

# Asymmetric hydride shift reactions catalysed by chiral aluminium complexes

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## Supporting Information

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## 1. General Experimental

**Reagents, solvents and techniques:** All reactions were performed under an inert atmosphere with constant magnetic stirring, unless otherwise stated, using clean, oven dried glassware. Reagents and solvents were obtained from commercial supplies and were used without further purification. All inert gases were sourced from the University of Oxford's internal supplies and dried through CaCl<sub>2</sub> drying columns. Anhydrous solvents were obtained from the University of Oxford internal solvent system and dried by passing through alumina columns, manufactured by Innovative Technology Inc. PS-400-7. Temperatures of -78 °C and 0 °C were achieved with a CO<sub>2</sub>(s)/acetone bath and ice/water bath respectively.

**Thin layer chromatography** was performed on Merck Kieselgel 60 F<sub>254</sub> 0.25 mm pre-coated aluminium plates. Product spots were visualized under UV light ( $\lambda = 254$  nm) and/or by staining with potassium permanganate solution, phosphomolybdic acid or vanillin. Flash chromatography was performed using VWR silica gel 60 (40-63  $\mu\text{m}$  particle size) using head pressure by means of a nitrogen line.

**NMR Spectroscopy:** <sup>1</sup>H and <sup>13</sup>C NMR samples were run on a Bruker AVIIIHD 400 MHz spectrometer, where required COSY and HSQC spectra were used to assign NMR spectra. In addition, Bruker AVIIIHD 500 MHz and Bruker NEO 600 MHz spectrometers were used to obtain NOESY and HMBC data where required. All NMR spectra were recorded at ambient temperature. Chemical shifts are quoted in ppm with signal splittings recorded as singlet (s), doublet (d), triplet (t), quartet (q), quintet (qn), sextet (sext), septet (sept), and multiplet (m). The abbreviation br denotes broad.

**Infrared spectra** were recorded neat on a Bruker Tensor 27 spectrometer equipped with an attenuated total reflectance attachment with internal calibration. Absorption maxima ( $\lambda_{\text{max}}$ ) are quoted in wavenumbers (cm<sup>-1</sup>). The abbreviation br denotes broad.

**Mass Spectroscopy:** Mass spectra were obtained through the University of Oxford mass spectrometry service by electrospray ionisation (ESI) using a Bruker Daltonics microTOF spectrometer. The m/z values were all recorded in Daltons to four decimal places, the mass found was compared to the mass calculated from the monoisotopic molecular formula.

**Optical rotations** were recorded on a Bellingham+Stanley ADP450 polarimeter in a cell with a path length of 0.5 dm in the solvent specified, at temperature T, expressed in °C, at concentration c, expressed in g/100 mL.

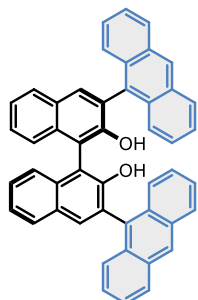
**Chiral normal phase HPLC** was performed on an Agilent 1260 Series HPLC unit equipped with UV-vis diode-array detector, fitted with the appropriate Daicel Chiralpak column (dimensions: 0.46 cm  $\phi$  x 25 cm) along with the corresponding guard column (0.4 cm  $\phi$  x 1 cm). Wavelengths ( $\lambda$ ) are reported in nm, retention times ( $t_{\text{R}}$ ) are reported in minutes and solvent flow rates are reported in mL min<sup>-1</sup>.

**Melting Points:** Melting points were obtained using Griffin melting point apparatus.

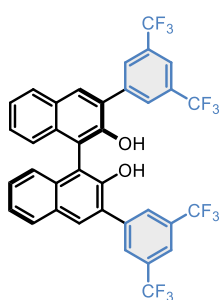
**Microwave:** Reactions in a microwave were completed on a Biotage® Initiator+.

## 2. Optimisation

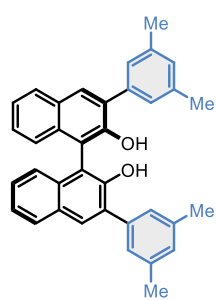
### 2.1 Index of ligands involved in the study



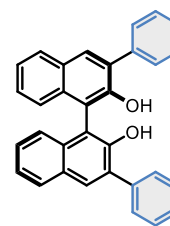
**L1**, CAS No: 361342-49-6



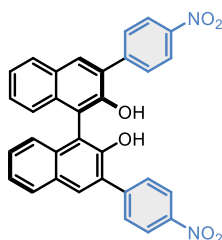
**L2**, CAS No: 756491-54-0



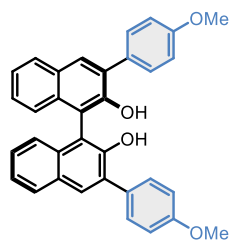
**L3**, CAS No: 215433-51-5



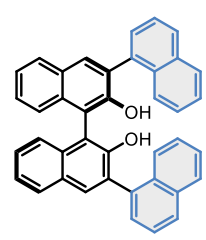
**L4**, CAS No: 39648-74-3



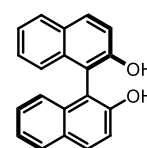
**L5**, CAS No: 791616-60-9



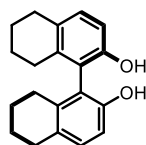
**L6**, CAS No: 756491-51-7



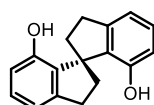
**L7**, CAS No: 851615-07-1



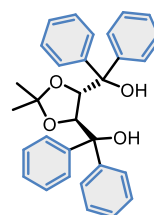
**L8**, CAS No: 18531-94-7



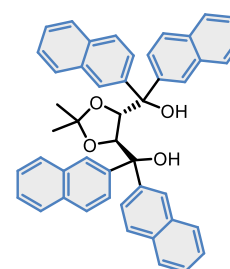
**L9**, CAS No: 65355-14-8



**L10**, CAS No: 223259-63-0

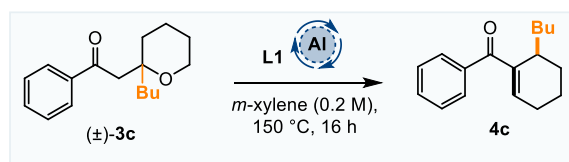


**L11**, CAS No: 93379-48-7



**L12**, CAS No: 137365-16-3

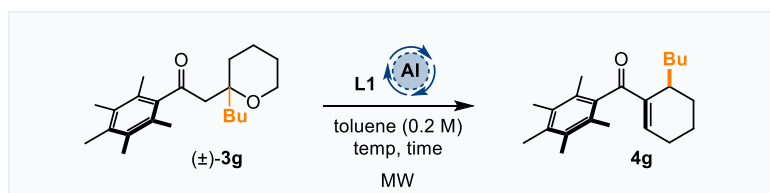
### 2.2 Representative example of irreproducibility in catalytic experiments with tBuOH additive.



Run	Me <sub>3</sub> Al (mol%)	Ligand (mol%)	tBuOH (mol%)	Yield (%)	e.r.
1	40	<b>L1</b> (40)	40	44	90:10
2	40	<b>L1</b> (40)	40	55	90:10
3	40	<b>L1</b> (40)	40	72	94:6

## 2.3 Extended optimisation table

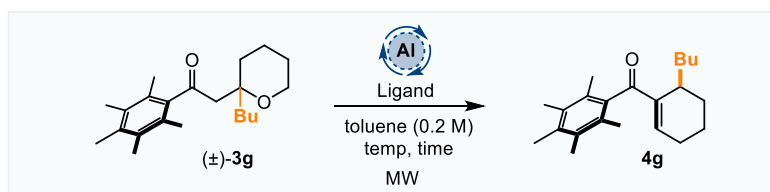
### 2.3.1 Screening of solvents, temperature, time on model substrate 3g



Entry	$\text{Me}_3\text{Al}$ (mol%)	Ligand (mol%)	Time (h)	Temp (°C)	Yield (%) <sup>[a]</sup>	e.r. <sup>[b]</sup>
1	30	<b>L1</b> (45)	1.5	130	79	92:8
2	20	<b>L1</b> (40)	1.5	130	85	88:12
3	20	<b>L1</b> (30)	72	RT	-	-
4	20	<b>L1</b> (30)	2.5	90	25	95:5
5	20	<b>L1</b> (30)	1.5	110	19	94:6
6	20	<b>L1</b> (30)	1.5	130	70	84:16
7	20	<b>L1</b> (30), (0.4 M)	1.5	130	68	86:14
8	20	<b>L1</b> (30)	0.75	150	59	87:13
9	20	<b>L1</b> (30)	0.75	170	65	80:20
10 <sup>a</sup>	20	<b>L1</b> (30)	1.5	130	40	96:4
11	10	<b>L1</b> (15)	1.5	130	19	85:15
12	20	<b>L1</b> (20)	1.5	130	68	79:21
13	20	<b>L1</b> (30) + 4A MS	1.5	130	27	81:19
14	20	<b>L1</b> (30) + 4A MS	3	130	61	85:15
15	20	<b>L1</b> (30), THF	1.5	130	56	87:13
16	20	<b>L1</b> (30), DCE	1.5	130	60	82:18
17	40	<b>L1</b> (60), DCE	1.5	130	74	86:14
18	40	<b>L1</b> (60), DCE	1.0	130	72	88:12
19	40	<b>L1</b> (60), DCE	1.0	150	78	80:20
20	40	<b>L1</b> (60), DCE	1.0	170	77	78:22
21	40	<b>L1</b> (60), DCE	0.5	190	69	79:21
22	20	<b>L1</b> ,(30), THF (9.25 equiv.) <sup>[c]</sup>	1.5	130	51	92:8
23	20	<b>L1</b> ,(30), THF (9.25 equiv.) <sup>[c]</sup>	1.5	130	54	90:10
24	40	<b>L1</b> ,(60), THF (9.25 equiv.) <sup>[c]</sup>	1.5	130	75	98.5:1.5
25	40	<b>L1</b> ,(60), THF (10 equiv.) <sup>[c]</sup>	1.5	130	75	98.3:1.7
26	20	<b>L2</b> (30)	1.5	130	70	84:16

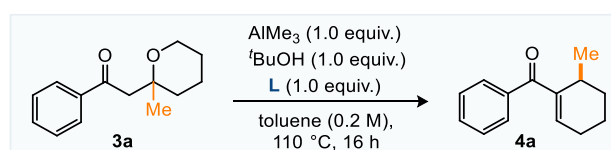
<sup>[a]</sup> Yield of isolated product, <sup>[b]</sup> Determined by normal phase HPLC analysis using a chiral stationary phase. <sup>[c]</sup> compared to  $\text{AlMe}_3$

### 2.3.2 Screening of different ligands on model substrate 3g



Entry	$\text{Me}_3\text{Al}$ (mol%)	Ligand (mol%)	Time (h)	Temp ( $^\circ\text{C}$ )	Yield (%) <sup>[a]</sup>	e.r. <sup>[c]</sup>
1	20	<b>L3</b> (30)	1.5	130	8	72:28
2	40	<b>L3</b> (60)	1.5	130	38	80:20
3	20	<b>L5</b> (30)	1.5	130	37	70:30
4	20	<b>L5</b> (30)	2.5	90	23	75:25
5	20	<b>L6</b> (30)	1.5	130	3	58:42
6	40	<b>L7</b> (60)	1.5	130	35	79:21
7	20	<b>L7</b> (30)	1.5	130	20	75:15
8	20	<b>L2</b> (20)	1.5	130	61	88:12
9	20	<b>L2</b> (20), $t\text{BuOH}$	1.5	130	50	85:15
8	20	<b>L2</b> (30), $\text{Al}(\text{SO}_3)_3$	1.5	130	50	80:20
9	20	<b>L2</b> (30)	1.5	130	48	88:12
10	20	<b>L2</b> (30), THF (9.25 equiv.)	1.5	130	45	92:8
11	40	<b>L2</b> (60)	1.5	130	72	90:10
12	40	<b>L2</b> (60), THF (9.25 equiv.)	1.5	130	74	93:7
13	40	<b>L2</b> (20)	1.5	130	60	87:13

### 2.3.3 Initial screening of different ligands on model substrate 3a



Entry	Ligand	Yield (%) <sup>[a]</sup>	e.r. <sup>[c]</sup>
1	<b>L8</b>	(12)	57:43
2	<b>L9</b>	(15)	52:48
3	<b>L10</b>	(20)	51:49
4	<b>L11</b>	(26)	56:44
5	<b>L12</b>	(15)	65:35

### 3. General procedures and characterization data

#### General Procedure 1 – Synthesis of Weinreb amides

Dimethylhydroxylamine hydrochloride (1.1 equiv.) was added to a solution of benzoyl chloride in CH<sub>2</sub>Cl<sub>2</sub> (0.3 M) under N<sub>2</sub>. The reaction mixture was cooled to 0 °C and triethylamine (3.0 equiv.) was added dropwise. The reaction was warmed to RT and stirred overnight. The mixture was quenched by the addition of sat. aq. ammonium chloride and extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic phases were dried over MgSO<sub>4</sub>, filtered and concentrated *in vacuo*. For details of purification, see experimental procedures.

#### General Procedure 2 – Synthesis of ynones

*n*-BuLi in hexanes (2.4 equiv.) was added dropwise to a solution of 5-hexyn-1-ol (1.2 equiv.) in THF (0.3 M) at –78 °C under N<sub>2</sub>. The reaction mixture was stirred for 1 h, and a solution of Weinreb amide (1.0 equiv.) in THF (3.0 M) was added dropwise. The reaction was warmed to RT and stirred for 1 h. The mixture was quenched by the addition of sat. aq. ammonium chloride and extracted with EtOAc. The combined organic phases were dried over MgSO<sub>4</sub>, filtered and concentrated *in vacuo*. For details of purification, see the experimental procedures.

#### General Procedure 3: DMP oxidation

*N*-Protected diol (0.39 mmol, 1 equiv.) was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (3.5 mL). NaHCO<sub>3</sub> (197 mg, 2.34 mmol, 6 equiv.) and Dess-Martin Periodinane (250 mg, 0.59 mmol, 1.5 equiv.) were added, and the mixture left to stir for 30 min at RT. The reaction was diluted with saturated aqueous NaHCO<sub>3</sub> solution (5 mL) and saturated aqueous Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> solution, and extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 15 mL). The organic layer was dried with MgSO<sub>4</sub>, filtered and the solvent removed *in vacuo*. For details of purification, see the experimental procedures.

#### General Procedure 4 – Synthesis of racemic cyclohexenes by aluminium promoted [1,5]-hydride shift

A 2–5 mL Biotage<sup>®</sup> microwave vial was charged with the tetrahydropyran (1.0 equiv.), basic alumina (Brockmann I, 5.0 equiv.) or Al(O<sup>*t*</sup>Bu)<sub>3</sub> (1.0 equiv.) and toluene (0.2 M). The vial was degassed, backfilled with N<sub>2</sub>, sealed with a microwave vial cap containing a Reseal<sup>™</sup> septum and heated at 110 °C for 16 h. The reaction was cooled to RT, diluted with Et<sub>2</sub>O, filtered through a plug of silica gel, and concentrated *in vacuo*. For details of purification, see the experimental procedures.

#### General Procedure 5A – Asymmetric synthesis of cyclohexenes by aluminium promoted [1,5]-hydride shift

A 2–5 mL Biotage<sup>®</sup> microwave vial was charged with (*R*)-3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol (1.0 equiv.), *tert*-butanol (1.0 equiv.) and *m*-xylene (0.2 M). The vial was degassed, backfilled with N<sub>2</sub>, and a solution of AlMe<sub>3</sub> in toluene (2.0 M, 1.0 equiv.) was added dropwise to the suspension. The mixture was stirred for 30 min, tetrahydropyran starting material (1.0 equiv.) was added, and the vial was sealed with a microwave vial cap containing a Reseal<sup>™</sup> septum. The reaction was heated at 130 °C for 16 h, cooled to RT, diluted with Et<sub>2</sub>O,

filtered through a plug of silica gel, and concentrated *in vacuo*. For details of purification, see the experimental procedures.

### **General Procedure 5B – Asymmetric synthesis of cyclohexenes by aluminium catalysed [1,5]-hydride shift**

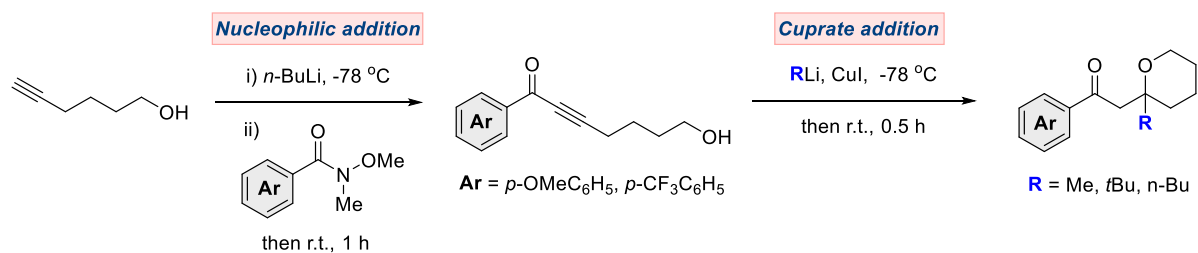
A 2–5 mL Biotage® microwave vial was charged with (*R*)-3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol (77 mg, 0.12 mmol, 0.6 equiv.) and toluene (0.2 M, 1.0 mL), and then degassed with argon. AlMe<sub>3</sub> in toluene (1.0 M, 0.08 mL, 0.08 mmol, 0.4 equiv.) was added dropwise to the suspension under N<sub>2</sub>, and the mixture stirred for 30 min. Tetrahydropyran starting material (0.20 mmol, 1.0 equiv.) was then added, and the reaction vessel was sealed with a microwave vial cap (containing a Reseal™ septum) and heated at 130 °C for 1.5 h in the microwave. The reaction mixture was cooled to room temperature, diluted with Et<sub>2</sub>O, filtered through a plug of silica gel, and concentrated *in vacuo*. For purification details, see the experimental procedures.

### **General Procedure 5C – Asymmetric synthesis of cyclohexenes by aluminium catalysed [1,5]-hydride shift with THF**

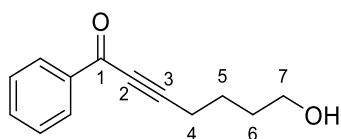
A 2–5 mL Biotage® microwave vial was charged with (*R*)-3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol (77 mg, 0.12 mmol, 0.6 equiv.) and toluene (0.2 M, 1.0 mL), and then degassed with N<sub>2</sub>. AlMe<sub>3</sub> in toluene (1.0 M, 0.08 mL, 0.08 mmol, 0.4 equiv.) was added dropwise to the suspension under N<sub>2</sub>, after which dry THF (60 μL, 0.73 mmol, 9.25 equiv. compared to AlMe<sub>3</sub>) was added and the mixture stirred for 30 min. Tetrahydropyran starting material (0.20 mmol, 1.0 equiv.) was then added, and the reaction vessel was sealed with a microwave vial cap (containing a Reseal™ septum) and heated at 130 °C for 1.5 h in the microwave. The reaction mixture was cooled to room temperature, diluted with Et<sub>2</sub>O, filtered through a plug of silica gel, and concentrated *in vacuo*. For purification details, see the experimental procedures.

Note: In **General Procedure (5A-C)**, (*R*)-3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol (L1, CAS No: 361342-49-6) was recycled and recovered after column chromatography (Pentane:Et<sub>2</sub>O, 60:40) as an off-white solid in (97-99% yield).

### 3.1 Synthesis of THP precursors 3a-3f



#### 7-Hydroxy-1-phenylhept-2-yn-1-one, **S1**



$n\text{-BuLi}$  in hexanes (23.0 mL, 2.5 M, 58.0 mmol, 2.4 equiv.), 5-hexyn-1-ol (2.83 g, 28.8 mmol, 1.2 equiv.), THF (0.3 M, 80 mL), and  $N\text{-methoxy-}N\text{-methylbenzamide}$  (3.96 g, 24.0 mmol, 1.0 equiv.) were subjected to **General Procedure 2**. Purification by column chromatography (pentane:EtOAc, 80:20 to 60:40) afforded the title compound **S1** as a yellow oil (4.15 g, 85% yield).

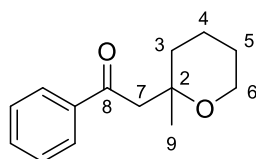
$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.17 – 8.07 (m, 2H, ArCH x 2), 7.64 – 7.54 (m, 1H, ArCH), 7.52 – 7.41 (m, 2H, ArCH x 2), 3.78 – 3.65 (m, 2H, H-7 x 2), 2.61 – 2.49 (m, 2H, H-4 x 2), 1.85 – 1.69 (m, 4H, H-5 x 2, H-6 x 2), 1.62 (s, 1H, OH).

$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  178.4 (C-1), 137.0 (ArC), 134.1 (ArC), 129.7 (ArC x 2), 128.7 (ArC x 2), 96.4 (C-3), 80.0 (C-2), 62.3 (C-7), 31.9 (C-6), 24.4 (C-5), 19.2 (C-4).

**HRMS** (ESI<sup>+</sup>): Found  $[\text{M}+\text{H}]^+ = 203.1071$ ;  $\text{C}_{13}\text{H}_{15}\text{O}_2$  requires 203.1067  $\Delta$  2.16 ppm

**IR** (film)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 3389, 2938, 2869, 2236, 2200, 1639.

#### (±)-2-(2-Methyltetrahydro-2H-pyran-2-yl)-1-phenylethan-1-one, **3a**



$\text{MeLi}$  in  $\text{Et}_2\text{O}$  (1.6 M, 11.2 mL, 18.0 mmol, 6.0 equiv.) was added dropwise to a solution of  $\text{CuI}$  (1.72 g, 9.00 mmol, 3.0 equiv.) in THF (0.3 M, 25 mL) at  $-78\text{ }^\circ\text{C}$ . The reaction mixture was warmed to  $0\text{ }^\circ\text{C}$  and stirred for 1 h, affording a colourless solution. The mixture was cooled to  $-78\text{ }^\circ\text{C}$ , and a solution of **S1** (606 mg, 3.00 mmol, 1.0 equiv.) in THF (1.0 M, 3 mL) was added dropwise and stirred for 30 min. The reaction was quenched by addition of saturated aqueous ammonium chloride (30 mL) and warmed to RT. The mixture was treated with 35% aqueous ammonium hydroxide solution (30 mL), affording a clear blue aqueous phase. The solution was extracted with EtOAc (3 x 60 mL) and the combined organic phases were washed with HCl (1.0 M, 50 mL), dried over  $\text{MgSO}_4$ , filtered, and concentrated *in vacuo*. Purification by column chromatography (pentane:Et<sub>2</sub>O, 95:5) afforded the title compound **3a** as a yellow oil (588 mg, 90% yield).

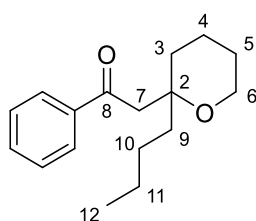
**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 8.02 – 7.94 (m, 2H, ArH x 2), 7.59 – 7.50 (m, 1H, ArH), 7.49 – 7.40 (m, 2H, ArH), 3.76 – 3.65 (m, 2H, H-6), 3.25 – 3.13 (m, 2H, H-7), 1.78 – 1.62 (m, 4H, H-3, H-4), 1.59 – 1.47 (m, 2H, H-5), 1.33 (s, 3H, H-9).

**<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) δ 199.2 (C-8), 138.5 (ArC), 133.0 (ArC), 128.6 (ArC x 4), 73.5 (C-2), 61.8 (C-6), 48.1 (C-7), 35.1 (C-3), 25.9 (C-5), 23.4 (C-9), 19.5 (C-4).

**HRMS** (ESI+): Found [M+H]<sup>+</sup> = 219.1373; C<sub>14</sub>H<sub>19</sub>O<sub>2</sub> requires 219.1380 Δ -3.01 ppm.

**IR** (film) ν<sub>max</sub>/cm<sup>-1</sup>: 2980, 1676, 1597, 1449, 1378, 1232.

### (±)-2-(2-Butyltetrahydro-2H-pyran-2-yl)-1-phenylethan-1-one, **3c**



*n*-BuLi in hexanes (2.5 M, 1.2 mL, 3.0 mmol, 6.0 equiv.) was added dropwise to a solution of CuI (285 mg, 1.5 mmol, 3.0 equiv.) in THF (0.3 M, 5 mL) at –78 °C. The reaction mixture was warmed to 0 °C and stirred for 1 h, affording a black precipitate. The mixture was cooled to –78 °C, and a solution of **S1** (101 mg, 0.50 mmol, 1.0 equiv.) in THF (1.0 M, 0.5 mL) was added dropwise and stirred for 30 min. The reaction was quenched by addition of saturated aqueous ammonium chloride (10 mL) and warmed to RT. The mixture was treated with 35% aqueous ammonium hydroxide solution (10 mL), affording a clear blue aqueous phase. The solution was extracted with EtOAc (3 x 20 mL) and the combined organic phases were washed with HCl (1.0 M, 20 mL), dried over MgSO<sub>4</sub>, filtered, and concentrated *in vacuo*. Purification by column chromatography (pentane:Et<sub>2</sub>O, 95:5) afforded the title compound **3c** as a yellow oil (101 mg, 78% yield).

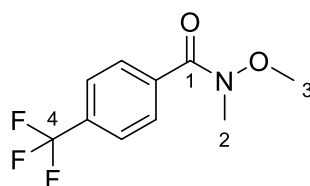
**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 8.00 – 7.93 (m, 2H, ArH), 7.58 – 7.50 (m, 1H, ArH), 7.49 – 7.40 (m, 2H, ArH), 3.66 (dd, *J* = 6.0, 5.0 Hz, 2H, H-6), 3.24 (d, *J* = 15.5 Hz, 1H, H-7), 3.14 (d, *J* = 15.5 Hz, 1H, H-7'), 1.91 – 1.56 (m, 6H, H-3, H-5, H-9), 1.55 – 1.45 (m, 2H, H-4), 1.41 – 1.13 (m, 4H, H-10, H-11), 0.86 (t, *J* = 7.0 Hz, 3H, H-12).

**<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) δ 199.3 (C-8), 138.6 (ArC), 132.9 (ArC), 128.6 (ArC x 2), 128.4 (ArC x 2), 75.4 (C-2), 61.5 (C-6), 44.8 (C-7), 34.3 (C-9), 33.7 (C-3), 25.9 (C-5), 25.4 (C-10), 23.3 (C-11), 19.2 (C-4), 14.2 (C-12).

**HRMS** (ESI+): Found [M+H]<sup>+</sup> = 261.1849; C<sub>17</sub>H<sub>25</sub>O<sub>2</sub> requires 261.1849 Δ -0.04 ppm

**IR** (film) ν<sub>max</sub>/cm<sup>-1</sup>: 2933, 2860, 1677, 1448, 1350, 1085.

### *N*-Methoxy-*N*-methyl-4-(trifluoromethyl)benzamide, **S2**



Dimethylhydroxylamine hydrochloride (3.22 g, 33.0 mmol, 1.1 equiv.), CH<sub>2</sub>Cl<sub>2</sub> (0.3 M, 100 mL), 4-(trifluoromethyl)benzoyl chloride (6.26 g, 30.0 mmol, 1.0 equiv.), and triethylamine (12.6 mL, 90.0 mmol, 3.0 equiv.) were subjected to **General Procedure 1**. Purification by column chromatography (pentane:EtOAc, 80:20) afforded the title compound **S2** as a colourless oil (6.42 g, 92% yield).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.78 (d, *J* = 8.0 Hz, 2H, ArCH x 2), 7.66 (d, *J* = 8.0 Hz, 2H, ArCH x 2), 3.52 (s, 3H, H-3 x 3), 3.37 (s, 3H, H-2 x 3).

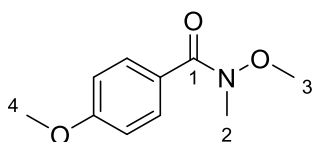
<sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>) δ -63.0.

<sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 168.6 (C-1), 137.7 (ArC), 132.3 (ArC), 128.7 (ArC x 2), 125.1 (ArC x 2), 122.8 (C-4), 61.4 (C-3), 33.4 (C-2).

The spectroscopic data matched that previously reported in the literature.<sup>[1]</sup>

[1] Radhoff, N.; Daniliuc, C. G.; Studer, A. *Angew. Chem., Int. Ed.* **2023**, *62*, e202304771.

### ***N*,4-Dimethoxy-*N*-methylbenzamide, S3**



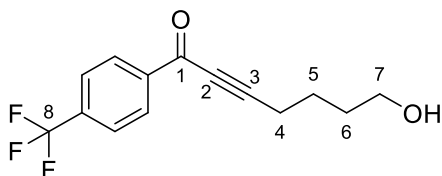
Dimethylhydroxylamine hydrochloride (1.61 g, 16.5 mmol, 1.1 equiv.), CH<sub>2</sub>Cl<sub>2</sub> (0.3 M, 50 mL), 4-methoxybenzoyl chloride (2.56 g, 15.0 mmol, 1.0 equiv.), and triethylamine (6.3 mL, 45.0 mmol, 3.0 equiv.) were subjected to **General Procedure 1**. Purification by column chromatography (pentane:EtOAc, 60:40) afforded the title compound **S3** as a colourless oil (1.51 g, 51% yield).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.77 – 7.68 (m, 2H, ArCH x 2), 6.94 – 6.86 (m, 2H, ArCH x 2), 3.84 (s, 3H, H-4 x 3), 3.56 (s, 3H, H-3 x 3), 3.35 (s, 3H, H-2 x 3).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 169.5 (C-1), 161.6 (ArC), 130.7 (ArC x 2), 126.1 (ArC), 113.4 (ArC x 2), 61.0 (C-3), 55.4 (C-4), 34.0 (C-2).

The spectroscopic data matched that previously reported in the literature.<sup>[1]</sup>

### **7-Hydroxy-1-(4-(trifluoromethyl)phenyl)hept-2-yn-1-one, S2a**



*n*-BuLi in hexanes (19.2 mL, 2.5 M, 48.0 mmol, 2.4 equiv.), 5-hexyn-1-ol (2.35 g, 24.0 mmol, 1.2 equiv.), THF (0.3 M, 67 mL) and *N*-methoxy-*N*-methyl-4-(trifluoromethyl)benzamide **S2** (4.66 g, 20.0 mmol, 1.0 equiv.) were subjected to **General Procedure 2**. The title compound was afforded after purification by FCC (10-40% EtOAc/Pentane) as a yellow oil (3.76 g, 13.9 mmol, 70% yield).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 8.23 (d, *J* = 8.0 Hz, 2H, ArCH x 2), 7.74 (d, *J* = 8.0 Hz, 2H, ArCH x 2), 3.73 (t, *J* = 6.0 Hz, 2H, H<sub>7</sub> x 2), 2.59 (t, *J* = 6.5 Hz, 2H, H<sub>4</sub> x 2), 1.86 – 1.71 (m, 4H, H<sub>5</sub> x 2, H<sub>6</sub> x 2), 1.39 (s, 1H, OH).

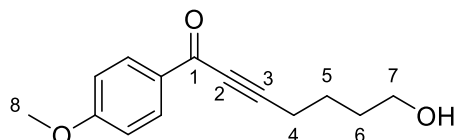
<sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>) δ -63.1.

$^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  177.0 ( $\text{C}_1$ ), 139.5 (ArC), 135.2 (ArC), 129.9 (ArC x 2), 125.8 (ArC x 2), 123.7 ( $\text{C}_8$ ), 97.9 ( $\text{C}_3$ ), 79.8 ( $\text{C}_2$ ), 62.3 ( $\text{C}_7$ ), 31.9 ( $\text{C}_6$ ), 24.4 ( $\text{C}_5$ ), 19.2 ( $\text{C}_4$ ).

HRMS (ESI+): Found  $[\text{M}+\text{H}]^+ = 271.0945$ ;  $\text{C}_{14}\text{H}_{14}\text{F}_3\text{O}_2$  requires 271.0940  $\Delta$  1.68 ppm

IR (film)  $\nu_{\text{max}}/\text{cm}^{-1}$  3394, 2920, 2865, 2231, 2188, 1642, 1254.

### 7-Hydroxy-1-(4-methoxyphenyl)hept-2-yn-1-one, **S3a**



*n*-BuLi in hexanes (9.8 mL, 2.5 M, 24.6 mmol, 2.4 equiv.), 5-hexyn-1-ol (1.21 g, 12.3 mmol, 1.2 equiv.), THF (0.3 M, 34 mL) and *N*-methoxy-*N*-methyl-4-(trifluoromethyl)benzamide **S3** (2.00 g, 10.2 mmol, 1.0 equiv.) were subjected to **General Procedure 2**. The title compound was afforded after purification by FCC (20-60% EtOAc/Pentane) as a yellow oil (2.11 g, 9.08 mmol, 89% yield).

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.13 – 8.04 (m, 2H, ArCH x 2), 6.98 – 6.89 (m, 2H, ArCH x 2), 3.88 (s, 3H,  $\text{H}_8$  x 3), 3.75 – 3.67 (m, 2H,  $\text{H}_7$  x 2), 2.58 – 2.48 (m, 2H,  $\text{H}_4$  x 2), 1.82 – 1.69 (m, 4H,  $\text{H}_5$  x 2,  $\text{H}_6$  x 2).

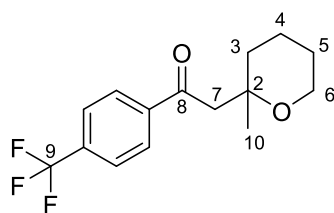
$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  177.1 ( $\text{C}_1$ ), 164.5 (ArC), 132.1 (ArC x 2), 130.4 (ArC), 113.9 (ArC x 2), 95.5 ( $\text{C}_3$ ), 80.0 ( $\text{C}_2$ ), 62.3 ( $\text{C}_7$ ), 55.7 ( $\text{C}_8$ ), 31.9 ( $\text{C}_6$ ), 24.4 ( $\text{C}_5$ ), 19.2 ( $\text{C}_4$ ).

HRMS (ESI+): Found  $[\text{M}+\text{H}]^+ = 233.1172$ ;  $\text{C}_{14}\text{H}_{17}\text{O}_3$  requires 233.1172  $\Delta$  -0.11 ppm

m.p.: 109-110 °C

IR (film)  $\nu_{\text{max}}/\text{cm}^{-1}$  3389, 2938, 2869, 2236, 2200, 1639, 1449, 1265, 701.

### (±)-2-(2-Methyltetrahydro-2H-pyran-2-yl)-1-(4-(trifluoromethyl)phenyl)ethan-1-one, **3b**



MeLi in Et<sub>2</sub>O (13.9 mL, 1.6 M, 22.2 mmol, 6.0 equiv.) was added dropwise to a solution of CuI (2.11 g, 11.1 mmol, 3.0 equiv.) in THF (0.3 M, 37 mL) at -78 °C. The reaction mixture was warmed to 0 °C and stirred for 1 h, affording a colourless solution. The mixture was cooled to -78 °C, and a solution of **S2a** (1.00 g, 3.70 mmol, 1.0 equiv.) in THF (1.0 M, 4 mL) was added dropwise and stirred for 30 min. The reaction was quenched by addition of saturated aqueous ammonium chloride (30 mL) and warmed to RT. The mixture was treated with 35% aqueous ammonium hydroxide solution (30 mL), affording a clear blue aqueous phase. The solution was extracted with EtOAc (3 x 60 mL), and the combined organic phases were washed with HCl (1.0 M, 60 mL), dried over MgSO<sub>4</sub>, filtered, and concentrated *in vacuo*. Purification by column chromatography (pentane:Et<sub>2</sub>O, 95:5) afforded the title compound **3b** as a yellow oil (911 mg, 86% yield).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 8.08 (d, *J* = 8.0 Hz, 2H, ArH), 7.71 (d, *J* = 8.0 Hz, 2H, ArH), 3.73 – 3.62 (m, 2H, H-6), 3.22 – 3.13 (m, 2H, H-7), 1.76 – 1.59 (m, 4H, H-3, H-4), 1.55 – 1.47 (m, 2H, H-5), 1.33 (s, 3H, H-10).

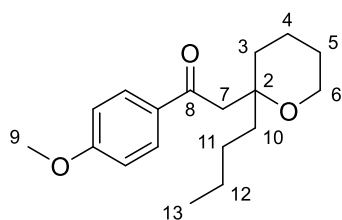
<sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>) δ -63.1.

<sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 198.4 (C-8), 141.1 (ArC), 134.1 (ArC), 129.0 (ArC x 2), 125.6 (ArC x 2), 122.7 (C-9), 73.5 (C-2), 61.8 (C-6), 49.1 (C-7), 35.1 (C-3), 25.8 (C-5), 22.9 (C-10), 19.4 (C-4).

HRMS (ESI+): Found [M+H]<sup>+</sup> = 287.1255; C<sub>15</sub>H<sub>18</sub>F<sub>3</sub>O<sub>2</sub> requires 287.1253 Δ 0.54 ppm

IR (film) ν<sub>max</sub>/cm<sup>-1</sup>: 3660, 2980, 1677, 1597, 1449, 1378.

### (±)-2-(2-Butyltetrahydro-2H-pyran-2-yl)-1-(4-methoxyphenyl)ethan-1-one, 3d



*n*-BuLi in hexanes (2.5 M, 7.2 mL, 18.1 mmol, 6.0 equiv.) was added dropwise to a solution of CuI (1.72 g, 9.03 mmol, 3.0 equiv.) in THF (0.3 M, 30 mL) at -78 °C. The reaction mixture was warmed to 0 °C and stirred for 1 h, affording a black precipitate. The mixture was cooled to -78 °C and a solution of **3a** (700 mg, 3.01 mmol, 1.0 equiv.) in THF (1.0 M, 3 mL) was added dropwise and stirred for 30 min. The reaction was quenched by addition of saturated aqueous ammonium chloride (30 mL) and warmed to RT. The mixture was treated with 35% aqueous ammonium hydroxide solution (30 mL), affording a clear blue aqueous phase. The solution was extracted with EtOAc (3 x 60 mL), and the combined organic phases were washed with HCl (1.0 M, 60 mL), dried over MgSO<sub>4</sub>, filtered, and concentrated *in vacuo*. Purification by column chromatography (pentane: Et<sub>2</sub>O, 85:15) afforded the title compound **3d** as a yellow oil (812 mg, 93% yield).

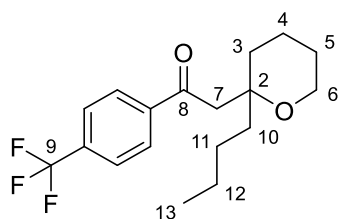
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.01 – 7.91 (m, 2H, ArH), 6.96 – 6.88 (m, 2H, ArH), 3.86 (s, 3H, H-9), 3.70 – 3.61 (m, 2H, H-6), 3.19 (d, *J* = 15.0 Hz, 1H, H-7), 3.08 (d, *J* = 15.0 Hz, 1H, H-7'), 1.87 – 1.58 (m, 6H, H-3, H-5, H-10), 1.54 – 1.44 (m, 2H, H-4), 1.39 – 1.17 (m, 4H, H-11, H-12), 0.87 (t, *J* = 7.0 Hz, 3H, H-13).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 197.7 (C-8), 163.4 (ArC), 131.7 (ArC), 130.8 (ArC x 2), 113.7 (ArC x 2), 75.4 (C-2), 61.5 (C-6), 55.6 (C-9), 44.6 (C-7), 34.3 (C-10), 33.7 (C-3), 25.9 (C-5), 25.4 (C-11), 23.3 (C-12), 19.2 (C-4), 14.3 (C-13).

HRMS (ESI+): Found [M+H]<sup>+</sup> = 291.1957; C<sub>18</sub>H<sub>27</sub>O<sub>3</sub> requires 291.1955 Δ 0.77 ppm

IR (film) ν<sub>max</sub>/cm<sup>-1</sup>: 2957, 2869, 1670, 1601, 1576, 1510.

### (±)-2-(2-Butyltetrahydro-2H-pyran-2-yl)-1-(4-(trifluoromethyl)phenyl)ethan-1-one, 3e



*n*-BuLi in hexanes (2.5 M, 8.9 mL, 22.2 mmol, 6.0 equiv.) was added dropwise to a solution of CuI (2.11 g, 11.1 mmol, 3.0 equiv.) in THF (0.3 M, 37 mL) at  $-78$  °C. The reaction mixture was warmed to 0 °C and stirred for 1 h, affording a black precipitate. The mixture was cooled to  $-78$  °C, and a solution of **S2** (1.00 g, 3.70 mmol, 1.0 equiv.) in THF (1.0 M, 4 mL) was added dropwise and stirred for 30 min. The reaction was quenched by addition of saturated aqueous ammonium chloride (30 mL) and warmed to RT. The mixture was treated with 35% aqueous ammonium hydroxide solution (30 mL), affording a clear blue aqueous phase. The solution was extracted with EtOAc (3 x 60 mL) and the combined organic phases were washed with HCl (1.0 M, 60 mL), dried over MgSO<sub>4</sub>, filtered, and concentrated *in vacuo*. Purification by column chromatography (pentane: Et<sub>2</sub>O, 95:5) afforded the title compound **3e** as a yellow oil (755 mg, 62% yield).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 8.07 (d, *J* = 8.0 Hz, 2H, ArH), 7.71 (d, *J* = 8.0 Hz, 2H, ArH), 3.68 – 3.58 (m, 2H, H-6), 3.26 (d, *J* = 15.0 Hz, 1H, H-7), 3.07 (d, *J* = 15.0 Hz, 1H, H-7'), 1.83 (ddd, *J* = 14.0, 12.0, 4.0 Hz, 1H, H-3), 1.77 – 1.56 (m, 5H, H-10, H-4, H-3'), 1.48 (p, *J* = 5.5 Hz, 2H, H-5), 1.42 – 1.15 (m, 4H, H-11, H-12), 0.88 (t, *J* = 7.0 Hz, 3H, H-13).

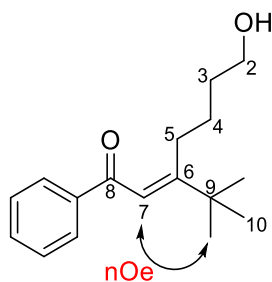
<sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>) δ -63.1.

<sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 198.6 (C-8), 141.3 (ArC), 134.1 (ArC), 128.9 (ArC x 2), 125.6 (ArC x 2), 123.8 (C-9), 75.5 (C-2), 61.5 (C-6), 45.8 (C-7), 34.0 (C-3), 33.4 (C-10), 25.7 (C-5), 25.5 (C-11), 23.3 (C-12), 19.2 (C-4), 14.2 (C-13).

HRMS (ESI<sup>+</sup>): Found [M+H]<sup>+</sup> = 329.1714; C<sub>18</sub>H<sub>24</sub>F<sub>3</sub>O<sub>2</sub> requires 329.1723 Δ -2.72 ppm.

IR (film)  $\nu_{\max}$ /cm<sup>-1</sup>: 2980, 1685, 1582, 1511, 1461, 1408.

### (*E*)-3-(*tert*-Butyl)-7-hydroxy-1-phenylhept-2-en-1-one, **3f**



*t*-BuLi in pentane (1.7 M, 3.5 mL, 6.0 mmol, 6.0 equiv.) was added dropwise to a solution of CuI (572 mg, 3.0 mmol, 3.0 equiv.) in THF (0.1 M, 10 mL) at  $-78$  °C. The reaction mixture was warmed to 0 °C and stirred for 1 h, affording a black precipitate. The mixture was cooled to  $-78$  °C, and a solution of **S1** (202 mg, 1.0 mmol, 1.0 equiv.) in THF (1.0 M, 1 mL) was added dropwise and stirred for 30 min. The reaction was quenched by addition of saturated aqueous ammonium chloride (10 mL) and warmed to RT. The mixture was treated with 35% aqueous ammonium hydroxide solution, affording a clear blue aqueous phase. The solution was extracted with EtOAc (3 x 30 mL), and the combined organic phases were dried over MgSO<sub>4</sub>, filtered, and concentrated *in vacuo*. Purification by column chromatography (Pentane:EtOAc, 80:20 to 60:40) afforded the title compound **3f** as a colourless oil (102 mg, 39% yield, >95:5 *E/Z*).

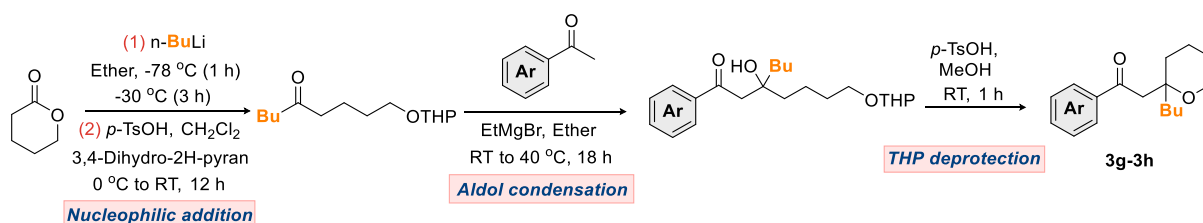
$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.95 – 7.88 (m, 2H, ArH), 7.59 – 7.49 (m, 1H, ArH), 7.50 – 7.40 (m, 2H, ArH), 6.86 (s, 1H, H-7), 3.81 – 3.73 (m, 2H, H-2), 2.67 – 2.57 (m, 2H, H-4), 2.26 (s, 1H, OH), 1.73 – 1.55 (m, 4H, H-3, H-5), 1.22 (s, 9H, H-10).

$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  192.2 (C-8), 173.5 (ArC), 140.1 (C-6), 132.4 (ArC), 128.6 (ArC x 2), 128.3 (ArC x 2), 117.1 (C-7), 61.4 (C-2), 39.0 (C-9), 32.7 (C-3), 29.5 (C-4), 29.0 (C-10), 26.3 (C-5).

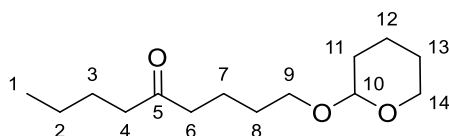
**HRMS (ESI+):** Found  $[\text{M}+\text{H}]^+ = 261.1848$ ;  $\text{C}_{17}\text{H}_{25}\text{O}_2$  requires 261.1849  $\Delta$  -0.59 ppm

**IR (film)**  $\nu_{\text{max}}/\text{cm}^{-1}$ : 3503, 2958, 2871, 1703, 1658, 1599.

### 3.2 Synthesis of THP precursors 3g-3h



#### ( $\pm$ )-1-((Tetrahydro-2H-pyran-2-yl)oxy)nonan-5-one, S4



A solution of commercially available  $\delta$ -valerolactone (6.00 g, 60.0 mmol, 1.0 equiv.) in dry  $\text{Et}_2\text{O}$  (120 mL) was cooled to  $-78^\circ\text{C}$  under Argon and  $n\text{-BuLi}$  (2.5 M, 24 mL, 60 mmol) was added dropwise. The reaction was stirred at  $-78^\circ\text{C}$  for 1 h and then warmed to  $-30^\circ\text{C}$  and stirred for 1 h, quenched by slow addition of sat. aq.  $\text{NH}_4\text{Cl}$  (100 mL) and extracted with  $\text{Et}_2\text{O}$  ( $3 \times 80$  mL). The combined organic layers were dried over  $\text{Na}_2\text{SO}_4$  and concentrated *in vacuo*. The crude product was used as is in the next step. To a solution of crude keto-alcohol (9.00 g, 56.9 mmol, 1.0 equiv.) and  $p\text{-TsOH}\cdot\text{H}_2\text{O}$  (541 mg, 2.85 mmol, 0.05 equiv.) in  $\text{CH}_2\text{Cl}_2$  (120 mL) was added dropwise 3,4-dihydro-2H-pyran (6.00 g, 71.1 mmol, 1.25 equiv.) at  $0^\circ\text{C}$  and stirred for 1.5 h at room temperature. After the addition of sat.  $\text{NaHCO}_3$  solution, the reaction mixture was extracted with  $\text{CH}_2\text{Cl}_2$ . The combined organic layers were dried over  $\text{MgSO}_4$ , filtered and concentrated *in vacuo*. Purification by column chromatography (pentane:  $\text{Et}_2\text{O}$ , 80:20 to 90:10) afforded the title compound **S4** as a transparent oil (12.1 g, 83%). This compound contained a small impurity from which it could not be separated and was used directly in the next step.

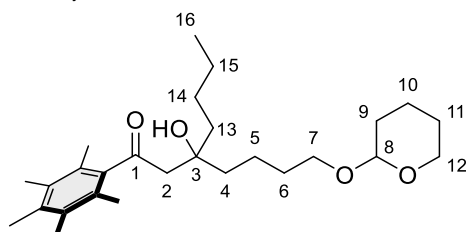
$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  4.60 – 4.51 (m, 1H, H10), 3.84 (ddd,  $J = 11.3, 7.7, 3.2$  Hz, 1H, H-14), 3.74 (dt,  $J = 9.7, 6.3$  Hz, 1H, H-9), 3.54 – 3.45 (m, 1H, H-14'), 3.45 – 3.29 (m, 1H, H-9'), 2.42 (m, 4H, H-4, H-6), 1.81 (m, 1H, H-12), 1.76 – 1.40 (m, 11H, H-3, H-7, H-8, H-11, H-12, H-13), 1.30 (m, 2H, H-2), 0.87 (t,  $J = 7.3$  Hz, 3H, H-1).

$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  211.3 (C-5), 99.0 (C-10), 67.2 (C-9), 62.3 (C-14), 42.6 (C-6), 42.44 (C-4), 30.7 (C-11), 29.3 (C-13), 26.0 (C-7), 25.5 (C-3), 22.3 (C-2), 20.7 (C-8), 19.6 (C-12), 14.0 (C-1).

HRMS (ESI+): Found  $[M+Na]^+ = 265.1777$ ;  $C_{14}H_{26}O_3Na$  requires 265.1774,  $\Delta$  1.07 ppm

IR (film)  $\nu_{max}/cm^{-1}$ : 2939, 2872, 1714, 1467, 1383, 1121.

**(±)-3-Hydroxy-1-(2,3,4,5,6-pentamethylphenyl)-3-(3-((tetrahydro-2H-pyran-2-yl)oxy)propyl)heptan-1-one, S5**



EtMgBr in Et<sub>2</sub>O (3.0 M, 5.00 mL, 14.8 mmol, 1.4 equiv.) was added dropwise to a solution of 1-(2,3,4,5,6-pentamethylphenyl)ethan-1-one (2.0 g, 10.6 mmol, 1.0 equiv.) in dry Et<sub>2</sub>O (0.3 M, 35 mL) at 0 °C under N<sub>2</sub>. The reaction mixture was heated 40 °C for 1 h, which resulted in the formation of a white precipitate. **S4** (2.56 g, 10.6 mmol, 1.0 equiv.) was added dropwise over 5 min. The reaction was maintained at 40 °C for 16 h, cooled to RT and quenched with an aqueous saturated solution of NH<sub>4</sub>Cl (10 mL). The resulting solution was extracted with Et<sub>2</sub>O (3×20 mL) and the combined organic phases were dried over MgSO<sub>4</sub>, filtered and concentrated in *vacuo*. Purification by column chromatography (pentane: Et<sub>2</sub>O, 95:5 to 80:20) afforded the title compound **S5** as a light yellow oil (3.0 g, 66%) and a 1:1 mixture of inseparable diastereoisomers.

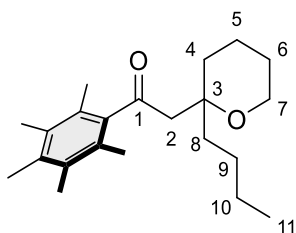
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  4.57 (dd,  $J = 4.6, 2.7$  Hz, 1H, H-8), 3.93 – 3.80 (m, 1H, H-12), 3.78 – 3.73 (m, 1H, H-7), 3.55 – 3.45 (m, 1H, H-12'), 3.44 – 3.36 (m, 1H, H-7'), 2.86 (s, 2H, H-2), 2.23 (s, 3H, 3×ArCH<sub>3</sub>), 2.18 (s, 6H, 6×ArCH<sub>3</sub>), 2.13 (s, 6H, 6×ArCH<sub>3</sub>), 1.89 – 1.77 (m, 1H, H-13/H-4), 1.77 – 1.66 (m, 3H), 1.66 – 1.44 (m, 10H), 1.40 – 1.21 (m, 4H), 0.91 (t,  $J = 7.0$  Hz, 3H, H-16).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  214.1 (C-1), 140.0 (ArC), 135.9 (ArC), 133.4 (ArC), 127.3 (ArC), 99.1 (C-8), 99.0 (C-8) 73.7 (C-3), 67.6 (C-7), 67.5 (C-7), 62.5 (C-12), 53.1 (C-2), 38.8 (C-4/C-13), 38.7 (C-4/C-13), 38.6 (C-9), 30.9 (C-6), 30.4 (C-4/C-13), 30.3 (C-4/C-13), 25.9 (C-11/C-14), 25.6 (C-11/C-14), 23.4 (C-5/C-10/C-15), 20.3 (C-5/C-10/C-15), 19.82 (C-5/C-10/C-15), 17.1 (ArCH<sub>3</sub>), 16.8 (ArCH<sub>3</sub>), 16.0 (ArCH<sub>3</sub>), 14.2 (C-16).

IR (film)  $\nu_{max}/cm^{-1}$ : 2940, 2871, 1702, 1602, 1454, 1120.

HRMS (ESI+): Found  $[M+Na]^+ = 455.3139$ ;  $C_{27}H_{44}O_4Na$  requires 455.3132,  $\Delta$  1.58 ppm.

**(±)-2-(2-Butyltetrahydro-2H-pyran-2-yl)-1-(2,3,4,5,6-pentamethylphenyl)ethan-1-one, 3g**



To a solution of **S5** (3.00 g, 6.93 mmol, 1.0 equiv.) in MeOH (0.2 M, 35 mL) was added *p*-TsOH·H<sub>2</sub>O (264 mg, 1.39 mmol, 0.2 equiv.) at RT for 3 h. After addition of sat. NaHCO<sub>3</sub>, extract with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic layers

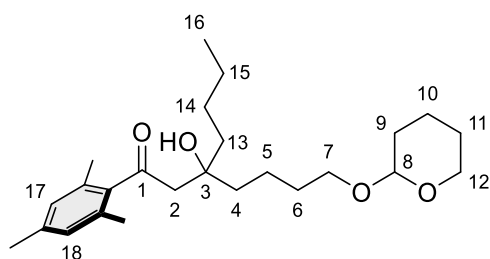
were dried over  $\text{MgSO}_4$ , filtered and concentrated under reduced pressure. Purification by column chromatography (Pentane:  $\text{Et}_2\text{O}$ , 98:2 to 95:5) afforded the title compound **3g** as a white solid (2.00 g, 87% yield).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  3.61 (qd,  $J = 11.7, 4.7$  Hz, 2H, H-7), 3.02 (d,  $J = 18.2$  Hz, 1H, H-2), 2.95 (d,  $J = 18.2$  Hz, 1H, H-2'), 2.23 (s, 3H,  $3\times\text{ArCH}_3$ ), 2.18 (s, 6H,  $6\times\text{ArCH}_3$ ), 2.15 (s, 6H,  $6\times\text{ArCH}_3$ ), 2.02 – 1.76 (m, 4H, H-4, H-6/8), 1.75 – 1.56 (m, 2H, H-6/8), 1.56 – 1.46 (m, 2H, H-5), 1.41 – 1.17 (m, 4H, H-9, H-10), 0.91 (t,  $J = 6.9$  Hz, 3H, H-11).  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  209.7 (C-1), 141.2 (ArC), 135.4 (ArC), 133.2 (ArC), 127.5 (ArC), 74.7 (C-3), 61.3 (C-7), 50.9 (C-2), 34.7 (C-8/C-4), 33.2 (C-4/C-8), 25.9 (C-6), 25.4 (C-9), 23.4 (C-10), 19.2 (C-5), 17.32 (ArCH<sub>3</sub>), 16.8 (ArCH<sub>3</sub>), 16.1 (ArCH<sub>3</sub>), 14.3 (C-11).

**IR** (film)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 2953, 2932, 2869, 1703, 1457, 1446, 1304.

**HRMS** (ESI<sup>+</sup>): Found  $[\text{M}+\text{H}]^+ = 331.2625$ ;  $\text{C}_{22}\text{H}_{35}\text{O}_2$  requires 331.2632  $\Delta$  -1.94 ppm.

**m.p.**: 47-49 °C.

### (±)3-Butyl-3-hydroxy-1-mesityl-7-((tetrahydro-2H-pyran-2-yl)oxy)heptan-1-one, **S6**



$\text{EtMgBr}$  in  $\text{Et}_2\text{O}$  (3.0 M, 2.87 mL, 8.6 mmol, 1.4 equiv.) was added dropwise to a solution of 1-mesitylethan-1-one (1.00 g, 6.2 mmol, 1.0 equiv.) in dry  $\text{Et}_2\text{O}$  (0.3 M, 17 mL) at 0 °C under  $\text{N}_2$ . The reaction mixture was heated 40 °C for 1 h, which resulted in the formation of a white precipitate. **S4** (1.50 g, 6.2 mmol, 1.0 equiv.) was added dropwise over 5 min. The reaction was maintained at 40 °C for a further 16 h, cooled to RT and quenched with an aqueous saturated solution of  $\text{NH}_4\text{Cl}$  (10 mL). The resulting solution was extracted with  $\text{Et}_2\text{O}$  ( $3\times 20$  mL) and the combined organic phases were dried over  $\text{MgSO}_4$ , filtered and concentrated *in vacuo*. The combined organic layers were dried ( $\text{MgSO}_4$ ) and concentrated *in vacuo*. Purification by column chromatography (Pentane: $\text{Et}_2\text{O}$ , 95:5) afforded the title compound **S6** as a colourless oil and a 1:1 mixture of inseparable diastereoisomers (1.53 g, 60% yield).

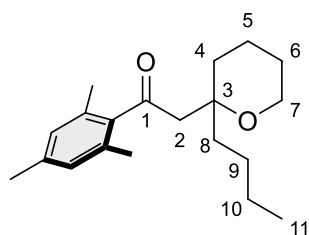
$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.82 (s, 2H, H17, H18), 4.56 (dd,  $J = 4.6, 2.7$  Hz, 1H, H-8), 3.89 – 3.80 (m, 1H, H-12), 3.77 – 3.68 (m, 1H, H-7), 3.53 – 3.43 (m, 1H, H-7'), 3.42 – 3.34 (m, 1H, H-12), 2.88 (s, 2H, H-2), 2.26 (s, 3H,  $3\times\text{ArCH}_3$ ), 2.21 (s, 6H,  $6\times\text{ArCH}_3$ ), 1.87 – 1.75 (m, 1H, H-13/H-4), 1.72 – 1.39 (m, 12H), 1.39 – 1.17 (m, 5H), 0.90 (t,  $J = 6.9$  Hz, 3H, H-16).

$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  212.8 (C-1), 139.2 (ArC), 138.8 (ArC), 132.5 (ArC), 128.8 (ArC), 99.0 (C-8), 98.9 (C-8), 73.9 (C-3), 67.5 (C-7), 67.4 (C-7), 62.4 (C-12), 52.3 (C-2), 38.9 (C-4/C-13), 38.8 (C-4/C-13), 38.7 (C-9), 30.9 (C-6), 30.4 (C-4/C-13), 30.3 (C-4/C-13), 25.9 (C-11/C-14), 25.6 (C-11/C-14), 23.3 (C-5/C-10/C-15), 21.1 (C-5/C-10/C-15), 20.5 (C-5/C-10/C-15), 19.8 (ArCH<sub>3</sub>), 19.2 (ArCH<sub>3</sub>), 14.2 (C-16).

**FTIR** (neat)  $\nu/\text{cm}^{-1} = 2940, 2871, 1702, 1600, 1460, 1338$ .

**HRMS** (ESI<sup>+</sup>)  $m/z$  Found  $[\text{M}+\text{Na}]^+ = 427.2811$ ;  $\text{C}_{25}\text{H}_{40}\text{O}_4\text{Na}$  requires 427.2819,  $\Delta$  -1.83 ppm.

### (±)-2-(2-Butyltetrahydro-2H-pyran-2-yl)-1-mesitylethan-1-one, 3h



To a solution of **S6** (500 mg, 1.24 mmol, 1.0 equiv.) in MeOH (0.2 M, 6 mL) was added *p*-TsOH·H<sub>2</sub>O (48 mg, 0.25 mmol, 0.2 equiv.) at RT for 3 h. After addition of sat. NaHCO<sub>3</sub>, extract with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic layers were dried over MgSO<sub>4</sub>, filtered and concentrated under reduced pressure. Purification by column chromatography (Pentane: Et<sub>2</sub>O, 98:2 to 95:5) afforded the title compound **3h** as a colourless oil (205 mg, 55% yield).

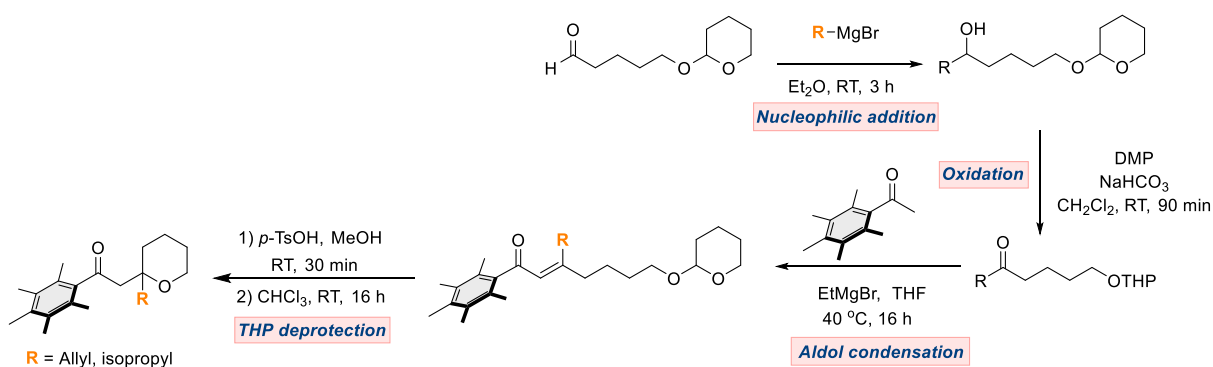
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.82 (s, 2H, ArH), 3.66 – 3.51 (m, 2H, H-7), 3.04 (d, *J* = 17.0 Hz, 1H, H-2), 2.97 (d, *J* = 17.0 Hz, 1H, H-2'), 2.27 (s, 3H, 3 × ArCH<sub>3</sub>), 2.25 (s, 6H, 6 × ArCH<sub>3</sub>), 1.96 – 1.84 (m, 1H, H-4), 1.84 – 1.70 (m, 3H, H-4', H-6/8), 1.74 – 1.53 (m, 2H, H-6/8), 1.56 – 1.46 (m, 2H, H-5), 1.41 – 1.15 (m, 4H, H-9, H-10), 0.90 (t, *J* = 6.9 Hz, 3H, H-11).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 208.5 (C-1), 140.3 (ArC), 138.3 (ArC), 132.8 (ArC), 128.8 (ArC), 75.1 (C-3), 61.3 (C-7), 50.0 (C-2), 34.9 (C-4/C-8), 33.4 (C-4/C-8), 25.8 (C-6), 25.4 (C-9), 23.3 (C-10), 21.1 (C-5), 19.4 (ArCH<sub>3</sub>), 19.2 (ArCH<sub>3</sub>), 14.2 (C-11).

HRMS (ESI<sup>+</sup>): Found [M+H]<sup>+</sup> = 303.2324; C<sub>20</sub>H<sub>31</sub>O<sub>2</sub> requires 303.2319 Δ 1.79 ppm.

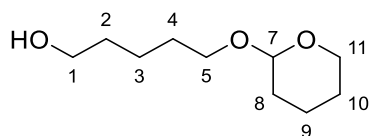
IR (film) ν<sub>max</sub>/cm<sup>-1</sup>: 2980, 2935, 2869, 2244, 1703, 1445.

### 3.3 Synthesis of THP precursors 3i-3j



## Synthesis of (±)-5-((tetrahydro-2H-pyran-2-yl)oxy)pentanal

### (±)-5-((Tetrahydro-2H-pyran-2-yl)oxy)pentan-1-ol, **S7**



To a solution of 1,5-pentanediol (7.40 g, 71.3 mmol, 3.0 equiv.) and *p*-TsOH·H<sub>2</sub>O (226 mg, 1.19 mmol, 0.05 equiv.) in CH<sub>2</sub>Cl<sub>2</sub> (100 mL) was added dropwise 3,4-dihydro-2H-pyran (2.00 g, 23.8 mmol, 1.0 equiv.) at 0 °C and stirred for 1.5 h at room temperature. After the addition of sat. NaHCO<sub>3</sub> solution, the reaction mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic layers were dried over MgSO<sub>4</sub>, filtered and concentrated under reduced pressure. Purification by column chromatography (pentane:EtOAc, 90:10 to 60:40) afforded the title compound **S7** as a colourless oil (2.79 g, 64% yield).

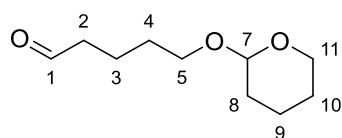
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 4.57 (dd, *J* = 4.6, 2.8 Hz, 1H, H7), 3.87 (ddd, *J* = 11.1, 7.4, 3.5 Hz, 1H, H-11), 3.76 (dt, *J* = 9.6, 6.7 Hz, 1H, H-5), 3.66 (td, *J* = 6.5, 5.4 Hz, 2H, H-1), 3.50 (dtd, *J* = 10.7, 4.1, 2.4 Hz, 1H, H-11'), 3.40 (dt, *J* = 9.6, 6.5 Hz, 1H, H-5'), 1.92 – 1.37 (m, 12H, H-2, H-3, H-4, H-8, H-9 and H-10).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 99.1 (C-7), 67.7 (C-5), 63.1 (C-1), 62.4 (C-11), 32.7 (C-2), 30.8 (C-8), 29.5 (C-4), 25.6 (C-10), 22.6 (C-3), 19.8 (C-9).

The data matched that previously reported in the literature. [2]

[2] H. Herrera, W. Barros-Parada, M. F. Flores, E. Fuentes-Contreras, J. Bergmann, *J. Chil. Chem. Soc.* **2018**, *63*, 4019 – 4022.

### (±)-5-((Tetrahydro-2H-pyran-2-yl)oxy)pentanal, **S8**



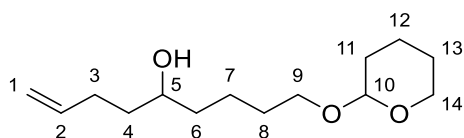
**S7** (2.00 g, 10.6 mmol, 1.0 equiv.), NaHCO<sub>3</sub> (3.57 g, 42.5 mmol, 4.0 equiv.), Dess-Martin Periodinane (9.00 g, 21.2 mmol, 2.0 equiv.) and CH<sub>2</sub>Cl<sub>2</sub> (11 mL) were subjected to **General Procedure 3**. Purification by column chromatography (pentane:EtOAc, 80:20) afforded the title compound **S8** as a colourless oil (1.30 g, 66% yield).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.78 (t, *J* = 1.8 Hz, 1H, H-1), 4.57 (dd, *J* = 4.5, 2.8 Hz, 1H, H-7), 3.85 (ddd, *J* = 11.0, 7.5, 3.4 Hz, 1H, H-11), 3.76 (dt, *J* = 9.7, 6.3 Hz, 1H, H-5), 3.56 – 3.45 (m, 1H, H-11'), 3.40 (dt, *J* = 9.7, 6.1 Hz, 1H, H-5'), 2.48 (td, *J* = 7.2, 1.7 Hz, 2H, H-2), 1.88 – 1.45 (m, 10H, H-3, H-4, H-8, H-9 and H-10).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 202.5 (C-1), 98.9 (C-7), 67.0 (C-5), 62.4 (C-11), 43.7 (C-2), 30.7 (C-8), 29.2 (C-3), 25.5 (C-4), 19.7 (C-10), 19.1 (C-9).

The data matched that previously reported in the literature. [2]

### (±)-9-((Tetrahydro-2H-pyran-2-yl)oxy)non-1-en-5-ol, **S9**



To a solution of **S8** (2.00 g, 10.8 mmol, 1.0 equiv.) in diethyl ether (25 mL) was added a solution of but-3-en-1-ylmagnesium bromide (1.0 M, 21.6 mL, 21.6 mmol, 2.0 equiv.) at 0 °C. The reaction solution was stirred for 3 h at room temperature. After reaction, the solution was cooled to 0 °C. To the solution was first added an aqueous saturated solution of NH<sub>4</sub>Cl (20 mL) dropwise and then H<sub>2</sub>O (20 mL). After stirring for 10 min, the two phases were separated. The aqueous phase was extracted with diethyl ether (2×20 mL). The combined organic phases were dried over MgSO<sub>4</sub> and concentrated in *vacuo* to give the title compound **S9** (1.62 g, 62% yield) as a clear oil and a 1:1 mixture of inseparable diastereoisomers.

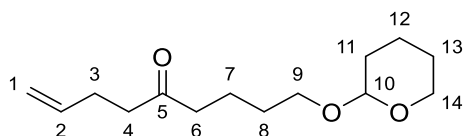
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.87 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H, H-2), 5.19 – 4.95 (m, 2H, H-1), 4.60 (dd, *J* = 4.6, 2.7 Hz, 1H, H-10), 3.89 (ddd, *J* = 11.1, 7.3, 3.4 Hz, 1H, H-14), 3.83 – 3.73 (m, 1H, H-9), 3.65 (m, 1H, H-5), 3.59 – 3.48 (m, 1H, H-14'), 3.43 (m, 1H, H-9'), 2.33 – 2.09 (m, 2H, H-3), 1.85 (tdd, *J* = 11.3, 7.1, 4.1 Hz, 1H, H-12), 1.79 – 1.40 (m, 13H, H-4, H-6, H-7, H-8, H-11, H-12', H-13).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 138.6 (C-2), 114.8 (C-1), 99.0 (C-10), 99.0 (C-10), 71.3 (C-5), 67.5 (C-9), 62.4 (C-14), 37.2 (C-6), 36.5 (C-4), 30.8 (C-11), 30.1 (C-3), 29.7 (C-13), 25.5 (C-4), 22.4 (C-8), 19.7 (C-12).

IR (film)  $\nu_{\max}/\text{cm}^{-1}$ : 2895, 2792, 1631, 1460, 1357, 1326.

HRMS (ESI<sup>+</sup>): Found [M+K]<sup>+</sup> = 281.1510; C<sub>14</sub>H<sub>26</sub>O<sub>3</sub>K requires 281.1514, Δ -1.26 ppm.

### (±)-9-((Tetrahydro-2H-pyran-2-yl)oxy)non-1-en-5-one, **S10**



**S9** (692 mg, 2.90 mmol, 1.0 equiv.), NaHCO<sub>3</sub> (1.00 g, 11.4 mmol, 4.0 equiv.), Dess-Martin Periodinane (2.4 g, 5.71 mmol, 2.0 equiv.) and CH<sub>2</sub>Cl<sub>2</sub> (20 mL) were subjected to **General Procedure A**. Purification by column chromatography (pentane: EtOAc, 90:10) afforded the title compound **S10** as a colourless oil (590 mg, 86% yield).

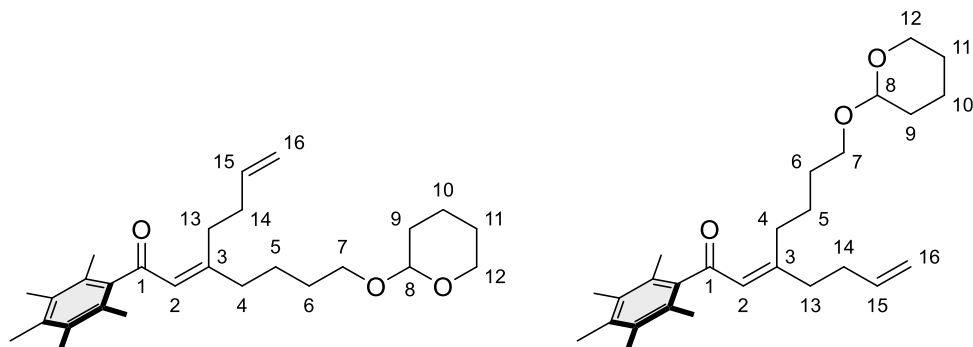
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.82 (ddt, *J* = 16.8, 10.2, 6.5 Hz, 1H, H-2), 5.10 – 4.95 (m, 2H, H-1), 4.58 (dd, *J* = 4.5, 2.8 Hz, 1H, H-10), 3.88 (ddd, *J* = 11.1, 7.5, 3.3 Hz, 1H, H-14), 3.76 (dt, *J* = 9.6, 6.3 Hz, 1H, H-9), 3.57 – 3.47 (m, 1H, H-14'), 3.40 (dt, *J* = 9.5, 6.1 Hz, 1H, H-9'), 2.50 (dt, *J* = 21.0, 7.3 Hz, 4H, H-4, H-6), 2.40 – 2.29 (m, 2H, H-3), 1.94 – 1.78 (m, 1H, H-12), 1.77 – 1.47 (m, 9H, H-7, H-8, H-11, H-12', H-13).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 210.2 (C-5), 137.2 (C-2), 115.2 (C-1), 98.9 (C-10), 67.2 (C-9), 62.4 (C-14), 42.6 (C-6), 41.8 (C-4), 30.8 (C-13), 29.3 (C-8), 27.8 (C-3), 25.5 (C-11), 20.6 (C-7), 19.7 (C-12).

IR (film)  $\nu_{\max}/\text{cm}^{-1}$ : 2895, 2792, 1715, 1631, 1460, 1357.

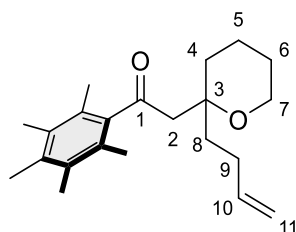
HRMS (ESI<sup>+</sup>): Found [M+H]<sup>+</sup> = 241.1791; C<sub>14</sub>H<sub>25</sub>O<sub>3</sub> requires 241.1798, Δ -3.02 ppm.

**(±)-1-(2,3,4,5,6-Pentamethylphenyl)-3-(4-((tetrahydro-2H-pyran-2-yl)oxy)butyl)hepta-2,6-dien-1-one, S11**



EtMgBr in Et<sub>2</sub>O (3.0 M, 1.50 mL, 4.5 mmol, 1.8 equiv.) was added dropwise to a solution of 1-(2,3,4,5,6-pentamethylphenyl)ethan-1-one (970 mg, 5.0 mmol, 2.0 equiv.) in THF (0.2 M, 8 mL) at 0 °C under N<sub>2</sub>. The reaction mixture was heated 40 °C for 1 h, which resulted in the formation of a white precipitate. **S10** (600 mg, 2.5 mmol, 1.0 equiv.) was added dropwise over 5 min. The reaction was maintained at 40 °C for a further 16 h, cooled to RT and quenched with an aqueous saturated solution of NH<sub>4</sub>Cl (10 mL). The resulting solution was extracted with Et<sub>2</sub>O (3×20 mL) and the combined organic phases were dried over MgSO<sub>4</sub>, filtered and concentrated in *vacuo*. The crude (680 mg) which was obtained as a 5:2 mixture of inseparable diastereoisomers (680 mg) was put into next reaction without purification.

**(±)-2-(2-(But-3-en-1-yl)tetrahydro-2H-pyran-2-yl)-1-(2,3,4,5,6-pentamethylphenyl)ethan-1-one, 3i**



To a solution of crude **S11** (680 mg) in MeOH (0.2 M, 8 mL) was added *p*-TsOH·H<sub>2</sub>O (64 mg, 0.33 mmol, 0.2 equiv.) portionwise at RT for 30 min. After addition of sat. NaHCO<sub>3</sub>, extract with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic layers were dried over MgSO<sub>4</sub>, filtered and concentrated under reduced pressure. The resulting crude product was dissolved in chloroform (20 mL) and stirred at RT for 16 h. The solvent was removed under reduced pressure, and purification by column chromatography (Pentane: Et<sub>2</sub>O, 97:3) afforded the title compound **3i** as a white solid (359 mg, 44% yield, over two steps).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.86 – 5.71 (m, 1H, H-10), 5.00 – 4.83 (m, 2H, H-11), 3.61 – 3.44 (m, 2H, H-7), 2.97 (d, *J* = 18.4 Hz, 1H, H-2), 2.86 (d, *J* = 18.4 Hz, 1H, H-2'), 2.15 (s, 3H, 3×ArCH<sub>3</sub>), 2.11 (s, 6H, 6×ArCH<sub>3</sub>), 2.07 (s, 6H, 6×ArCH<sub>3</sub>), 2.06 – 1.94 (m, 3H, H-8, H-9), 1.92 – 1.83 (m, 1H, H-8'), 1.77 (dd, *J* = 6.8, 5.4 Hz, 2H, H-4), 1.70 – 1.51 (m, 2H, H-5), 1.49 – 1.39 (m, 2H, H-6).

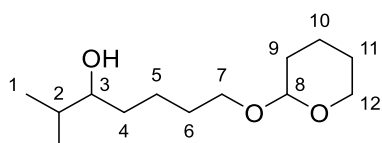
<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 209.4 (C-1), 141.0 (ArC), 139.0 (C-10), 135.4 (ArC), 133.1 (ArC), 127.4 (ArC), 114.3 (C-11), 74.3 (C-3), 61.2 (C-7), 50.9 (C-2), 33.9 (C-8), 32.9 (C-4), 27.5 (C-9), 25.8 (C-6), 19.0 (C-5), 17.2 (ArCH<sub>3</sub>), 16.71 (ArCH<sub>3</sub>), 16.0 (ArCH<sub>3</sub>).

IR (film)  $\nu_{\max}/\text{cm}^{-1}$ : 2980, 2888, 1703, 1640, 1473, 1461.

HRMS (ESI<sup>+</sup>): Found [M+H]<sup>+</sup> = 329.2484; C<sub>22</sub>H<sub>33</sub>O<sub>2</sub> requires 329.2475, Δ 2.71ppm.

m.p.: 53-55 °C.

### (±)-2-Methyl-7-((tetrahydro-2H-pyran-2-yl)oxy)heptan-3-ol, S12



To a solution of aldehyde **S8** (376 mg, 2.00 mmol, 1.0 equiv.) in diethyl ether (20 mL) was added a solution of isopropylmagnesium bromide (2.0 M, 2.00 ml, 4.00 mmol, 2.0 equiv.) at 0 °C. The reaction solution was stirred for 3 h at room temperature. Afterwards, the solution was cooled to 0 °C. To the solution was first added an aqueous saturated solution of NH<sub>4</sub>Cl (20 ml) dropwise and then H<sub>2</sub>O (20 ml). After stirring for 10 min, the two phases were separated. The aqueous phase was extracted with diethyl ether (2×20 ml). The combined organic phases were dried over MgSO<sub>4</sub> and concentrated in *vacuo* to give the title compound **S12** (390 mg, 85%) as a colourless oil and a 1:1 mixture of inseparable diastereoisomers.

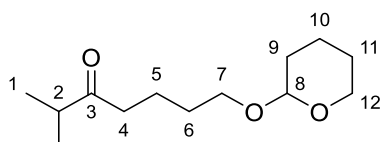
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 4.51 (dd, *J* = 4.5, 2.8 Hz, 1H, H8), 3.80 (ddd, *J* = 11.1, 7.4, 3.4 Hz, 1H, H-12), 3.69 (ddt, *J* = 10.5, 6.8, 3.3 Hz, 1H, C-7), 3.49 – 3.39 (m, 1H, H-12'), 3.33 (m, 2H, H3, H-7'), 1.86 – 1.23 (m, 13H, H-2, H-4, H-5, H-6, H-9, H-10, H-11), 0.85 (d, *J* = 3.9 Hz, 3H, H-1), 0.84 (d, *J* = 3.9 Hz, 3H, H-1').

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 99.0 (C-8), 98.9 (C-8'), 76.9 (C-3), 67.6 (C-7), 62.4 (C-12), 33.9 (C-4), 33.5 (C-2), 30.8 (C-9), 29.7 (C-6), 25.5 (C-11), 22.8 (C-5), 19.7 (C-10), 18.8 (C-1), 17.1 (C-1').

IR (film)  $\nu_{\max}/\text{cm}^{-1}$ : 3445, 2941, 2870, 1672, 1467, 1352.

HRMS (ESI<sup>+</sup>): Found [M+H]<sup>+</sup> = 231.1890; C<sub>13</sub>H<sub>27</sub>O<sub>3</sub> requires 231.1882, Δ 3.46 ppm.

### (±)-2-Methyl-7-((tetrahydro-2H-pyran-2-yl)oxy)heptan-3-one, S13



Alcohol **S12** (2.53 g, 11.0 mmol, 1.0 equiv.), NaHCO<sub>3</sub> (3.68 g, 44 mmol, 4.0 equiv.), Dess-Martin Periodinane (9.35 g, 22.0 mmol, 2.0 equiv.) and CH<sub>2</sub>Cl<sub>2</sub> (17.5 mL) were subjected to **General Procedure 3**. Purification by column chromatography (pentane:Et<sub>2</sub>O, 90:10) afforded the title compound **S13** as a colourless oil (2.13 g, 88% yield).

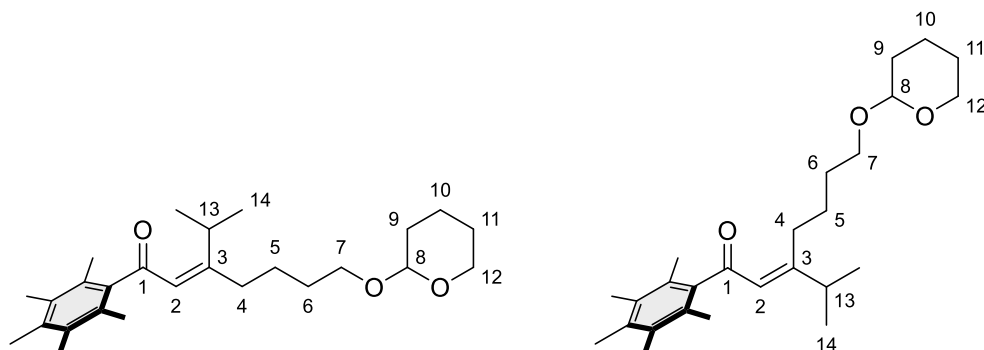
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 4.57 (dd, *J* = 4.5, 2.8 Hz, 1H, H8), 3.85 (ddd, *J* = 11.1, 7.6, 3.4 Hz, 1H, H-12), 3.74 (dt, *J* = 9.6, 6.4 Hz, 1H, H-7), 3.55 – 3.45 (m, 1H, H-12'), 3.38 (dt, *J* = 9.6, 6.2 Hz, 1H, H-7'), 2.59 (hept, *J* = 6.9 Hz, 1H, H-2), 2.49 (t, *J* = 7.1 Hz, 2H, H-4), 1.90 – 1.45 (m, 10H, H-5, H-6, H-9, H-10 and H-11), 1.09 (d, *J* = 6.9 Hz, 6H, H-1).

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  214.7 (C-3), 98.9 (C-8), 67.3 (C-7), 62.3 (C-12), 40.8 (C-2), 40.0 (C-4), 30.8 (C-9), 29.3 (C-6), 25.5 (C-11), 20.6 (C-5), 19.7 (C-10), 18.3 (C-1).

IR (film)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 2941, 2872, 1713, 1467, 1383, 1353.

HRMS (ESI+): Found  $[\text{M}+\text{H}]^+ = 229.1721$ ;  $\text{C}_{13}\text{H}_{25}\text{O}_3$  requires 229.1725,  $\Delta$  -1.75 ppm.

**(±)-3-Isopropyl-1-(2,3,4,5,6-pentamethylphenyl)-7-((tetrahydro-2H-pyran-2-yl)oxy)hept-2-en-1-one, S14**



$\text{EtMgBr}$  in  $\text{Et}_2\text{O}$  (3.0 M, 0.640 ml, 1.92 mmol, 1.4 equiv.) was added dropwise to a solution of 1-(2,3,4,5,6-pentamethylphenyl)ethan-1-one (302 mg, 1.58 mmol, 1.2 equiv.) in THF (0.2 M, 7.5 ml) at 0 °C under  $\text{N}_2$ . The reaction mixture was heated 40 °C for 1 h, which resulted in the formation of a white precipitate. **S13** (300 mg, 1.34 mmol, 1.0 equiv.) was added dropwise over 5 min. The reaction was maintained at 40 °C for a further 3 h, cooled to RT and quenched with an aqueous saturated solution of  $\text{NH}_4\text{Cl}$  (10 mL). The resulting solution was extracted with  $\text{Et}_2\text{O}$  (3×20 mL) and the combined organic phases were dried over  $\text{MgSO}_4$ , filtered and concentrated in *vacuo*. Purification by column chromatography (pentane: $\text{Et}_2\text{O}$ , 90:10) afforded the title compound **S14** as a mixture of inseparable (unassigned) diastereoisomers (220 mg, 40%, 4:1) as a colourless oil. Data is reported on the mixture.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) **Major diastereoisomer**:  $\delta$  6.19 (s, 1H, H-2), 4.59 (m, 1H, H-8), 3.88 (td,  $J = 7.6, 3.8$  Hz, 1H, H-12), 3.76 (dt,  $J = 9.8, 6.5$  Hz, 1H, H-7), 3.56 – 3.47 (m, 1H, H-12'), 3.42 (dt,  $J = 9.6, 6.5$ , 1H, H-7'), 2.62 (m, 2H, H-4), 2.41 (m, 1H, H-13), 2.24 (s, 3H, 3×ArCH<sub>3</sub>), 2.19 (s, 6H, 6×ArCH<sub>3</sub>), 2.15 (s, 6H, 6×ArCH<sub>3</sub>), 1.76 – 1.46 (m, 10H, H-5, H-6, H-9, H-10, H-11), 1.07 (d,  $J = 6.9$ , 6H, H-14).

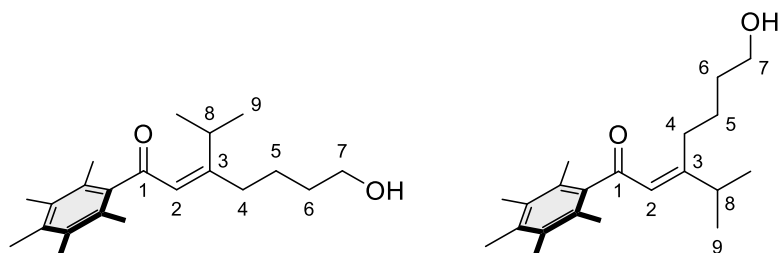
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) **Minor diastereoisomer**:  $\delta$  6.14 (s, 1H, H2), 4.55 (m, 1H, H-8), 3.88 (td,  $J = 7.6, 3.8$  Hz, 1H, H-12), 3.76 (dt,  $J = 9.8, 6.5$  Hz, 1H, H-7), 3.56 – 3.47 (m, 1H, H-12'), 3.42 (dt,  $J = 9.6, 6.5$ , 1H, H-7'), 2.62 (m, 2H, H-4), 2.41 (m, 1H, H-13), 2.24 (s, 3H, 3×ArCH<sub>3</sub>), 2.19 (s, 6H, 6×ArCH<sub>3</sub>), 2.15 (s, 6H, 6×ArCH<sub>3</sub>), 1.76 – 1.46 (m, 10H, H-5, H-6, H-9, H-10, H-11), 1.07 (d,  $J = 6.9$ , 6H, H-14).

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  215.1 (C-1), 170.5 (C-3), 142.5 (ArC), 133.3 (ArC), 132.9 (ArC), 128.4 (ArC), 123.6 (C-2), 99.3 (C-8), 67.9 (C-12), 62.8 (C-7), 36.8 (C-13), 32.6 (C-4), 31.3 (C-9), 30.6 (C-6), 26.0 (C-11), 22.2 (C-14), 20.2 (C-10), 20.1 (C-5), 17.6 (ArCH<sub>3</sub>), 17.4 (ArCH<sub>3</sub>), 16.4 (ArCH<sub>3</sub>).

IR (film)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 2992, 2946, 1702, 1442, 1387, 1352.

HRMS (ESI+): Found  $[\text{M}+\text{H}]^+ = 401.3065$ ;  $\text{C}_{26}\text{H}_{41}\text{O}_3$  requires 401.3050,  $\Delta$  3.67 ppm.

### 7-Hydroxy-3-isopropyl-1-(2,3,4,5,6-pentamethylphenyl)hept-2-en-1-one, **S15**



To a solution of an *E/Z* mixture (4:1) of **S14** (127 mg, 0.32 mmol, 1.0 equiv.) in MeOH (0.2 M, 2 mL) was added *p*-TsOH·H<sub>2</sub>O (12 mg, 0.06 mmol, 0.2 equiv.) and then stirred at RT for 30 min. After addition of sat. NaHCO<sub>3</sub>, the reaction was extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic layers were dried over MgSO<sub>4</sub>, filtered and concentrated under reduced pressure. Purification by column chromatography (pentane:EtOAc, 90:10) afforded the title compound **S15** as a mixture of inseparable diastereoisomers (70 mg, 70%, 5:1) as a colourless oil. Data is reported on the mixture.

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) **Major diastereoisomer:** δ 6.22 (s, 1H, H-2), 3.76 (m, 2H, H-7), 2.67 – 2.58 (m, 2H, H-4), 2.41 (hept, *J* = 6.9 Hz, 1H, H-8), 2.24 (s, 3H, 3×ArCH<sub>3</sub>), 2.19 (s, 6H, 6×ArCH<sub>3</sub>), 2.12 (s, 6H, 6×ArCH<sub>3</sub>), 1.72 – 1.59 (m, 4H, H-5, H-6), 1.08 (d, *J* = 6.8 Hz, 6H, H-9).

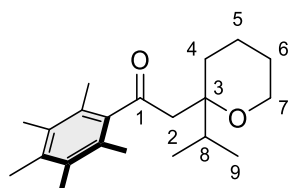
**Minor diastereoisomer:** δ 6.14 (s, 1H, H-2), 3.65 (m, 1H, H-7), 2.41 (hept, *J* = 6.9 Hz, 1H, H-8), 2.24 (s, 3H, 3×ArCH<sub>3</sub>), 2.19 (s, 6H, 6×ArCH<sub>3</sub>), 2.12 (s, 6H, 6×ArCH<sub>3</sub>), 1.72 – 1.59 (m, 4H, H-5, H-6), 1.08 (d, *J* = 6.8 Hz, 6H, H-9).

**<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) δ 201.4 (C-1), 171.0 (C-3), 141.9 (ArC), 135.1 (ArC), 133.0 (ArC), 127.9 (ArC), 122.9 (C-2), 61.6 (C-7), 36.9 (C-8), 32.4 (C-6), 31.5 (C-4), 25.0 (C-5), 21.6 (C-9), 17.1 (ArCH<sub>3</sub>), 16.7 (ArCH<sub>3</sub>), 16.0 (ArCH<sub>3</sub>).

**IR** (film)  $\nu_{\max}/\text{cm}^{-1}$ : 3415, 2925, 1670, 1598, 1462, 1384.

**HRMS** (ESI+): Found [M+H]<sup>+</sup> = 317.2475; C<sub>21</sub>H<sub>33</sub>O<sub>2</sub> requires 317.2470, Δ -1.47 ppm.

### (±)-2-(2-Isopropyltetrahydro-2H-pyran-2-yl)-1-(2,3,4,5,6-pentamethylphenyl)ethan-1-one **3j**



**S15** (65.4 mg, 0.16 mmol, 1 equiv.) was dissolved in chloroform (20 mL) and the resulting solution was stirred at RT for 16 h. The reaction mixture was then concentrated under reduced pressure, and purification by column chromatography (Pentane: Et<sub>2</sub>O, 97:3) afforded the title compound **3j** as a white solid (60 mg, 86% yield).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 3.49 (m, 2H, H-7), 3.03 (d, *J* = 17.1 Hz, 1H, H-2), 2.70 (d, *J* = 17.1 Hz, 1H, H-2'), 2.44 (hept, *J* = 6.9 Hz, 1H, H-8), 2.16 (s, 3H, 3×ArCH<sub>3</sub>), 2.11 (d, *J* = 3.2 Hz, 12H, 12×ArCH<sub>3</sub>), 1.91 – 1.80 (m, 1H, H-4), 1.68 – 1.32 (m, 5H, H-4', H-5, H-6), 0.85 (d, *J* = 1.5 Hz, 3H, H-9), 0.83 (d, *J* = 1.5 Hz, 3H, H-9').

**<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) δ 210.1 (C-1), 141.7 (ArC), 135.3 (ArC), 133.1 (ArC), 127.7 (ArC), 77.1 (C-3) 61.2 (C-7), 46.1 (C-2), 30.8 (C-8), 27.8 (C-4), 25.6 (C-6), 19.1 (C-5), 17.4 (ArCH<sub>3</sub>), 17.2 (ArCH<sub>3</sub>), 16.8 (ArCH<sub>3</sub>), 16.4 (C-9), 16.0 (C-9').

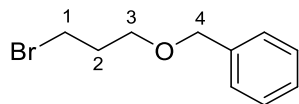
**IR** (film)  $\nu_{\max}/\text{cm}^{-1}$ : 2980, 2925, 1704, 1598, 1461, 1383.

HRMS (ESI+): Found  $[M+H]^+ = 317.2475$ ;  $C_{21}H_{33}O_2$  requires 317.2472,  $\Delta -0.97$  ppm.

m.p.: 65-67 °C

HRMS (ESI+): Found  $[M+H]^+ = 317.2475$ ;  $C_{21}H_{33}O_2$  requires 317.2472,  $\Delta -0.97$  ppm.

### ((3-Bromopropoxy)methyl)benzene, S16



To a solution of benzyloxypropan-1-ol (3.40 g, 20.5 mmol) in dry  $CH_2Cl_2$  (50 mL) was added  $CBr_4$  (8.5 g, 25.6 mmol). After cooling the solution to 0 °C,  $PPh_3$  (9.62 g, 36.7 mmol) was added in portions. The resulting red solution was stirred at room temperature for 18 h. The solvent was removed under reduced pressure, and the precipitate washed several times with ether (6 x 100 mL) and filtered. The collective ether extracts were concentrated to afford a yellow oil. Purification by column chromatography (pentane:Et<sub>2</sub>O, 99:1) afforded the title compound **S16** as a pale yellow oil (3.46 g, 76% yield).

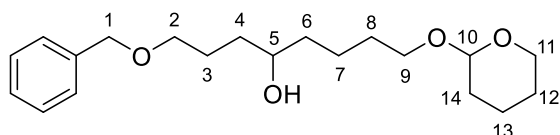
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.47 – 7.24 (m, 5H, 5×ArH), 4.55 (s, 2H, H-4), 3.64 (t,  $J = 6.5$  Hz, 2H, H-1), 3.57 (t,  $J = 6.5$  Hz, 2H, H-3), 2.17 (p,  $J = 6.2$  Hz, 2H, H-2).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  138.3 (ArC), 128.4 (ArC), 127.7 (ArC), 127.7 (ArC), 73.2 (C-4), 67.7 (C-1), 32.9 (C-2), 30.7 (C-3).

The data matched that previously reported in the literature. [3]

[3] K. J. Frankowski, J. E. Golden, Y. Zeng, Y. Lei, J. Aube, *J. Am. Chem. Soc.* **2008**, *130*, 6018 – 6024.

### (±)-1-(Benzyloxy)-8-((tetrahydro-2H-pyran-2-yl)oxy)octan-4-ol, S17



To a solution of **S8** (980 mg, 5.26 mmol, 1.0 equiv.) in diethyl ether (25 mL) was added a solution of (3-(benzyloxy)propyl)magnesium bromide (1.0 M, 10.6 mL, 10.6 mmol, 2.0 equiv.) at 0 °C. The reaction solution was stirred for 3 h at room temperature. After reaction, the solution was cooled to 0 °C. To the solution was first added an aqueous saturated solution of  $NH_4Cl$  (20 mL) dropwise and then  $H_2O$  (20 mL). After stirring for 10 min, the two phases were separated. The aqueous phase was extracted with diethyl ether (2×20 mL). The combined organic phases were dried over  $MgSO_4$  and concentrated in *vacuo* to give the title compound **S17** as a mixture of diastereomers (980 mg, 55%, 70:30 d.r.) as a colourless oil.

**Major diastereomer:** <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.30 – 7.15 (m, 5H, 5×ArH), 4.49 (t,  $J = 3.6$  Hz, 1H, H-10), 4.43 (d,  $J = 1.7$  Hz, 2H, H-1), 3.78 (ddd,  $J = 11.0, 7.4, 3.3$  Hz, 1H, H-11), 3.71 – 3.61 (m, 1H, H-9), 3.51 (m, 1H, H-5), 3.42 (m, 3H, H-2, H-11'), 3.31 (dt,  $J = 9.5, 6.5$  Hz, 1H, H-9'), 1.83 – 1.24 (m, 16H, H-3, H-4, H-6, H-7, H-8, H-12, H-13, H-14).

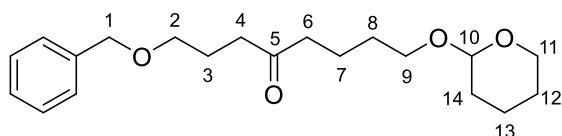
$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  138.3 (ArC), 128.4 (ArC), 127.8 (ArC), 127.6 (ArC), 98.9 (C10), 73.2 (C-1), 71.4 (C-5), 70.6 (C-2), 67.6 (C-9), 62.4 (C-11), 37.3 (C-6), 34.6 (C-4), 30.8 (C-14), 29.7 (C-3), 26.2 (C-7), 25.5 (C-12), 22.5 (C-13), 19.7 (C-8).

**Diagnostic peaks for minor diastereomer:**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  3.67 (m, 2H), 3.56 (t,  $J = 5.9$  Hz, 2H), 1.77 (m, 2H).

IR (film)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 3405, 2980, 2886, 1460, 1381, 1252.

HRMS (ESI $^+$ ): Found  $[\text{M}+\text{Na}]^+ = 359.2200$ ;  $\text{C}_{20}\text{H}_{32}\text{O}_4\text{Na}$  requires 359.2193,  $\Delta$  2.00 ppm.

### ( $\pm$ )-1-(Benzyloxy)-8-((tetrahydro-2H-pyran-2-yl)oxy)octan-4-one, **S18**



**S17** (672 mg, 2.00 mmol, 1 equiv.),  $\text{NaHCO}_3$  (670 mg, 8.0 mmol, 4.0 equiv.), Dess-Martin Periodinane (1.70 g, 4.01 mmol, 2.0 equiv.) and  $\text{CH}_2\text{Cl}_2$  (20 mL) were subjected to **General Procedure 3**. Purification by column chromatography (pentane:EtOAc, 90:10) afforded the title compound **S18** as a colourless oil (493 mg, 75% yield).

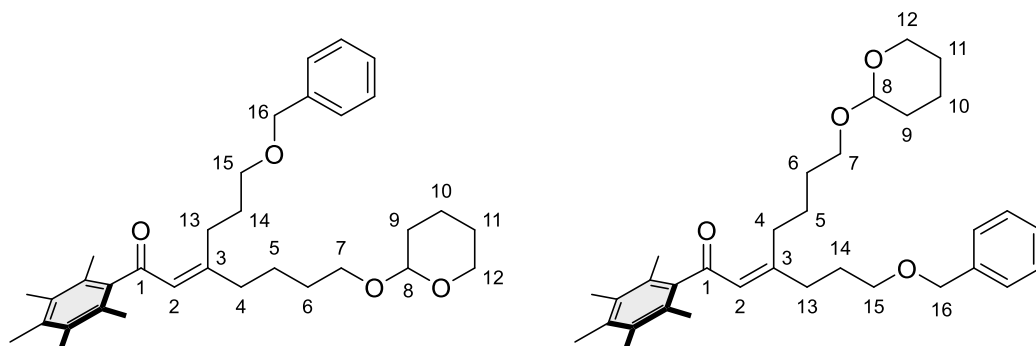
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.32 – 7.17 (m, 5H, 5 $\times$ ArH), 4.49 (t,  $J = 3.6$  Hz, 1H, H-10), 4.41 (s, 2H, H-1), 3.78 (ddd,  $J = 11.1, 7.5, 3.4$  Hz, 1H, H-11), 3.66 (dt,  $J = 9.5, 6.3$  Hz, 1H, H-9), 3.41 (m, 3H, H2, H-11'), 3.30 (dt,  $J = 9.5, 6.1$  Hz, 1H, H-9'), 2.45 (t,  $J = 7.2$  Hz, 2H, H-4), 2.37 (t,  $J = 7.2$  Hz, 2H, H-6), 1.93 – 1.39 (m, 12H, H3, H7, H8, H12, H-13, H-14).

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  210.9 (C-5), 138.4 (ArC), 128.4 (ArC), 127.7 (ArC), 127.6 (ArC), 98.9 (C-10), 72.9 (C-1), 69.4 (C-2), 67.2 (C-9), 62.3 (C-11), 42.6 (C-6), 39.4 (C-4), 30.7 (C-7), 29.3 (C-13), 25.5 (C-12), 23.9 (C-3), 20.7 (C-8), 19.7 (C-14).

IR (film)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 2942, 2870, 1715, 1641, 1440, 1413.

HRMS (ESI $^+$ ): Found  $[\text{M}+\text{H}]^+ = 335.2229$ ;  $\text{C}_{20}\text{H}_{31}\text{O}_4$  requires 335.2217,  $\Delta$  3.71 ppm.

### ( $\pm$ )-3-(3-(Benzyloxy)propyl)-1-(2,3,4,5,6-pentamethylphenyl)-7-((tetrahydro-2H-pyran-2-yl)oxy)hept-2-en-1-one, **S19**



$\text{EtMgBr}$  in  $\text{Et}_2\text{O}$  (3.0 M, 0.93 mL, 2.80 mmol, 2.0 equiv.) was added dropwise to a solution of 1-(2,3,4,5,6-pentamethylphenyl)ethan-1-one (532 mg, 2.80 mmol, 2.0 equiv.) in THF (0.2 M, 7.5 mL) at 0  $^\circ\text{C}$  under  $\text{N}_2$ . The reaction mixture was heated 40  $^\circ\text{C}$  for 1 h, which resulted in the formation of a white precipitate. **S18** (468 mg,

1.40 mmol, 1.0 equiv.) was added dropwise over 10 min. The reaction was maintained at 40 °C for a further 16 h, cooled to RT and quenched with an aqueous saturated solution of NH<sub>4</sub>Cl (10 mL). The resulting solution was extracted with Et<sub>2</sub>O (3×20 mL) and the combined organic phases were dried over MgSO<sub>4</sub>, filtered and concentrated *in vacuo*. Purification by column chromatography (pentane:Et<sub>2</sub>O, 90:10) afforded the title compound **S19** as a mixture of inseparable isomers (513 mg, 72% yield, 1:1) as a colourless oil. Data is reported on the mixture.

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) **Major diastereoisomer:** δ 7.31 – 7.14 (m, 5H, 5×ArH), 6.13 (s, 1H, H-2), 4.51 (t, *J* = 3.6 Hz, 1H, H-8), 4.44 (s, 2H, H-16), 3.77 (ddd, *J* = 15.1, 11.3, 7.8 Hz, 1H, H-12), 3.72 – 3.59 (m, 1H, H-7), 3.45 (m, 3H, H12', H-15), 3.31 (td, *J* = 9.6, 5.5 Hz, 1H, H-7'), 2.61 (m, 2H, H-13), 2.20 (t, *J* = 7.7 Hz, 2H, H-4), 2.15 (s, 3H, 3×ArCH<sub>3</sub>), 2.10 (s, 6H, 6×ArCH<sub>3</sub>), 2.02 (s, 6H, 6×ArCH<sub>3</sub>), 1.86 – 1.68 (m, 4H, H-5, H-14), 1.50 (m, 8H, H-6, H-9, H-10, H-11).

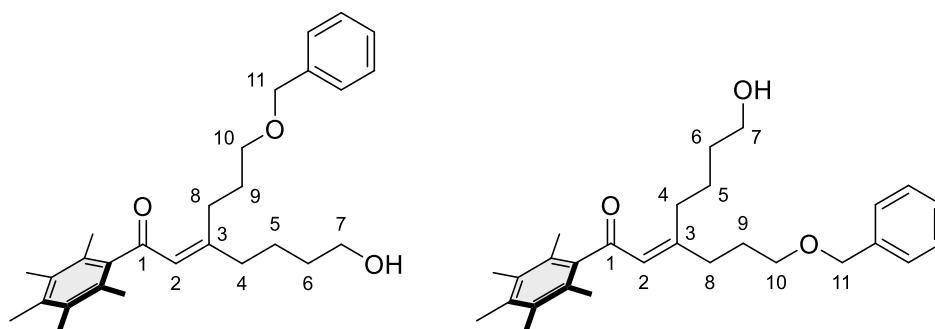
**Minor diastereoisomer:** δ 7.31 – 7.14 (m, 5H, 5×ArH), 6.11 (s, 1H, H-2), 4.47 (m, 1H, H-8), 4.40 (s, 2H, H-16), 3.77 (ddd, *J* = 15.1, 11.3, 7.8 Hz, 1H, H-12), 3.72 – 3.59 (m, 1H, H-7), 3.39 (m, 3H, H-12', H-15), 3.31 (td, *J* = 9.6, 5.5 Hz, 1H, H-7'), 2.61 (m, 2H, H-13), 2.20 (t, *J* = 7.7 Hz, 2H, H-4), 2.15 (s, 3H, 3×ArCH<sub>3</sub>), 2.10 (s, 6H, 6×ArCH<sub>3</sub>), 2.02 (s, 6H, 6×ArCH<sub>3</sub>), 1.86 – 1.68 (m, 4H, H-5, H-14), 1.50 (m, 8H, H-6, H-9, H-10, H-11).

**<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) δ 200.7 (C-1), 200.7 (C-1'), 163.3 (C-3), 141.8 (ArC), 138.6 (ArC), 138.4 (ArC'), 135.0 (ArC), 132.9 (ArC), 128.4 (ArC), 128.4 (ArC'), 127.9 (ArC), 127.8 (ArC'), 127.7 (ArC), 127.6 (ArC), 127.6 (ArC'), 127.5 (C-2), 125.8 (ArC), 125.8 (ArC'), 98.9 (C-8), 98.9 (C-8'), 73.0 (C-16), 72.9 (C-16'), 70.5 (C-15), 69.5 (C-15'), 67.4 (C-7), 67.2 (C-7'), 62.4 (C-12), 35.2 (C-13), 32.3 (C-4), 30.8 (C-9), 30.7 (C-9'), 30.0 (C-6), 29.4 (C-6'), 28.7 (C-14), 27.9 (C-5), 25.5 (C-11), 25.5 (C-11'), 19.7 (C-10), 19.7 (C-10'), 17.2 (ArCH<sub>3</sub>), 16.7 (ArCH<sub>3</sub>), 16.0 (ArCH<sub>3</sub>).

**IR** (film)  $\nu_{\max}/\text{cm}^{-1}$ : 2923, 2886, 1702, 1532, 1460, 1344.

**HRMS** (ESI<sup>+</sup>): Found [M+H]<sup>+</sup> = 507.3458; C<sub>33</sub>H<sub>47</sub>O<sub>4</sub> requires 507.3469, Δ -2.09 ppm.

### 3-(3-(Benzyloxy)propyl)-7-hydroxy-1-(2,3,4,5,6-pentamethylphenyl)hept-2-en-1-one, **S20**



To a solution of E/Z mixture (1:1) of **S19** (140 mg, 0.28 mmol, 1.0 equiv.) in MeOH (0.2 M, 1.5 mL) was added *p*-TsOH·H<sub>2</sub>O (10 mg, 0.06 mmol, 0.2 equiv.) portionwise at RT for 30 min. After addition of sat. NaHCO<sub>3</sub>, extract with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic layers were dried over MgSO<sub>4</sub>, filtered and concentrated under reduced pressure. Purification by column chromatography (pentane:EtOAc, 90:10) afforded the title compound **S20** as a inseparable mixture diastereoisomers as a colourless oil (108 mg, 91% yield, 1:1). Data is reported on the mixture.

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) **Major diastereoisomer:** δ 7.30 – 7.15 (m, 5H, 5×ArH), 6.13 (s, 1H, H-2), 4.45 (s, 2H, H-11), 3.69 – 3.61 (m, 2H, H-7), 3.46 (t, *J* = 6.6 Hz, 2H, H-10), 2.67 – 2.59 (m, 2H, H-8), 2.22 (t, *J* = 7.7 Hz, 2H, H-4),

2.16 (s, 3H, 3×ArCH<sub>3</sub>), 2.11 (s, 6H, 6×ArCH<sub>3</sub>), 2.03 (s, 6H, 6×ArCH<sub>3</sub>), 1.84 – 1.66 (m, 2H, H-9), 1.61 – 1.42 (m, 4H, H-5, H-6).

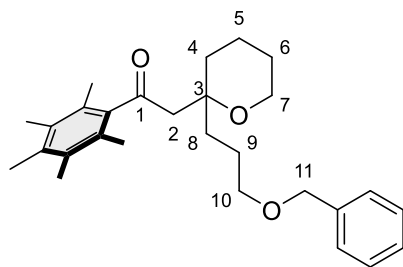
**Minor diastereoisomer:** δ 7.30 – 7.15 (m, 5H, 5×ArH), 6.13 (s, 1H, H<sub>2</sub>), 4.40 (s, 2H, H-11), 3.58 – 3.53 (m, 2H, H-7), 3.39 (t, *J* = 6.3 Hz, 2H, H-7), 2.56 (m, 2H, H-8), 2.22 (t, *J* = 7.7 Hz, 1H, H-4), 2.16 (s, 3H, 3×ArCH<sub>3</sub>), 2.11 (s, 6H, 6×ArCH<sub>3</sub>), 2.03 (s, 6H, 6×ArCH<sub>3</sub>), 1.84 – 1.66 (m, 2H, H-9), 1.61 – 1.42 (m, 4H, H-5, H-6).

**<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) δ 200.9 (C1), 200.7 (C1'), 164.2 (C-3), 163.4 (C-3'), 141.7 (ArC), 138.3 (ArC), 135.1 (ArC), 135.1 (ArC'), 133.0 (ArC), 128.4 (ArC), 128.4 (ArC'), 127.8 (ArC), 127.8 (ArC'), 127.7 (ArC), 127.7 (ArC'), 127.5 (C-2), 125.7 (ArC), 73.0 (C-11), 70.5 (C-10), 62.6 (C-7), 38.6 (C-4), 32.3 (C-6), 29.4 (C-8), 28.7 (C-9), 24.5 (C-5), 17.1 (ArCH<sub>3</sub>), 16.7 (ArCH<sub>3</sub>), 16.0 (ArCH<sub>3</sub>).

**IR** (film)  $\nu_{\max}/\text{cm}^{-1}$ : 3405, 2923, 2886, 1670, 1597, 1460.

**HRMS** (ESI<sup>+</sup>): Found [M+H]<sup>+</sup> = 423.2900; C<sub>28</sub>H<sub>39</sub>O<sub>3</sub> requires 423.2894, Δ 1.48 ppm.

### 2-(2-(3-(Benzyloxy)propyl)tetrahydro-2H-pyran-2-yl)-1-(2,3,4,5,6-pentamethylphenyl)ethan-1-one, **3k**



Compound **S20** (168 mg, 0.400 mmol, 1.0 equiv.) was dissolved in chloroform (20 mL) and the resulting solution was stirred at RT for 16 h. The reaction mixture was then concentrated under reduced pressure, and purification by column chromatography (Pentane: Et<sub>2</sub>O, 90:10) afforded the title compound as a white solid (119 mg, 70% yield).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.44 – 7.05 (m, 5H, 5×ArH), 4.44 (s, 2H, H-11), 3.47 (m, 2H, H-10), 3.42 (t, *J* = 6.7 Hz, 2H, H-7), 2.96 (d, *J* = 18.2 Hz, 1H, H-2), 2.86 (d, *J* = 18.2 Hz, 1H, H-2'), 2.15 (s, 3H, 3×ArCH<sub>3</sub>), 2.10 (s, 6H, 6×ArCH<sub>3</sub>), 2.06 (s, 6H, 6×ArCH<sub>3</sub>), 1.98 (ddd, *J* = 14.1, 11.9, 4.8 Hz, 1H, H-4), 1.83 (ddd, *J* = 14.0, 11.5, 5.1 Hz, 1H, H-4'), 1.75 (t, *J* = 6.1 Hz, 2H, H-8), 1.71 – 1.46 (m, 4H, H-5, H-6), 1.44 (ddt, *J* = 10.0, 6.1, 3.7 Hz, 2H, H-9).

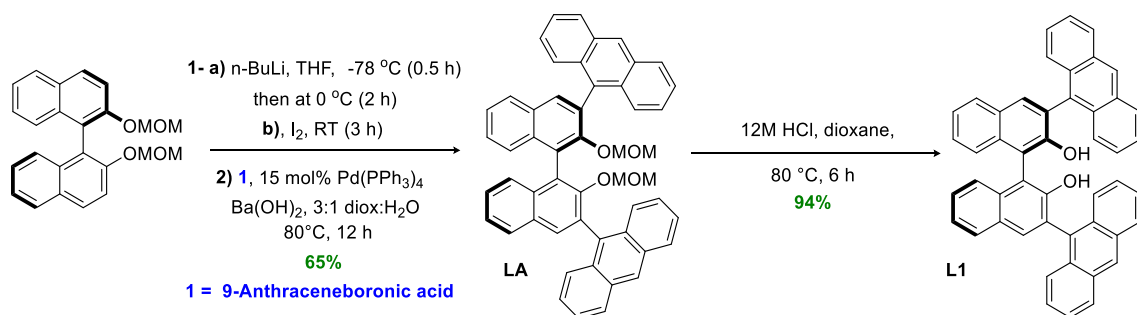
**<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) δ 209.5 (C-1), 141.0 (ArC), 138.8 (ArC), 135.4 (ArC), 133.1 (ArC), 128.4 (ArC), 127.6 (ArC), 127.5 (ArC), 127.4 (ArC), 74.3 (C-3), 72.8 (C-11), 70.8 (C-7), 61.2 (C-10), 50.9 (C-2), 32.9 (C-8), 31.1 (C-4), 25.7 (C-9), 23.5 (C-5), 19.1 (C-6), 17.2 (ArCH<sub>3</sub>), 16.7 (ArCH<sub>3</sub>), 16.0 (ArCH<sub>3</sub>).

**IR** (film)  $\nu_{\max}/\text{cm}^{-1}$ : 2980, 1700, 1453, 1403, 1257, 1081.

**HRMS** (ESI<sup>+</sup>): Found [M+K]<sup>+</sup> = 461.2463; C<sub>28</sub>H<sub>38</sub>O<sub>3</sub>K requires 461.2453, Δ 2.27 ppm.

**m.p.:** 54-56 °C.

## Synthesis of Binol ligand L1



A solution of commercially available of (*R*)-OMOM BINOL (CAS number: 173831-50-0) (5.00 g, 13.4 mmol, 1.00 equiv.) in dry THF (265 mL) was cooled to -78 °C under N<sub>2</sub> and n-BuLi (16 mL, 2.50 M in hexanes, 40.2 mmol, 3.00 equiv.) was added dropwise. The reaction was stirred at -78 °C for 30 min and then warmed to 0 °C and stirred for 2 h. Then the reaction mixture was cooled to -78 °C, I<sub>2</sub> (10.2 g, 40.2 mmol, 3.00 equiv.) was added as a solid, and the reaction mixture was warmed to RT for 5 h and quenched with an aqueous saturated solution of NH<sub>4</sub>Cl (30 mL). The resulting solution was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 200 mL). The combined organic phases were washed with saturated solution Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> (3 × 200 mL), then the combined organic phases were washed with brine (1 × 200 mL) and the organic phase was dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. The crude product was used as is in the next step. In a flask A crude (*R*)-Iodo BINOL (8.00 g, 12.8 mmol, 1.0 equiv.), 9-anthracenylboronic acid (6.80 g, 30.7 mmol, 2.4 equiv.), Pd(PPh<sub>3</sub>)<sub>4</sub> (2.22 g, 1.92 mmol, 0.15 equiv.), and Ba(OH)<sub>2</sub> (11.0 g, 64.0 mmol, 5.0 equiv.) were combined and purged with nitrogen for 15 min. A mixture of 3:1 dioxane:H<sub>2</sub>O (130 mL) was added and stirred at 80 °C for 12 h. The resulting reaction was cooled to RT, then diluted with 1M AcOH and CH<sub>2</sub>Cl<sub>2</sub> until a homogeneous biphasic solution resulted. The aqueous layer was extracted twice with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic layers were washed with H<sub>2</sub>O (3 × 200 mL) and brine (3 × 200 mL). The organic layer was then dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. Purification by column chromatography (Pentane: CH<sub>2</sub>Cl<sub>2</sub>, 95:5 to 60:40) afforded **LA** as a pale yellow solid (6.00 g, 65% yield).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.54 (s, 2H, 2 × ArH), 8.11 – 7.96 (m, 8H, 8 × ArH), 7.91 (d, *J* = 7.1 Hz, 2H, 2 × ArH), 7.80 (d, *J* = 8.8 Hz, 2H, 2 × ArH), 7.65 (d, *J* = 8.8 Hz, 2H, 2 × ArH), 7.55 – 7.37 (m, 10H, 10 × ArH), 7.27 – 7.18 (m, 2H, 2 × ArH), 4.32 – 4.20 (m, 4H, 2 × CH<sub>2</sub>), 1.88 (s, 6H, 3 × OCH<sub>3</sub>).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 152.8 (ArC), 134.3 (ArC), 133.5 (ArC), 133.2 (ArC), 132.6 (ArC), 131.5 (ArC), 131.5 (ArC), 131.0 (ArC), 130.9 (ArC), 130.8 (ArC), 128.6 (ArC), 128.4 (ArC), 128.2 (ArC), 127.2 (ArC), 126.9 (ArC), 126.8 (ArC), 126.5 (ArC), 126.0 (ArC), 125.8 (ArC), 125.5 (ArC), 125.32 (ArC), 125.28 (ArC), 98.38 (OCH<sub>2</sub>), 55.53 (OCH<sub>3</sub>). The spectral data matched that previously reported in the literature.<sup>[4]</sup>

[4] I. T. Crouch, R. K. Neff, D. E. Frantz, *J. Am. Chem. Soc.* **2013**, 135, 4970.

A solution of **LA** (6.00 g, 9.40 mmol, 1.00 equiv.) in dioxane (70 mL) and 37% HCl (9 mL, 108.7 mmol, 11.6 equiv.) and stirred at 60 °C for 6 h. The reaction was monitored by TLC (Pentane: CH<sub>2</sub>Cl<sub>2</sub>, 60:40). The reaction was concentrated *in vacuo* to give a crude brown solid. This solid resuspended in CH<sub>2</sub>Cl<sub>2</sub> and stirred with Na<sub>2</sub>SO<sub>4</sub> for 10 min to get rid of residual water and filtered off. The resulting solution was then concentrated *in vacuo* to form a yellow solid. Purification by column chromatography (Pentane: CH<sub>2</sub>Cl<sub>2</sub>, 87:13 to 60:40) afforded the title ligand

**L1** as an off-white solid (4.90 g, 94% yield).

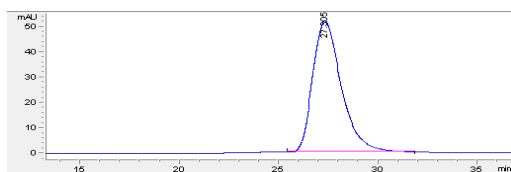
**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)** δ 8.58 (s, 2H, 2 × ArH), 8.13 – 8.00 (m, 6H, 6 × ArH), 7.90 (dd, *J* = 22.7, 8.2 Hz, 4H, 4 × ArH), 7.68 (d, *J* = 8.8 Hz, 2H, 2 × ArH), 7.60 (d, *J* = 8.2 Hz, 2H, 2 × ArH), 7.55 – 7.38 (m, 10H, 10 × ArH), 7.26 (d, *J* = 15.5 Hz, 2H, 2 × ArH), 5.11 (s, 2H, 2 × OH).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)** δ 151.2 (ArC), 134.1 (ArC), 133.2 (ArC), 131.7 (ArC), 131.6 (ArC), 131.0 (ArC), 130.9 (ArC), 129.4 (ArC), 128.8 (ArC), 128.7 (ArC), 128.6 (ArC), 127.9 (ArC), 127.5 (ArC), 127.3 (ArC), 126.4 (ArC), 126.3 (ArC), 126.3 (ArC), 125.6 (ArC), 125.5 (ArC), 125.0 (ArC), 124.4 (ArC), 113.7 (ArC).

**HPLC conditions:** Enantiopurity of commercial ligand **L1** (*R*) was determined by HPLC with a Chiralpak® IA column (95:5 hexane:IPA, 1.0 mL min<sup>-1</sup>, 254 nm, room temperature); *t<sub>r</sub>* (minor) = 27.30 min.

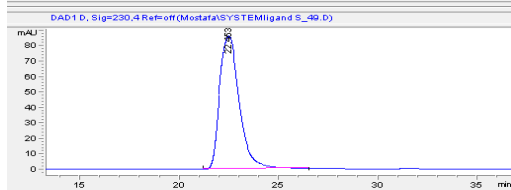
**HPLC conditions:** Enantiopurity of commercial ligand **L1** (*S*) was determined by HPLC with a Chiralpak® IA column (95:5 hexane:IPA, 1.0 mL min<sup>-1</sup>, 254 nm, room temperature); *t<sub>r</sub>* = 22.45 min.

**HPLC conditions:** Enantiopurity of synthesised and recycled ligand **L1** (*R*) was determined by HPLC with a Chiralpak® IA column (95:5 hexane:IPA, 1.0 mL min<sup>-1</sup>, 254 nm, room temperature); *t<sub>r</sub>* = 27.77 min.



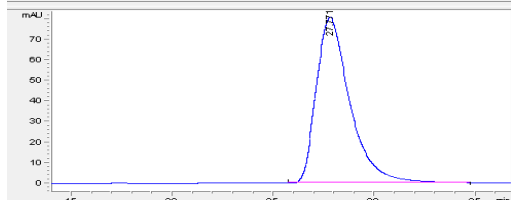
**Commercial Ligand L1 (*R*)**  
**(*R*)-3,3'-Di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol,**  
CAS No: 361342-49-6

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	27.305	BB	5231.9	52.1	1.4766	100.000	0.704



**Commercial Ligand L1 (*S*)**  
**(*S*)-3,3'-Di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol,**  
CAS No: 361342-50-9

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	22.453	BB	5952.6	86.3	1.0849	100.000	0.774

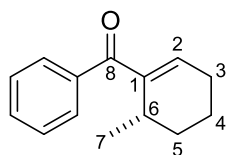


**Recycled Ligand L1 (*R*)**  
**(*R*)-3,3'-Di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol**

#	Time	Type	Area	Height	Width	Area%	Symmetry
1	27.771	BB	9323.3	80.4	1.743	100.000	0.645

## Synthesis of cyclohexenes 4a-4k

### (6-Methylcyclohex-1-en-1-yl)(phenyl)methanone, 4a



**Racemic:** 2-(2-Methyltetrahydro-2H-pyran-2-yl)-1-phenylethan-1-one **3a** (65.4 mg, 0.30 mmol, 1.0 equiv.),  $\text{Al}(\text{O}^t\text{Bu})_3$  (73.9 mg, 0.30 mmol, 1.0 equiv.), and toluene (0.2 M, 1.5 mL) were subjected to **General Procedure 4**. The title compound was afforded after purification by FCC (pentane: Et<sub>2</sub>O, 98:2) as a colourless oil (50.2 mg, 83% yield).

**Enantioenriched:** (*R*)-3,3'-Di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol **L1** (128 mg, 0.20 mmol, 1.0 equiv.), *tert*-butanol (14.8 mg, 0.20 mmol, 1.0 equiv.), *m*-xylene (1.0 mL, 0.2 M),  $\text{AlMe}_3$  in toluene (2.0 M, 0.1 mL, 0.20 mmol, 1.0 equiv.) and 2-(2-methyltetrahydro-2H-pyran-2-yl)-1-phenylethan-1-one **3a** (43.7 mg, 0.20 mmol, 1.0 equiv.) were subjected to **General Procedure 5A**. Purification by column chromatography (pentane:Et<sub>2</sub>O, 98:2) afforded the title compound as a colourless oil (23.2 mg, 58% yield).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.73 – 7.62 (m, 2H, ArH), 7.55 – 7.47 (m, 1H, ArH), 7.45 – 7.37 (m, 2H, ArH), 6.40 (td,  $J$  = 4.0, 1.5 Hz, 1H, H-2), 3.09 – 2.88 (m, 1H, H-6), 2.37 – 2.05 (m, 2H, H-3), 1.86– 1.50 (m, 4H, H-4, H-5), 1.07 (d,  $J$  = 7.0 Hz, 3H, H-7).

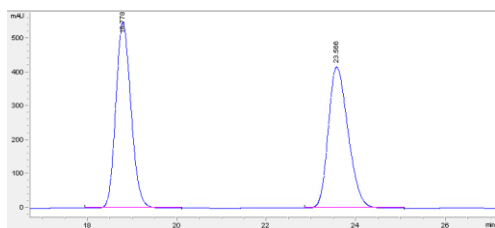
<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  198.6 (C-8), 144.1 (C-1), 141.8 (C-2), 139.2 (ArC), 131.7 (ArC), 129.5 (ArC x 2), 128.2 (ArC x 2), 30.2 (C-5), 28.1 (C-6), 26.3 (C-3), 19.9 (C-7), 18.6 (C-4).

**HRMS** (ESI<sup>+</sup>): Found  $[\text{M}+\text{H}]^+ = 201.1273$ ; C<sub>14</sub>H<sub>17</sub>O requires 201.1274  $\Delta$  -0.45 ppm.

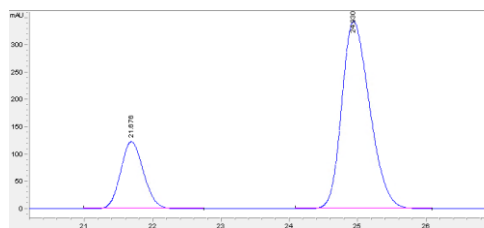
**IR** (film)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 2933, 2870, 1649, 1598, 1579, 1447.

$[\alpha]_{\text{D}}^{25} = +5.34$  ( $c = 1.0$ , CHCl<sub>3</sub>).

**HPLC:** Enantiomeric excess was determined by HPLC with a Chiralpak® IG column (99.5:0.5 hexane:IPA, 1.0 mL min<sup>-1</sup>, 254 nm, room temperature);  $t_{\text{r}}$  (minor) = 21.7 min,  $t_{\text{r}}$  (major) = 24.9 min, 23:77 e.r. ).

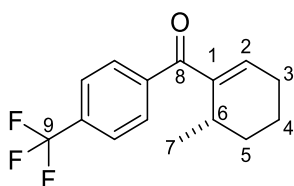


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	18.778	BB	12977.7	549.7	0.3675	50.244	0.825
2	23.566	BB	12851.6	418.5	0.4782	49.756	0.709



#	Time	Type	Area	Height	Width	Area%	Symmetry
1	21.676	BB	2887.8	123.7	0.3645	22.794	0.857
2	24.933	BB	9781.3	344	0.4398	77.206	0.701

## (6-Methylcyclohex-1-en-1-yl)(4-(trifluoromethyl)phenyl)methanone, 4b



**Racemic: 3b** (57.3 mg, 0.20 mmol, 1.0 equiv.), Al(O<sup>t</sup>Bu)<sub>3</sub> (49.3 mg, 0.20 mmol, 1.0 equiv.), and toluene (0.2 M, 1.0 mL) were subjected to **General Procedure 4**. Purification by column chromatography (pentane: Et<sub>2</sub>O, 97:3) afforded the title compound as a colourless oil (38.9 mg, 72% yield).

**Enantioenriched: (R)-3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol L1** (128 mg, 0.20 mmol, 1.0 equiv.), *tert*-butanol (14.8 mg, 0.20 mmol, 1.0 equiv.), *m*-xylene (1.0 mL, 0.2 M), AlMe<sub>3</sub> in toluene (2.0 M, 0.1 mL, 0.20 mmol, 1.0 equiv.), and **3b** (57.3 mg, 0.20 mmol, 1.0 equiv.) were subjected to **General Procedure 5A**. Purification by column chromatography (pentane:Et<sub>2</sub>O, 97:3) afforded the title compound as a colourless oil (35 mg, 66% yield).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.73 (d, *J* = 8.0 Hz, 2H, ArCH x 2), 7.67 (d, *J* = 8.0 Hz, 2H, ArCH x 2), 6.43 (td, *J* = 4.0, 1.0 Hz, 1H, H-2), 3.04 – 2.94 (m, 1H, H-6), 2.34 – 2.23 (m, 1H, H-3), 2.22 – 2.10 (m, 1H, H-3'), 1.83 – 1.68 (m, 2H, H-4), 1.68 – 1.54 (m, 2H, H-5), 1.09 (d, *J* = 7.0 Hz, 3H, H-7).

<sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>) δ -63.0.

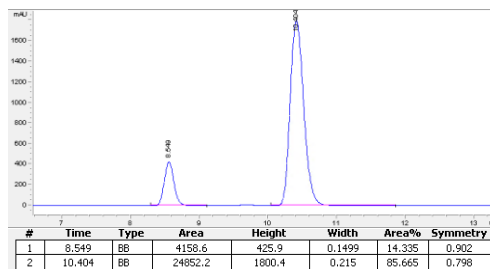
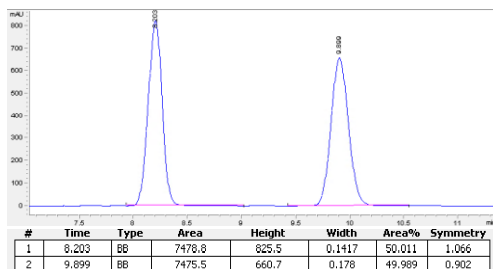
<sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 197.1 (C-8), 144.0 (ArC), 143.9 (C-2), 142.4 (C-1), 133.1 (q, *J* = 33 Hz, ArC<sub>ipso</sub>), 129.5 (ArC x 2), 125.2 (q, *J* = 4 Hz, ArC<sub>ortho</sub> x 2), 123.9 (q, *J* = 273 Hz, C-9), 29.9 (C-5), 27.8 (C-6), 26.5 (C-3), 19.9 (C-7), 18.2 (C-4).

**HRMS** (ESI<sup>+</sup>): Found [M+H]<sup>+</sup> = 269.1143; C<sub>15</sub>H<sub>16</sub>F<sub>3</sub>O requires 269.1148 Δ -1.60 ppm.

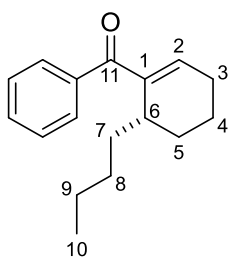
**IR** (film) ν<sub>max</sub>/cm<sup>-1</sup>: 2937, 2873, 1654, 1579, 1512, 1457.

[α]<sub>D</sub><sup>25</sup> = +4.84 (c = 1.0, CHCl<sub>3</sub>).

**HPLC**: Enantiomeric excess was determined by HPLC with a Chiralpak® IC column (99.5:0.5 hexane:IPA, 1.0 mL min<sup>-1</sup>, 230 nm, room temperature); t<sub>r</sub> (minor) = 8.5 min, t<sub>r</sub> (major) = 10.4 min, 14:86 e.r.).



### (6-Butylcyclohex-1-en-1-yl)(phenyl)methanone, **4c**



**Racemic:** **3c** (52.1 mg, 0.20 mmol, 1.0 equiv.),  $\text{Al}(\text{O}^t\text{Bu})_3$  (49.3 mg, 0.20 mmol, 1.0 equiv.), and toluene (0.2 M, 1.0 mL) were subjected to **General Procedure 4**. The title compound was afforded after purification by FCC (pentane:  $\text{Et}_2\text{O}$ , 98:2) as a colourless oil (32.6 mg, 67% yield).

**Enantioenriched:** (*R*)-3,3'-Di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol **L1** (128 mg, 0.20 mmol, 1.0 equiv.), *tert*-butanol (14.8 mg, 0.20 mmol, 1.0 equiv.), *m*-xylene (1.0 mL, 0.2 M),  $\text{AlMe}_3$  in toluene (2.0 M, 0.1 mL, 0.20 mmol, 1.0 equiv.), and **3c** (52.1 mg, 0.20 mmol, 1.0 equiv.) were subjected to **General Procedure 5A**. Purification by column chromatography (pentane: $\text{Et}_2\text{O}$ , 98:2) afforded the title compound **4c** as a colourless oil (31 mg, 64% yield).

**$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.73 – 7.64 (m, 2H, ArH x 2), 7.54 – 7.46 (m, 1H, ArH), 7.46 – 7.36 (m, 2H, ArH x 2), 6.38 (td,  $J = 4.0, 1.0$  Hz, 1H, H-2), 3.08 – 2.75 (m, 1H, H-6), 2.39 – 2.02 (m, 2H, H-3), 1.80 – 1.54 (m, 4H, H-4, H-5), 1.53 – 1.39 (m, 1H, H-7), 1.42 – 1.13 (m, 5H, H-7', H-8, H-9), 0.85 (t,  $J = 7.0$  Hz, 3H, H-10).

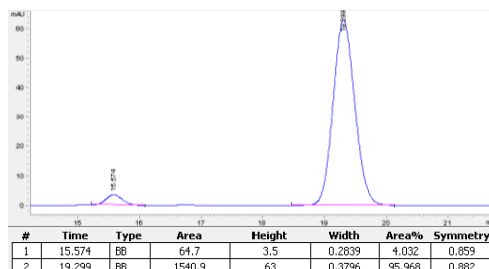
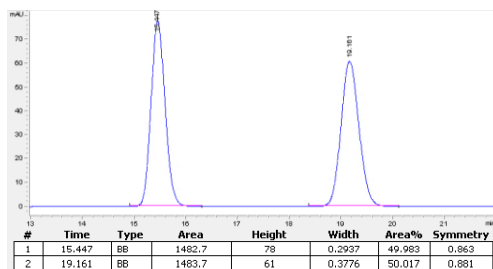
**$^{13}\text{C}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  198.6 (C-11), 143.7 (C-1), 141.8 (C-2), 139.0 (ArC), 131.8 (ArC), 129.6 (ArC x 2), 128.2 (ArC x 2), 33.5 (C-7), 32.8 (C-6), 29.8 (C-9), 26.4 (C-5), 26.3 (C-3), 22.9 (C-8), 18.4 (C-4), 14.2 (C-10).

**HRMS** (ESI<sup>+</sup>): Found  $[\text{M}+\text{H}]^+ = 243.1741$ ;  $\text{C}_{17}\text{H}_{23}\text{O}$  requires 243.1743  $\Delta$  -0.82 ppm.

**IR** (film)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 2980, 2970, 2931, 1650, 1598, 1579, 1447.

$[\alpha]_{\text{D}}^{25} = +9.80$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).

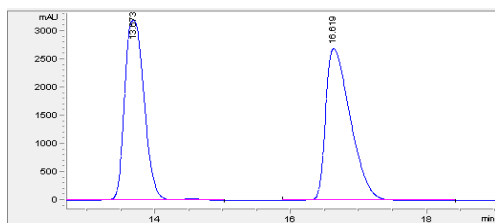
**HPLC:** Enantiomeric excess was determined by HPLC with a Chiralpak® IG column (99.5:0.5 hexane:IPA, 1.0 mL  $\text{min}^{-1}$ , 254 nm, room temperature);  $t_{\text{r}}$  (minor) = 15.6 min,  $t_{\text{r}}$  (major) = 19.3 min, 4:96 e.r.).



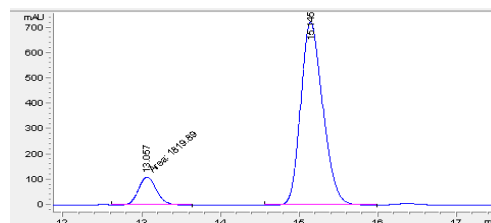
**Enantioenriched:** (*R*)-3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol **L1** (77 mg, 0.12 mmol, 0.6 equiv.), toluene (0.2 M, 1 mL),  $\text{AlMe}_3$  in toluene (1.0 M, 0.08 mL, 0.08 mmol, 0.4 equiv.) and **3c** (52.1 mg, 0.20 mmol, 1.0

equiv.) were subjected to **General procedure 5C**. Purification by column chromatography (pentane:Et<sub>2</sub>O, 98:2) afforded the title compound **4c** as a colourless oil (30 mg, 62% yield).

**HPLC**: Enantiomeric excess was determined by HPLC with a Chiralpak® IG column (99.5:0.5 hexane:IPA, 1.0 mL min<sup>-1</sup>, 254 nm, room temperature); t<sub>r</sub> (minor) = 13.1 min, t<sub>r</sub> (major) = 15.1 min, 11:89 e.r.).



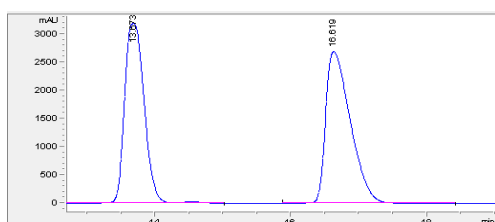
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	13.673	BV R	63870.7	3193.1	0.3135	48.533	0.762
2	16.619	BB	67732.2	2700.7	0.3866	51.467	0.449



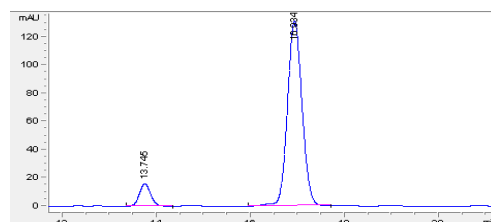
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	13.057	MM T	1819.9	111.2	0.3502	11.395	3.08E-2
2	15.145	BB	14164.7	721.6	0.305	88.615	0.753

**Enantioenriched**: (*R*)- 3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol **L1** (77 mg, 0.12 mmol, 0.6 equiv.), toluene (0.2 M, 1 mL), AlMe<sub>3</sub> in toluene (1.0 M, 0.08 mL, 0.08 mmol, 0.4 equiv.) after which dry THF (60 μL, 0.73 mmol, 9.25 equiv.) and **3c** (52.1 mg, 0.20 mmol, 1.0 equiv.) were subjected to **General procedure 5C**. Purification by column chromatography (pentane:Et<sub>2</sub>O, 98:2) afforded the title compound **4c** as a colourless oil (29 mg, 60% yield).

**HPLC**: Enantiomeric excess was determined by HPLC with a Chiralpak® IG column (99.5:0.5 hexane:IPA, 1.0 mL min<sup>-1</sup>, 254 nm, room temperature); t<sub>r</sub> (minor) = 13.7 min, t<sub>r</sub> (major) = 16.9 min, 8.5:91.5 e.r.).

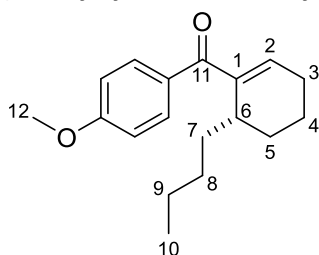


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	13.673	BV R	63870.7	3193.1	0.3135	48.533	0.762
2	16.619	BB	67732.2	2700.7	0.3866	51.467	0.449



#	Time	Type	Area	Height	Width	Area%	Symmetry
1	13.745	BB	262.6	15.8	0.2581	8.493	0.901
2	16.934	BB	2829.8	130.7	0.3366	91.507	0.916

#### (6-Butylcyclohex-1-en-1-yl)(4-methoxyphenyl)methanone, **4d**



**Racemic**: **3d** (58.1 mg, 0.20 mmol, 1.0 equiv.), Al(O<sup>t</sup>Bu)<sub>3</sub> (49.3 mg, 0.20 mmol, 1.0 equiv.), and toluene (0.2 M, 1.0 mL) were subjected to **General Procedure 4**. Purification by column chromatography (Pentane:Et<sub>2</sub>O, 98:2) afforded the title compound **4d** as a colourless oil (19.5 mg, 36% yield).

**Enantioenriched:** (*R*)-3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol **L1** (128 mg, 0.20 mmol, 1.0 equiv.), *tert*-butanol (14.8 mg, 0.20 mmol, 1.0 equiv.), *m*-xylene (1.0 mL, 0.2 M), AlMe<sub>3</sub> in toluene (2.0 M, 0.1 mL, 0.20 mmol, 1.0 equiv.), and **3d** (58.1 mg, 0.20 mmol, 1.0 equiv.) were subjected to **General Procedure 5A**. Purification by column chromatography (Pentane:Et<sub>2</sub>O, 98:2) afforded the title compound **4d** as a colourless oil (34.9 mg, 64% yield).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.78 – 7.70 (m, 2H, ArH x 2), 6.95 – 6.87 (m, 2H, ArH x 2), 6.29 (td, *J* = 4.0, 1.0 Hz, 1H, H-2), 3.86 (s, 3H, H-12), 2.93 – 2.84 (m, 1H, H-6), 2.35 – 2.06 (m, 2H, H-3), 1.79 – 1.53 (m, 4H, H-4 x 2, H-5), 1.49 – 1.16 (m, 6H, H-7, H-8, H-9), 0.83 (t, *J* = 6.5 Hz, 3H, H-10).

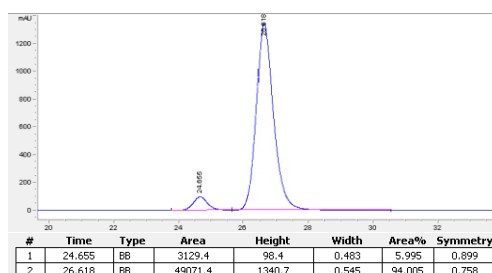
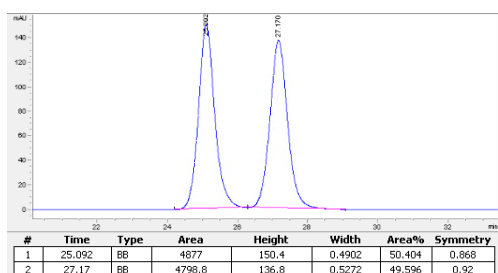
<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 197.6 (C-11), 162.9 (ArC), 143.7 (C-1), 139.2 (C-2), 132.0 (ArC x 2), 131.4 (ArC), 113.5 (ArC x 2), 55.5 (C-12), 33.6 (C-7), 33.3 (C-6), 29.8 (C-8), 26.7 (C-5), 26.1 (C-3), 22.9 (C-9), 18.7 (C-4), 14.2 (C-10).

**HRMS** (ESI<sup>+</sup>): Found [M+H]<sup>+</sup> = 273.1845; C<sub>18</sub>H<sub>25</sub>O<sub>2</sub> requires 273.1849 Δ -1.47 ppm.

**IR** (film) ν<sub>max</sub>/cm<sup>-1</sup>: 2932, 2858, 1643, 1600, 1575, 1509.

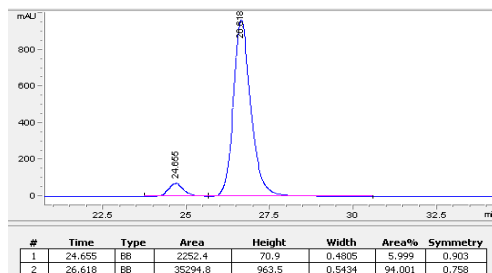
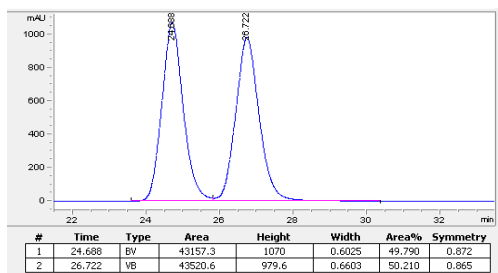
[α]<sub>D</sub><sup>25</sup> = +8.08 (c = 1.0, CHCl<sub>3</sub>).

**HPLC:** Enantiomeric excess was determined by HPLC with a Chiralpak® IA column (99.5:0.5 hexane:IPA, 0.5 mL min<sup>-1</sup>, 254 nm, room temperature); t<sub>r</sub> (minor) = 24.7 min, t<sub>r</sub> (major) = 26.6 min, 6:94 e.r.).



**Enantioenriched:** (*R*)-3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol **L1** (77 mg, 0.12 mmol, 0.6 equiv.), toluene (0.2 M, 1 mL), AlMe<sub>3</sub> in toluene (1.0 M, 0.08 mL, 0.08 mmol, 0.4 equiv.) and **3d** (58.1 mg, 0.20 mmol, 1.0 equiv.) were subjected to **General procedure 5B**. Purification by column chromatography (Pentane:Et<sub>2</sub>O, 98:2) afforded the title compound **4d** as a colourless oil (34 mg, 62% yield).

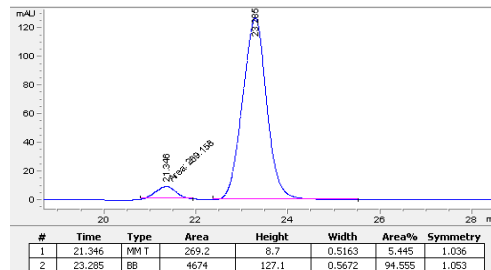
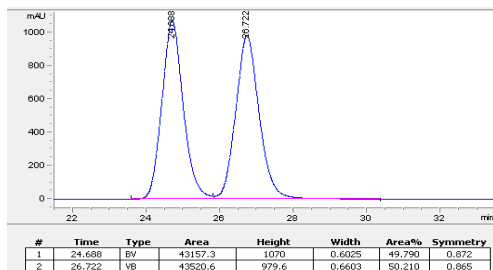
**HPLC:** Enantiomeric excess was determined by HPLC with a Chiralpak® IA column (99:1 hexane:IPA, 0.5 mL min<sup>-1</sup>, 254 nm, room temperature); t<sub>r</sub> (minor) = 24.7 min, t<sub>r</sub> (major) = 26.6 min, 6:94 e.r.).



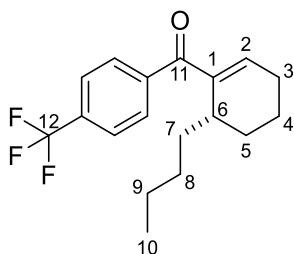
**Enantioenriched:** (*R*)-3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol **L1** (77 mg, 0.12 mmol, 0.6 equiv.), toluene (0.2 M, 1 mL), AlMe<sub>3</sub> in toluene (1.0 M, 0.08 mL, 0.08 mmol, 0.4 equiv.) after which dry THF (60 μL, 0.73

mmol, 9.25 equiv.) and **3d** (58.1 mg, 0.20 mmol, 1.0 equiv.) were subjected to **General procedure 5C**. Purification by column chromatography (Pentane:Et<sub>2</sub>O, 98:2) afforded the title compound **4d** as a colourless oil (35 mg, 64% yield).

**HPLC**: Enantiomeric excess was determined by HPLC with a Chiralpak® IA column (99:1 hexane:IPA, 0.5 mL min<sup>-1</sup>, 254 nm, room temperature); t<sub>r</sub> (minor) = 24.7 min, t<sub>r</sub> (major) = 26.6 min, 5.5:94.5 e.r.).



### (6-Butylcyclohex-1-en-1-yl)(4-(trifluoromethyl)phenyl)methanone, **4e**



**Racemic**: **3e** (65.7 mg, 0.20 mmol, 1.0 equiv.), Al(O<sup>t</sup>Bu)<sub>3</sub> (49.3 mg, 0.20 mmol, 1.0 equiv.), and toluene (0.2 M, 1.0 mL) were subjected to **General Procedure 4**. Purification by column chromatography (Pentane:Et<sub>2</sub>O, 98:2) afforded the title compound **4e** as a colourless oil (40.6 mg, 65% yield).

**Enantioenriched**: (*R*)-3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol **L1** (128 mg, 0.20 mmol, 1.0 equiv.), *tert*-butanol (14.8 mg, 0.20 mmol, 1.0 equiv.), *m*-xylene (1.0 mL, 0.2 M), AlMe<sub>3</sub> in toluene (2.0 M, 0.1 mL, 0.20 mmol, 1.0 equiv.), and **3e** (65.7 mg, 0.20 mmol, 1.0 equiv.) were subjected to **General Procedure 5A**. Purification by column chromatography (Pentane:Et<sub>2</sub>O, 98:2) afforded the title compound **4e** as a colourless oil (37.2 mg, 60% yield).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.75 (d, *J* = 8.0 Hz, 2H), 7.67 (d, *J* = 8.1 Hz, 2H), 6.43 – 6.38 (m, 1H), 2.94 – 2.86 (m, 1H), 2.34 – 2.23 (m, 1H), 2.21 – 2.08 (m, 1H), 1.79 – 1.56 (m, 4H), 1.53 – 1.42 (m, 1H), 1.41 – 1.17 (m, 4H), 0.91 – 0.81 (m, 3H).

<sup>19</sup>F NMR (471 MHz, CDCl<sub>3</sub>) δ -63.0.

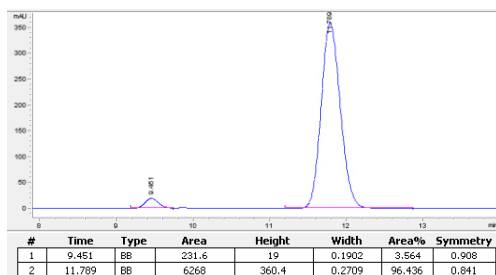
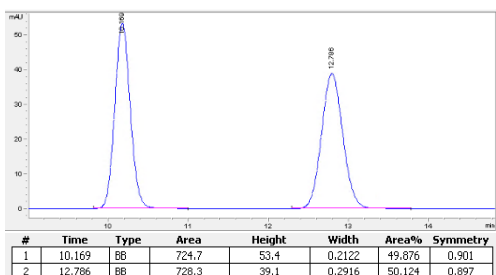
<sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 197.1 (C-11), 143.7 (ArC), 143.7 (C-2), 142.3 (C-1), 133.1 (q, *J* = 32 Hz, ArC<sub>ipso</sub>), 129.6 (ArC x 2), 125.2 (q, *J* = 4 Hz, ArC x 2), 123.9 (q, *J* = 272 Hz, C-12), 33.4 (C-7), 32.5 (C-6), 29.8 (C-8), 26.4 (C-3), 26.2 (C-5), 22.9 (C-9), 18.1 (C-4), 14.2 (C-10).

**HRMS** (ESI<sup>+</sup>): Found [M+H]<sup>+</sup> = 311.1612; C<sub>18</sub>H<sub>22</sub>F<sub>3</sub>O requires 311.1617 Δ -1.72 ppm.

IR (film) ν<sub>max</sub>/cm<sup>-1</sup>: 2935, 2861, 1655, 1510, 1459, 1407.

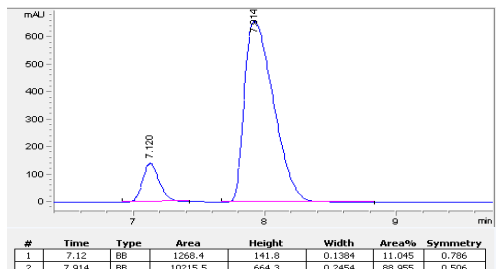
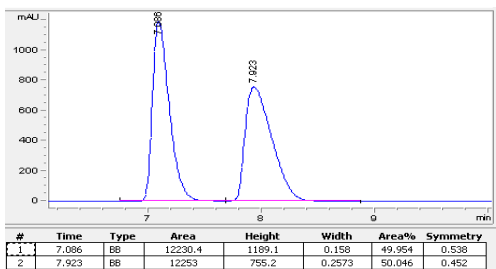
[α]<sub>D</sub><sup>25</sup> = +8.16 (c = 1.0, CHCl<sub>3</sub>).

**HPLC**: Enantiomeric excess was determined by HPLC with a Chiralpak® IC column (99.5:0.5 hexane:IPA, 1.0 mL min<sup>-1</sup>, 254 nm, room temperature); t<sub>r</sub> (minor) = 9.5 min, t<sub>r</sub> (major) = 11.8 min, 3.5:96.5 e.r.).



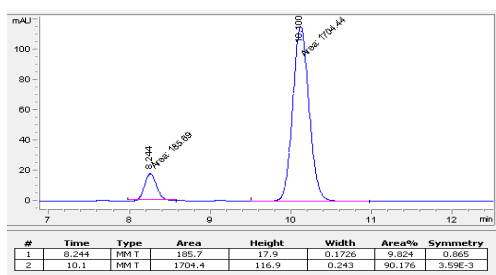
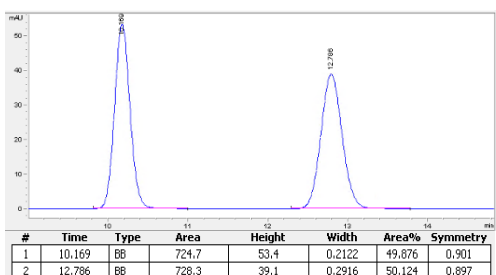
**Enantioenriched:** (*R*)- 3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol **L1** (77 mg, 0.12 mmol, 0.6 equiv.), toluene (0.2 M, 1 mL), AlMe<sub>3</sub> in toluene (1.0 M, 0.08 mL, 0.08 mmol, 0.4 equiv.) and **3e** (65.7 mg, 0.20 mmol, 1.0 equiv.) were subjected to **General procedure 5B**. Purification by column chromatography (Pentane:Et<sub>2</sub>O, 98:2) afforded the title compound **4e** as a colourless oil (40 mg, 64% yield).

**HPLC:** Enantiomeric excess was determined by HPLC with a Chiralpak® IG column (99.5:0.5 hexane:IPA, 1.0 mL min<sup>-1</sup>, 254 nm, room temperature); t<sub>r</sub> (minor) = 7.1 min, t<sub>r</sub> (major) = 7.9 min, 11:89 e.r.).

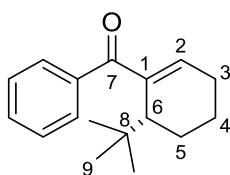


**Enantioenriched:** (*R*)- 3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol **L1** (77 mg, 0.12 mmol, 0.6 equiv.), toluene (0.2 M, 1 mL), AlMe<sub>3</sub> in toluene (1.0 M, 0.08 mL, 0.08 mmol, 0.4 equiv.) after which dry THF (60 μL, 0.73 mmol, 9 equiv.) and **3e** (65.7 mg, 0.20 mmol, 1.0 equiv.) were subjected to **General procedure 5C**. Purification by column chromatography (Pentane:Et<sub>2</sub>O, 98:2) afforded the title compound **4e** as a colourless oil (38 mg, 61% yield).

**HPLC:** Enantiomeric excess was determined by HPLC with a Chiralpak® IG column (99.5:0.5 hexane:IPA, 1.0 mL min<sup>-1</sup>, 254 nm, room temperature); t<sub>r</sub> (minor) = 8.2 min, t<sub>r</sub> (major) = 10.1 min, 10:90 e.r.).



## (6-(*tert*-Butyl)cyclohex-1-en-1-yl)(phenyl)methanone, 4f



**Racemic:** **3f** (78.1 mg, 0.30 mmol, 1.0 equiv.),  $\text{Al}(\text{O}^t\text{Bu})_3$  (73.9 mg, 0.30 mmol, 1.0 equiv.), and toluene (0.2 M, 1.5 mL) were subjected to **General Procedure 4**. The title compound **4f** was afforded after purification by FCC (Pentane:Et<sub>2</sub>O, 97:3) as a colourless oil (47.0 mg, 65% yield).

**Enantioenriched:** (*R*)-3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol **L1** (128 mg, 0.20 mmol, 1.0 equiv.), *tert*-butanol (14.8 mg, 0.20 mmol, 1.0 equiv.), *m*-xylene (1.0 mL, 0.2 M),  $\text{AlMe}_3$  in toluene (2.0 M, 0.1 mL, 0.20 mmol, 1.0 equiv.), and **3f** (52.1 mg, 0.30 mmol, 1.0 equiv.) were subjected to **General Procedure 5A**. Purification by column chromatography (Pentane:Et<sub>2</sub>O, 98:2) afforded the title compound **4f** as a colourless oil (29.6 mg, 61% yield).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.87 – 7.81 (m, 2H, ArH), 7.57 – 7.49 (m, 1H, ArH), 7.48 – 7.39 (m, 2H, ArH), 6.44 (ddd, *J* = 4.5, 3.5, 1.0 Hz, 1H, H-2), 3.09 – 2.95 (m, 1H, H-6), 2.32 – 2.05 (m, 2H, H-3), 2.00 – 1.78 (m, 2H, H-4, H-5), 1.77 – 1.60 (m, 1H, H-5), 1.57 – 1.47 (m, 1H, H-4), 0.93 (s, 9H, H-9).

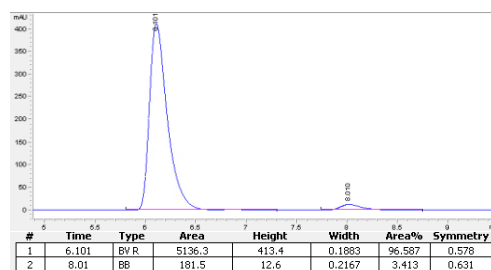
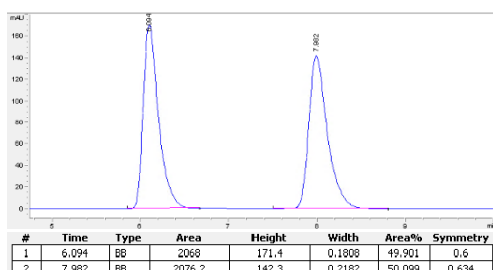
<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  198.9 (C-7), 142.5 (C-1), 142.0 (C-2), 137.7 (ArC), 132.2 (ArC), 130.2 (ArC x 2), 128.3 (ArC x 2), 41.9 (C-6), 35.9 (C-8), 29.5 (C-9 x 3), 25.5 (C-3), 24.5 (C-5), 20.3 (C-4).

HRMS (ESI<sup>+</sup>): Found  $[\text{M}+\text{H}]^+ = 243.1741$ ; C<sub>17</sub>H<sub>23</sub>O requires 243.1743  $\Delta$  -0.82 ppm.

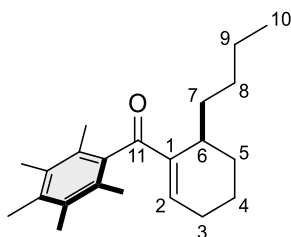
IR (film)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 2980, 1655, 1598, 1579, 1448.

$[\alpha]_{\text{D}}^{25} = -8.20$  (*c* = 1.0, CHCl<sub>3</sub>).

**HPLC:** Enantiomeric excess was determined by HPLC with a Chiralpak® OD column (99.5:0.5 hexane:IPA, 1.0 mL min<sup>-1</sup>, 230 nm, room temperature); *t*<sub>r</sub> (major) = 6.1 min, *t*<sub>r</sub> (minor) = 8.0 min, 96.5:3.5 e.r.).



## (6-Butylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 4g



**Racemic: 3g** (66.1 mg, 0.20 mmol, 1.0 equiv.), Al(O<sup>t</sup>Bu)<sub>3</sub> (49.3 mg, 0.20 mmol, 1.0 equiv.), and toluene (0.2 M, 1.0 mL) were subjected to **General Procedure 4**. The title compound was afforded after purification by FCC (Pentane:Et<sub>2</sub>O, 98:2) as a white solid (45.9 mg, 73% yield).

**Enantioenriched: (R)-3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol L1** (128 mg, 0.20 mmol, 1.0 equiv.), *tert*-butanol (14.8 mg, 0.20 mmol, 1.0 equiv.), *m*-xylene (1.0 mL, 0.2 M), AlMe<sub>3</sub> in toluene (2.0 M, 0.1 mL, 0.20 mmol, 1.0 equiv.), and **3g** (66.1 mg, 0.20 mmol, 1.0 equiv.) were subjected to **General Procedure 5A**. Purification by column chromatography (Pentane:Et<sub>2</sub>O, 98:2) afforded the title compound **4g** as a white solid (45 mg, 72% yield).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.46 (t, *J* = 4.0 Hz, 1H, H-2), 2.90 – 2.80 (m, 1H, H-6), 2.24 (s, 3H, ArCH<sub>3</sub>), 2.21 – 2.08 (m, 8H, 2xArCH<sub>3</sub>, H-3), 2.04 (s, 3H, 3xArCH<sub>3</sub>), 2.02 (s, 3H, 3xArCH<sub>3</sub>), 1.92 – 1.71 (m, 2H), 1.70 – 1.55 (m, 2H), 1.55 – 1.22 (m, 6H), 0.94 (t, *J* = 7.0 Hz, 3H, H-10).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 202.9 (C-11), 146.1 (C-2), 145.1 (C1), 138.4 (ArC), 134.9 (ArC), 132.6 (ArC), 132.6 (ArC), 129.4 (ArC), 129.2 (ArC), 32.7 (C<sub>7</sub>), 31.1 (C-6), 30.2 (C-5), 26.6 (C-3), 25.0 (C-8), 22.9 (C-9), 17.5 (ArCH<sub>3</sub>), 17.3 (ArCH<sub>3</sub>), 17.1 (C-4), 16.8 (ArCH<sub>3</sub>), 16.1 (ArCH<sub>3</sub>), 16.0 (ArCH<sub>3</sub>), 14.3 (C-10).

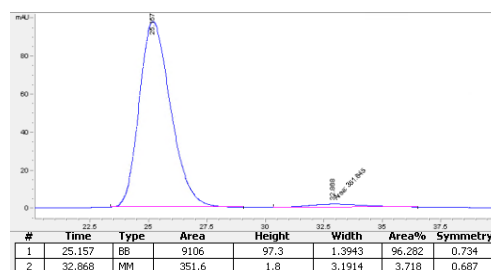
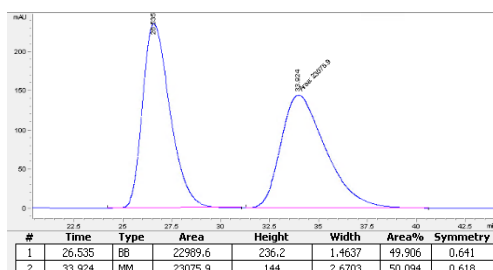
HRMS (ESI<sup>+</sup>): Found [M+H]<sup>+</sup> = 313.2521; C<sub>22</sub>H<sub>33</sub>O requires 313.2526 Δ -1.55 ppm.

IR (film) ν<sub>max</sub>/cm<sup>-1</sup>: 2928, 2859, 1650, 1631, 1601, 1456.

[α]<sub>D</sub><sup>25</sup> = -8.38 (c = 1.0, CHCl<sub>3</sub>).

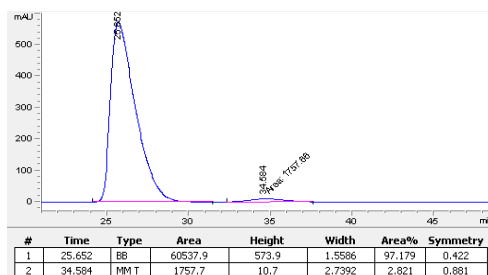
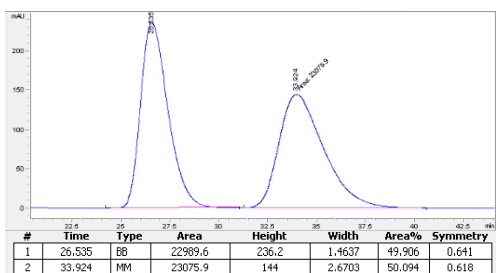
m.p.: 58-60 °C.

**HPLC:** Enantiomeric excess was determined by HPLC with a Chiralpak® IG column (99.5:0.5 hexane:IPA, 1.0 mL min<sup>-1</sup>, 210 nm, room temperature); t<sub>r</sub> (major) = 25.1 min, t<sub>r</sub> (minor) = 32.9 min, 96.5:3.5 e.r.).



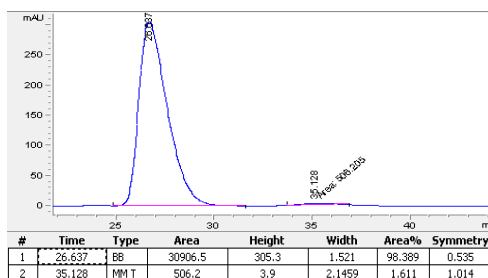
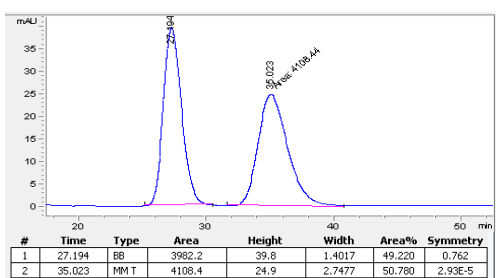
**Enantioenriched: (R)- 3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol L1** (77 mg, 0.12 mmol, 0.6 equiv.), toluene (0.2 M, 1 mL), AlMe<sub>3</sub> in toluene (1.0 M, 0.08 mL, 0.08 mmol, 0.4 equiv.) and **3g** (66 mg, 0.20 mmol, 1 equiv.) were subjected to **General procedure 5B**. Purification by column chromatography (Pentane:Et<sub>2</sub>O, 98:2) afforded the title compound **4g** as a white solid (46 mg, 74% yield).

**HPLC:** Enantiomeric excess was determined by HPLC with a Chiralpak® IG column (99.5:0.5 hexane:IPA, 1.0 mL min<sup>-1</sup>, 210 nm, room temperature); t<sub>r</sub> (major) = 25.6 min, t<sub>r</sub> (minor) = 34.6 min, 97:3 e.r.).



**Enantioenriched:** (*R*)- 3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol **L1** (77 mg, 0.12 mmol, 0.6 equiv.), toluene (0.2 M, 1 mL), AlMe<sub>3</sub> in toluene (1.0 M, 0.08 mL, 0.08 mmol, 0.4 equiv.), after which dry THF (60 μL, 0.73 mmol, 9.25 equiv.) and **3g** (66 mg, 0.20 mmol, 1 equiv.) were subjected to **General procedure 5C**. Purification by column chromatography (Pentane:Et<sub>2</sub>O, 98:2) afforded the title compound **4g** as a white solid (47 mg, 75% yield).

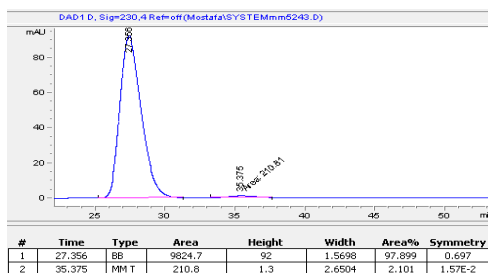
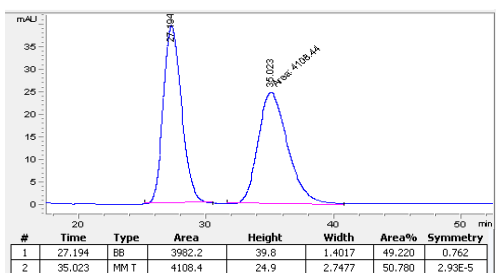
**HPLC:** Enantiomeric excess was determined by HPLC with a Chiralpak® IG column (99.5:0.5 hexane:IPA, 1.0 mL min<sup>-1</sup>, 210 nm, room temperature); t<sub>r</sub> (major) = 26.6 min, t<sub>r</sub> (minor) = 35.1 min, 98.5:1.5 e.r.).



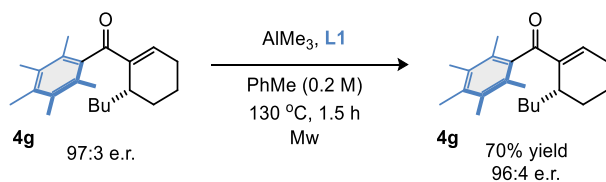
**Scale-Up Procedure:** (*R*)- 3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol **L1** (1.90 g, 3.0 mmol, 0.6 equiv.), toluene (0.2 M, 25 mL), AlMe<sub>3</sub> in toluene (1.0 M, 2.0 mL, 2.0 mmol, 0.4 equiv.), after which dry THF (1.50 mL, 18.5 mmol, 9.25 equiv.) and **3g** (1.65 g, 5.00 mmol, 1.0 equiv.) were subjected to **General procedure 5C**. Purification by column chromatography (Pentane:Et<sub>2</sub>O, 98:2) afforded the title compound **4g** as a white solid (1.25 g, 80% yield). (*R*)- 3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol **L1** was recycled and recovered after column chromatography (Pentane:Et<sub>2</sub>O, 60:40) as an off-white solid (1.85 g, 97% yield) and RSM is (183 mg, 11% yield).

The spectroscopic data were identical to that given above.

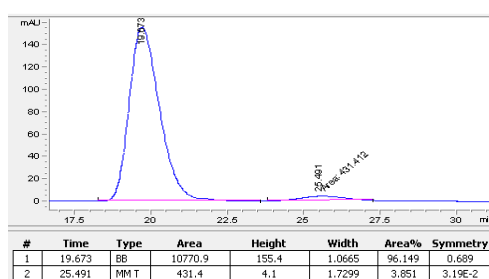
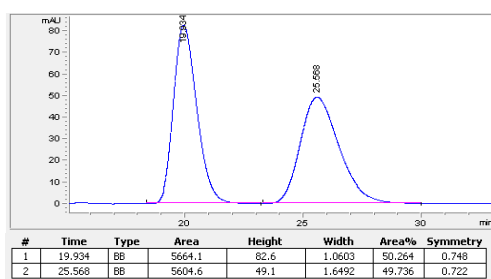
**HPLC:** Enantiomeric excess was determined by HPLC with a Chiralpak® IG column (99.5:0.5 hexane:IPA, 1.0 mL min<sup>-1</sup>, 210 nm, room temperature); t<sub>r</sub> (major) = 27.4 min, t<sub>r</sub> (minor) = 35.4 min, 98:2 e.r.).



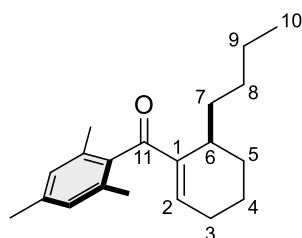
**Control experiment:** enantioenriched (6-butylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone (63 mg, 0.20 mmol, 1.0 equiv.) was subjected to **General procedure 5B** and recovered as a white solid **4g** (44 mg, 70% yield).



**HPLC:** Enantiomeric excess was determined by HPLC with a Chiralpak® IG column (99.5:0.5 hexane:IPA, 1.0 mL min<sup>-1</sup>, 210 nm, room temperature);  $t_r$  (major) = 19.7 min,  $t_r$  (minor) = 25.5 min, 96:4 e.r.).



### (6-Butylcyclohex-1-en-1-yl)(mesityl)methanone, **4h**



**Racemic:** **3h** (60.5 mg, 0.20 mmol, 1.0 equiv.),  $\text{Al}(\text{O}^t\text{Bu})_3$  (49.3 mg, 0.20 mmol, 1.0 equiv.), and toluene (0.2 M, 1.0 mL) were subjected to **General Procedure 4**. The title compound was afforded after purification by FCC (Pentane:Et<sub>2</sub>O, 98:2) as a colourless oil **4h** (37.0 mg, 65% yield).

**Enantioenriched:** (*R*)-3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol **L1** (128 mg, 0.20 mmol, 1.0 equiv.), *tert*-butanol (14.8 mg, 0.20 mmol, 1.0 equiv.), *m*-xylene (1.0 mL, 0.2 M),  $\text{AlMe}_3$  in toluene (2.0 M, 0.1 mL, 0.20 mmol, 1.0 equiv.), and **3h** (60.5 mg, 0.20 mmol, 1.0 equiv.) were subjected to **General Procedure 5A**. Purification by column chromatography (Pentane:Et<sub>2</sub>O, 98:2) afforded the title compound **4h** as a colourless oil (50.5 mg, 89% yield).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  6.81 (s, 2H, ArH), 6.45 (t,  $J$  = 3.9 Hz, 1H, H-2), 2.90 – 2.78 (m, 1H, H-6), 2.28 (s, 3H, 3×ArCH<sub>3</sub>), 2.22 – 2.12 (m, 2H), 2.10 (s, 6H, 2×ArCH<sub>3</sub>), 1.88-1.78 (m, 1H), 1.74 – 1.57 (m, 3H), 1.54 – 1.36 (m, 4H), 1.35 – 1.29 (m, 1H), 1.25 – 1.19 (m, 1H), 0.93 (t,  $J$  = 6.8 Hz, 3H, H-10).

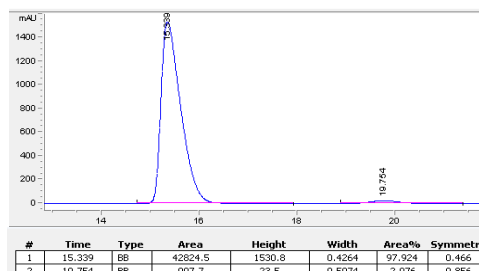
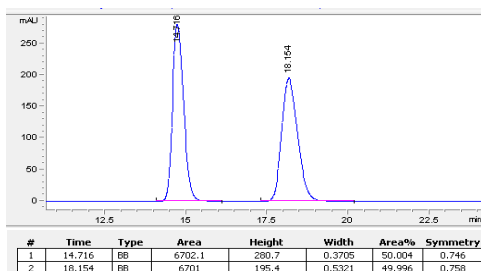
$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  201.7 (C-11), 145.7 (C-2), 145.0 (C1), 137.8 (ArC), 137.8 (ArC), 134.3 (ArC), 128.2 (ArC), 32.8, 31.2, 30.2, 26.6, 25.09, 22.9, 21.2, 19.3 (ArCH<sub>3</sub>), 17.2 (ArCH<sub>3</sub>), 14.3 (C-10).

HRMS (ESI<sup>+</sup>): Found  $[\text{M}+\text{Na}]^+ = 307.2046$ ;  $\text{C}_{20}\text{H}_{28}\text{ONa}$  requires 307.2032  $\Delta$  4.44 ppm.

IR (film)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 2926, 2855, 1654, 1629, 1612, 1457, 1262.

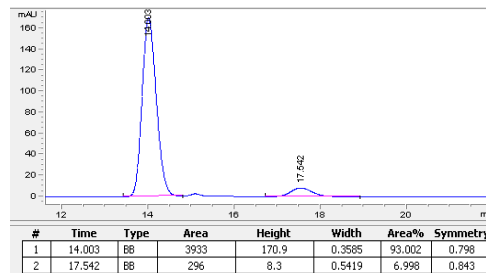
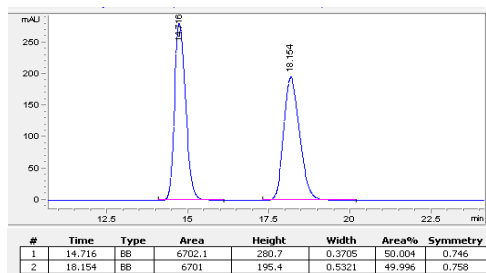
$[\alpha]_{\text{D}}^{20} = -66.6$  ( $c = 0.4$ ,  $\text{CHCl}_3$ ).

HPLC: Enantiomeric excess was determined by HPLC with a Chiralpak<sup>®</sup> IG column (99.5:0.5 hexane:IPA, 1.0 mL  $\text{min}^{-1}$ , 210 nm, room temperature);  $t_{\text{r}}$  (major) = 15.3 min,  $t_{\text{r}}$  (minor) = 19.7 min, 98:2 e.r.).

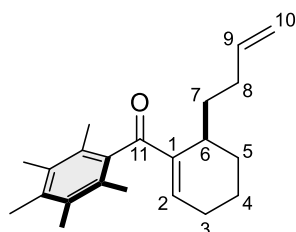


**Enantioenriched:** (*R*)- 3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol **L1** (77 mg, 0.12 mmol, 0.6 equiv.), toluene (0.2 M, 1 mL),  $\text{AlMe}_3$  in toluene (1.0 M, 0.08 mL, 0.08 mmol, 0.4 equiv.) and **3h** (60.5 mg, 0.20 mmol, 1 equiv.) were subjected to **General procedure 5B**. Purification by column chromatography (Pentane:Et<sub>2</sub>O, 98:2) afforded the title compound as a white solid **4h** (41.5 mg, 73% yield).

HPLC: Enantiomeric excess was determined by HPLC with a Chiralpak<sup>®</sup> IG column (99.5:0.5 hexane:IPA, 1.0 mL  $\text{min}^{-1}$ , 210 nm, room temperature);  $t_{\text{r}}$  (major) = 14.0 min,  $t_{\text{r}}$  (minor) = 17.5 min, 93:7 e.r.).



### (6-(But-3-en-1-yl)cyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, **4i**



**Racemic:** *tert*-Butanol (22 mg, 0.30 mmol, 3.0 equiv.), toluene (0.2 M, 0.5 mL),  $\text{AlMe}_3$  in toluene (1.0 M, 0.10 mL, 0.10 mmol, 1.0 equiv.) and **3i** (66 mg, 0.20 mmol, 1.0 equiv.) were subjected to **General procedure 4**. Purification

by column chromatography (Pentane:Et<sub>2</sub>O, 98:2) afforded the title compound **4i** as a white solid (30 mg, 50% yield).

**Enantioenriched:** (*R*)-3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol **L1** (128 mg, 0.20 mmol, 1.0 equiv.), *tert*-butanol (14.8 mg, 0.20 mmol, 1.0 equiv.), *m*-xylene (1.0 mL, 0.2 M), AlMe<sub>3</sub> in toluene (2.0 M, 0.1 mL, 0.20 mmol, 1.0 equiv.) and **3i** (66 mg, 0.20 mmol, 1.0 equiv.) were subjected to **General procedure 5A**. Purification by column chromatography (Pentane:Et<sub>2</sub>O, 98:2) afforded the title compound **4i** as a white solid (57 mg, 87% yield, 90.5:9.5 e.r.).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.40 (t, *J* = 3.9 Hz, 1H, H-2), 5.84 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H, H-9), 5.00 (m, 1H, H-10), 4.91 (dd, *J* = 10.1, 2.4, 1H, H-10'), 2.81 (m, 1H, H-6), 2.16 (m, 5H, H-8, 3×ArCH<sub>3</sub>), 2.12 – 1.99 (m, 8H, H-3, 6×ArCH<sub>3</sub>), 1.95 (s, 3H, 3×ArCH<sub>3</sub>), 1.93 (s, 3H, 3×ArCH<sub>3</sub>), 1.81 (m, 2H, H-5, H-7), 1.64 – 1.51 (m, 2H, H-4), 1.42 (tt, *J* = 18.4, 5.8 Hz, 1H, H-5'), 1.34 – 1.11 (m, 1H, H-7').

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 202.7 (C-11), 146.2 (C-2), 144.7 (ArC), 139.0 (C-9), 138.2 (ArC), 134.8 (C-1), 132.5 (ArC), 132.5 (ArC'), 129.3 (ArC), 129.1 (ArC'), 114.4 (C-10), 32.08 (C-8), 32.1 (C-7), 30.7 (C-6), 26.4 (C-3), 24.8 (C-5), 17.4 (ArCH<sub>3</sub>), 17.2 (ArCH<sub>3</sub>'), 16.9 (C-4), 16.7 (ArCH<sub>3</sub>), 16.0 (ArCH<sub>3</sub>), 15.9 (ArCH<sub>3</sub>').

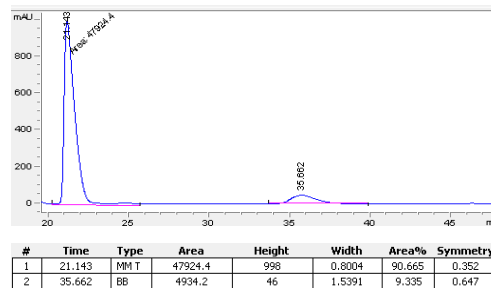
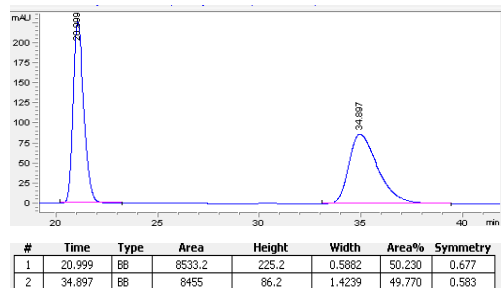
IR (film) ν<sub>max</sub>/cm<sup>-1</sup>: 2933, 2858, 1653, 1630, 1452, 1420.

HRMS (ESI+): Found [M+K]<sup>+</sup> = 349.1932; C<sub>22</sub>H<sub>30</sub>OK requires 349.1928, Δ 1.08 ppm.

m.p.: 82-84 °C.

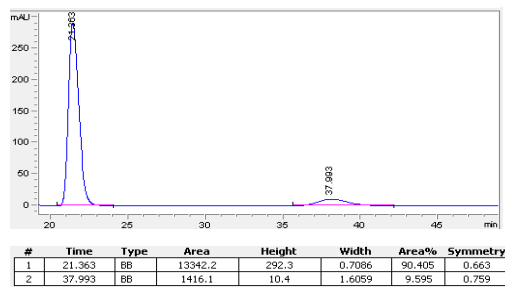
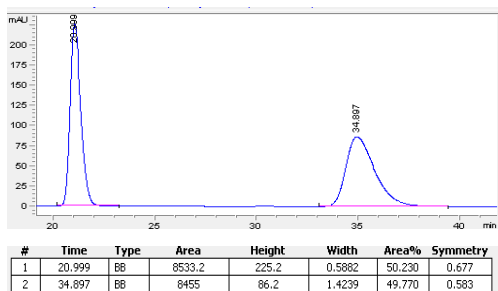
[α]<sub>D</sub><sup>20</sup> = + 27.0 (c = 0.7, CHCl<sub>3</sub>).

**HPLC:** Enantiomeric excess was determined by HPLC with a Chiralpak<sup>®</sup> IG column (99:1 hexane: IPA, 1.0 ml min<sup>-1</sup>, 254 nm, room temperature); t<sub>r</sub> (minor) = 21.1 min, t<sub>r</sub> (major) = 35.7 min, 90.5:9.5 e.r.



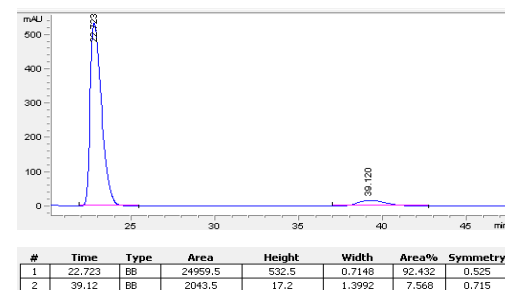
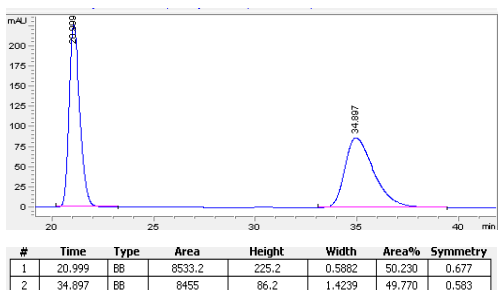
**Enantioenriched:** (*R*)-3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol **L1** (77 mg, 0.12 mmol, 0.6 equiv.), toluene (0.2 M, 1 mL), AlMe<sub>3</sub> in toluene (1.0 M, 0.080 mL, 0.080 mmol, 0.4 equiv.) and **3i** (66 mg, 0.20 mmol, 1.0 equiv.) were subjected to **General procedure 5B**. Purification by column chromatography (Pentane:Et<sub>2</sub>O, 98:2) afforded the title compound **4i** as a white solid (47 mg, 74% yield, 90.5:9.5 e.r.).

**HPLC:** Enantiomeric excess was determined by HPLC with a Chiralpak<sup>®</sup> IG column (99:1 hexane: IPA, 1.0 ml min<sup>-1</sup>, 254 nm, room temperature); t<sub>r</sub> (minor) = 21.4 min, t<sub>r</sub> (major) = 38.0 min, 90.5:9.5 e.r.

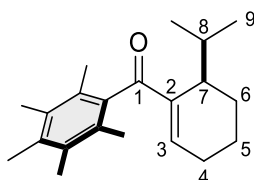


**Enantioenriched:** (*R*)- 3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol **L1** (77 mg, 0.12 mmol, 0.6 equiv.), toluene (0.2 M, 1 mL), AlMe<sub>3</sub> in toluene (1.0 M, 0.080 mL, 0.080 mmol, 0.4 equiv.) and **3i** (66 mg, 0.20 mmol, 1.0 equiv.) were subjected to **General procedure 5C**. Purification by column chromatography (Pentane:Et<sub>2</sub>O, 98:2) afforded the title compound **4i** as a white solid (43 mg, 70% yield, 92.5:7.5 e.r.).

**HPLC:** Enantiomeric excess was determined by HPLC with a Chiralpak<sup>®</sup> IG column (99:1 hexane: IPA, 1.0 ml min<sup>-1</sup>, 254 nm, room temperature); t<sub>r</sub> (minor) = 22.7 min, t<sub>r</sub> (major) = 39.1 min, 92.5:7.5 e.r.



### (6-Isopropylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone **4j**



**Racemic:** *tert*-Butanol (22 mg, 0.30 mmol, 3.0 equiv.), toluene (0.2 M, 0.5 ml), AlMe<sub>3</sub> in toluene (1.0 M, 0.1 mL, 0.1 mmol, 1.0 equiv.) and mixture of *E/Z* (5:1) 7-hydroxy-3-isopropyl-1-(2,3,4,5,6-pentamethylphenyl)hept-2-en-1-one (32 mg, 0.10 mmol, 1.0 equiv.) were subjected to **General procedure 4**. Purification by column chromatography (Pentane:Et<sub>2</sub>O, 98:2) afforded the title compound as a colourless oil (5.4 mg, 0.017 mmol, 17%).

**Enantioenriched A:** (*R*)-3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol **L1** (128 mg, 0.20 mmol, 1.0 equiv.), *tert*-butanol (14.8 mg, 0.20 mmol, 1.0 equiv.), *m*-xylene (1.0 mL, 0.2 M), AlMe<sub>3</sub> in toluene (2.0 M, 0.1 mL, 0.20 mmol, 1.0 equiv.) and **3j** (63 mg, 0.20 mmol, 1.0 equiv.) were subjected to **General procedure 5A**. Purification by column chromatography (Pentane:Et<sub>2</sub>O, 98:2) afforded the title compound **4j** as a white solid (41 mg, 68% yield, 91:9 e.r.).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.63 (t, *J* = 4.2 Hz, 1H, H-3), 2.84 (q, *J* = 5.2 Hz, 1H, H-7), 2.41 – 2.28 (m, 1H, H-8), 2.24 (s, 3H, 3×ArCH<sub>3</sub>), 2.18 (s, 6H, 6×ArCH<sub>3</sub>), 2.16 – 2.09 (m, 2H, H-4), 2.06 (s, 3H, 3×ArCH<sub>3</sub>), 2.00 (s, 3H, 3×ArCH<sub>3</sub>), 1.81 (ddt, *J* = 12.8, 9.2, 4.9 Hz, 1H, H-6), 1.71 (qd, *J* = 10.1, 4.4 Hz, 1H, H-5), 1.62 – 1.45 (m, 2H, H-5', H-6'), 1.07 (d, *J* =

6.9 Hz, 3H, H-9), 0.88 (d,  $J$  = 6.9, 3H, H-9).

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  203.1 (C-1), 148.3 (C-3), 143.8 (ArC), 138.6 (ArC), 134.7 (C-2), 132.5 (ArC), 129.12 (ArC), 128.9 (ArC') 36.8 (C-7), 29.5 (C-8), 26.2 (C-4), 22.5 (C-6), 21.6 (C-9), 19.3 (C-5), 18.8 (C-9'), 17.4 (ArCH<sub>3</sub>), 17.3 (ArCH<sub>3</sub>'), 16.7 (ArCH<sub>3</sub>), 16.0 (ArCH<sub>3</sub>), 16.0 (ArCH<sub>3</sub>').

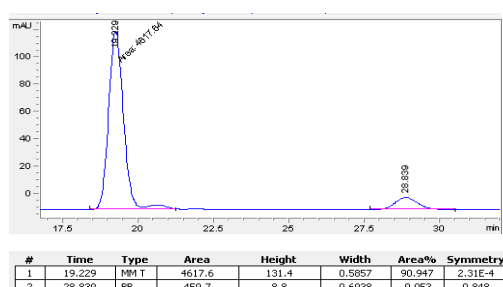
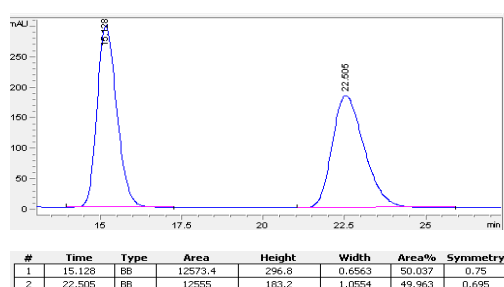
IR (film)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 2947, 2870, 1710, 1662, 1462, 1358.

HRMS (ESI+): Found  $[\text{M}+\text{H}]^+ = 299.2366$ ;  $\text{C}_{21}\text{H}_{31}\text{O}$  requires 299.2369,  $\Delta$  -1.23 ppm.

m.p.: 100 - 102 °C.

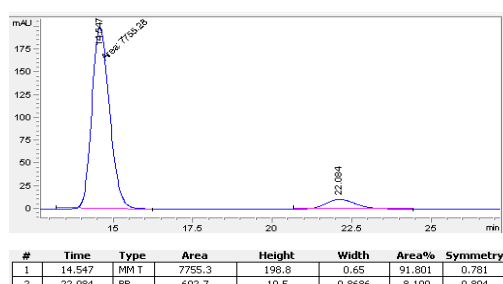
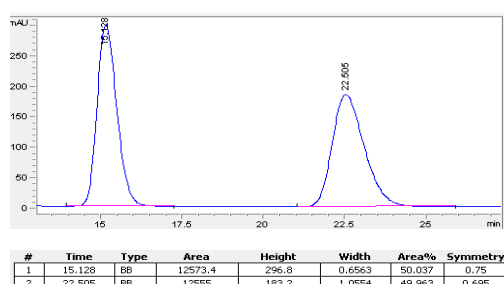
$[\alpha]_{\text{D}}^{20} = -30.7$  ( $c = 0.3$ ,  $\text{CHCl}_3$ ).

**HPLC:** Enantiomeric excess was determined by HPLC with a Chiralpak<sup>®</sup> IG column (99:1 hexane: IPA, 1.0 ml min<sup>-1</sup>, 254 nm, room temperature);  $t_r$  (minor) = 19.2 min,  $t_r$  (major) = 28.8 min, 91:9 e.r.



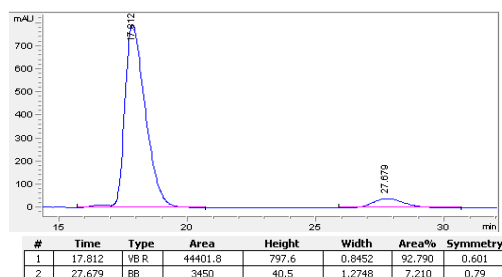
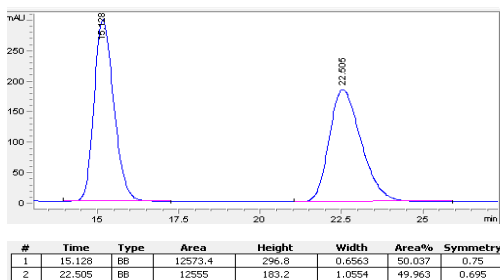
**Enantioenriched B:** (*R*)- 3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol (77 mg, 0.12 mmol, 0.6 equiv.), toluene (0.2 M, 1 ml),  $\text{AlMe}_3$  in toluene (1.0 M, 0.08 mL, 0.08 mmol, 0.4 equiv.) and **3j** (63 mg, 0.20 mmol, 1.0 equiv.) were subjected to **General procedure 5B**. Purification by column chromatography (Pentane:Et<sub>2</sub>O, 98:2) afforded the title compound **4j** as a colourless oil (40 mg, 67% yield, 92:8 e.r.).

**HPLC:** Enantiomeric excess was determined by HPLC with a Chiralpak<sup>®</sup> IG column (99:1 hexane:IPA, 1.0 mL min<sup>-1</sup>, 210 nm, room temperature);  $t_r$  (major) = 14.5 min,  $t_r$  (minor) = 22.1 min, 92:8 e.r.).

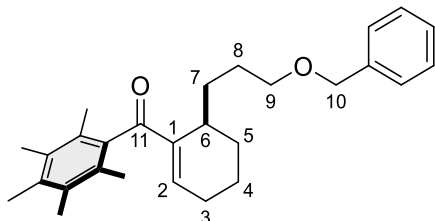


**Enantioenriched C:** (*R*)- 3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol **L1** (77 mg, 0.12 mmol, 0.6 equiv.), toluene (0.2 M, 1 ml),  $\text{AlMe}_3$  in toluene (1.0 M, 0.08 mL, 0.08 mmol, 0.4 equiv.) and **3j** (63 mg, 0.20 mmol, 1.0 equiv.) were subjected to **General procedure 5C**. Purification by column chromatography (Pentane:Et<sub>2</sub>O, 98:2) afforded the title compound **4j** as a colourless oil (35 mg, 58% yield, 93:7 e.r.).

**HPLC:** Enantiomeric excess was determined by HPLC with a Chiralpak<sup>®</sup> IG column (99:1 hexane:IPA, 1.0 mL min<sup>-1</sup>, 210 nm, room temperature);  $t_r$  (major) = 14.5 min,  $t_r$  (minor) = 22.1 min, 93:7 e.r.).



### (6-(3-(Benzyloxy)propyl)cyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, **4k**



**Racemic:** *tert*-Butanol (22 mg, 0.30 mmol, 3 equiv.), toluene (0.2 M, 0.5 ml), AlMe<sub>3</sub> in toluene (1.0 M, 0.10 mL, 0.10 mmol, 1.0 equiv.) and mixture of E/Z (1:1) **S20** (84 mg, 0.20 mmol, 1.0 equiv.) were subjected to **General procedure 4**. Purification by column chromatography (Pentane:Et<sub>2</sub>O, 98:2) afforded the title compound **4k** as a colourless oil (25 mg, 31% yield).

**Enantioenriched:** (*R*)-3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol **L1** (128 mg, 0.20 mmol, 1.0 equiv.), *tert*-butanol (14.8 mg, 0.20 mmol, 1.0 equiv.), *m*-xylene (1.0 mL, 0.2 M), AlMe<sub>3</sub> in toluene (2.0 M, 0.1 mL, 0.20 mmol, 1.0 equiv.), and **3k** (84 mg, 0.20 mmol, 1.0 equiv.) were subjected to **General Procedure 5A**. Purification by column chromatography (Pentane:Et<sub>2</sub>O, 95:5) afforded the title compound **4k** as a white solid (54 mg, 67% yield, 96.5:3.5 e.r.).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.33 – 7.16 (m, 5H, 5×ArH), 6.40 (t, *J* = 3.9 Hz, 1H, H-2), 4.46 (s, 2H, H-10), 3.57 – 3.38 (m, 2H, H-9), 2.83 – 2.75 (m, 1H, H-6), 2.16 (s, 3H, 3×ArCH<sub>3</sub>), 2.10 (s, 6H, 6×ArCH<sub>3</sub>), 2.10 – 2.02 (m, 2H, H-3), 1.95 (s, 3H, 3×ArCH<sub>3</sub>), 1.93 (s, 3H, 3×ArCH<sub>3</sub>), 1.82 – 1.61 (m, 3H, H-7, H-8), 1.59 – 1.50 (m, 2H, H-4), 1.48 – 1.12 (m, 3H, H-5, H-7').

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 202.8 (C-11), 146.3 (C-2), 144.7 (ArC), 138.8 (ArC), 138.2 (ArC), 134.8 (ArC), 132.5 (ArC), 129.3 (ArC), 129.1 (ArC'), 128.3 (ArC), 127.7 (ArC), 127.4 (C-1), 72.8 (C-10), 70.7 (C-9), 31.0 (C-6), 29.3 (C-5), 28.1 (C-8), 26.4 (C-3), 25.0 (C-7), 17.4 (ArCH<sub>3</sub>), 17.2 (ArCH<sub>3</sub>'), 17.0 (C-4), 16.7 (ArCH<sub>3</sub>), 16.0 (ArCH<sub>3</sub>), 15.9 (ArCH<sub>3</sub>').

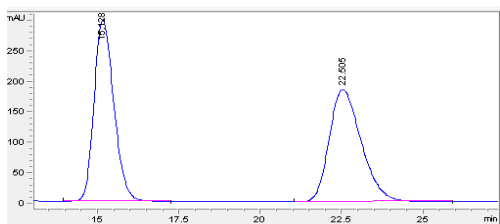
IR (film)  $\nu_{\max}$ /cm<sup>-1</sup>: 2978, 2923, 1660, 1423, 1336, 1197.

HRMS (ESI<sup>+</sup>): Found [M+H]<sup>+</sup> = 405.2782; C<sub>28</sub>H<sub>37</sub>O<sub>2</sub> requires 405.2788, Δ -1.50 ppm.

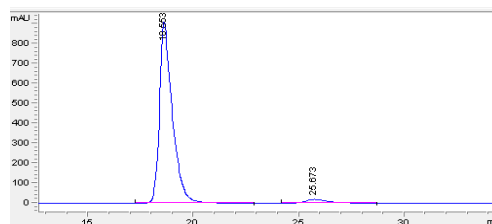
m.p.: 64 - 65 °C.

[α]<sub>D</sub><sup>20</sup> = -40.0 (c = 0.1, CHCl<sub>3</sub>).

**HPLC:** Enantiomeric excess was determined by HPLC with a Chiralpak® IA column (99.5:0.5 hexane: IPA, 1.0 ml min<sup>-1</sup>, 254 nm, room temperature); t<sub>r</sub> (minor) = 18.6 min, t<sub>r</sub> (major) = 25.7 min, 96.5:3.5 e.r.



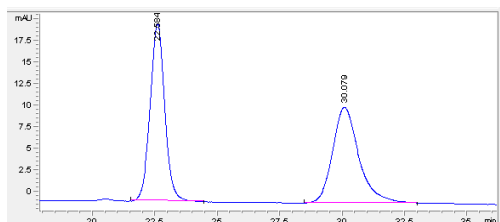
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	15.128	BB	12573.4	296.8	0.6563	50.037	0.75
2	22.505	BB	12555	183.2	1.0554	49.963	0.695



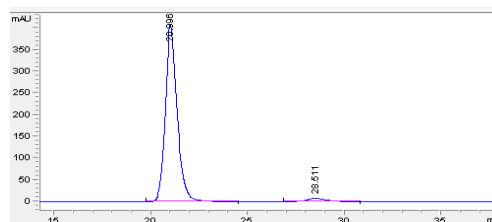
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	18.553	BB	38268.7	910.4	0.5944	96.356	0.502
2	25.673	BB	1447.3	19.1	1.0467	3.644	0.618

**Enantioenriched:** (*R*)-3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol **L1** (77 mg, 0.12 mmol, 0.6 equiv.), toluene (0.2 M, 1 ml), AlMe<sub>3</sub> in toluene (1.0 M, 0.080 mL, 0.08 mmol, 0.4 equiv.) and **3k** (84 mg, 0.20 mmol, 1.0 equiv.) were subjected to **General procedure 5C**. Purification by column chromatography (Pentane:Et<sub>2</sub>O, 95:5) afforded the title compound **4k** as a white solid (28 mg, 35% yield, 97:3 e.r.) and RSM is (29 mg, 35% yield).

**HPLC:** Enantiomeric excess was determined by HPLC with a Chiralpak® IA column (99.5:0.5 hexane: IPA, 1.0 ml min<sup>-1</sup>, 254 nm, room temperature); t<sub>r</sub> (minor) = 21.0 min, t<sub>r</sub> (major) = 28.5 min, 97:3 e.r.



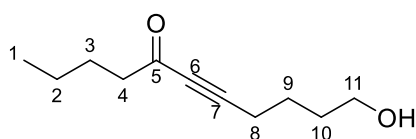
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	22.584	BB	836.9	20.6	0.6132	50.750	0.999
2	30.079	BB	812.2	11.1	0.9307	49.250	0.784



#	Time	Type	Area	Height	Width	Area%	Symmetry
1	20.996	BB	17333.1	410.9	0.6202	96.847	0.744
2	28.511	BB	564.3	7.8	0.8711	3.153	0.812

### 3.4 Synthesis of alkylketone substrate **3l** and cyclohexene **4l**

#### 11-Hydroxyundec-6-yn-5-one **S21**



*n*-BuLi in hexanes (14.4 mL, 2.5 M, 36.0 mmol, 2.4 equiv.) was added dropwise to a solution of 5-hexyn-1-ol (1.77 g, 18.0 mmol, 1.2 equiv.) in THF (0.3 M, 50 mL) at -78 °C. The reaction mixture was stirred for 1 h, after which a solution of *N*-methoxy-*N*-methylpentanamide (2.18 g, 15.0 mmol, 1.0 equiv.) in THF (3.0 M) was added dropwise. The mixture was then warmed to RT and stirred for a further 1 h. The reaction was quenched by the addition of saturated aqueous ammonium chloride and extracted with EtOAc. The combined organic phases were dried over MgSO<sub>4</sub>, filtered and concentrated *in vacuo*. The title compound was afforded after purification by FCC (20→60% EtOAc/Pentane) as a yellow oil (1.92 g, 10.5 mmol, 70% yield).

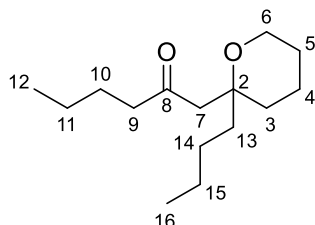
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 3.72 – 3.64 (m, 2H, H<sub>11</sub> x 2), 2.52 (t, *J* = 7.5 Hz, 2H, H<sub>4</sub> x 2), 2.47 – 2.37 (m, 2H, H<sub>8</sub> x 2), 1.75 – 1.56 (m, 6H, H<sub>9</sub> x 2, H<sub>10</sub> x 2, H<sub>3</sub> x 2), 1.46 (s, 1H, OH), 1.41 – 1.27 (m, 2H, H<sub>2</sub> x 2), 0.91 (t, *J* = 7.5 Hz, 3H, H<sub>1</sub> x 3).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 188.7 (C<sub>5</sub>), 93.7 (C<sub>7</sub>), 81.3 (C<sub>6</sub>), 62.3 (C<sub>11</sub>), 45.4 (C<sub>4</sub>), 31.8 (C<sub>10</sub>), 26.3 (C<sub>3</sub>), 24.3 (C<sub>9</sub>), 22.3 (C<sub>2</sub>), 18.9 (C<sub>8</sub>), 13.9 (C<sub>1</sub>).

HRMS (ESI<sup>+</sup>): Found [M+H]<sup>+</sup> = 183.1383; C<sub>11</sub>H<sub>19</sub>O<sub>2</sub> requires 183.1380 Δ 1.85 ppm

IR (film) ν<sub>max</sub>/cm<sup>-1</sup>: 3432, 2980, 2214, 1672, 1618, 1461.

### 1-(2-Butyltetrahydro-2H-pyran-2-yl)hexan-2-one **3l**



*n*-BuLi in hexanes (2.5 M, 13.2 mL, 3.0 mmol, 6.0 equiv.) was added dropwise to a solution of CuI (3.13 g, 16.5 mmol, 3.0 equiv.) in THF (0.3 M, 55 mL) at -78 °C. The reaction mixture was warmed to 0 °C and stirred for 1 h, affording a black precipitate. The mixture was cooled to -78 °C and a solution of 11-hydroxyundec-6-yn-5-one **S21** (1.00 g, 5.49 mmol, 1.0 equiv.) in THF (1.0 M, 4 mL) was added dropwise and stirred for 30 min. The reaction was quenched by the addition of saturated aqueous ammonium chloride (50 mL) and warmed to RT. The reaction was treated with 35% aqueous ammonium hydroxide solution (50 mL), affording a clear blue aqueous phase. The solution was extracted with EtOAc (3 x 100 mL), and the combined organic phases were washed with HCl (1.0 M, 100 mL), dried over MgSO<sub>4</sub>, filtered, and concentrated *in vacuo*. The title compound was afforded after purification by FCC (5% Et<sub>2</sub>O/pentane) as a yellow oil (536 mg, 2.23 mmol, 41% yield).

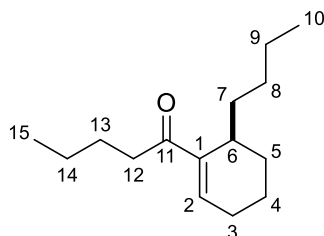
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 3.69 – 3.60 (m, 2H, H<sub>6</sub> x 2), 2.60 (d, *J* = 2.5 Hz, 2H, H<sub>7</sub> x 2), 2.47 (td, *J* = 7.0, 1.0 Hz, 2H, H<sub>9</sub> x 2), 1.74 – 1.45 (m, 10H, H<sub>3</sub> x 2, H<sub>4</sub> x 2, H<sub>13</sub> x 2, H<sub>10</sub> x 2, H<sub>5</sub> x 2), 1.38 – 1.10 (m, 6H, H<sub>14</sub> x 2, H<sub>11</sub> x 2, H<sub>15</sub> x 2), 0.94 – 0.84 (m, 6H, H<sub>12</sub> x 3, H<sub>16</sub> x 3).

<sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 210.5 (C<sub>8</sub>), 74.9 (C<sub>2</sub>), 61.5 (C<sub>6</sub>), 49.2 (C<sub>7</sub>), 44.7 (C<sub>9</sub>), 35.1 (C<sub>3</sub>), 33.4 (C<sub>13</sub>), 25.9 (C<sub>5</sub> or C<sub>10</sub>), 25.8 (C<sub>5</sub> or C<sub>10</sub>), 25.4 (C<sub>14</sub>), 23.3 (C<sub>15</sub>), 22.4 (C<sub>11</sub>), 19.2 (C<sub>4</sub>), 14.2 (C<sub>12</sub> or C<sub>16</sub>), 14.0 (C<sub>12</sub> or C<sub>16</sub>).

HRMS (ESI<sup>+</sup>): Found [M+H]<sup>+</sup> = 241.2161; C<sub>15</sub>H<sub>29</sub>O<sub>2</sub> requires 241.2162 Δ -0.34 ppm.

IR (film) ν<sub>max</sub>/cm<sup>-1</sup>: 2957, 2871, 1709, 1460, 1379, 1284.

### 1-(6-Butylcyclohex-1-en-1-yl)pentan-1-one **4l**



**Racemic:** 1-(2-Butyltetrahydro-2H-pyran-2-yl)hexan-2-one **3l** (48.1 mg, 0.200 mmol, 1.0 equiv.), Al(*Ot*-Bu)<sub>3</sub> (49.3 mg, 0.200 mmol, 1.0 equiv.), and PhMe (0.2 M, 1.0 mL) were subjected to **General Procedure 4**. The title

compound was afforded after purification by FCC (5% Et<sub>2</sub>O/pentane) as a colourless oil (32.2 mg, 0.145 mmol, 72% yield).

**Enantioenriched:** (*R*)-3,3'-di(anthracen-9-yl)-[1,1'-binaphthalene]-2,2'-diol **L1** (128 mg, 0.200 mmol, 1.0 equiv.), *tert*-butanol (14.8 mg, 0.200 mmol, 1.0 equiv.), *m*-xylene (1.0 mL, 0.2 M), AlMe<sub>3</sub> in PhMe (2.0 M, 0.1 mL, 0.200 mmol, 1.0 equiv.), and 1-(2-butyltetrahydro-2*H*-pyran-2-yl)hexan-2-one **3I** (48.1 mg, 0.200 mmol, 1.0 equiv.) were subjected to **General Procedure 5A**. The title compound was afforded after purification by FCC (3% Et<sub>2</sub>O/pentane) as a colourless oil (30.1 mg, 0.135 mmol, 68% yield).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.78 (s, 1H, H<sub>2</sub>), 2.70 – 2.50 (m, 3H, H<sub>6</sub>, H<sub>12</sub> x 2), 2.31 – 2.10 (m, 2H, H<sub>3</sub> x 2), 1.77 – 1.67 (m, 1H, H<sub>5a</sub>), 1.67 – 1.53 (m, 4H, H<sub>4</sub> x 2, H<sub>13</sub> x 2), 1.51 – 1.06 (m, 9H, H<sub>5b</sub>, H<sub>7</sub> x 2, H<sub>8</sub> x 2, H<sub>9</sub> x 2, H<sub>14</sub> x 2), 0.95 – 0.84 (m, 6H, H<sub>10</sub> x 3, H<sub>15</sub> x 3).

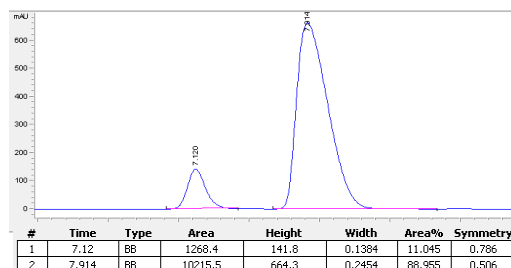
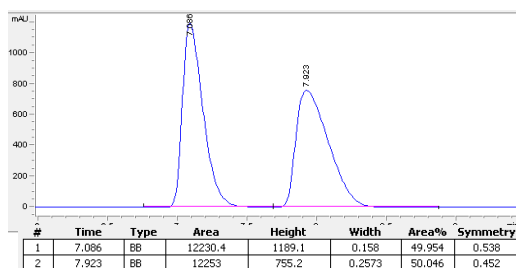
<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 202.1 (C<sub>11</sub>), 144.4 (C<sub>1</sub>), 138.9 (C<sub>2</sub>), 37.5 (C<sub>12</sub>), 33.3 (C<sub>7</sub>), 31.6 (C<sub>6</sub>), 30.1 (C<sub>8</sub>), 27.2 (C<sub>13</sub>), 26.2 (C<sub>3</sub>), 25.4 (C<sub>5</sub>), 22.9 (C<sub>14</sub> or C<sub>9</sub>), 22.7 (C<sub>14</sub> or C<sub>9</sub>), 17.3 (C<sub>4</sub>), 14.2 (C<sub>15</sub> or C<sub>10</sub>), 14.1 (C<sub>15</sub> or C<sub>10</sub>).

**HRMS** (ESI<sup>+</sup>): Found [M+H]<sup>+</sup> = 223.2054; C<sub>15</sub>H<sub>27</sub>O requires 223.2056 Δ -1.16 ppm.

**IR** (film) ν<sub>max</sub>/cm<sup>-1</sup>: 2957, 2933, 2872, 1671, 1464, 1381.

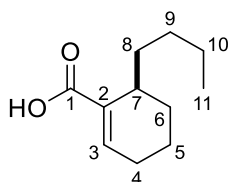
[α]<sub>D</sub><sup>25</sup> = -5.86 (c = 1.0, CHCl<sub>3</sub>).

**HPLC:** Enantiomeric excess was determined by HPLC with a Chiralpak® IG column (99.5:0.5 hexane:IPA, 1.0 mL min<sup>-1</sup>, 230 nm, room temperature); t<sub>r</sub> (minor) = 7.12 min, t<sub>r</sub> (major) = 7.91 min, 11:89 e.r.



### 3.5 Derivatization of the Acyl Cyclohexenes

#### 6-Butylcyclohex-1-ene-1-carboxylic acid, **5**



A 2–5 mL Biotage® microwave vial was charged with **4g** (31 mg, 0.10 mmol, 1.0 equiv.), hexafluoroisopropanol (0.88 mL) and 37% aq. HCl (12 M, 0.13 mL). The reaction vessel was sealed with a microwave vial cap (containing a Reseal™ septum) and heated at 65 °C for 15 h. The reaction was then cooled to RT, diluted with water (5 ml) and extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 10 mL), dried over MgSO<sub>4</sub>, filtered and concentrated in vacuo. Purification by column chromatography (CH<sub>2</sub>Cl<sub>2</sub>:MeOH, 98:2) afforded the title compound **5** as brown oil (15 mg, 81% yield).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.07 (t, *J* = 4.0 Hz, 1H, H-3), 2.53 (tt, *J* = 6.6, 3.1 Hz, 1H, H-7), 2.38 – 1.94 (m, 2H, H-4), 1.80 – 1.70 (m, 1H, H-6), 1.70 – 1.46 (m, 4H, H-6', H-8, H-9), 1.46 – 1.16 (m, 5H, H-5, H-8', H-10), 0.97 – 0.82 (m, 3H, H-11).

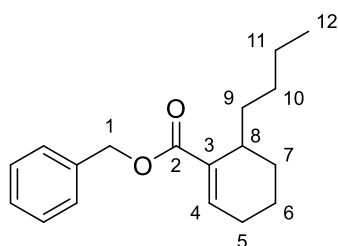
**<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) δ 173.2 (C-1), 142.1 (C-3), 134.5 (C-2), 33.1 (C-8), 32.4 (C-7), 29.9 (C-5 or C-9), 26.1 (C-4), 25.2 (C-6), 22.8 (C-5 or C-9), 17.0 (C-10), 14.1 (C-11).

**IR** (film)  $\nu_{\max}/\text{cm}^{-1}$ : 2933, 1683, 1638, 1421, 1273, 1155.

**HRMS** (ESI<sup>+</sup>): Found  $[\text{M}+\text{H}]^+ = 183.1377$ ; C<sub>11</sub>H<sub>19</sub>NO<sub>2</sub> requires 183.1380 Δ -1.40 ppm.

$[\alpha]_{\text{D}}^{20} = -30.0$  (c = 0.1, CHCl<sub>3</sub>).

### Benzyl 6-butylcyclohex-1-ene-1-carboxylate, **S22**



To a solution of **5** (8.0 mg, 0.040 mmol, 1.0 equiv) in anhydrous EtOH (0.5 mL) was added Cs<sub>2</sub>CO<sub>3</sub> (7.8 mg, 0.024 mmol, 0.6 equiv) and the mixture was stirred at RT for 15 min. Benzyl bromide (5 μL, 0.044 mmol, 1.1 equiv) was then added, and the reaction mixture was stirred at RT for 16 h. The solvent was removed under reduced pressure, and the residue was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (2 × 10 mL), dried over MgSO<sub>4</sub>, and concentrated in vacuo. Purification by column chromatography (pentane/Et<sub>2</sub>O = 97:3) afforded the title compound **S22** as a yellow oil (6 mg, 55% yield).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.47 – 7.17 (m, 5H, 5×ArH), 6.98 (d, *J* = 3.5 Hz, 1H, H-4), 5.24 (d, *J* = 12.5 Hz, 1H, H-1), 5.16 (d, *J* = 12.5 Hz, 1H, H-1'), 2.58 (m, 1H, H-8), 2.29 – 2.07 (m, 2H, H-5), 1.80 – 1.69 (m, 1H, H-7), 1.65 – 1.47 (m, 4H, H-7', H-9, H-10), 1.44 – 1.16 (m, 5H, H-6, H-9', H-11), 0.95 – 0.83 (m, 3H, H-12).

**<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) δ 167.5 (C-2), 139.7 (C4), 136.4 (C-3), 135.0 (ArC), 128.4 (ArC), 128.0 (ArC), 128.0 (ArC), 65.9 (C-1), 33.2 (C-9), 32.7 (C-8), 29.9 (C-11), 25.9 (C-5), 25.4 (C-7), 22.7 (C-6), 17.1 (C-10), 14.0 (C12).

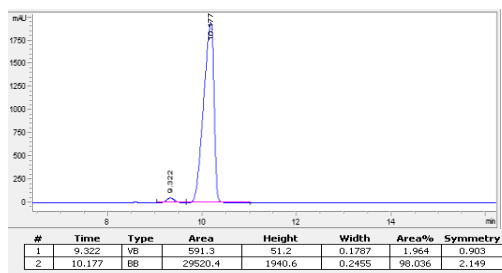
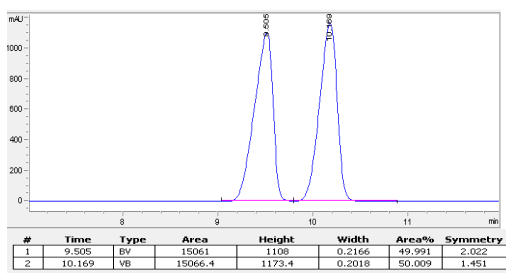
**IR** (film)  $\nu_{\max}/\text{cm}^{-1}$ : 3020, 2918, 2360, 1712, 1498, 1230.

**HRMS** (ESI<sup>+</sup>): Found  $[\text{M}+\text{Na}]^+ = 273.1848$ ; C<sub>18</sub>H<sub>24</sub>O<sub>2</sub> requires 273.1849 Δ -0.39 ppm.

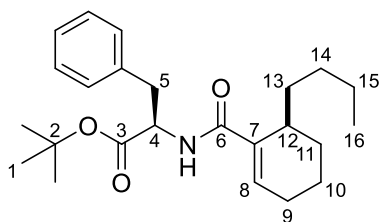
$[\alpha]_{\text{D}}^{20} = -50.4$  (c = 0.1, CHCl<sub>3</sub>)

To enable determination of the enantiomeric ratio of the title compound, a racemic sample was prepared following the same synthetic procedure.

**HPLC**: Enantiomeric excess was determined by HPLC with a Chiralpak® IG column (99.5:0.5 hexane: IPA, 1.0 ml min<sup>-1</sup>, 254 nm, room temperature); t<sub>r</sub> (minor) = 9.3 min, t<sub>r</sub> (major) = 10.2 min, 98:2 e.r.



### **tert-Butyl (6-butylcyclohex-1-ene-1-carbonyl)-D-phenylalaninate, 6**



A solution of **5** (18 mg, 0.10 mmol, 1 equiv.) in CH<sub>2</sub>Cl<sub>2</sub> (2 mL) was added to a solution of D-Phenylalanine tert-butyl ester hydrochloride (77 mg, 0.30 mmol, 3 equiv.) and DMAP (0.1 g, 0.8 mmol, 8 equiv.) in CH<sub>2</sub>Cl<sub>2</sub> (3 mL) at 25 °C. Then EDCI · HCl (77 mg, 0.40 mmol, 4 equiv.) was added and the mixture was stirred under inert conditions for 24 h. Saturated NaHCO<sub>3</sub> solution (10 mL) was added, the layers separated and the aqueous layer was extracted with chloroform (3 x 10 mL). The combined organic extracts were washed with brine (2 x 10 mL), dried (MgSO<sub>4</sub>) and the solvent was removed under reduced pressure. Purification by column chromatography (pentane:Et<sub>2</sub>O, 90:10) afforded the title compound as white solid (25 mg, 65% yield).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.33 – 7.24 (m, 3H, 3×ArH), 7.21 – 7.16 (m, 2H, 2×ArH), 6.37 (t, *J* = 3.9, 1H, H-8), 6.15 (d, *J* = 7.9 Hz, 1H, N-H), 4.84 (dt, *J* = 7.9, 6.0 Hz, 1H, H-4), 3.15 (d, *J* = 5.9 Hz, 2H, H-5), 2.54 (m, 1H, H-12), 2.14 – 2.07 (m, 2H, H-9), 1.75 – 1.60 (m, 4H, H-10, H-11), 1.43 (m, 10H, H-1, H-13), 1.38 – 1.17 (m, 5H, H-13', H-14, H-15), 0.93 – 0.85 (m, 3H, H-16).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 170.9 (C-4), 169.0 (C-6), 139.5 (ArC), 136.4 (C-7), 131.8 (C-8), 129.5 (ArC), 128.3 (ArC), 126.9 (ArC), 82.2 (C-2), 53.4 (C-4), 38.2 (C-5), 33.3 (C-13), 33.1 (C-6), 29.7 (C-14), 28.0 (C-1), 26.0 (C-11), 25.4 (C-9), 22.8 (C-15), 18.1 (C-10), 14.1 (C-16).

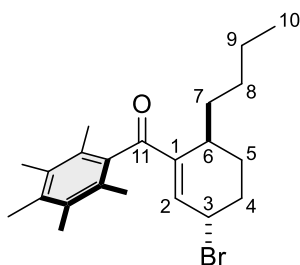
IR (film)  $\nu_{\max}/\text{cm}^{-1}$ : 2980, 2360, 1746, 1660, 1626, 1381.

HRMS (ESI<sup>+</sup>): Found [M+H]<sup>+</sup> = 386.2703; C<sub>24</sub>H<sub>36</sub>NO<sub>3</sub> requires 386.2690 Δ 3.44 ppm.

m.p.: 110-111 °C.

$[\alpha]_{\text{D}}^{20} = -72.0$  (c = 0.1, CHCl<sub>3</sub>).

### **(3-Bromo-6-butylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 7**



A stirred solution of **4g** (33 mg, 0.10 mmol, 1.0 equiv.) in CHCl<sub>3</sub> (1 mL) was cooled to -17 °C and Br<sub>2</sub> (5 μL, 1.0 equiv.) was added dropwise. The resulting solution was stirred at -17 °C for 15 min and then was warmed to RT and stirred for 3 h. The reaction mixture was concentrated *in vacuo*, and purification by column chromatography (Pentane:Et<sub>2</sub>O, 99:1) afforded the title compound **7** as a mixture of diastereomers (31.5 mg, 86%, 70:30 d.r.) as a white solid. NMR of the crude reaction mixture showed a ratio of 80:20 d.r. Careful chromatography allowed isolation of a small sample of the major diastereoisomer for X-ray analysis.

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) **Major diastereoisomer:** δ 6.42 (d, *J* = 4.7 Hz, 1H, H-2), 4.83 (td, *J* = 4.7, 1.8 Hz, 1H, H-3), 3.01 – 2.86 (m, 1H, H-6), 2.24 (s, 3H, 3×ArCH<sub>3</sub>), 2.18 (s, 6H, 6×ArCH<sub>3</sub>), 2.14 – 2.05 (m, 2H, ), 2.01 (brs, *J* = 5.6 Hz, 6H, 6×ArCH<sub>3</sub>), 1.98 – 1.90 (m, 1H), 1.84 (brd, *J* = 13.8 Hz, 1H), 1.68 (s, 1H), 1.50 – 1.34 (m, 4H), 1.23 – 1.17 (m, 1H), 0.93 (t, *J* = 7.0 Hz, 3H, H-10).

**<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) **Major diastereoisomer:** δ 203.1 (C-11), 144.5, 141.9 (C-2), 137.4 (ArC), 135.5 (ArC), 133.0 (ArC), 132.8 (ArC), 47.3 (C-3), 32.1, 30.7 (C-6), 30.2, 27.2, 22.8, 20.0, 17.5 (ArCH<sub>3</sub>), 16.8 (ArCH<sub>3</sub>), 16.1 (ArCH<sub>3</sub>), 14.3 (C-10).

**IR** (film)  $\nu_{\max}/\text{cm}^{-1}$ : 2958, 2918, 2854, 1654, 1625, 1458, 1186.

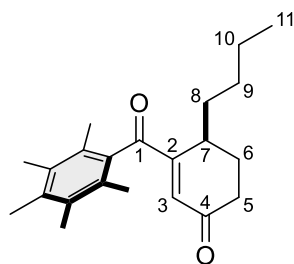
**HRMS** (ESI<sup>+</sup>): Found [M+Na]<sup>+</sup> = 413.1462.; C<sub>22</sub>H<sub>31</sub>BrONa requires 413.1450, Δ 2.79 ppm

**m.p.:** 105-107 °C.

$[\alpha]_{\text{D}}^{20} = -163.3$  (*c* = 0.1, CHCl<sub>3</sub>).

**Diagnostic peaks for minor diastereomer:** **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 4.73 (td, *J* = 6.6, 1.4 Hz, 1H, H-3), 2.89 – 2.79 (m, 1H, H-6).

#### 4-Butyl-3-(2,3,4,5,6-pentamethylbenzoyl)cyclohex-2-en-1-one, **8**



To a suspension of sodium bicarbonate (42 mg, 0.50 mmol, 5.0 equiv.) in a mixture of dry DMSO (0.25 mL) and dry MeCN (0.25 mL) was added mixture (ca 4:1 d.r.) of the bromide substrate **7** (39 mg, 0.10 mmol, 1.0 equiv.) under nitrogen. The reaction mixture was stirred at 80 °C for 8 h. After cooling to RT, the mixture was diluted with H<sub>2</sub>O (10 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with saturated aqueous NaHCO<sub>3</sub> (10 mL) and brine (10 mL), dried (Na<sub>2</sub>SO<sub>4</sub>), filtered, and concentrated *in vacuo*. Purification by column chromatography (pentane:Et<sub>2</sub>O, 90:10) afforded the title compound **8** as yellow solid (20 mg, 61% yield).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 6.08 (s, 1H, H-3), 3.09 – 3.06 (m, 1H, H-7), 2.57 (ddd, *J* = 17.9, 14.5, 5.2 Hz, 1H, H-5), 2.48 – 2.36 (m, 1H, H-5'), 2.23 (m, 4H, H-6, ArCH<sub>3</sub>), 2.16 (s, 6H, 2×ArCH<sub>3</sub>), 2.04 (dt, *J* = 14.2, 4.8 Hz, 1H, H-6'), 1.98 (s, 6H, 6×ArCH<sub>3</sub>), 1.80 – 1.68 (m, 2H, H-8), 1.56 – 1.30 (m, 4H, H-9, H-10), 0.95 (t, *J* = 7.1 Hz, 3H, H-11).

**<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) δ 204.2 (C-4), 202.39 (C-1), 159.05 (ArC), 136.2 (ArC), 136.1 (ArC'), 134.6 (C-3), 133.0

(ArC), 129.0 (ArC), 33.4 (C-5), 31.4 (C-7), 30.7 (C-8), 30.5 (C-9), 24.8 (C-6), 22.6 (C-10), 17.4 (ArCH<sub>3</sub>), 16.7 (ArCH<sub>3</sub>), 15.9 (ArCH<sub>3</sub>), 14.0 (C-11).

IR (film)  $\nu_{\max}/\text{cm}^{-1}$ : 2980, 2360, 1746, 1660, 1626, 1381.

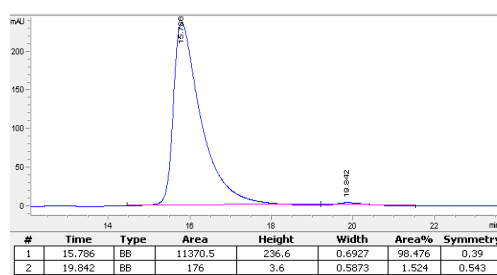
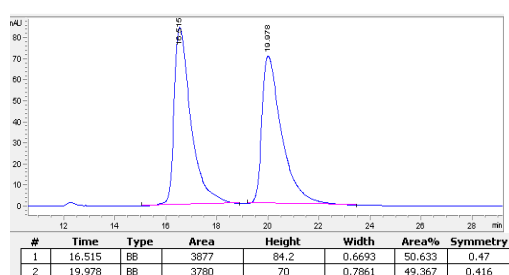
HRMS (ESI<sup>+</sup>): Found  $[\text{M}+\text{H}]^+ = 327.2331$ ; C<sub>22</sub>H<sub>31</sub>NO<sub>2</sub> requires 327.2319  $\Delta$  1.83 ppm.

m.p.: 62-64 °C.

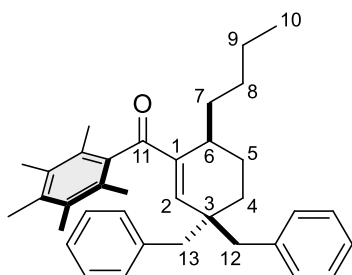
$[\alpha]_{\text{D}}^{20} = -126.0$  (c = 0.1, CHCl<sub>3</sub>).

To enable determination of the enantiomeric ratio of the title compound, a racemic sample was prepared following the same synthetic procedure.

HPLC: Enantiomeric excess was determined by HPLC with a Chiralpak® IA column (99.9:0.1 hexane: IPA, 1.0 ml min<sup>-1</sup>, 254 nm, room temperature); t<sub>r</sub> (minor) = 15.7 min, t<sub>r</sub> (major) = 19.8 min, 98.5:1.5 e.r.



### (3,3-Dibenzyl-6-butylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 9



A 2–5 mL Biotage® microwave vial was charged with **4g** (33 mg, 0.10 mmol, 1.0 equiv.) in dry THF (1 mL) under N<sub>2</sub> and LiHMDS (0.25 mL, 1.0 M in THF, 0.25 mmol, 2.5 equiv.) was added dropwise the resulting solution was stirred at RT for 1 h. Then a solution of benzyl iodide (87 mg, 0.4 mmol, 4.0 equiv.) in dry THF (1 mL) was added and was stirred at RT for 4 h until the full consumption of starting material **4g**. The reaction mixture was quenched by addition of sat. aq. NH<sub>4</sub>Cl. The layers were separated and the aqueous layer was extracted with Et<sub>2</sub>O (3 x 10 mL), dried over MgSO<sub>4</sub>, filtered and concentrated in vacuo. The title compound **9** was afforded after purification by FCC (Pentane:Et<sub>2</sub>O, 98:2) as a colourless oil (36.4 mg, 70% yield).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.21 (dd,  $J = 5.0, 1.9$  Hz, 3H), 7.18 – 7.12 (m, 3H), 7.10 – 6.95 (m, 2H), 6.90 – 6.80 (m, 2H), 6.33 (s, 1H), 2.73 – 2.60 (m, 4H), 2.47 (d,  $J = 13.2$  Hz, 1H), 2.29 (s, 3H, ArCH<sub>3</sub>), 2.25 (s, 6H, 2xArCH<sub>3</sub>), 2.08 (s, 3H, ArCH<sub>3</sub>), 2.00 (s, 3H, ArCH<sub>3</sub>), 1.68 – 1.56 (m, 2H), 1.45 – 1.26 (m, 4H), 1.22 – 1.02 (m, 3H), 0.79 (t,  $J = 6.9$  Hz, 3H), 0.59 – 0.45 (m, 1H, H-12'/13').

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 202.9 (C-11), 151.8 (ArC), 145.4 (ArC), 138.2 (ArC), 137.9 (ArC), 137.6 (ArC), 135.1 (ArC), 132.8 (ArC), 132.7 (ArC), 130.8 (ArC), 130.6 (ArC), 129.2 (ArC), 129.1 (ArC), 128.0 (ArC), 127.8 (ArC), 126.5 (ArC), 126.3 (ArC), 46.9 (C-12/C-13), 46.4 (C12/C-13), 42.1 (C-3), 31.8 (C-12/13), 30.9 (C-6), 25.3, 22.7, 21.8, 17.9 (ArCH<sub>3</sub>), 17.5 (ArCH<sub>3</sub>), 16.9 (ArCH<sub>3</sub>), 16.2 (ArCH<sub>3</sub>), 16.1 (ArCH<sub>3</sub>), 14.1 (C-10).

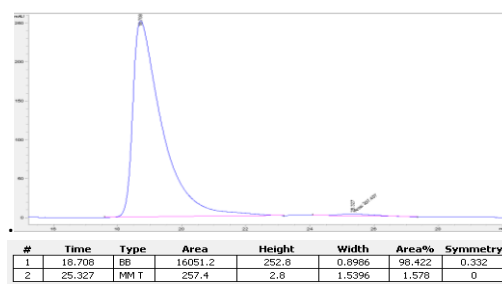
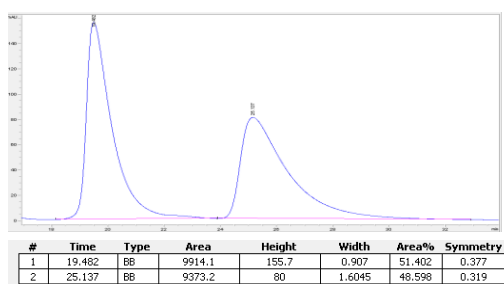
IR (film)  $\nu_{\max}$ /cm<sup>-1</sup>: 3028, 2931, 2359, 1652, 1496, 1218.

HRMS (ESI+): Found [M+Na]<sup>+</sup> = 515.3298; C<sub>36</sub>H<sub>44</sub>O requires 515.3284 Δ 2.65 ppm.

[α]<sub>D</sub><sup>20</sup> = -16.8 (c = 0.2, CHCl<sub>3</sub>).

To enable determination of the enantiomeric ratio of the title compound, a racemic sample was prepared following the same synthetic procedure.

HPLC: Enantiomeric excess was determined by HPLC with a Chiralpak<sup>®</sup> IA column (99.9:0.1 hexane: IPA, 1.0 ml min<sup>-1</sup>, 254 nm, room temperature); t<sub>r</sub> (minor) = 18.7 min, t<sub>r</sub> (major) = 25.3 min, 98.5:1.5 e.r.



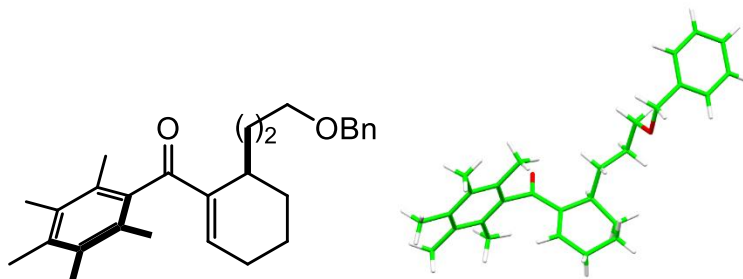
#### 4. Crystallographic data

Single crystal X-ray data collection and structure determination were performed by Akvile Mazeikaite in the Chemistry Research Laboratory, University of Oxford. Crystals were mounted on MiTeGen loops using perfluoropolyether oil and rapidly transferred to a goniometer head on a diffractometer fitted with an Oxford CryoSystems CryoStream open-flow nitrogen cooling device.<sup>1</sup> Data collections were either carried out at 100 K using a high flux Rigaku Synergy DW rotating anode diffractometer using mirror-monochromated Cu K $\alpha$  radiation ( $\lambda = 1.54184 \text{ \AA}$ ). Data were processed using CryAlisPro, the structure was then solved using charge-flipping algorithm SUPERFLIP<sup>2</sup> and refined by full-matrix least squares using CRYSTALS.<sup>3,4</sup> Structures are visualised and represented using Mercury.

1. Cosier, J.; Glazer, A. M., *J. Appl. Cryst.* 1986, 19, 105-107.
2. Palatinus, L.; Chapuis, G., *J. Appl. Cryst.* 2007, 40, 786-790.
3. Cooper, R. I. T., A. L.; Watkin, D. J., *J. Appl. Cryst.* 2010, 43, 1100-1107.
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**Crystallographic data:****(R)-(6-(2-(benzyloxy)ethyl)cyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone (4k)**

Recrystallised via vapour diffusion using THF/EtOH

Formula C<sub>28</sub> H<sub>36</sub> O<sub>2</sub>

Crystal class	monoclinic	Space group	P2 <sub>1</sub>
a	8.4999(1)	alpha	90
b	31.6705(1)	beta	93.0936(4)
c	8.6223(1)	gamma	90
Volume	2317.71(4)	Z	4
Radiation type	Cu K $\alpha$	Wavelength	1.54184
Dx	1.159	Mr	404.57
Mu	0.543	Temperature (K)	100
Size	0.076 × 0.112 × 0.152		
Colour	Clear pale colourless	Shape	block
Cell from	70363 reflections	Theta range	3 to 76
Diffractometer type	multi-scan	Scan type	OMEGA
Absorption type	multi-scan	Transmission range	0.81 – 0.96
Rint	0.030	Independent reflections	9420
Hmin, Hmax	-10, 10	Theta max	75.96
Kmin, Kmax	-39, 36		
Lmin, Lmax	-10, 10		
Refinement on Fsqd			
R-factor	0.0308	Weighted R-factor	0.0792
Max shift/su	0.0007365		
Delta Rho min	-0.14	Delta Rho max	0.13
Reflections used	9085	sigma(I) limit	-3.00
Number of parameters	580	Goodness of fit	0.994
Flack parameter	0.03(4)		

35 Y

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Z 110

4k

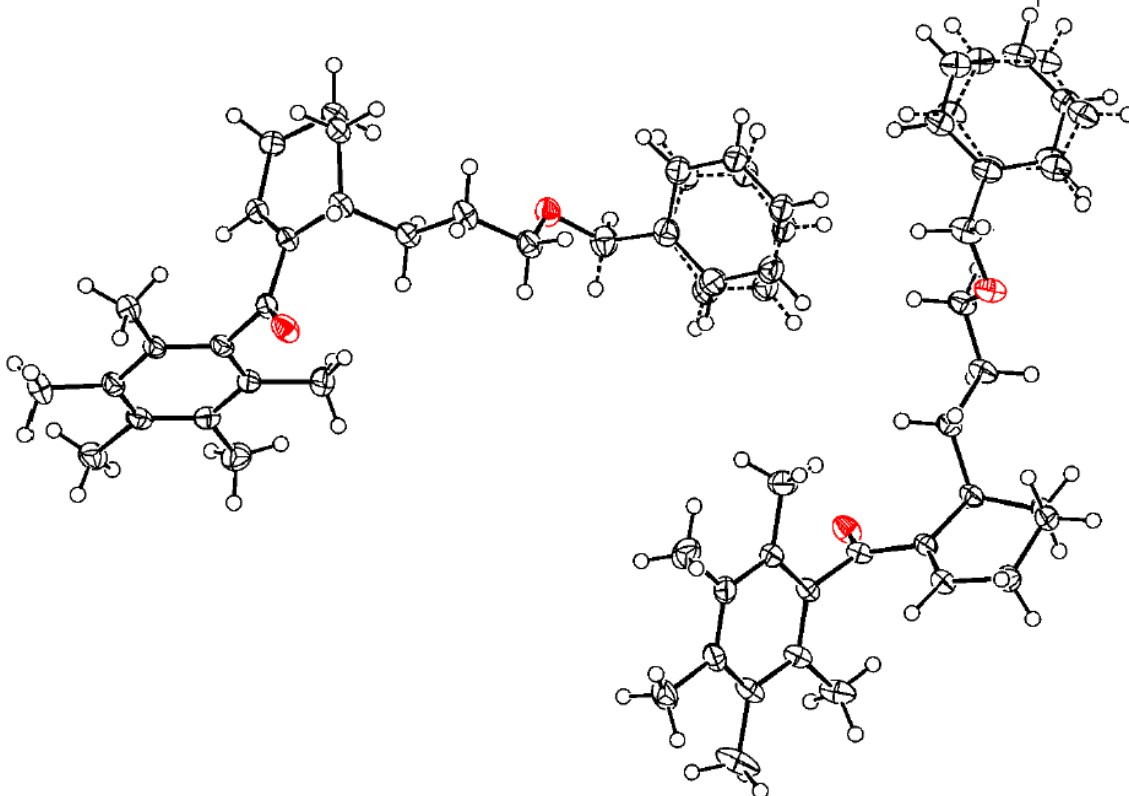
P 21

R = 0.03

RES= 0-135 X

NOMOVE FORCED

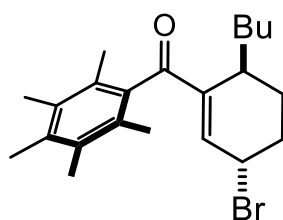
Prob = 50%  
Temp = 100K



Thermal ellipsoids are drawn at the 50% probability level.

**((3S,6S)-3-bromo-6-butylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone (7)**

Recrystallised via vapour diffusion using CH<sub>2</sub>Cl<sub>2</sub>/ DMSO-EtOH (9:1)



Formula C<sub>22</sub> H<sub>31</sub> Br O

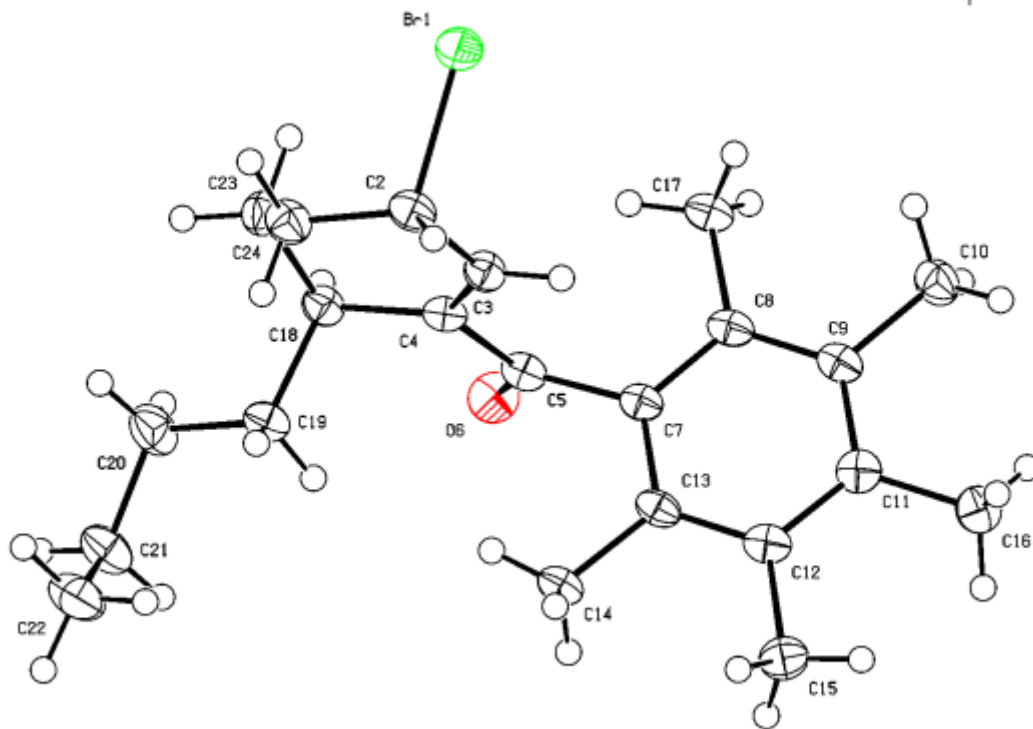
Crystal class	orthorhombic	Space group	P2 <sub>1</sub> 2 <sub>1</sub> 2 <sub>1</sub>
a	7.3986(1)	alpha	90
b	8.6217(1)	beta	90
c	31.2132(2)	gamma	90
Volume	1991.04(4)	Z	4
Radiation type	Cu K $\alpha$	Wavelength	1.54184
Dx	1.306	Mr	391.39
Mu	2.833	Temperature (K)	100
Size	0.014 $\times$ 0.071 $\times$ 0.086		
Colour	Clear pale colourless	Shape	plate
Cell from	75898 reflections	Theta range	3 to 76
Diffractometer type	multi-scan	Scan type	OMEGA
Absorption type	multi-scan	Transmission range	0.74 – 0.96
Rint	0.063	Independent reflections	4132
Hmin, Hmax	-9, 9	Theta max	76.078
Kmin, Kmax	-10, 9		
Lmin, Lmax	-38, 39		
Refinement on Fsqd			
R-factor	0.0351	Weighted R-factor	0.0965
Max shift/su	0.0007464		
Delta Rho min	-0.33	Delta Rho max	0.62
Reflections used	4132	sigma(I) limit	-3.00
Number of parameters	218	Goodness of fit	1.0017
Flack parameter	-0.021(5)		

72 Y

NOMOVE FORCED

Prob = 50%  
Temp = 100K

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Z -78 I

P 21 21 21 R = 0.04

RES= 0 109 X

Thermal ellipsoids are drawn at the 50% probability level.