Highly Diastereoselective Synthesis of Homoallylic Alcohols Bearing Adjacent Quaternary Centers Using Substituted Allylic Zinc Reagents**

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Supporting Information

1. General

All reactions were carried out under nitrogen using standard Schlenk techniques. Melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded on a Bruker AMX 300 or AMX 600 or Varian VXR 400 S instrument. Chemical shifts are given as ppm relative to the residual solvent peak (chloroform-*d*1: 7.26 ppm/77.0 ppm; benzene-*d*6 7.16 ppm/128.0 ppm). IR spectra were recorded on a Perkin Elmer 1420 Infrared Spectrometer. Mass spectra were recorded on a Finnigan Mat 95 Q spectrometer. Column chromatography purification was performed on Merck silica gel 60 (230-400 mesh ASTM). THF and toluene were dried with sodium/benzophenone and distilled. Elemental analysis was performed on an Elementar vario EL and with a Metrohm Titroprocessor 686. Yields referred to isolated yields of compounds estimated to be > 95% pure as determined by ^1H -NMR, capillary GC and combustion analysis (new compounds).

Synthesis of 3-chloro-1-methyl-cyclohexene

Triphenylphosphine (14.70 g, 56.0 mmol) was slowly added to a solution of 3-methylcyclohex-2-en-1-ol (4.50 g, 40.0 mmol) in carbon tetrachloride (50 mL) and the resulting mixture was refluxed for 5 h. Then, the mixture was cooled and pentane (150 mL) was added. The suspension was filtered off and washed with pentane (50 mL). The solvent was removed under vacuum. Distillation (40 $^\circ\text{C}$ /3.0 mmHg) of the residual oil provided the compound **I** (3.13 g, 60%) as a colourless oil, as a ratio of 90: 10 mixture of **I**: **II**. The mixture was used in the subsequent step without further purification.

^1H NMR (CDCl_3 , 300 MHz): 5.50-5.60 (m, 1 H), 4.60-4.70 (m, 1 H), 1.80-2.10 (m, 6 H), 1.68 (s, 3 H);

^{13}C NMR (CDCl_3 , 75 MHz): 139.8, 122.6, 57.1, 32.0, 29.8, 23.7, 18.5;

IR (neat): 2934 (m), 1665 (m), 1444 (s), 1436 (w), 1222 (s) cm^{-1} ;

MS (EI, 70 ev): m/z (%) = 132 (M^+ (^{37}Cl), 9), 130 (3), 95 (100), 79 (29), 67 (28).

The spectral data is in accordance with that reported in the literature.¹

Synthesis of 2-chloromethyl-6,6-dimethyl-bicyclo[3.1.1]hept-2-ene

¹ T. Carrillo-Marquez, L. Caggiano, R. F. W. Jackson, U. Grabowska, A. Rae, M. J. Tozer, *Org. Biomol. Chem.*, **2005**, 3, 4117.

Triphenylphosphine (36.68 g, 140 mmol) was slowly added to a solution of (-)-myrtenol (15.20 g, 100 mmol) in carbon tetrachloride (140 mL) and the resulting mixture was refluxed for 5 h. After the mixture was cooled, the pentane (250 mL) was added. The suspension was filtered off and washed with pentane (100 mL). The solvent was removed under vacuum. Distillation (40 °C/2.0 mmHg) of the oil provided the compound (12.44 g, 73%) as a colourless oil. $[\alpha]_D^{20} = -40$ ($c = 0.8$, CH_2Cl_2).

^1H NMR (CDCl_3 , 600 MHz): 5.60 (s, 1 H), 3.94-4.01 (m, 2 H), 2.41 (dt, $J_1 = 8.8$ Hz, $J_2 = 5.5$ Hz, 1 H), 2.20-2.32 (m, 3 H), 2.06-2.11 (m, 1 H), 1.29 (s, 3 H), 1.16 (d, $J = 8.8$ Hz, 1 H), 0.82 (s, 3 H);

^{13}C NMR (CDCl_3 , 150 MHz): 144.1, 122.4, 48.6, 44.2, 40.4, 38.0, 31.5, 31.2, 26.0, 21.1;

IR (neat): 2919 (m), 1650 (w), 1469 (m), 1429 (m), 1366 (m), 1256 (s) cm^{-1} ;

MS (EI, 70 eV): m/z (%) = 172 (M^+ , 1), 170 (3), 126 (13), 91 (100), 79 (15);

HRMS (EI): calcd. for $\text{C}_{10}\text{H}_{15}\text{Cl}$ (^{35}Cl): 170.0862; **found**: 170.0849 (^{35}Cl).

Preparation of 2-cyclohexenylzinc chloride (1a)

Zinc dust ²(3.20 g, 50.0 mmol) and dry LiCl (500 mg, 12.0 mmol) were covered with dry THF (5 mL) and activated by the addition of a few drops of 1,2-dibromoethane and TMSCl. After stirring for 10 min, a solution of 3-chloro-cyclohexene (1.17 g, 10.0 mmol) in THF (10 mL) was added in with a syringe pump at 0 °C within 2 h. The resulting mixture was stirred under nitrogen at 0 °C for 36 h. The zinc suspension was settled using centrifuge machine. The concentration and the yield were determined as follows:

Iodine (254 mg, 1.0 mmol) was placed into a dry 10 mL round-bottomed flask equipped with a magnetic stirrer bar and septum under nitrogen. Dry THF (5 mL) was added with syringe. The allylic zinc solution was added dropwise with syringe until the red colour disappeared. The volume of the allylic zinc reagent was determined and the following equation used to determine the molarity of the solution: molarity of allylic zinc reagent = 1/volume of allylic zinc reagent.

The concentration of the allylic zinc reagent was 0.60 mol/l; volume = 14.0 mL; yield: 84%.

Preparation of 2-cyclopentenylzinc chloride (1b)

Zinc dust (3.20 g, 50.0 mmol) and dry LiCl (500 mg, 12.0 mmol) were covered with dry THF (5 mL) and activated by the addition of a few drops of 1, 2-dibromoethane and TMSCl. After stirring for 10 min, a solution of 3-chloro-cyclopentene (1.03 g, 10.0 mmol) in THF (10 mL) was added with a syringe pump at -10 °C within 2 h. The resulting mixture was stirred under nitrogen at -10 °C for 40 h. The zinc suspension was allowed to settle using a centrifuge machine. The concentration and the yield were determined as the method described above.

The concentration of the allylic zinc reagent was 0.40 mol/l; volume = 14.5 mL; yield: 58%.

² From Aldrich.

Preparation of 1-methyl-1-cyclohexenylzinc chloride (1c)

Zinc dust (3.20 g, 50.0 mmol) and dry LiCl (500 mg, 12.0 mmol) were covered with dry THF (5 mL) and activated by the addition of a few drops of 1,2-dibromoethane and TMSCl. After stirring for 10 min, a solution of 3-chloro-1-methyl-cyclohexene (mixture of 3-chloro-1-methyl-cyclohexene and 3-chloro-3-methyl-cyclohexene, 1.30 g, 10.0 mmol) in THF (10 mL) was added in with a syringe pump at -10 °C within 2 h. The resulting mixture was stirred under nitrogen at -10 °C for 12 h. The zinc suspension was allowed to settle using a centrifuge machine. The concentration and the yield were determined as the method described above. The concentration of allylic zinc reagent: 0.38 mol/l; volume = 14.5 mL; yield: 55%.

Preparation of 2-methyl-6,6-dimethyl-bicyclo[3.1.1]hept-2-enylzinc chloride (1d)

Zinc dust (1.60 g, 25.0 mmol) and dry LiCl (500 mg, 12.0 mmol) were covered with dry THF (5 mL) and activated by the addition of a few drops of 1, 2-dibromoethane and TMSCl. After stirring for 10 min, a solution of 2-chloromethyl-6, 6-dimethyl-bicyclo[3.1.1]hept-2-ene (1.71 g, 10.0 mmol) in THF (10 mL) was added in with a syringe pump at room temperature within 2 h. The resulting mixture was stirred under nitrogen at room temperature for 40 h. The zinc suspension was allowed to settle using a centrifuge machine. The concentration and the yield were determined as the method described above.

Preparation of cinnamylzinc chloride (1e) :

Zinc dust (2.00 g, 30.0 mmol) and dry LiCl (1.00 g, 24.0 mmol) were covered with dry THF (5 mL) and activated by the addition of a few drops of 1, 2-dibromoethane and TMSCl. After stirring for 10 min, a solution of cinnamyl chloride (1.52 g, 10.0 mmol) in THF (15 mL) was added at room temperature within 10 min. The resulting mixture was stirred under nitrogen at room temperature for 1 h. The zinc suspension was allowed to settle using a centrifuge machine. The concentration and the yield were determined as the method described above.

Preparation of cinnamylzinc chloride (1f) :

Zinc dust (2.00 g, 30.0 mmol) and dry LiCl (1.00 g, 24.0 mmol) were covered with dry THF (5 mL) and activated by the addition of a few drops of 1, 2-dibromoethane and TMSCl. After stirring for 10 min, a solution of cinnamyl phosphate (2.70 g, 10.0 mmol) in THF (15 mL)

was added at room temperature within 10 min. The resulting mixture was stirred under nitrogen at room temperature for 18 h. The zinc suspension was allowed to settle using a centrifuge machine. The concentration and the yield were determined as the method described above.

Typical procedure for preparation of homoallylic alcohols by the addition of an allylic zinc reagent to an aldehyde or a ketone.

Procedure A: The allylic zinc chloride (1.2 mmol) was added to the solution of aldehyde or ketone (1.0 mmol) in THF (2 mL) at -78 °C and the resulting mixture was stirred at this temperature for 1 h. After quenching with water (10 mL), the reaction mixture was extracted with ether (3 x 30 mL). The combined extracts were washed with brine, dried over Na₂SO₄ and concentrated *in vacuo*. Purification by flash chromatography (The silica gel was buffered with 1% Et₃N in pentane) provided the pure compound.

Synthesis of 4-((1*R)-cyclohex-2-enyl)-((1*S**)-hydroxy-ethyl)-benzonitrile (**3a**)**

It was prepared from 4-acetylbenzonitrile (145 mg, 1.0 mmol) and 2-cyclohexenylzinc chloride (**1a**, 1.2 mmol) according to **Procedure A**. Purification by flash chromatography (eluent: pentane: ether = 2: 1) provided the pure compound **3a** (220 mg, 97%) as a colourless oil. dr > 99:1.

¹H NMR (CDCl₃, 300 MHz): 7.55 (d, *J* = 8.3 Hz, 2 H), 7.49 (d, *J* = 8.3 Hz, 2 H), 5.86-5.94 (m, 1 H), 5.72 (d, *J* = 10.5 Hz, 1 H), 2.43-2.53 (m, 1 H), 2.08 (s, 1 H), 1.84-1.94 (m, 2 H), 1.59-1.69 (m, 1 H), 1.54 (s, 3 H), 1.05-1.44 (m, 3 H);

¹³C NMR (CDCl₃, 75 MHz): 152.5, 132.3, 131.6, 126.0, 125.2, 118.8, 109.9, 75.7, 46.1, 27.8, 24.9, 24.1, 21.5;

IR (neat): 3481 (m), 2931 (m), 2227 (m), 1606 (m), 1372 (m) cm⁻¹;

MS (EI, 70 ev): *m/z* (%) = 227 (0.5), 146 (100), 130 (8), 102 (7);

HRMS (EI): calcd. for C₁₅H₁₈NO (*M*⁺+H): 228.1388; **found**: 228.1388 (*M*⁺+H).

Synthesis of ((1*S)-((1*R**)-cyclohex-2-enyl)-2-methyl-phenyl-propan-1-ol (**3b**)**

It was prepared from 2-methyl-1-phenyl-propan-1-one (148 mg, 1.0 mmol) and 2-cyclohexenylzinc chloride (**1a**, 1.2 mmol) according to **Procedure A**. This reaction was carried out at -30 °C for 12 h. Purification by flash chromatography (eluent: pentane: ether = 100: 1) provided the pure compound **3b** (216 mg, 94%) as a colourless oil. dr > 99:1.

¹H NMR (CDCl₃, 300 MHz): 7.22-7.47 (m, 5 H), 5.86-6.00 (m, 2 H), 2.85-3.05 (m, 1 H), 2.27-2.42 (m, 1 H), 1.83-2.03 (m, 2 H), 1.69-1.80 (m, 1 H), 1.63 (s, 1 H), 1.42-1.60 (m, 2 H), 1.17-1.33 (m, 1 H), 0.91 (d, *J* = 7.0 Hz, 3 H), 0.83 (d, *J* = 7.0 Hz, 3 H);

¹³C NMR (CDCl₃, 75 MHz): 142.2, 131.3, 127.2, 126.6, 126.4, 126.1, 80.4, 41.6, 34.7, 25.2, 24.4, 22.2, 17.6, 16.8;

IR (neat): 3568 (w), 2933 (m), 1494 (w), 1468 (m), 1445 (m) cm⁻¹;

MS (EI, 70 ev): *m/z* (%) = 213 (*M*⁺-OH, 1), 187 (8), 149 (100), 105 (79);

HRMS (EI): calcd. for C₁₆H₂₀ (*M*⁺-H₂O): 212.1565; **found**: 212.1574 (*M*⁺-H₂O).

To determine the structures of **3a** and **3b**, another compound was synthesized and crystallized:

Synthesis of (1*S)-{(1*R**)-cyclohex-2-enyl}-1-3,5-bis(2,5-dichloro-benzenesulfonate)-phenyl-ethanol (**3l**).**

ORTEP representation of **3l** with thermal ellipsoids set at 30% probability level (See the complete X-ray data at the end of the manuscript)

It was prepared from 3,5-bis(2,5-dichloro-benzenesulfonate)-acetophenone³ (570 mg, 1.0 mmol) and 2-cyclohexenylzinc chloride (**1a**, 1.2 mmol) according to **Procedure A**. Purification by flash chromatography (eluent: pentane: ether = 6: 1) provided the pure compound **3o** (600 mg, 92%) as a white solid, mp.: 149.6-150.8 °C. dr > 99:1.

¹H NMR (CDCl₃, 300 MHz): 7.78 (d, *J* = 2.6 Hz, 2 H), 7.53 (s, 4 H), 7.03 (d, *J* = 2.6 Hz, 2 H), 6.85 (t, *J* = 2.6 Hz, 1 H), 5.85-5.96 (m, 1 H), 5.59 (d, *J* = 10.6 Hz, 1 H), 2.14-2.29 (m, 1 H), 1.50-2.00 (m, 4 H), 1.41 (s, 3 H), 1.19-1.36 (m, 1 H), 0.73-0.97 (m, 2 H);

¹³C NMR (CDCl₃, 75 MHz): 151.2, 149.0, 135.2, 134.1, 133.4, 133.3, 133.0, 132.1, 131.5, 124.7, 118.3, 114.5, 75.3, 46.2, 27.9, 25.0, 24.0, 21.7;

IR (neat): 3559 (m), 2930 (s), 1612 (w), 1588 (s), 1452 (s), 1434, 1394, 1384 cm⁻¹;

MS (EI, 70 ev): *m/z* (%) = 634 (M⁺-H₂O, 0.5), 571 (100), 360 (20), 145 (30);

Anal. Calcd for C₂₆H₂₂Cl₄O₇S₂: C, 47.87; H, 3.40;

Found: C, 47.76; H, 3.46.

Synthesis of (1*S)-(2-amino-5-chloro-phenyl)-{(1*R**)-cyclohex-2-enyl}-methanol (**3c**).**

It was prepared from 2-amino-5-chloro-benzaldehyde (156 mg, 1.0 mmol) and 2-cyclohexenylzinc chloride (**1a**, 1.2 mmol) according to **Procedure A**. Purification by flash chromatography (eluent: pentane: ether = 1: 1) provided the pure compound **7** (213 mg, 90%) as a white solid, mp.: 112.0-112.5 °C. dr > 99:1 (determined by ¹H NMR).

¹H NMR (CDCl₃, 300 MHz): 6.97-7.08 (m, 2 H), 6.55 (d, *J* = 8.8 Hz, 1 H), 5.72-5.83 (m, 1 H), 5.17-5.29 (m, 1 H), 4.43 (d, *J* = 7.9 Hz, 1 H), 3.00-4.31 (bs, 2 H), 2.61-2.74 (m, 1 H), 1.94-2.05 (m, 2 H), 1.69-1.93 (m, 2 H), 1.45-1.65 (m, 2 H);

³ Prepared from 3,5-dihydroxyacetophenone and 2,5-dichlorobenzenesulfonylchloride using a usual method.

^{13}C NMR (CDCl_3 , 75 MHz): 143.2, 130.4, 128.2, 128.00, 127.97, 127.5, 122.8, 117.9, 76.7, 39.6, 25.2, 24.9, 20.7;

IR (neat): 3384 (m), 3357 (m), 3162 (m), 1487 (s), 1420 (m), 1200 (m) cm^{-1} ;

MS (EI, 70 ev): m/z (%) = 219 ($\text{M}^+ - \text{H}_2\text{O}$, 100), 191 (91), 164 (48), 140 (79), 77 (29);

HRMS (EI): calcd. for $\text{C}_{13}\text{H}_{15}\text{ClNO}$ ($\text{M}^+ - \text{H}$): 236.0842; found: 236.0852 ($\text{M}^+ - \text{H}$).

Synthesis of (1*S**)-{(1*R**)-cyclohex-2-enyl}-6-methoxy-1,2,3,4-tetrahydro-naphthalen-1-ol (3d)

It was prepared from 6-methoxyl-1-tetralone (176 mg, 1.0 mmol) and 2-cyclohexenylzinc chloride (**1a**, 1.2 mmol) according to **Procedure A**. Purification by flash chromatography (eluent: pentane: ether = 3: 1) provided the pure compound **3d** (250 mg, 97%) as a colourless oil. dr > 97:3.

^1H NMR (CDCl_3 , 400 MHz): 7.45 (d, $J = 8.6$ Hz, 1 H), 6.76 (dd, $J_1 = 8.6$ Hz, $J_2 = 2.7$ Hz, 1 H), 6.59 (d, $J = 2.7$ Hz, 1 H), 5.57-5.67 (m, 1 H), 4.97-5.06 (m, 1 H), 3.76 (s, 3 H), 2.84-2.93 (m, 1 H), 2.55-2.75 (m, 2 H), 1.65-2.08 (m, 9 H), 1.44-1.62 (m, 2 H);

^{13}C NMR (CDCl_3 , 100 MHz): 158.2, 139.7, 133.4, 128.9, 128.4, 127.8, 113.0, 112.7, 73.7, 55.0, 46.4, 33.1, 30.7, 25.3, 23.4, 22.3, 19.3;

IR (neat): 3446 (m), 2928 (s), 1607 (s), 1498 (s), 1253 (s) cm^{-1} ;

MS (EI, 70 ev): m/z (%) = 240 ($\text{M}^+ - \text{H}_2\text{O}$, 100), 225 (9), 211 (22), 199 (33), 159 (24);

HRMS (EI): calcd. for $\text{C}_{17}\text{H}_{20}\text{O}$ ($\text{M}^+ - \text{H}_2\text{O}$): 240.1514; found: 240.1520 ($\text{M}^+ - \text{H}_2\text{O}$).

Synthesis of (1*S**)-{(1*R**)-cyclohex-2-enyl}-ferrocenyl-ethanol (3e).

ORTEP representation of **3e** with thermal ellipsoids set at 30% probability level (See the complete X-ray data at the end of the manuscript).

It was prepared from acetylferrocene (228 mg, 1.0 mmol) and 2-cyclohexenylzinc chloride (**1a**, 1.2 mmol) according to **Procedure A**. Purification by flash chromatography (eluent: pentane: ether = 10: 1) provided the pure compound **3e** (288 mg, 93%) as a red solid, mp.: 83.1-84.4 °C. dr > 99:1.

^1H NMR (C_6D_6 , 400 MHz): 5.81-5.88 (m, 1 H), 5.67-5.75 (m, 1 H), 4.24-4.29 (m, 1 H), 3.99 (s, 5 H), 3.89-3.92 (m, 2 H), 3.86-3.88 (m, 1 H), 2.46-2.56 (m, 1 H), 2.09 (s, 1 H), 1.94-2.03 (m, 1 H), 1.76-1.85 (m, 2 H), 1.60-1.70 (m, 1 H), 1.49 (s, 3 H), 1.32-1.52 (m, 2 H);

^{13}C NMR (C_6D_6 , 100 MHz): 128.7, 128.6, 68.6, 68.5, 68.1, 67.6, 66.1, 47.8, 25.9, 25.5, 25.2, 22.6;

IR (neat): 3545 (m), 2926 (m), 1446 (m), 1369 (m), 1318 (s) cm^{-1} ;

MS (EI, 70 ev): m/z (%) = 292 ($\text{M}^+ - \text{H}_2\text{O}$, 100), 275 (10), 225 (11), 166 (9), 121 (12);

HRMS (EI): calcd. for $\text{C}_{18}\text{H}_{20}\text{Fe}$ ($\text{M}^+ - \text{H}_2\text{O}$): 292.0914; found: 292.0906 ($\text{M}^+ - \text{H}_2\text{O}$).

Synthesis of (1*S**)-2-chloro-{(1*R**)-cyclohex-2-enyl}-1-phenyl-ethanol (**3f**)

It was prepared from 2-chloro-1-phenyl-ethanone (161 mg, 1.0 mmol) and 2-cyclohexenylzinc chloride (**1a**, 1.2 mmol) according to **Procedure A**. Purification by flash chromatography (eluent: pentane: ether = 5: 1) provided the pure compound **4a** (230 mg, 97%) as a colourless oil. dr > 99:1.

¹H NMR (CDCl₃, 300 MHz): 7.28-7.51 (m, 5 H), 5.85-5.93 (m, 1 H), 5.70-5.85 (m, 1 H), 3.99-4.20 (m, 2 H), 2.70-2.82 (m, 1 H), 2.58 (s, 1 H), 1.84-2.10 (m, 2 H), 1.69-1.80 (m, 1 H), 1.29-1.66 (m, 3 H);

¹³C NMR (CDCl₃, 75 MHz): 141.9, 131.1, 127.9, 127.1, 126.0, 125.4, 77.9, 52.4, 44.3, 24.9, 24.3, 21.8;

IR (neat): 3550 (m), 1495 (m), 1446 (s), 1433 (m), 1054 (m) cm⁻¹;

MS (EI, 70 ev): m/z (%) = 219 (M⁺-H₂O, 0.1), 155 (100), 105 (8), 91 (9), 77 (32);

HRMS (EI): calcd. for C₁₄H₁₆Cl (M⁺-OH): 219.0941; **found**: 219.0924 (M⁺-OH).

Synthesis of (1*S**)-2-azido-{(1*R**)-cyclohex-2-enyl}-1-phenyl-ethanol (**3g**)

It was prepared from 2-azido-1-phenyl-ethanone (161 mg, 1.0 mmol) and 2-cyclohexenylzinc chloride (**1a**, 1.2 mmol) according to **Procedure A**. Purification by flash chromatography (eluent: pentane: ether = 5: 1) provided the pure compound **4b** (226 mg, 93%) as a colourless oil. dr > 99:1.

¹H NMR (CDCl₃, 300 MHz): 7.20-7.50 (m, 5 H), 5.84-5.96 (m, 1 H), 5.70-5.80 (m, 1 H), 3.74 (s, 2 H), 2.57-2.71 (m, 1 H), 2.33 (bs, 1 H), 1.83-2.00 (m, 2 H), 1.62-1.75 (m, 1 H), 1.34-1.49 (m, 2 H), 1.17-1.31 (m, 1 H);

¹³C NMR (CDCl₃, 75 MHz): 142.4, 132.1, 128.1, 127.1, 125.6, 125.2, 78.3, 59.2, 43.7, 24.9, 24.0, 21.6;

IR (neat): 3547 (w), 2130 (vs), 1495 (w), 1446 (m) cm⁻¹;

MS (EI, 70 ev): m/z (%) = 197 (M⁺-H₂O-N₂, 95), 169 (100), 115 (8);

HRMS (ESI): calcd. for C₁₅H₁₈N₃O₃ ([M+FA-H]⁻): 288.1348; **found**: 288.1375 ([M+FA-H]⁻);
calcd. for C₁₆H₂₀N₃O₃ ([M+AA-H]⁻): 302.1505; **found**: 302.1535 ([M+AA-H]⁻).

Synthesis of (1*S**)-(4-bromo-phenyl)-{(1*R**)-cyclohex-2-enyl}-2-(4-phenyl-[1,2,3]triazol-1-yl)-ethanol (**3g'**)

ORTEP representation of **3g'** with thermal ellipsoids set at 30% probability level (See the complete X-ray data at the end of the manuscript).

2-Cyclohexenylzinc chloride **1a** (2.0 mL, 1.2 mmol, 0.6 M in THF) was added to the solution of 2-azido-1-(4-bromo-phenyl)ethanone (240 mg, 1.0 mmol) and ethynylbenzene (153 mg, 1.5 mmol) in THF (2.0 mL) at -78 °C and the resulting mixture was stirred for 1 h at this temperature. The solution of CuCN·2LiCl (0.05 mL, 5 mol%, 1.0 M in THF) was added and the reaction mixture was stirred overnight at room temperature. After quenching with water (10 mL), the reaction mixture was extracted with CH₂Cl₂ (3 x 30 mL). The combined extracts were washed with brine and dried over Na₂SO₄ and concentrated *in vacuo*. Purification by flash chromatography (eluent: pentane: ether = 10: 1 then ether: CH₂Cl₂ = 1: 1) provided the pure compound **3g'** (400 mg, 94%) as a white solid, mp.: 157.0-158.5 °C.

¹H NMR (CDCl₃, 600 MHz): 7.66 (d, *J* = 7.6 Hz, 2 H), 7.51 (s, 1 H), 7.32-7.41 (m, 4 H), 7.28 (t, *J* = 7.5 Hz, 1 H), 7.19 (d, *J* = 7.6 Hz, 2 H), 5.99-6.05 (m, 1 H), 5.81 (d, *J* = 10.1 Hz, 1 H), 4.84 (d, *J* = 14.1 Hz, 1 H), 4.77 (d, *J* = 14.1 Hz, 1 H), 3.19 (s, 1 H), 2.68-2.76 (m, 1 H), 1.87-2.02 (m, 2 H), 1.64-1.75 (m, 1 H), 1.36-1.48 (m, 2 H), 1.18-1.30 (m, 1 H), ;

¹³C NMR (CDCl₃, 150 MHz): 147.2, 140.2, 133.8, 131.3, 130.3, 128.8, 128.1, 127.5, 125.6, 124.2, 121.4, 121.0, 77.9, 58.2, 43.8, 25.0, 24.1, 21.4;

IR (neat): 3327 (m), 2939 (m), 1609 (m), 1590 (m), 1487 (m), 1466 (m), 1005 (s) cm⁻¹;

MS (EI, 70 ev): *m/z* (%) = 425 (M⁺ (⁸¹Br), 1), 423 (M⁺ (⁷⁹Br), 1), 342 (18), 296 (6), 183 (88), 159 (100), 130 (42);

HRMS (EI): calcd. for C₂₂H₂₂BrN₃O (M⁺, ⁷⁹Br): 423.0946; **found**: 423.0926 (M⁺, ⁷⁹Br).

Synthesis of 4-((1*R**)-cyclopent-2-enyl)-((1*S**)-hydroxy-ethyl)-benzoic acid methyl ester (**3h**)

It was prepared from 4-acetyl-benzoic acid methyl ester (178 mg, 1.0 mmol) and 2-cyclopentylzinc chloride (**1b**, 1.2 mmol) according to **Procedure A**. This reaction was carried out in THF (5.0 mL). Purification by flash chromatography (eluent: pentane: ether = 3: 1) provided the pure compound **3i** (236 mg, 96%) as a colourless oil. dr > 99:1.

¹H NMR (CDCl₃, 300 MHz): 7.96 (d, *J* = 8.5 Hz, 2 H), 7.49 (d, *J* = 8.5 Hz, 2 H), 5.95-6.00 (m, 1 H), 5.72-5.77 (m, 1 H), 3.87 (s, 3 H), 3.17-3.25 (m, 1 H), 2.10-2.33 (m, 2 H), 1.87 (s, 1 H), 1.46-1.65 (m, 2 H), 1.53 (s, 3 H);

¹³C NMR (CDCl₃, 75 MHz): 167.0, 152.7, 135.9, 129.3 (2 X C), 128.1, 125.2, 75.8, 57.1, 51.9, 32.2, 29.0, 24.6;

IR (neat): 3499 (m), 2951 (m), 1705 (s), 1609 (m), 1436 (m), 1406 (m), 1276 (vs) cm⁻¹;

MS (EI, 70 ev): *m/z* (%) = 228 (M⁺-H₂O, 1), 179 (100), 163 (8), 137 (9), 77 (9);

HRMS (EI): calcd. for C₁₅H₁₉O₃ (M⁺+H): 247.1334; **found**: 247.1349 (M⁺+H).

Synthesis of (1*S**)-((1*R**)-1-methyl-cyclohex-2-enyl)-phenyl-methanol (**3i**)

It was prepared from benzaldehyde (106 mg, 1.0 mmol) and 1-methyl-1-cyclohexenylzinc chloride (**1c**, 1.2 mmol) according to **Procedure A**. Purification by flash chromatography (eluent: pentane: ether = 4: 1) provided the pure compound **3i** (198 mg, 98%) as a colourless oil. dr > 97:3.

¹H NMR (CDCl₃, 300 MHz): 7.25-7.36 (m, 5 H), 5.86 (dt, *J*₁ = 10.2 Hz, *J*₂ = 3.7 Hz, 1 H), 5.49 (d, *J* = 10.2 Hz, 1 H), 4.48 (d, *J* = 2.2 Hz, 1 H), 1.99 (d, *J* = 2.2 Hz, 1 H), 1.91-1.98 (m, 2 H), 1.81-1.91 (m, 1 H), 1.47-1.76 (m, 2 H), 1.17-1.27 (m, 1 H), 0.93 (s, 3 H);

^{13}C NMR (CDCl_3 , 75 MHz): 140.6, 133.7, 129.4, 127.9, 127.4, 127.2, 80.8, 40.4, 29.7, 25.1, 23.7, 18.8;

IR (neat): 3439 (w), 2930 (m), 1493 (w), 1452 (m), 1186 (m), 1022 (s) cm^{-1} ;

MS (EI, 70 ev): m/z (%) = 184 ($\text{M}^+ - \text{H}_2\text{O}$, 0.5), 107 (100), 96 (85), 79 (59), 67 (13);

HRMS (EI): calcd. for $\text{C}_{14}\text{H}_{17}$ ($\text{M}^+ - \text{OH}$): 185.1330; **found**: 185.1345 ($\text{M}^+ - \text{OH}$).

Synthesis of (1S*)-(4-bromo-phenyl)-1-((1R*)-1-methyl-cyclohex-2-enyl)-ethanol (3j)

It was prepared from 4-bromoacetophenone (199 mg, 1.0 mmol) and 1-methyl-1-cyclohexenylzinc chloride (**1c**, 1.2 mmol) according to **Procedure A**. Purification by flash chromatography (eluent: pentane: ether = 10: 1) provided the pure compound **3j** (292 mg, 99%) as a colourless oil. dr > 98:2.

^1H NMR (CDCl_3 , 300 MHz): 7.40 (d, J = 8.8 Hz, 2 H), 7.31 (d, J = 8.8 Hz, 2 H), 5.81-5.87 (m, 1 H), 5.67-5.72 (m, 1 H), 1.93 (s, 1 H), 1.78-1.93 (m, 2 H), 1.59-1.77 (m, 2 H), 1.56 (s, 3 H), 1.36-1.53 (m, 1 H), 0.98 (s, 3 H), 0.93-1.92 (m, 1 H);

^{13}C NMR (CDCl_3 , 75 MHz): 144.2, 131.5, 130.3, 130.1, 129.0, 120.5, 78.0, 42.7, 30.6, 25.0, 24.9, 23.2, 19.4;

IR (neat): 3476 (m), 2937 (m), 1589 (w), 1486 (s), 1368 (m), 1076 (s) cm^{-1} ;

MS (EI, 70 ev): m/z (%) = 276 ($\text{M}^+ - \text{H}_2\text{O}$, 0.5), 201 (^{81}Br , 100), 199 (^{79}Br , 100), 185 (9), 95 (21);

HRMS (EI): calcd. for $\text{C}_{15}\text{H}_{18}\text{Br}$ ($\text{M}^+ (^{79}\text{Br}) - \text{OH}$): 277.0592; **found**: 277.0589 ($\text{M}^+ (^{79}\text{Br}) - \text{OH}$).

Synthesis of (1R)-((1R)-(6,6-dimethyl-2-methylene-bicyclo[3.1.1]hept-3-yl)-2,2-dimethylpropan-1-ol (3k)

It was prepared from 2, 2-dimethyl-propionaldehyde (86 mg, 1.0 mmol) and ((6, 6-dimethyl bicyclo[3.1.1]hept-2-en-2-yl)methyl)zinc chloride (**1d**, 1.2 mmol) according to **Procedure A**. Purification by flash chromatography (eluent: pentane: ether = 3: 1) provided the pure compound **3k** (200 mg, 90%) as a colourless oil. dr > 99:1. $[\alpha]_{\text{D}}^{20} = +8.4$ ($c = 0.5$, CH_2Cl_2).

^1H NMR (CDCl_3 , 600 MHz): 4.94 (s, 1 H), 4.62 (s, 1 H), 3.08 (t, J = 5.4 Hz, 1 H), 2.57 (t, J = 7.5 Hz, 1 H), 2.47 (d, J = 5.3 Hz, 1 H), 2.33 (d, J = 5.0 Hz, 1 H), 2.22-2.29 (m, 1 H), 2.06-2.14 (m, 1 H), 1.95 (q, J = 5.5 Hz, 1 H), 1.63 (dd, J_1 = 13.8 Hz, J_2 = 4.4 Hz, 1 H), 1.35 (d, J = 10.2 Hz, 1 H), 1.23 (s, 3 H), 0.91 (s, 9 H), 0.72 (s, 3 H);

^{13}C NMR (CDCl_3 , 150 MHz): 153.7, 111.9, 83.6, 51.7, 41.4, 40.5, 37.3, 36.4, 33.5, 25.77, 25.75, 25.6, 21.6;

IR (neat): 3532 (m), 2920 (s), 2948 (s), 1630 (m), 1479 (m), 1458 (m), 1364 (s), 1076 (s) cm^{-1} ;

MS (EI, 70 ev): m/z (%) = 222 (M^+ , 1), 189 (5), 165 (8), 147 (9), 136 (39), 121 (30), 93 (100), 69 (23);

HRMS (EI): calcd. for $\text{C}_{15}\text{H}_{27}\text{O}$ ($\text{M}^+ + \text{H}$): 223.2062; **found**: 223.2077 ($\text{M}^+ + \text{H}$).

Synthesis of 3,5-dinitro-benzoic acid (1R)-{(1R)-(6,6-dimethyl-2-methylene-bicyclo[3.1.1]hept-3-yl)-2,2-dimethyl-propyl ester (3k')

ORTEP representation of **10'** with thermal ellipsoids set at 30% probability level (See the complete X-ray data at the end of the manuscript).

A solution of 1-(6, 6-dimethyl-2-methylene-bicyclo[3.1.1]hept-3-yl)-2,2-dimethyl-propan-1-ol **3k** (44 mg, 0.2 mmol), 3,5-dinitro-benzoyl chloride (69 mg, 0.3 mmol), NEt₃ (61 mg, 0.6 mmol) and DMAP (10 mol %) in CH₂Cl₂ (10 mL) was stirred at room temperature for 12 h. The reaction mixture was diluted with ether (30 mL) and then washed with water. The organic layer was dried over anhydrous Na₂SO₄, filtered, and concentrated. The residue was chromatographed on silica gel (eluent: pentane: ether = 8: 1), providing '**3k**' (71 mg, 85%) as a white solid; mp.: 171.5-172.8 °C. [α]_D²⁰ = -59.2 (c = 0.5, CH₂Cl₂).

¹H NMR (CDCl₃, 300 MHz): 9.17 (t, *J* = 2.0 Hz, 1 H), 9.11 (d, *J* = 2.0 Hz, 2 H), 4.93 (d, *J* = 8.8 Hz, 1 H), 4.62-4.70 (m, 2 H), 2.92 (t, *J* = 8.5 Hz, 1 H), 2.06-2.34 (m, 3 H), 1.91-2.02 (m, 1 H), 1.69-1.82 (m, 1 H), 1.54 (d, *J* = 9.7 Hz, 1 H), 1.19 (s, 3 H), 1.07 (s, 9 H), 0.70 (s, 3 H);

¹³C NMR (CDCl₃, 75 MHz): 161.6, 150.5, 148.6, 134.7, 129.4, 122.0, 112.7, 87.5, 51.9, 40.9, 40.5, 36.2, 35.4, 32.9, 26.5, 26.1, 25.5, 21.8;

IR (neat): 2912 (m), 1719 (s), 1628 (w), 1542 (vs), 1482(w), 1460 (w), 1339 (vs) cm⁻¹;

MS (EI, 70 ev): *m/z* (%) = 401 (M⁺-CH₃, 0.5), 330 (25), 194 (80), 105 (90), 91 (100);

Anal. Calcd for C₂₂H₂₈N₂O₆: C, 63.45; H, 6.78; N, 6.73; **Found**: C, 63.24; H, 6.56, N, 6.70.

Synthesis of (2R*)-(3S*)-2-(4-bromo-phenyl)-3-phenyl-pent-4-en-2-ol (4a)

It was prepared from 4-bromoacetophenone (199 mg, 1.0 mmol) and cinnamylzinc chloride (**1e**, 1.2 mmol) according to **Procedure A**. Purification by flash chromatography (eluent: pentane: ether = 8: 2 + 1 % Et₃N) provided the pure compound **4a** (315 mg, 99%) as a colourless oil. dr > 99:1.

¹H NMR (CDCl₃, 300 MHz): 7.42 (d, *J* = 8.5 Hz, 2 H), 7.05-7.32 (m, 7 H), 6.07-6.17 (m, 1 H), 5.08 (d, *J* = 10.3 Hz, 1 H), 4.96 (d, *J* = 17.1 Hz, 1 H), 3.58 (d, *J* = 8.8 Hz, 1 H), 2.00 (br s, 1 H), 1.43 (s, 3 H).

¹³C NMR (CDCl₃, 75 MHz): 145.4, 139.8, 137.0, 130.8, 129.5, 128.2, 127.5, 127.0, 120.6, 118.4, 76.0, 61.8, 28.4.

IR (neat): 3560, 2974, 2924, 1638, 1598, 1486, 1452, 1394, 1084, 1008, 920, 743 cm^{-1} .
Spectral data matching those reported by Baba and collaborators.⁴

Synthesis of (2*S**)-(3*S**)-2,3-dimethyl-4-phenyl-hex-5-en-3-ol (**4b**)

It was prepared from 3-methyl-butan-2-one (86 mg, 1.0 mmol) and cinnamylzinc chloride (**1e**, 1.2 mmol) according to **Procedure A**. Purification by flash chromatography (eluent: pentane: ether = 8: 2 + 1 % Et_3N) provided the pure compound **4b** (196 mg, 96%) as a colourless oil. dr > 99:1.

^1H NMR (CDCl_3 , 300 MHz): 7.22-7.38 (m, 5 H), 6.39 (dt, $J = 17.2$ Hz, $J = 9.9$ Hz, 1 H), 5.19 (dd, $J = 10.2$ Hz, $J = 1.9$ Hz, 1 H), 5.13 (ddd, $J = 17.2$ Hz, $J = 1.8$ Hz, $J = 0.7$ Hz, 1 H), 3.46 (d, $J = 9.6$ Hz, 1 H), 2.00 (hept, $J = 6.8$ Hz, 1 H), 1.40 (br s, 1 H), 1.02 (d, $J = 6.9$ Hz, 3 H), 0.96 (d, $J = 6.8$ Hz, 3 H), 0.91 (s, 3 H).

^{13}C NMR (CDCl_3 , 75 MHz): 142.1, 138.1, 129.6, 128.5, 126.7, 117.1, 76.3, 57.9, 34.3, 20.4, 17.8, 17.1.

IR (neat): 3480, 3074, 3027, 2976, 2962, 2877, 1636, 1601, 1491, 1470, 1452, 1387, 1376, 1156, 1080, 1001, 912, 734 cm^{-1} ;

MS (EI, 70 ev): m/z (%) = 161 (3), 119 (8), 118 (87), 117 (28), 115 (14), 91 (9), 87 (100), 69 (27).

HRMS (EI): calcd. for $[\text{C}_{14}\text{H}_{20}\text{O} - \text{OH}]^+$: 187.1487; **found**: 187.1466.

Synthesis of (2*S**)-(3*S**)-2-cyclopropyl-3-phenyl-pent-4-en-2-ol (**4c**)

It was prepared from 1-cyclopropyl-ethanone (85 mg, 1.0 mmol) and cinnamylzinc chloride (**1e**, 1.2 mmol) according to **Procedure A**. Purification by flash chromatography (eluent: pentane: ether = 8: 2 + 1 % Et_3N) provided the pure compound **4c** (188 mg, 93%) as a colourless oil. dr > 99:1.

^1H NMR (CDCl_3 , 300 MHz): 7.23-7.39 (m, 5 H), 6.44 (dt, $J = 16.9$ Hz, $J = 9.9$ Hz, 1 H), 5.15-5.26 (m, 2 H), 3.44 (d, $J = 9.4$ Hz, 1 H), 1.33 (s, 1 H), 1.11 (s, 3 H), 0.84-0.95 (m, 1 H), 0.28-0.47 (m, 4 H).

^{13}C NMR (CDCl_3 , 75 MHz): 140.9, 137.8, 129.4, 128.1, 126.6, 117.7, 72.4, 62.1, 24.3, 19.5, 1.1, 0.8.

IR (neat): 3570, 3475, 3082, 3006, 2977, 2932, 1636, 1601, 1493, 1452, 1418, 1372, 1307, 1138, 1020, 915, 734 cm^{-1} .

MS (EI, 70 ev): m/z (%) = 128 (1), 119 (3), 118 (29), 117 (13), 115 (10), 86 (3), 85 (52), 67 (4), 43 (100).

HRMS (EI): calcd. for $[\text{C}_{14}\text{H}_{18}\text{O} - \text{H}_2\text{O}]^+$: 184.1252; **found**: 184.1264.

Note: The same reaction carried out at 0 $^\circ\text{C}$ afforded **4c** in 92 % yield and 92: 8 diastereoselectivity.

⁴ Yasuda, M.; Hirata, K.; Nishino, M.; Yamamoto, A.; Baba, A. *J. Am. Chem. Soc.* **2002**, *124*, 13442-13447.

Synthesis of (2*S**)-(3*S**)-2-cyclohexyl-3-phenyl-pent-4-en-2-ol (**4d**)

It was prepared from 1-cyclohexyl-ethanone (127 mg, 1.0 mmol) and cinnamylzinc chloride (**1e**, 1.2 mmol) according to **Procedure A**. Purification by flash chromatography (eluent: pentane: ether = 8: 2 + 1 % Et₃N) provided the pure compound **4d** (231 mg, 95%) as a colourless oil. dr > 99:1.

¹H NMR (CDCl₃, 300 MHz): 7.21-7.37 (m, 5 H), 6.37 (dt, *J* = 17.2 Hz, *J* = 9.9 Hz, 1 H), 5.18 (dd, *J* = 10.2 Hz, *J* = 1.9 Hz, 1 H), 5.10 (dd, *J* = 17.2 Hz, *J* = 1.6 Hz, 1 H), 3.47 (d, *J* = 9.7 Hz, 1 H), 1.58-2.06 (m, 6 H), 0.94-1.58 (m, 6 H), 0.91 (s, 3 H).

¹³C NMR (CDCl₃, 75 MHz): 141.9, 137.9, 129.4, 128.2, 126.4, 116.8, 75.6, 57.3, 44.5, 27.8, 26.7, 26.7, 21.5.

IR (neat): 3477, 3072, 3027, 2976, 2903, 2852, 1635, 1600, 1490, 1451, 1378, 1062, 909, 746, 701 cm⁻¹.

MS (EI, 70 ev): *m/z* (%) = 161 (4), 128 (6), 127 (68), 119 (9), 118 (100), 117 (25), 115 (13), 109 (37), 83 (40), 43 (30).

HRMS (EI): calcd. for [C₁₇H₂₄O – H₂O]⁺: 226.1721; **found**: 226.1716.

Synthesis of (2*S**)-(3*S**)-1,1,1-trifluoro-2-methyl-3-phenyl-pent-4-en-2-ol (**4e**)

It was prepared from 1,1,1-trifluoro-propan-2-one (111 mg, 1.0 mmol) and cinnamylzinc chloride (**1e**, 1.2 mmol) according to **Procedure A**. Purification by flash chromatography (eluent: pentane: ether = 9: 1 + 1 % Et₃N) provided the pure compound **4e** (177 mg, 77 %) as a colourless oil. dr > 99:1.

¹H NMR (CDCl₃, 300 MHz): 7.24-7.39 (m, 5 H), 6.29-6.44 (m, 1 H), 5.24 (dd, *J* = 10.2 Hz, *J* = 1.3 Hz, 1 H), 5.18 (ddd, *J* = 17.0 Hz, *J* = 1.4 Hz, *J* = 1.1 Hz, 1 H), 3.65 (d, *J* = 9.0 Hz, 1 H), 2.21 (br s, 1 H), 1.28 (q, *J* = 1.1 Hz, 3 H).

¹³C NMR (CDCl₃, 75 MHz): 138.9, 135.6, 129.2, 128.5, 127.3, 126.1 (q, *J* = 286.9 Hz), 118.6, 76.8 (q, *J* = 26.6 Hz), 55.1, 20.6 (m).

IR (neat): 3452, 3083, 2982, 2936, 1639, 1602, 1492, 1455, 1384, 1251, 1176, 1120, 1091, 996, 924, 751, 706 cm⁻¹.

MS (EI, 70 ev): *m/z* (%) = 230 (5), 118 (17), 117 (100), 116 (9), 115 (37), 91 (17), 65 (4), 43 (12).

HRMS (EI): calcd. for [C₁₂H₁₃F₃O]⁺: 230.0918; **found**: 230.0895.

Synthesis of (2*S**)-(3*S**)-2-isopropyl-2-methyl-3-phenyl-tetrahydro-furan (**5**)

BH₃·Me₂S (1.8 mL, 19 mmol, 3 equiv) was added at room temperature to a solution of homoallylic alcohol **4b** (1.2 g, 6.0 mmol) in dry THF (20 mL). The resulting solution was stirred at room temperature under nitrogen for 4 h, then it was quenched with water (7 mL) at 0 °C. Sodium perborate (8.5 g, 55 mmol, 9 equiv) and NaOH (2.2 g, 55 mmol, 9 equiv) were

subsequently added, and the reaction mixture was heated to 45 °C for 4 h. The phases were separated and the aqueous phase was extracted with Et₂O. The combined organic phases were dried over MgSO₄, and concentrated *in vacuo*. Purification by flash chromatography (eluent: ether + 1 % Et₃N) provided (4*S**)-(3*S**)-4,5-dimethyl-3-phenyl-hexane-1,4-diol (1.1 g, 84 %) as a colourless oil. dr > 99:1.

¹H NMR (CDCl₃, 300 MHz): 7.21-7.36 (m, 5 H), 3.48-3.60 (m, 1 H), 3.29-3.42 (m, 1H), 2.95 (dd, *J* = 11.1 Hz, *J* = 3.6 Hz, 1 H), 2.11-2.25 (m, 1 H), 1.89-2.09 (m, 2 H), 1.44 (br s, 2 H), 1.02 (d, *J* = 6.7 Hz, 3 H), 0.95 (d, *J* = 6.9 Hz, 3 H), 0.91 (s, 3 H).

¹³C NMR (CDCl₃, 75 MHz): 141.8, 129.6, 128.2, 126.6, 76.4, 61.5, 49.2, 34.0, 31.8, 20.7, 17.8, 17.0.

IR (neat): 3317, 2966, 2912, 2877, 1601, 1451, 1364, 1158, 1054, 1031, 931, 733, 700 cm⁻¹.

MS (EI, 70 ev): *m/z* (%) = 189 (2), 161 (32), 136 (16), 118 (100), 117 (31), 105 (18), 91 (16), 87 (58), 69 (11), 43 (26).

HRMS (EI): calcd. for [C₁₄H₂₂O₂]⁺: 222.1620; **found**: 222.1607.

Mesyl chloride (0.5 mL, 6.5 mmol, 1.5 equiv) was added at 0 °C to a solution of the diol (0.9 g, 4.1 mmol), Et₃N (1.1 mL, 8 mmol, 2.0 equiv) and DMAP (30 mg) in CH₂Cl₂ (15 mL). After 90 min, water was added and the aqueous phase extracted with CH₂Cl₂. The combined organic phases were dried over MgSO₄, and concentrated *in vacuo*. Purification by flash chromatography (eluent: pentane: ether = 98: 2) the pure tetrahydrofuran **5** (571 mg, 69 %) as a colourless oil. dr > 99:1.

¹H NMR (CDCl₃, 600 MHz): 7.19-7.32 (m, 5 H), 4.06-4.11 (m, 1 H), 3.87 (q, *J* = 8.1 Hz, 1 H), 2.25-2.40 (m, 2 H), 1.88 (hept, *J* = 6.8 Hz, 1 H), 1.00 (d, *J* = 6.8 Hz, 3 H), 0.95 (d, *J* = 6.9 Hz, 3 H), 0.79 (s, 3 H).

¹³C NMR (CDCl₃, 75 MHz): 142.4, 128.6, 128.1, 126.2, 87.3, 65.5, 50.3, 35.5, 33.7, 19.0, 18.3, 17.1.

IR (neat): 3029, 2964, 2875, 1603, 1495, 1453, 1386, 1372, 1082, 1052, 852, 767 cm⁻¹.

MS (EI, 70 ev): *m/z* (%) = 167 (3), 162 (6), 119 (10), 118 (100), 117 (59), 91 (13), 65 (2), 43 (17).

HRMS (EI): calcd. for [C₁₄H₂₀O + H]⁺: 205.1592; **found**: 205.1584.

Synthesis of (2*R**)-(3*S**)-2-methyl-3-phenyl-2-trifluoromethyl-tetrahydro-furan (**6**)

BH₃·Me₂S (1.8 mL, 19 mmol, 3 equiv) was added at room temperature to a solution of homoallylic alcohol **4e** (1.4 g, 6.0 mmol) in dry THF (20 mL). The resulting solution was stirred at room temperature under nitrogen for 4 h, then it was quenched with water (7 mL) at 0 °C. Sodium perborate (8.5 g, 55 mmol, 9 equiv) and NaOH (2.2 g, 55 mmol, 9 equiv) were subsequently added, and the reaction mixture was heated to 45 °C for 4 h. The phases were separated and the aqueous phase was extracted with Et₂O. The combined organic phases were dried over MgSO₄, and concentrated *in vacuo*. Purification by flash chromatography (eluent: pentane: ether = 6: 4 + 1 % Et₃N) provided (4*R**)-(3*S**)-5,5,5-trifluoro-4-methyl-3-phenyl-pentane-1,4-diol (554 mg, 37 %) as a white solid. dr > 99:1.

¹H NMR (CDCl₃, 300 MHz): 7.20-7.34 (m, 5 H), 3.57 (quint, *J* = 5.3 Hz, 1 H), 3.22-3.41 (m, 1H), 3.18 (dd, *J* = 10.1 Hz, *J* = 3.8 Hz, 1 H), 2.11-2.25 (m, 1 H), 2.16-2.50 (m, 3 H), 2.01-2.13 (m, 1 H), 1.27 (br s, 3 H).

¹³C NMR (CDCl₃, 75 MHz): 139.1, 129.5 (br), 128.4, 127.3, 126.5 (q, *J* = 287.2 Hz), 75.9 (q, *J* = 26.4 Hz), 60.6, 47.1, 32.6, 19.8 (m).

IR (neat): 3335, 3119, 2888, 1604, 1488, 1455, 1297, 1242, 1188, 1168, 1132, 1037, 706, 669 cm^{-1} .

MS (EI, 70 eV): m/z (%) = 137 (2), 136 (23), 135 (16), 118 (37), 117 (19), 106 (9), 105 (100), 91 (51), 43 (10).

HRMS (EI): calcd. for $[\text{C}_{12}\text{H}_{15}\text{F}_3\text{O}_2 - \text{H}_2\text{O}]^+$: 230.0918; **found**: 230.0906.

Mesyl chloride (0.16 mL, 1.5 equiv) was added at 0 °C to a solution of the diol (345 mg, 1.4 mmol), Et_3N (0.4 mL, 2.0 equiv) and DMAP (8 mg) in CH_2Cl_2 (3 mL) and Et_2O (3 mL). After 40 min, water was added and the aqueous phase extracted with Et_2O . The combined organic phases were dried over MgSO_4 , and concentrated *in vacuo*. Purification by flash chromatography (eluent: pentane: ether = 98: 2) the pure tetrahydrofuran **6** (151 mg, 47 %) as a colourless oil. dr > 99:1.

^1H NMR (CDCl_3 , 300 MHz): 7.23-7.40 (m, 5 H), 4.19-4.29 (m, 1 H), 4.04 (q, J = 8.0 Hz, 1 H), 3.73 (t, J = 8.6 Hz, 1 H), 2.37-2.48 (m, 2H), 0.99 (q, J = 1.1 Hz, 3 H).

^{13}C NMR (CDCl_3 , 75 MHz): 138.4, 128.8, 128.4, 127.3, 127.0 (q, J = 286.2 Hz), 84.2 (q, J = 27.4 Hz), 68.6, 48.3, 32.8, 18.5 (m).

IR (neat): 3034, 2994, 2952, 2885, 1604, 1495, 1456, 1383, 1286, 1208, 1179, 1117, 1084, 1044, 916, 883, 773, 700 cm^{-1} .

MS (EI, 70 eV): 231 (4), 230 (29), 161 (11), 118 (100), 117 (96), 115 (13), 91 (17), 43 (7).

HRMS (EI): calcd. for $[\text{C}_{12}\text{H}_{13}\text{F}_3\text{O}]^+$: 230.0918; **found**: 230.0914.

3f

3f

4d

4d

31

31