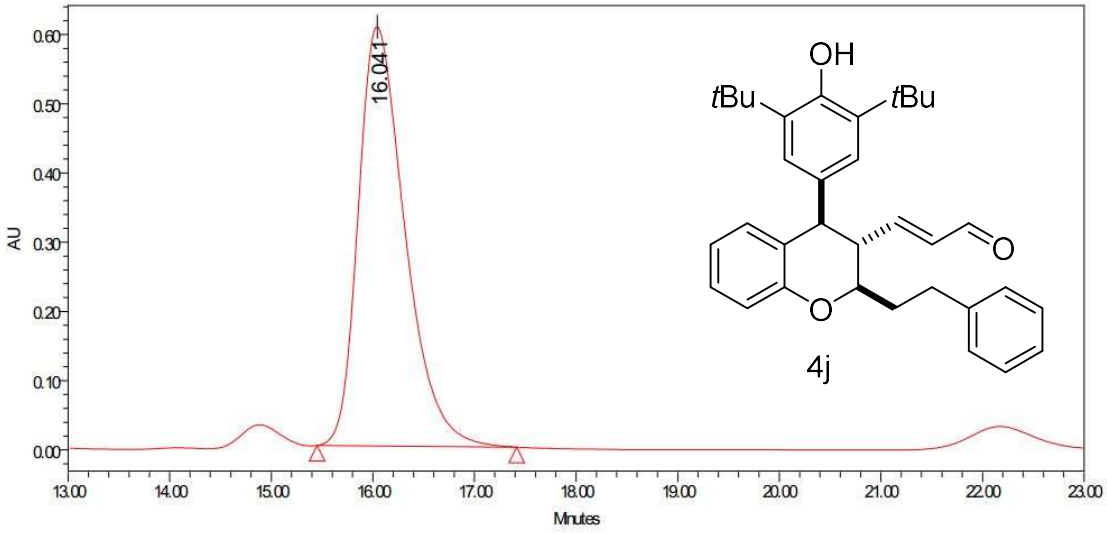
Peak Results

	RT	Area	%Area	Height
1	9.399	12096569	96.48	636516
2	10.407	438611	3.52	26048



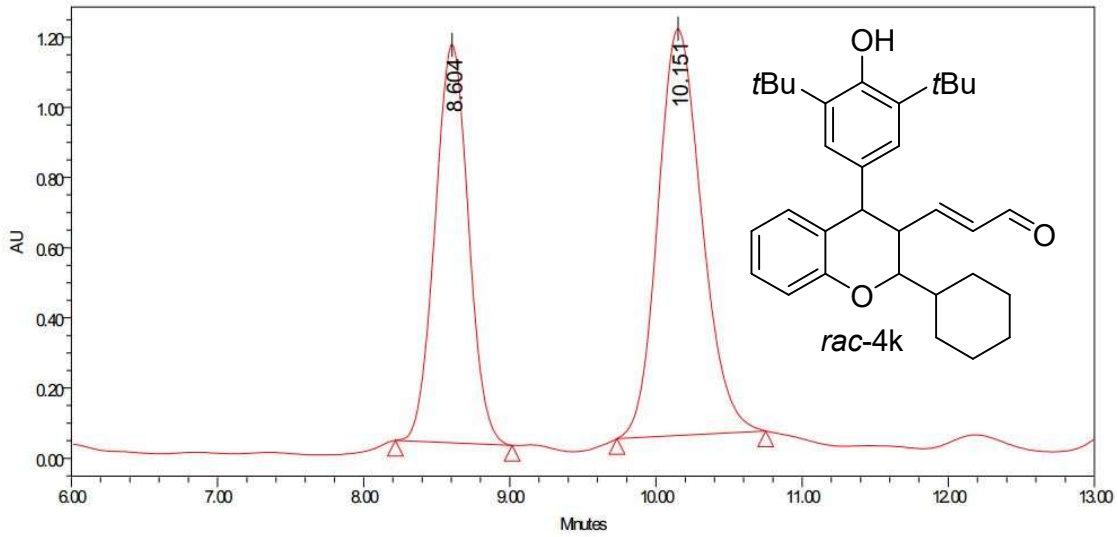
Peak Results

	RT	Area	%Area	Height
1	16.556	15877102	57.16	470236
2	18.264	1190133E	42.84	322307



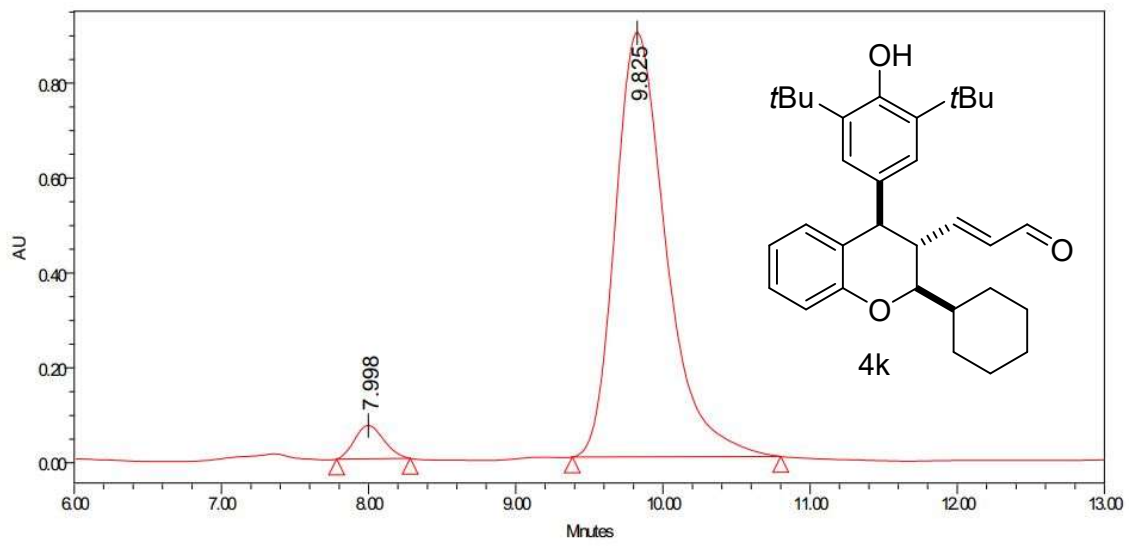
Peak Results

	RT	Area	%Area	Height
1	16.041	19343443	100.00	606172



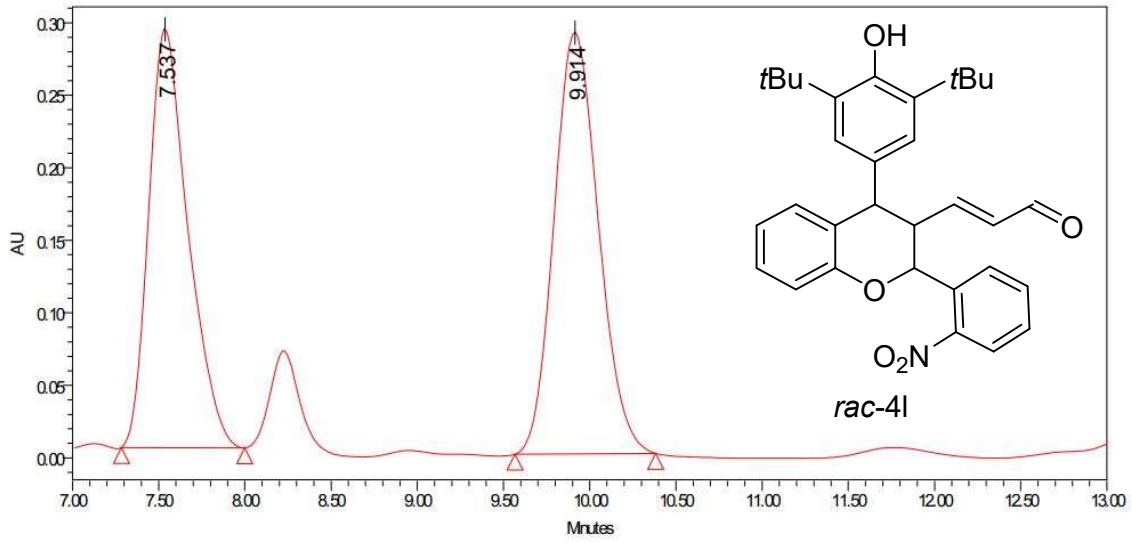
Peak Results

	RT	Area	%Area	Height
1	8.604	18047640	42.78	113618
2	10.151	24138486	57.22	1159974



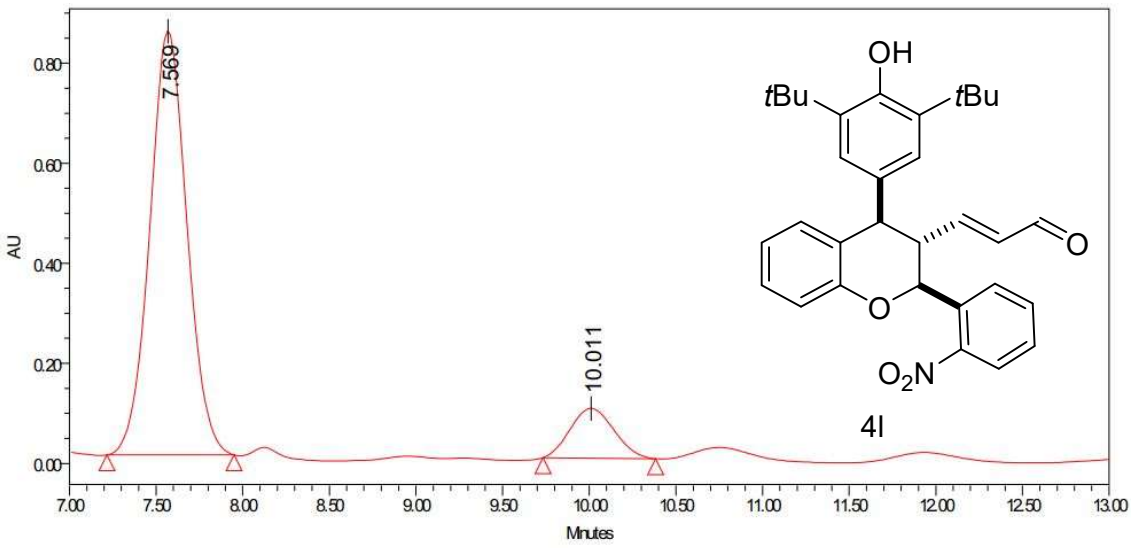
Peak Results

	RT	Area	%Area	Height
1	7.998	966673	4.32	70073
2	9.825	21428750	95.68	894827



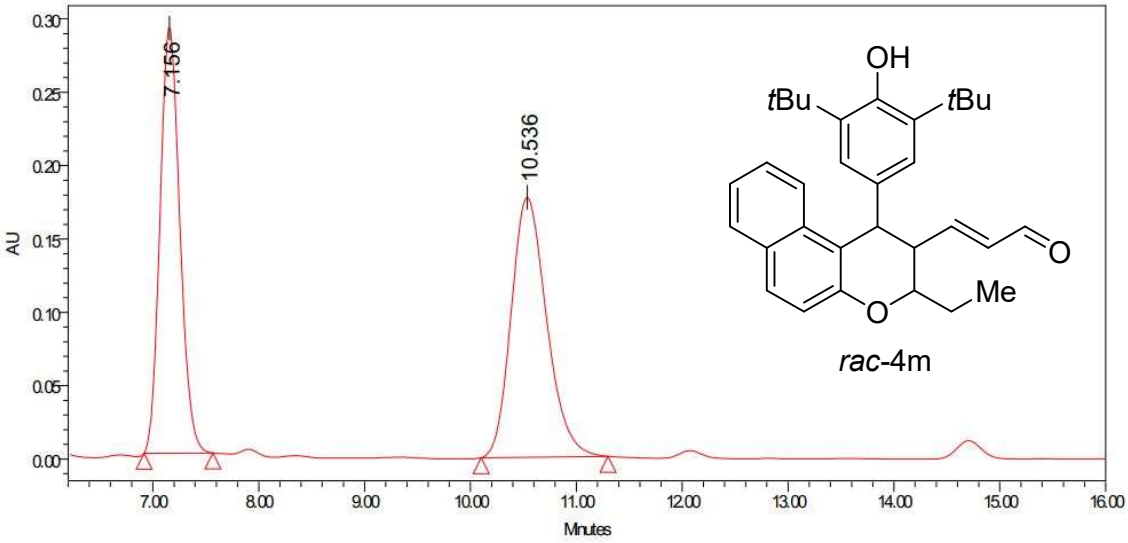
Peak Results

	RT	Area	%Area	Height
1	7.537	4581203	46.81	289251
2	9.914	5206123	53.19	290836



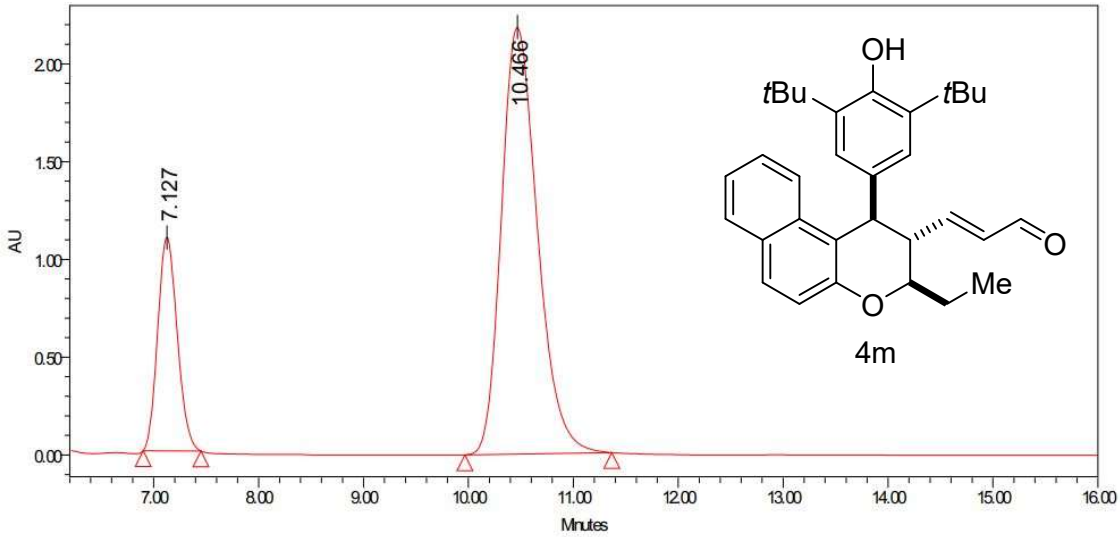
Peak Results

	RT	Area	%Area	Height
1	7.569	12655274	87.88	848422
2	10.011	1745815	12.12	99484



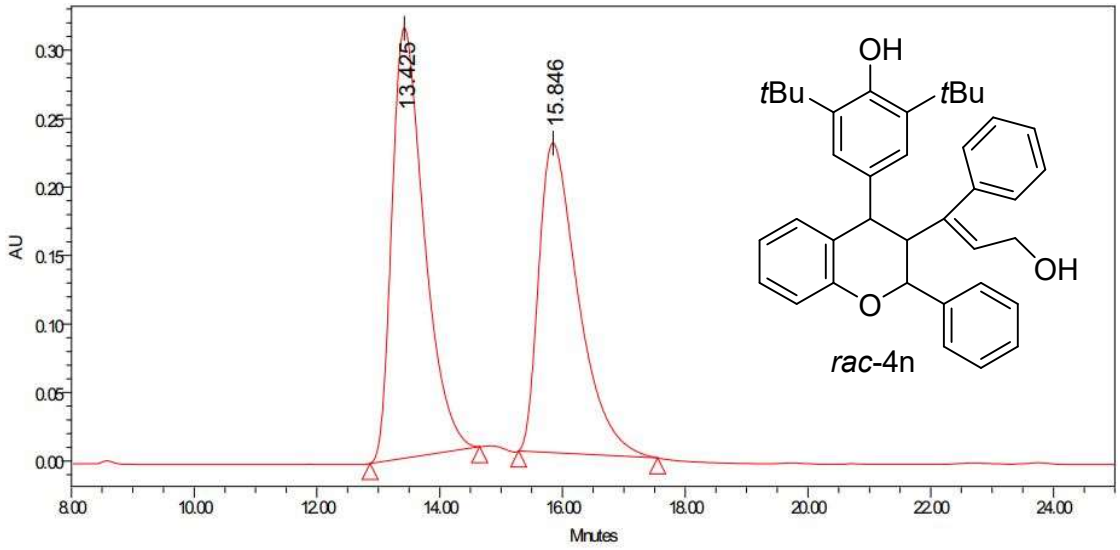
Peak Results

	RT	Area	%Area	Height
1	7.156	3775474	47.78	291083
2	10.536	4125580	52.22	177368



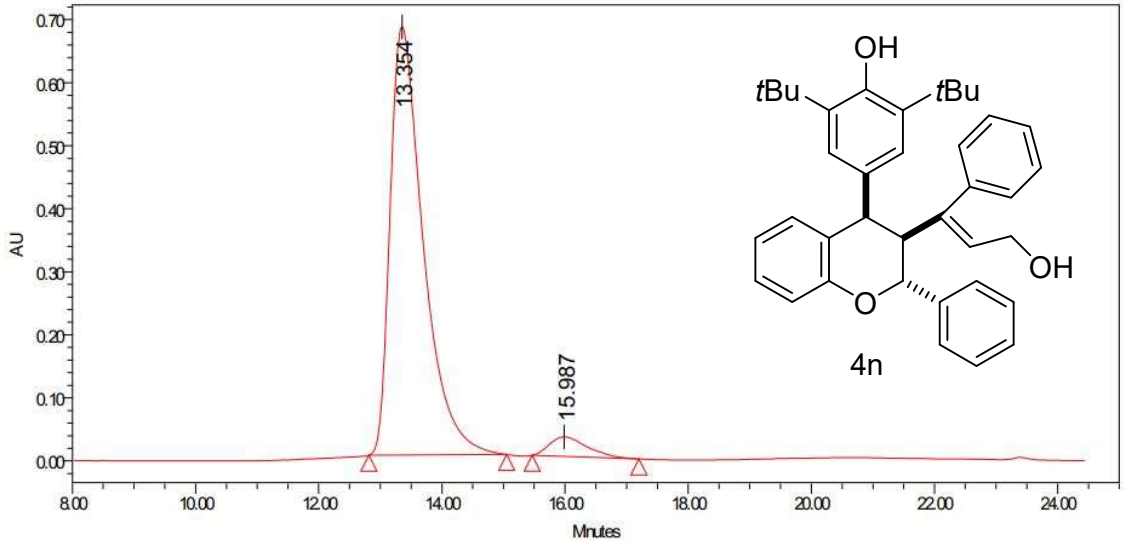
Peak Results

	RT	Area	%Area	Height
1	7.127	14121423	21.32	1094379
2	10.466	52102869	78.68	2183607



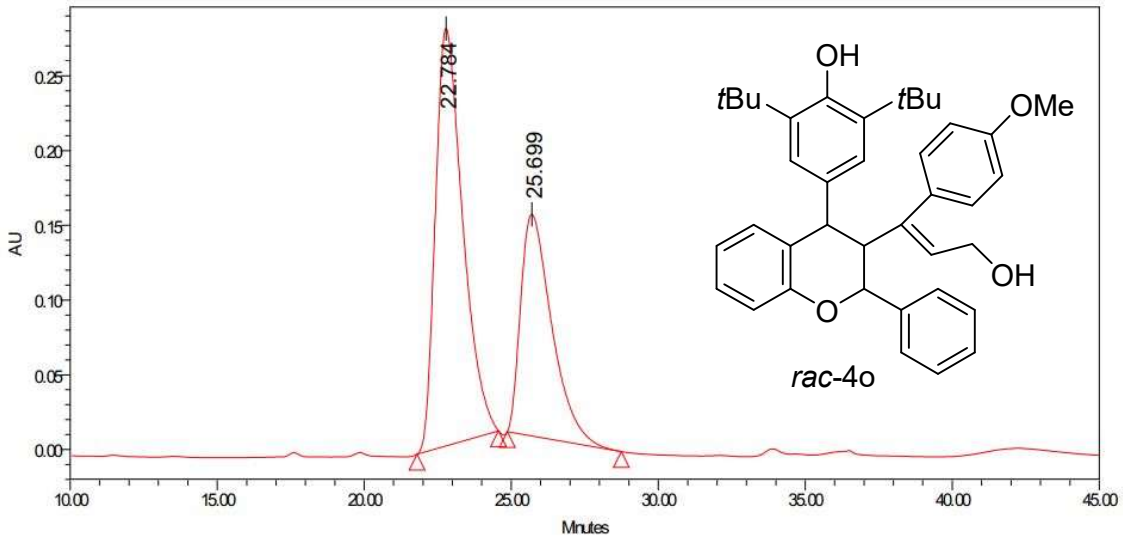
Peak Results

	RT	Area	%Area	Height
1	13.425	11472875	53.12	314156
2	15.846	10123394	46.88	226310



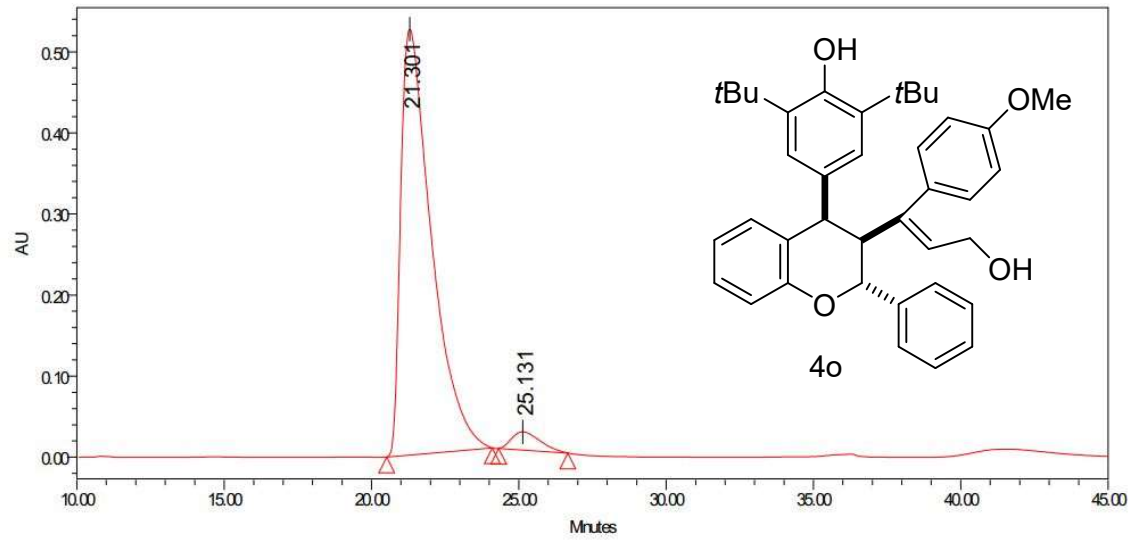
Peak Results

	RT	Area	%Area	Height
1	13.354	25357507	95.05	679443
2	15.987	1321790	4.95	30966



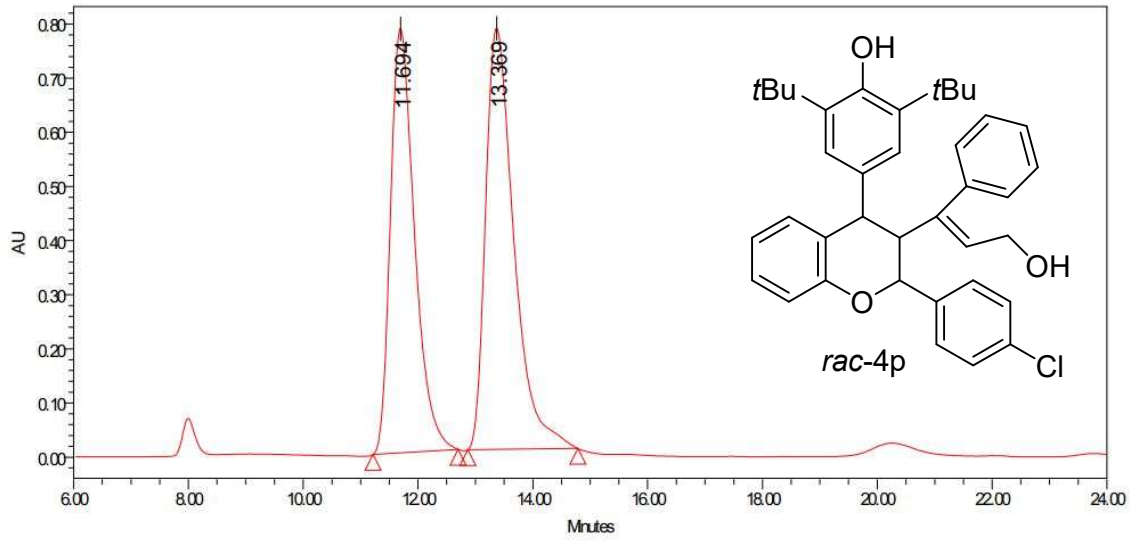
Peak Results

	RT	Area	%Area	Height
1	22.784	18071331	62.32	279198
2	25.699	10926306	37.68	148310



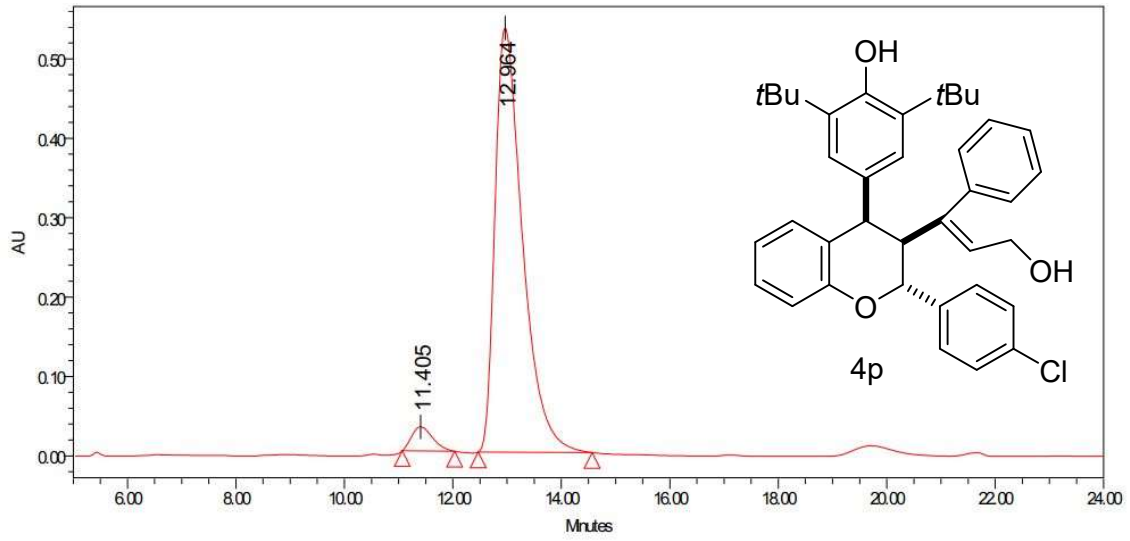
Peak Results

	RT	Area	%Area	Height
1	21.301	38056790	96.18	525207
2	25.131	1511703	3.82	22447



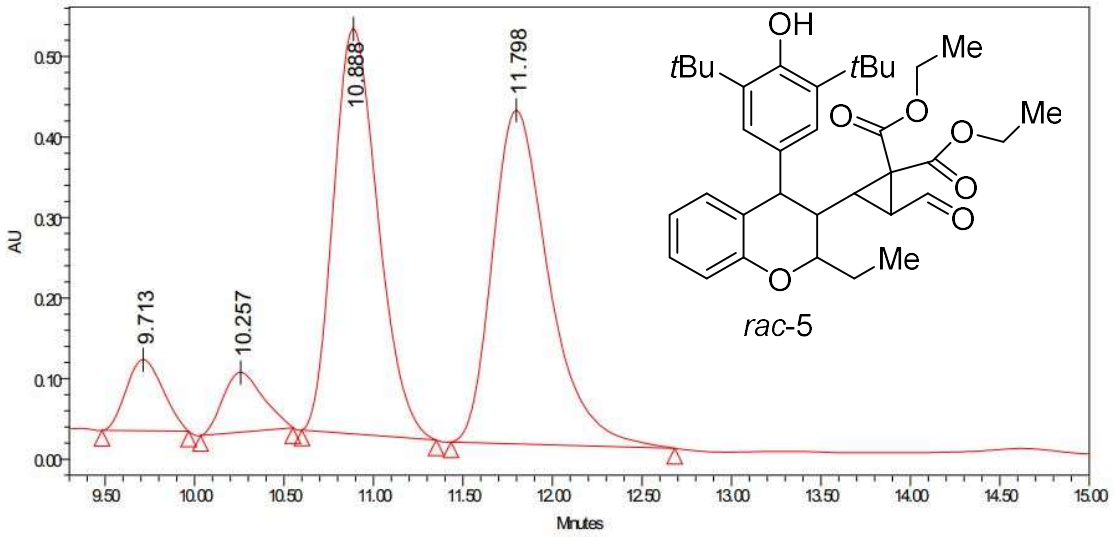
Peak Results

	RT	Area	%Area	Height
1	11.694	22842913	46.10	784212
2	13.369	26711098	53.90	778421



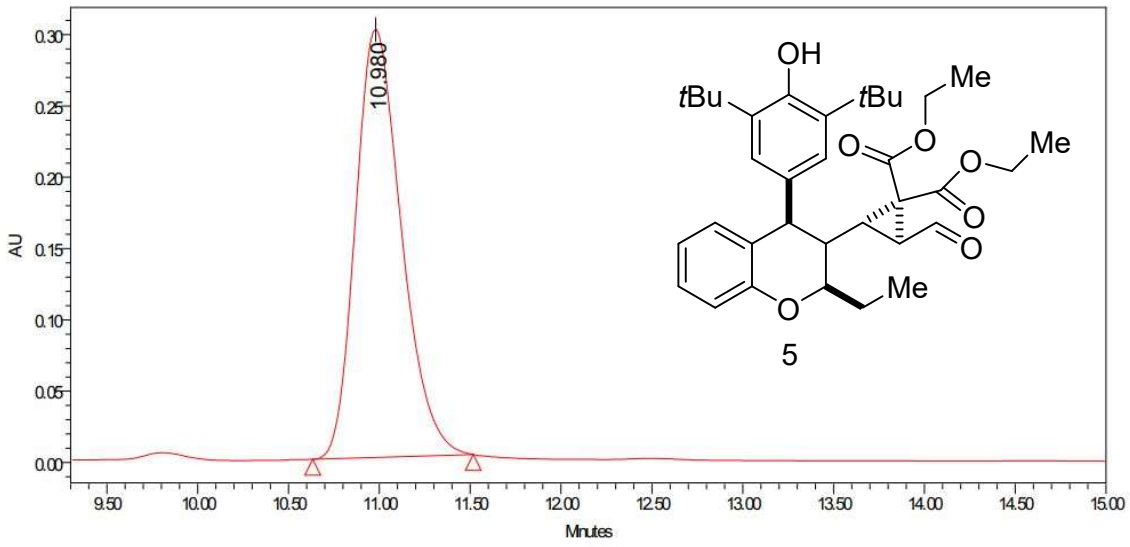
Peak Results

	RT	Area	%Area	Height
1	11.405	821942	4.19	30435
2	12.964	18807149	95.81	534160



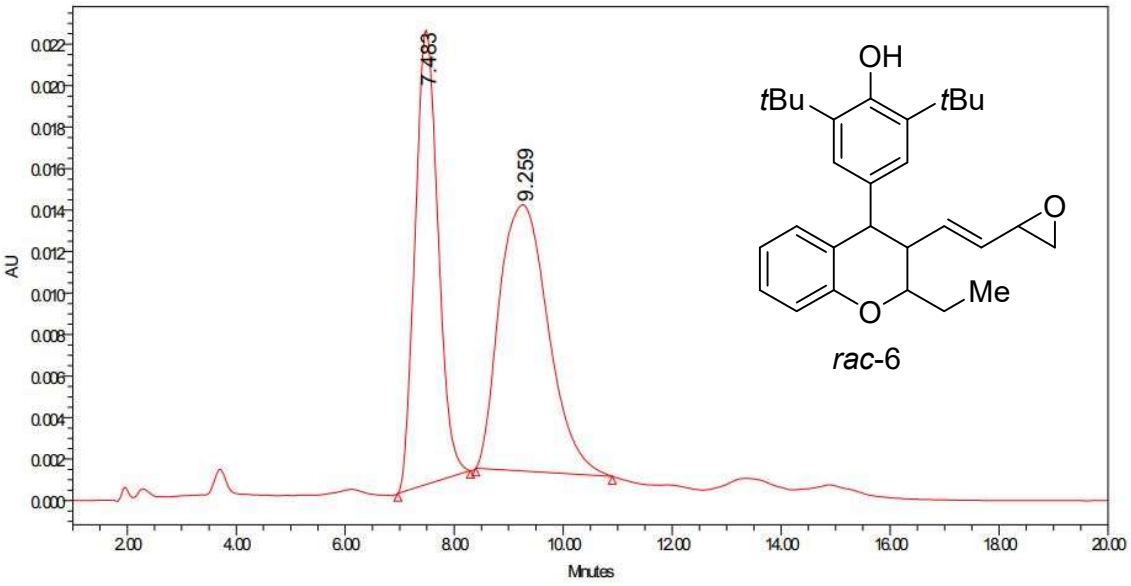
Peak Results

	RT	Area	%Area	Height
1	9.713	1255113	6.22	88455
2	10.257	1145709	5.68	74267
3	10.888	8710431	43.15	504041
4	11.798	9076166	44.96	414599



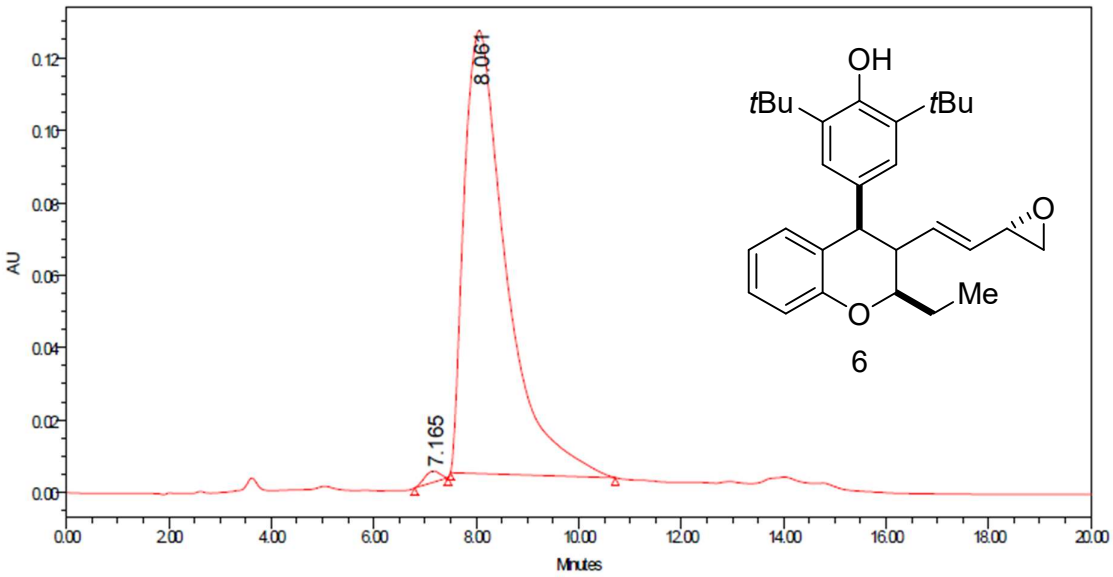
Peak Results

	RT	Area	%Area	Height
1	10.980	5271147	100.00	300489



rac-6

	RT	Area	%Area	Height
1	7.483	640791	44.40	21895
2	9.259	802472	55.60	12824



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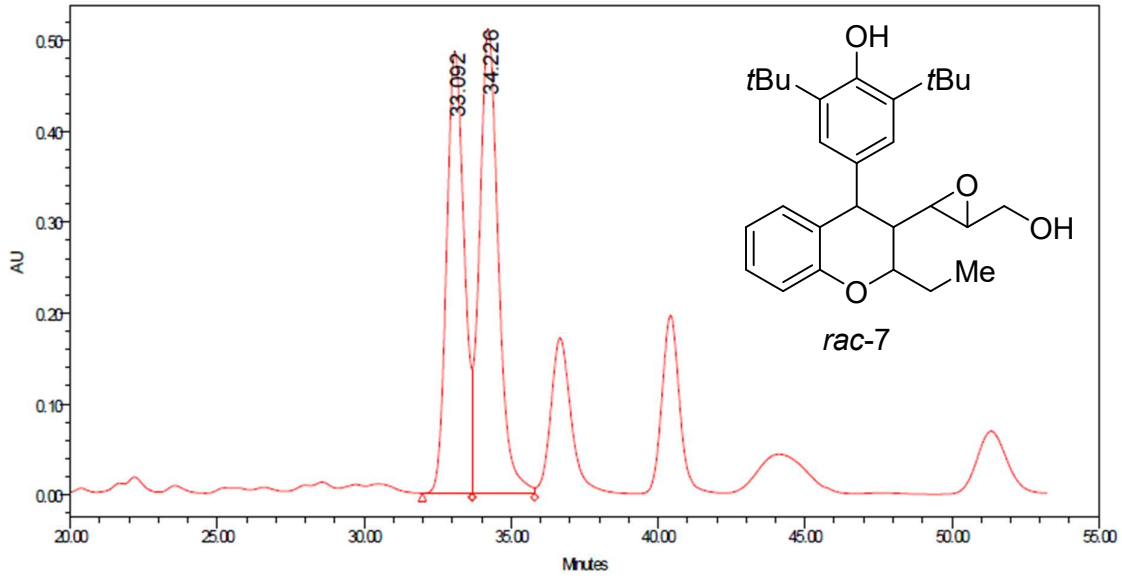
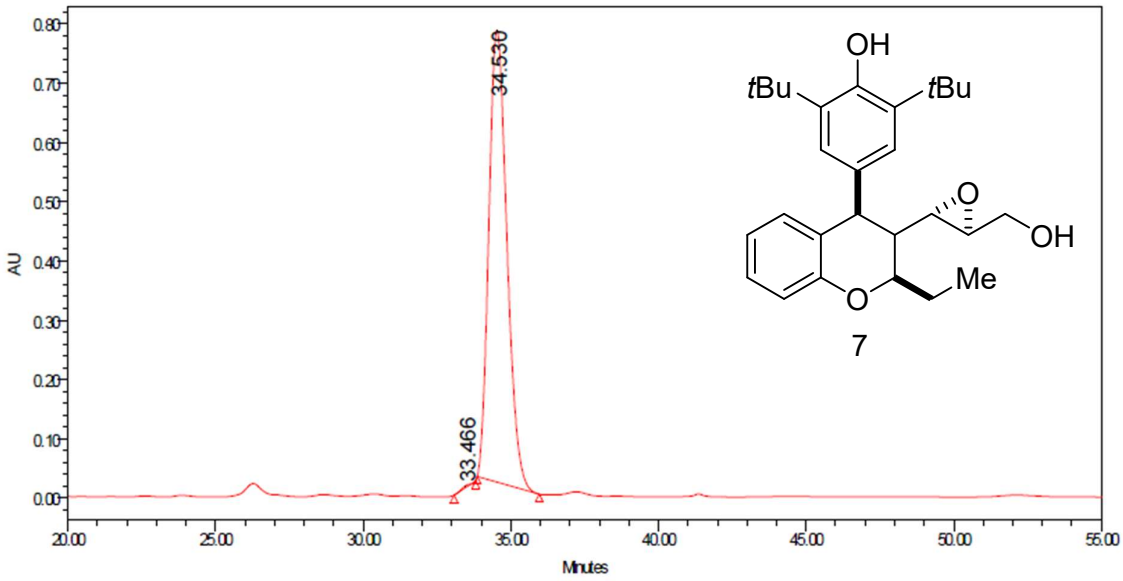
	RT	Area	%Area	Height
1	7.165	65017	0.92	3093
2	8.061	6973259	99.08	122343

Supporting Information



	RT	Area	%Area	Height
1	33.092	20085187	46.77	485792
2	34.226	22861993	53.23	510986



	RT	Area	%Area	Height
1	33.466	67028	0.21	3368
2	34.530	32388512	99.79	763009