Highly *Anti*-Selective S_N2'-Substitutions of Chiral α-Iodo Allylic Alcohol Derivatives with Mixed Zinc-Copper Reagents

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Supporting Information

General considerations

Unless otherwise indicated, all reactions were carried out under argon. Solvents were dried and freshly distilled. Reactions were monitored by gas chromatography (GC and GC-MS) or thin layer chromatography (TLC). Enantiomeric purity was determined by chiral HPLC or capillary GC analysis. In all cases, the analysis was calibrated with a sample of the racemate.

Chiral HPLC:

column A: Chiralcel OD-H, 0.46 cm x 25 cm

column B: Chiralcel OJ, 0.46 cm x 25 cm

Chiral GC:

column A: Chiraldex B-PH, 30.0 m x 250 μm

column B: TFA gamma-cyclodextrin, 30.0 m x 250 μm

method A: 40 °C (2 min), ramp of 20 °C/min to 160 °C (45 min)

method B: 40 °C (0.5 min), ramp of 20 °C/min to 150 °C

method C: 40 °C (10 min), ramp of 2 °C/min to 150 °C (90 min)

method D: 40 °C (8 min), ramp of 7 °C/min to 150 °C

method E: 110 °C

method F: 130 °C

Starting materials

α-Iodoenones 2-iodo-2-cyclohexenone^[1] and 2-iodo-2-cyclopentenone^[1] are literature known. (R)-2-Iodo-2-cyclohexen-1-ol (**6**) and (R)-2-iodo-2-cyclopenten-1-ol (**5**) are literature known.^[2]

(R)-2-Iodo-2-cyclopenten-1-yl diethylphosphate (**1**):^[3]

To a solution of (R)-2-iodo-2-cyclopenten-1-ol (**5**) (1.6 g, 7.6 mmol) in dry CH₂Cl₂ (20 mL) cooled at 0 °C, *N*-methylimidazole (1.2 mL, 15.2 mmol, 2.0 equiv) and diethylchlorophosphate (1.1 mL, 7.6 mmol, 1.0 equiv) were added dropwise. The resulting mixture was stirred 7 h 30 min at 0 °C. The reaction mixture was poured into pH 7 buffer (KH₂PO₄ / Na₂HPO₄, 20 mL) and the phases were separated. After extraction with CH₂Cl₂ (2 x 15 mL) the combined organic phase was dried over Na₂SO₄. The solvent was removed and the crude product purified by fast column chromatography (neutral Al₂O₃, grade III, Et₂O: pentane = 1:3 and then Et₂O containing 0.1 % of Et₃N) to give the phosphate ((R)-**1**) (2.0 g, 5.8 mmol, 76 %) as a colourless oil. This compound, sensitive to SiO₂ purification, was kept under argon in the refrigerator.

HPLC (column B, heptane: *i*PrOH = 99:1, 0.6 mL/min): *t*_R/min = 27.0 (*S*), 32.5 (*R*); 94 % *ee*.

[α]_D²⁰ + 4.5° (c, 1.025, CH₂Cl₂).

¹H NMR (CDCl₃, 300 MHz): δ = 6.43 (m, 1H), 5.25-5.30 (m, 1H), 4.08-4.24 (m, 4H), 2.48-2.60 (m, 1H), 2.26-2.43 (m, 2H), 2.06-2.17 (m, 1H), 1.31-1.39 (m, 6H) ppm.

¹³C NMR (CDCl₃, 75 MHz): δ = 146.0, 93.5, 93.4, 87.8, 87.7, 64.1, 64.0, 63.8, 63.7, 32.9, 30.8, 30.7, 16.2, 16.15, 16.1, 16.06 ppm.

m/z (%): 220 (10), 219 (100, M⁺-I), 209 (6), 193 (14), 192 (51), 163 (51), 155 (28), 138 (3), 127 (24), 111 (5), 99 (37), 83 (20), 66 (22), 65 (45).

HRMS (EI): calcd. for C₉H₁₅IO₄P [M-H⁺]: 344.9753, found: 344.9747.

IR (film): 2983 (m), 2932 (w), 1443 (w), 1393 (w), 1265 (s), 1165 (m), 1027 (vs), 989 (vs), 818 (m), 571 (w).

(*R*)-2-Iodo-2-cyclohexen-1-yl diethylphosphate (2a):^[3]

To a solution of (*R*)-2-iodo-2-cyclohexen-1-ol (**6**) (2.5 g, 11.2 mmol) and *N*-methylimidazole (2.1 mL, 26.8 mmol, 2.4 equiv) in dry CH₂Cl₂ (30 mL) at 25 °C, diethylchlorophosphate (1.9 mL, 13.4 mmol, 1.2 equiv) was added dropwise. The resulting mixture was stirred overnight at 25 °C. The reaction mixture was poured into saturated aqueous NaCl sol. (20 mL) and the phases were separated. After extraction with CH₂Cl₂ (2 x 15 mL) the combined organic phase was dried over Na₂SO₄. The solvent was removed and the crude product purified by column chromatography (Et₂O) to give the phosphate ((*R*)-**2a**) (3.5 g, 9.7 mmol, 87 %) as a colourless oil.

HPLC (column B, heptane: *i*PrOH = 99:1, 0.6 mL/min): *t_R*/min = 21.2 (*S*), 25.5 (*R*); 94 % *ee*.

$[\alpha]_D^{20} + 38.2^\circ$ (c 1.08, CH₂Cl₂).

¹H NMR (CDCl₃, 300 MHz): δ = 6.61 (t, *J* = 4.0 Hz, 1H), 4.73-4.89 (m, 1H), 4.03-4.24 (m, 4H), 1.91-2.21 (m, 4H), 1.63-1.82 (m, 2H), 1.29-1.37 (m, 6H) ppm.

¹³C NMR (CDCl₃, 75 MHz): δ = 143.9, 95.2, 95.1, 78.1, 78.0, 64.1, 64.0, 63.8, 63.7, 31.1, 29.1, 16.4, 16.2, 16.1, 16.0, 15.9 ppm.

m/z (%): 356 (1), 315 (1), 234 (11, M⁺-I), 233 (100), 207 (5), 206 (12), 205 (24), 177 (30), 155 (12), 127 (15), 99 (47), 97 (15), 81 (10), 80 (9), 79 (50), 78 (10), 77 (22), 67 (3), 52 (4).

HRMS (EI): calcd. for C₁₀H₁₈IO₄P [M⁺]: 359.9987, found: 359.9977.

IR (film): 2982 (m), 2035 (m), 1443 (w), 1273 (s), 1164 (m), 1032 (vs), 988 (vs), 805 (w), 763 (w).

anal. calcd. for C₁₀H₁₈IO₄P (360.13): C 33.35, H 5.04, I 35.24; found: C 33.58, H 5.03, I 35.23.

(*R*)-2-Iodo-2-cyclohexen-1-yl 2,3,4,5,6-pentafluorobenzoate (2b):

To a solution of (*R*)-2-iodo-2-cyclohexen-1-ol (**6**) (3.0 g, 13.4 mmol), pyridine (1.4 mL, 17.4 mmol, 1.3 equiv) and DMAP (0.164 g, 1.34 mmol, 0.1 equiv) in dry CH₂Cl₂ (67 mL) at 25 °C, pentafluorobenzoyl chloride (2.51 mL, 17.4 mmol, 1.3 equiv) was added dropwise. The resulting mixture was stirred for 2 h at 25 °C. The reaction mixture was poured into saturated aqueous NH₄Cl sol (60 mL) and the phases were separated. After extraction with Et₂O (2 x 50 mL) the combined organic phase was washed with saturated aqueous NaHCO₃ sol., brine, and dried over Na₂SO₄. The solvent was removed and the crude product purified by column chromatography (pentane:Et₂O = 20:1) to give the pentafluorobenzoate ester ((*R*)-**2b**) (5.2 g, 12.5 mmol, 93 %) as a colourless oil.

HPLC (column A, heptane: *i*PrOH = 98:2, 0.2 mL/min): *t_R*/min = 30.3 (*R*), 33.1 (*S*); 94 % *ee*.

$[\alpha]_D^{20} + 58.9^\circ$ (c 1.42, CH₂Cl₂).

¹H NMR (CDCl₃, 300 MHz): δ = 6.65 (dd, *J* = 4.4, 3.5 Hz, 1H), 5.62 (t, *J* = 4.3 Hz, 1H), 2.10-2.22 (m, 2H), 1.92-2.05 (m, 2H), 1.64-1.73 (m, 2H) ppm.

¹³C NMR (CDCl₃, 75 MHz): δ = 158.3, 147.0, 145.1, 145.0, 143.6, 141.4, 139.4, 135.9, 92.3, 76.5, 29.9, 29.1, 16.8 ppm.

m/z (%): 292 (12, M⁺-I), 291 (90), 247 (5), 206 (4), 196 (22), 195 (100), 167 (31), 148 (3), 117 (15), 80 (8), 79 (31), 77 (17).

IR (film): 2949 (m), 1738 (vs), 1652 (m), 1504 (vs), 1425 (m), 1341 (vs), 1225 (vs), 1102 (w), 998 (vs), 913 (m), 771 (m), 728 (w).

anal. calcd. for $C_{13}H_8F_5IO_2$ (418.1): C 37.35, H 1.93; found: C 37.40, H 1.93.

Method A: Typical procedure for the copper(I)-mediated addition of dialkylzinc reagents to pentafluorobenzoates or diethylphosphates.

The dialkylzinc reagent (1.12 mmol, 2.24 equiv) was added dropwise to a solution stirred at $-30\text{ }^{\circ}\text{C}$, under an argon atmosphere, of $CuCN\cdot 2LiCl$ (1 M solution in THF; 0.56 mL, 1.12 mmol) in NMP (sufficient to give an overall ratio of solvents THF:NMP = 2.8:1). The resulting mixture was stirred 0.5 h at $-30\text{ }^{\circ}\text{C}$; then, the pentafluorobenzoate ester or the diethylphosphate (0.5 mmol, 1.0 equiv) was added dropwise as a solution in THF (0.8 mL) and the reaction mixture was allowed to warm to $-10\text{ }^{\circ}\text{C}$ over approx. 1.5 h, and stirred at this temperature until the conversion was complete (14 h). Then, saturated aqueous NH_4Cl sol. (20 mL) was added followed by 25 % aqueous ammonia solution (1 mL), and the reaction mixture was stirred at $25\text{ }^{\circ}\text{C}$ until the copper salts had dissolved. The mixture was extracted with Et_2O (3 x 20 mL). The combined extracts were washed with brine and dried over Na_2SO_4 . Evaporation of the solvents and purification by column chromatography afforded the desired vinylic iodides.

(R)-1-Iodo-5-methyl-1-cyclopentene (3a):

Following general procedure A, Me_2Zn (4 M solution in THF, 1.5 mmol, 3.0 equiv) was dropwise added to a solution stirred at $-30\text{ }^{\circ}\text{C}$, under an argon atmosphere, of $CuCN\cdot 2LiCl$ (1 M solution in THF; 0.75 mL, 0.75 mmol, 1.5 equiv). The mixture was stirred 0.5 h at $-30\text{ }^{\circ}\text{C}$ and then cooled to $-50\text{ }^{\circ}\text{C}$. Then, (*R*)-2-iodo-2-cyclopenten-1-yl diethylphosphate (**1**) (0.173 g, 0.5 mmol, 1.0 equiv) was added dropwise as a solution in THF (0.8 mL) and the reaction mixture was stirred at $-50\text{ }^{\circ}\text{C}$ for 16 h. After purification by column chromatography (pentane) and careful removal of solvent, **3a** was obtained as a colourless oil (0.078 g, 0.37 mmol, 75 % yield).

GC (column B, method B): $t_R/\text{min} = 3.87$ (*R*), 3.92 (*S*); 94 % *ee*.

$[\alpha]_D^{20} +17.8^{\circ}$ (c 1.11, CH_2Cl_2).

1H NMR ($CDCl_3$, 300 MHz): $\delta = 6.07$ (m, 1H), 2.69-2.79 (m, 1H), 2.24-2.39 (m, 2H), 2.08-2.23 (m, 1H), 1.49-1.60 (m, 1H), 1.06 (d, $J = 6.7$ Hz, 3H) ppm.

^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 139.1$, 103.2, 47.2, 33.2, 30.6, 20.8 ppm.

m/z (%): 208 (98, M^+), 193 (7), 127 (5), 81 (100), 79 (34), 77 (100), 66 (38), 65 (11), 53 (18), 51 (9).

HRMS (EI): calcd. for C_6H_9I [M^+]: 207.9749, found: 207.9741.

IR (film): 3401 (m), 2957 (s), 2926 (vs), 2854 (s), 1713 (m), 1454 (m), 1377 (w), 1040 (m), 743 (w), 698 (w).

(R)-1-Iodo-6-pentyl-1-cyclohexene (3b):

Following general procedure A and starting from (*R*)-2-iodo-2-cyclohexen-1-yl diethylphosphate (**2a**) (0.180 g, 0.5 mmol, 1.0 equiv), the vinylic iodide **3b** was obtained as a colourless oil, after purification by column chromatography (pentane, 0.126 g, 0.455 mmol, 91 % yield).

GC (column A, method A): $t_R/\text{min} = 11.8$ (*S*), 12.0 (*R*); 93 % *ee*.

$[\alpha]_D^{20} -2.33^{\circ}$ (c 1.12, CH_2Cl_2).

1H NMR ($CDCl_3$, 300 MHz): $\delta = 6.36$ (dt, $J = 4.0$, 1.3 Hz, 1H), 2.19-2.31 (m, 1H), 1.93-2.10 (m, 2H), 1.51-1.87 (m, 5H), 1.10-1.45 (m, 7H), 0.75-0.94 (m, 3H) ppm.

^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 138.2$, 107.3, 44.9, 34.6, 31.8, 29.6, 28.1, 26.4, 22.6, 18.4, 14.1 ppm.

m/z (%): 278 (38, M^+), 208 (26), 151 (16), 109 (17), 95 (56), 91 (10), 81 (100), 77 (21), 69 (11), 67 (39), 55 (12).

HRMS (EI): calcd. for $C_{11}H_{19}I$ [M^+]: 278.0531, found: 278.0503.

IR (film): 2929 (vs), 2857 (s), 1683 (m), 1456 (s), 961 (w), 802 (w), 723 (w).

(R)-6-Ethyl-1-iodo-1-cyclohexene (3c):

Following general procedure A, and starting from (*R*)-2-iodo-2-cyclohexen-1-yl 2,3,4,5,6-pentafluorobenzoate (**2b**) (0.210 g, 0.5 mmol, 1.0 equiv), the vinylic iodide **3c** was obtained, after purification by column chromatography (pentane) as a colourless oil (0.100 g, 0.425 mmol, 85 % yield). The enantiomeric excess was determined by capillary GC analysis on the corresponding α,β -unsaturated phenyl ketone (**10**).^[4]

$[\alpha]_D^{20} -1.7^\circ$ (c 1.38, CH₂Cl₂).

¹H NMR (CDCl₃, 300 MHz): δ = 6.31 (dt, *J* = 4.0, 1.3 Hz, 1H), 2.09-2.21 (m, 1H), 1.87-2.01 (m, 2H), 1.46-1.65 (m, 3H), 1.67-1.81 (m, 2H), 1.15-1.33 (m, 1H), 0.83 (t, *J* = 7.5 Hz, 3H) ppm.

¹³C NMR (CDCl₃, 75 MHz): δ = 138.5, 107.0, 46.2, 29.6, 27.6, 27.5, 18.7, 11.1 ppm.

m/z (%): 236 (86, M⁺), 207 (2), 127 (3), 109 (100), 91 (9), 81 (28), 80 (29), 79 (72), 77 (29), 67 (99), 55 (20).

HRMS (EI): calcd. for C₈H₁₃I [M⁺]: 236.0062, found: 236.0067.

IR (film): 2962 (vs), 2873 (vs), 1628 (w), 1459 (m), 1319 (m), 974 (m), 937 (w), 890 (w), 802 (w), 725 (m).

(R)-6-Cyclohexyl-1-iodo-1-cyclohexene (3d):

Following general procedure A, and starting from (*R*)-2-iodo-2-cyclohexen-1-yl 2,3,4,5,6-pentafluorobenzoate (**2b**) (0.210 g, 0.5 mmol, 1.0 equiv), the vinylic iodide **3d** was obtained, after purification by column chromatography (pentane) as a colourless oil (0.131 g, 0.45 mmol, 90 % yield). The enantiomeric excess (91 % *ee*) was determined by ¹³C NMR analysis on the diastereisomeric (2*R*)-4-[(6*S*)-6-cyclohexyl-1-cyclohexen-1-yl]-3butyn-2-ol (**11**) obtained by cross-coupling **3d** with (*R*)-3-butyn-2-ol.^[5]

$[\alpha]_D^{20} -76.4^\circ$ (c 1.12, CH₂Cl₂).

¹H NMR (CDCl₃, 300 MHz): δ = 6.52 (m, 1H), 2.12-2.32 (m, 1H), 0.84-2.09 (m, 17 H) ppm.

¹³C NMR (CDCl₃, 75 MHz): δ = 140.3, 108.6, 48.6, 43.1, 31.2, 29.7, 27.1, 26.7, 26.6, 26.5, 25.2, 21.4 ppm.

m/z (%): 290 (51, M⁺), 208 (100), 163 (24), 121 (2), 105 (3), 91 (12), 83 (56), 81 (63), 79 (41), 67 (12), 55 (44).

HRMS (EI): calcd. for C₁₂H₁₉I [M⁺]: 290.0531, found: 290.0505.

IR (film): 2925 (vs), 2851 (vs), 1148 (s), 986 (w), 875 (w), 704 (w).

(R)-1-Iodo-6-isopropyl-1-cyclohexene (3e):

Following general procedure A, and starting from (*R*)-2-iodo-2-cyclohexen-1-yl 2,3,4,5,6-pentafluorobenzoate (**2b**) (0.210 g, 0.5 mmol, 1.0 equiv), the vinylic iodide **3e** was obtained, after purification by column chromatography (pentane) as a colourless oil (0.088 g, 0.35 mmol, 70 % yield).

GC (column B, method B): *t_R*/min = 6.86 (*S*), 6.97 (*R*); 93 % *ee*.

$[\alpha]_D^{20} -79.1^\circ$ (c 1.12, CH₂Cl₂).

¹H NMR (CDCl₃, 300 MHz): δ = 6.52 (m, 1H), 2.17-2.32 (m, 2H), 1.94-2.08 (m, 2H), 1.63-1.80 (m, 2H), 1.47-1.61 (m, 2H), 0.96 (d, *J* = 6.6 Hz, 3H), 0.75 (d, *J* = 6.6 Hz, 3H) ppm.

¹³C NMR (CDCl₃, 75 MHz): δ = 140.4, 109.0, 48.7, 32.2, 29.7, 23.6, 21.3, 20.4, 15.5 ppm.

m/z (%): 251 (9, M⁺), 250 (91), 209 (2), 208 (30), 207 (11), 206 (5), 123 (68), 91 (9), 81 (70), 80 (38), 79 (100), 78 (8), 77 (27), 67 (23), 53 (8).

HRMS (EI): calcd. for C₉H₁₅I [M⁺]: 250.0218, found: 250.0214.

IR (film): 2959 (vs), 2928 (vs), 2870 (s), 1682 (w), 1464 (m), 1386 (w), 1368 (w), 1030 (w), 1003 (w), 805 (w), 692 (w).

Method B :Typical procedure for the copper(I)-mediated addition of alkylzinc halide reagents to diethylphosphates.

The freshly prepared of alkylzinc halide reagent (solution in THF, 1.0 mmol, 2.0 equiv) was added dropwise to a solution stirred at -30 °C, under an argon atmosphere, of CuCN·2LiCl (1 M solution in THF; 1.0 mL, 1.0 mmol, 2.0 equiv). The resulting mixture was stirred 0.5 h at -30 °C, then the phosphate ester (0.5 mmol, 1.0 equiv) was added dropwise as a solution in NMP (sufficient to give an overall ratio of THF:NMP = 2.8:1) and the reaction mixture was allowed to warm to the temperature and to stir during the time stated for each compound. Then, saturated aqueous NH₄Cl sol. (20 mL) was added followed by 25 % aqueous ammonia solution (1 mL), and the reaction mixture was stirred at rt until the copper salts had dissolved. The mixture was extracted with Et₂O (3 x 20 mL). The combined extracts were washed with brine and dried over Na₂SO₄. Evaporation of the solvents and purification by column chromatography afforded the desired vinylic iodides.

(*R*)-4-(2-Iodo-2-cyclopenten-1-yl) ethylbutanoate (**3f**):

3-Carboethoxypropylzinc iodide^[6] was freshly prepared by treatment of 3-carboethoxypropyl iodide (0.726 g, 3.0 mmol, 1.0 equiv) with activated Zn foil (0.6 g, 9.0 mmol, 3.0 equiv) in THF (2 mL) at 48 °C for 4.5 h. The insertion of Zn was monitored by GC analysis of hydrolyzed aliquots and, after completion, the resulting solution was titrated with sodium thiosulfate.

Following general procedure B, after addition of (*R*)-2-iodo-2-cyclopenten-1-yl diethylphosphate (**1**) (0.173 g, 0.5 mmol, 1.0 equiv) in NMP (0.8 mL) over the mixed cuprate cooled at -30 °C, the reaction mixture was stirred for 14 h while warming up to 25 °C. The vinylic iodide **3f** was obtained, after purification by column chromatography (SiO₂, pentane:Et₂O = 20:1) as a colourless oil (0.125 g, 0.405 mmol, 81 % yield).

GC (column B, method C): t_R /min = 64.5 (*R*), 64.8 (*S*); 93 % *ee*.

$[\alpha]_D^{20}$ -10.4° (c 1.5, CH₂Cl₂).

¹H NMR (CDCl₃, 300 MHz): δ = 6.05 (m, 1H), 4.07 (q, J = 7.1 Hz, 2H), 2.54-2.76 (m, 1H), 2.14-2.34 (m, 4H), 1.94-2.07 (m, 1H), 1.41-1.69 (m, 4H), 1.19 (t, J = 7.1 Hz, 3H), 1.06-1.20 (m, 1H) ppm.

¹³C NMR (CDCl₃, 75 MHz): δ = 173.5, 139.6, 101.2, 60.2, 51.8, 34.4, 34.0, 33.3, 27.7, 22.0, 14.2 ppm.

m/z (%): 263 (2, M⁺-C₂H₅O), 245 (4), 219 (9), 206 (5), 193 (7), 181 (52), 153 (4), 135 (100), 118 (8), 107 (15), 93 (81), 79 (27), 66 (38), 55 (6).

HRMS (CI): calcd. for C₁₁H₁₈IO₂ [M+H⁺]: 309.0352, found: 309.0326.

IR (film): 2931 (s), 1736 (vs), 1453 (m), 1174 (m), 1028 (w), 757 (w), 692 (w).

anal. calcd. for C₁₁H₁₇IO₂ (308.16): C 42.87, H 5.56, found: C 42.91, H 5.46.

(*S*)-4-(2-Iodo-2-cyclohexen-1-yl) ethylbutanoate (**3g**):

3-Carboethoxypropylzinc iodide^[6] was freshly prepared by treatment of 3-carboethoxypropyl iodide (0.726 g, 3.0 mmol, 1.0 equiv) with activated Zn foil (0.6 g, 9.0 mmol, 3.0 equiv) in THF (2 mL) at 48 °C for 4.5 h. After insertion of Zn was complete (monitored by GC analysis of hydrolyzed aliquots), the resulting solution was titrated with sodium thiosulfate.

Following general procedure B, after addition of (*R*)-2-iodo-2-cyclohexen-1-yl diethylphosphate (**2a**) (0.180 g, 0.5 mmol, 1.0 equiv) in NMP (0.8 mL) over the mixed cuprate cooled at -30 °C, the reaction mixture was stirred for 12 h while warming up to 25 °C. The vinylic iodide **3g** was obtained, after purification by column chromatography (SiO₂, pentane:Et₂O = 20:1) as a colourless oil (0.110 g, 0.34 mmol, 68 % yield).

GC (column A, method A): t_R /min = 38.8 (*R*), 39.5 (*S*); 93 % *ee*.

$[\alpha]_D^{20}$ -1.7° (c 1.08, CH₂Cl₂).

¹H NMR (CDCl₃, 300 MHz): δ = 6.27 (dt, J = 4.0, 1.3 Hz, 1H), 4.03 (q, J = 7.0 Hz, 2H), 2.18-2.40 (m, 3H), 1.94-2.16 (m, 2H), 1.45-1.90 (m, 7H), 1.30-1.45 (m, 1H), 1.26 (t, J = 7.0 Hz, 3H) ppm.

^{13}C NMR (CDCl_3 , 75 MHz): δ = 173.5, 138.7, 106.2, 60.2, 44.6, 34.3, 34.1, 29.5, 27.9, 22.2, 18.4, 14.2 ppm.

m/z (%): 277 (2), 259 (2), 234 (3), 195 (100), 149 (84), 131 (74), 121 (39), 107 (96), 91 (25), 80 (20), 79 (72), 77 (23), 67 (15), 55 (8).

HRMS (EI): calcd. for $\text{C}_{12}\text{H}_{19}\text{IO}_2$ [$\text{M}+\text{H}^+$]: 322.0430, found: 323.0484.

IR (film): 2934 (s), 1733 (vs), 1446 (m), 1179 (s), 1035 (m), 964 (w), 724 (w).

anal. calcd. for $\text{C}_{12}\text{H}_{19}\text{IO}_2$ (322.18): C 44.74, H 5.94, I 39.39; found: C 44.61, H 5.97, I 39.38.

(S)-3-(2-Iodo-2-cyclopenten-1-yl)propyl acetate (3h):

3-Acetoxypropylzinc iodide^[6] was freshly prepared by treatment of 3-acetoxypropyl iodide (0.684 g, 3.0 mmol, 1.0 equiv) with activated Zn foil (0.6 g, 9.0 mmol, 3.0 equiv) in THF (2 mL) at 40 °C for 4 h. After insertion of Zn was complete (monitored by GC analysis of hydrolyzed aliquots), the resulting solution was titrated with sodium thiosulfate.

Following general procedure B, after preparation of the mixed cuprate by treatment of $\text{CuCN}\cdot 2\text{LiCl}$ (1 M solution in THF; 1.0 mL, 1.0 mmol, 2.0 equiv) with 3-acetoxypropylzinc iodide (1.45 M solution in THF, 1.45 mL, 1.0 mmol, 2.0 equiv) at -30 °C for 30 min, (*R*)-2-iodo-2-cyclopenten-1-yl diethylphosphate (**1**) (0.173 g, 0.5 mmol, 1.0 equiv), in NMP (0.8 mL), was dropwise added and the reaction mixture was stirred for 16 h while warming up to 25 °C. The vinylic iodide **3h** was obtained, after purification by column chromatography (SiO_2 , pentane: Et_2O = 6:1) as a colourless oil (0.134 g, 0.455 mmol, 91 % yield).

GC (column B, method C): t_R/min = 60.8 (*S*), 61.1 (*R*); 94 % *ee*.

$[\alpha]_D^{20}$ -7.7° (c 1.06, CH_2Cl_2).

^1H NMR (CDCl_3 , 300 MHz): δ = 6.06 (m, 1H), 3.92-4.13 (m, 2H), 2.47-2.66 (m, 1H), 2.20-2.28 (m, 2H), 1.99 (s, 3H), 1.95-2.07 (m, 1H), 1.46-1.72 (m, 4H), 1.03-1.24 (m, 1H) ppm.

^{13}C NMR (CDCl_3 , 75 MHz): δ = 171.1, 139.8, 101.1, 64.5, 51.6, 33.3, 30.7, 27.7, 25.5, 21.0 ppm.

m/z (%): 234 (19, M^+-HOAc), 219 (3), 206 (100), 193 (9), 167 (6, M^+-I), 123 (2), 107 (53), 91 (15), 79 (50), 77 (11), 66 (34), 65 (11).

HRMS (CI): calcd. for $\text{C}_{10}\text{H}_{16}\text{IO}_2$ [$\text{M}+\text{H}^+$]: 295.0195, found: 295.0230.

IR (film): 2944 (s), 2851 (m), 1740 (vs), 1450 (m), 1364 (m), 1239 (vs), 1048 (s), 799 (w), 606 (w).

anal. calcd. for $\text{C}_{10}\text{H}_{15}\text{IO}_2$ (294.13): C 40.83, H 5.14, found: C 41.15, H 4.85.

(S)-3-(2-Iodo-2-cyclohexen-1-yl)propyl acetate (3i):

3-Acetoxypropylzinc iodide^[6] was freshly prepared by treatment of 3-acetoxypropyl iodide (0.684 g, 3.0 mmol, 1.0 equiv) with activated Zn foil (0.6 g, 9.0 mmol, 3.0 equiv) in THF (2 mL) at 40 °C for 4 h. After insertion of Zn was complete (monitored by GC analysis of hydrolyzed aliquots), the resulting solution was titrated with sodium thiosulfate.

According to general procedure B, the freshly prepared 3-acetoxypropylzinc iodide (1.45 M solution in THF, 1.4 mmol, 2.0 equiv) was added dropwise to a solution stirred at -30 °C of $\text{CuCN}\cdot 2\text{LiCl}$ (1 M solution in THF; 1.4 mL, 1.4 mmol, 2.0 equiv). The resulting mixture was stirred 0.5 h at -30 °C, then (*R*)-2-iodo-2-cyclohexen-1-yl diethylphosphate (**2a**) (0.252 g, 0.7 mmol, 1.0 equiv) in NMP (0.8 mL) was added dropwise. The reaction mixture was stirred for 16 h while warming up to 25 °C. The vinylic iodide **3i** was obtained, after purification by column chromatography (SiO_2 , pentane: Et_2O = 6:1) as a colourless oil (0.181 g, 0.59 mmol, 84 % yield).

GC (column A, method A): t_R/min = 31.2 (*R*), 32.0 (*S*); 97.8 % *ee*.^[7]

$[\alpha]_D^{20}$ -3.2° (c 1.64, CH_2Cl_2).

^1H NMR (CDCl_3 , 300 MHz): δ = 6.39 (dt, J = 4.0, 1.4 Hz, 1H), 3.90-4.15 (m, 2H), 2.19-2.37 (m, 1H), 2.05 (s, 3H), 2.04 (m, 2H), 1.35-1.87 (m, 8H) ppm.

^{13}C NMR (CDCl_3 , 75 MHz): δ = 171.1, 138.9, 106.0, 64.4, 44.4, 31.0, 29.5, 28.0, 25.7, 21.0, 18.5 ppm.

m/z (%): 248 (13, M^+-HOAc), 220 (100), 206 (4), 181 (3, M^+-I), 121 (76), 105 (5), 93 (42), 91 (19), 80 (13), 79 (48), 77 (22), 67 (9), 55 (6).

HRMS (CI): calcd. for $C_{11}H_{18}IO_2$ $[M+H]^+$: 309.0352, found: 309.0386.

IR (film): 2934 (s), 1740 (vs), 1450 (m), 1364 (m), 1241 (vs), 1048 (m), 963 (w), 724 (w).

anal. calcd. for $C_{11}H_{17}IO_2$ (308.16): C 42.87, H 5.56, found: C 42.40, H 5.40.

(S)-2-[2-(2-Iodo-2-cyclopenten-1-yl)ethyl]-1,3-dioxolane (3j):

[2-(1,3-Dioxolan-2-yl)ethyl]zinc iodide^[6] was freshly prepared by treatment of 2-(2-iodoethyl)-1,3-dioxolane (0.684 g, 3.0 mmol, 1.0 equiv) with activated Zn foil (0.6 g, 9.0 mmol, 3.0 equiv) in THF (2 mL) at 45 °C for 3 h. After insertion of Zn was complete (monitored by GC analysis of hydrolyzed aliquots), the resulting solution was titrated with sodium thiosulfate.

According to general procedure B, the freshly prepared zinc iodide (1.5 M solution in THF, 1.2 mL, 1.7 mmol, 2.0 equiv) was added dropwise to a solution stirred at -30 °C of $CuCN \cdot 2LiCl$ (1 M solution in THF; 1.7 mL, 1.7 mmol, 2.0 equiv). The resulting mixture was stirred 0.5 h at -30 °C, then (*R*)-2-iodo-2-cyclopenten-1-yl diethylphosphate (**1**) (0.300 g, 0.87 mmol, 1.0 equiv) in NMP (1.0 mL) was added dropwise. The reaction mixture was allowed to warm up overnight (~14 h). The vinylic iodide **3j** was obtained, after purification by column chromatography (SiO_2 , pentane:Et₂O = 9:1) as a colourless oil (0.198 g, 0.67 mmol, 77 % yield).

GC (column B, method D): t_R/min = 30.1 (*S*), 30.3 (*R*); 94 % *ee*.

$[\alpha]_D^{20}$ -5.54° (c 1.3, CH₂Cl₂).

¹H NMR (CDCl₃, 300 MHz): δ = 6.09 (m, 1H), 4.85 (t, *J* = 4.4 Hz, 1H), 3.91-4.0 (m, 2H), 3.77-3.86 (m, 2H), 2.63-2.77 (m, 1H), 2.17-2.37 (m, 2H), 1.98-2.12 (m, 1H), 1.52-1.84 (m, 4H), 1.21-1.35 (m, 1H) ppm.

¹³C NMR (CDCl₃, 75 MHz): δ = 139.7, 104.5, 101.1, 64.8, 64.7, 51.6, 33.3, 30.7, 28.6, 27.6 ppm.

m/z (%): 293 (3, M^+-H), 232 (3), 206 (86), 168 (6), 167 (50), 149 (2), 127 (2), 123 (5), 105 (18), 99 (19), 91 (5), 79 (39), 77 (11), 73 (100), 66 (22), 65 (10).

HRMS (EI): calcd. for $C_{10}H_{14}IO_2$ $[M-H]^+$: 293.0039, found: 293.0035.

IR (film): 2949 (vs), 2882 (vs), 1602 (w), 1450 (m), 1410 (m), 1133 (vs), 1036 (s), 943 (w), 910 (w), 801 (w), 554 (w).

(S)-2-[2-(2-Iodo-2-cyclohexen-1-yl)ethyl]-1,3-dioxolane (3k):

[2-(1,3-Dioxolan-2-yl)ethyl]zinc iodide^[6] was freshly prepared by treatment of 2-(2-iodoethyl)-1,3-dioxolane (0.684 g, 3.0 mmol, 1.0 equiv) with activated Zn foil (0.6 g, 9.0 mmol, 3.0 equiv) in THF (2 mL) at 45 °C for 3 h. After insertion of Zn was complete (monitored by GC analysis of hydrolyzed aliquots), the resulting solution was titrated with sodium thiosulfate.

According to general procedure B, the freshly prepared zinc iodide (1.5 M solution in THF, 1.0 mL, 1.5 mmol, 2.0 equiv) was added dropwise to a solution stirred at -30 °C of $CuCN \cdot 2LiCl$ (1 M solution in THF; 1.5 mL, 1.5 mmol, 2.0 equiv). The resulting mixture was stirred 0.5 h at -30 °C, then 2-iodo-2-cyclohexen-1-yl diethylphosphate (**2a**) (0.270 g, 0.75 mmol, 1.0 equiv) in NMP (0.9 mL) was added dropwise. The reaction mixture was allowed to warm up overnight (~14 h). The vinylic iodide **3k** was isolated, after purification by column chromatography (SiO_2 , pentane:Et₂O = 9:1) as a colourless oil (0.143 g, 0.46 mmol, 62 % yield).

GC (column A, method A): t_R/min = 40.9 (*R*), 41.6 (*S*); 97 % *ee*.^[7]

$[\alpha]_D^{20}$ -3.65° (c 1.15, CH₂Cl₂).

¹H NMR (CDCl₃, 300 MHz): δ = 6.30 (dt, *J* = 4.0, 1.8 Hz, 1H), 4.87 (t, *J* = 4.4 Hz, 1H), 3.90-4.02 (m, 2H), 3.79-3.88 (m, 2H), 2.26-2.40 (m, 1H), 1.98-2.07 (m, 2H), 1.37-1.96 (m, 8H) ppm.

¹³C NMR (CDCl₃, 75 MHz): δ = 138.8, 106.1, 104.5, 64.9, 64.8, 44.5, 31.0, 29.5, 29.0, 28.0, 18.5 ppm.

m/z (%): 307 (3, M^+-H), 220 (83), 181 (65), 137 (4), 119 (28), 99 (21), 93 (33), 91 (20), 79 (26), 77 (17), 73 (100), 65 (4), 55 (5).

HRMS (EI): calcd. For $C_{11}H_{16}IO_2$ $[M-H]^+$: 307.0195, found: 307.0192.

IR (film): 2931 (vs), 2875 (vs), 1626 (w), 1451 (m), 1409 (m), 1327 (w), 1135 (s), 1038 (s), 943 (m), 870 (m), 726 (w).

(S)-3-(2-Iodo-2-cyclopenten-1-yl)propanenitrile (3l):

2-Cyanoethylzinc iodide^[8] was freshly prepared by treatment of 3-iodopropionitrile (0.543 g, 3.0 mmol, 1.0 equiv) with activated Zn foil (0.6 g, 9.0 mmol, 3.0 equiv) in THF (2 mL) at 25 °C for 3 h. After insertion of Zn was complete (monitored by GC analysis of hydrolyzed aliquots), the resulting solution was titrated with sodium thiosulfate.

According to general procedure B, the freshly prepared zinc iodide (1.5 M solution in THF, 0.7 mL, 1.0 mmol, 2.0 equiv) was added dropwise to a solution stirred at -30 °C of CuCN·2LiCl (1 M solution in THF; 1.0 mL, 1.0 mmol, 2.0 equiv). The resulting mixture was stirred 0.5 h at -30 °C, then (*R*)-2-iodo-2-cyclopenten-1-yl diethylphosphate (**1**) (0.173 g, 0.5 mmol, 1.0 equiv) in NMP (0.8 mL) was added dropwise. The reaction mixture was stirred overnight while warming up to 25 °C (~16 h). The vinylic iodide **3l** was isolated, after purification by column chromatography (SiO₂, pentane:Et₂O = 3:1) as a colourless oil (0.111 g, 0.45 mmol, 90 % yield).

GC (column B, method C): *t_R*/min = 61.9 (*S*), 64.6 (*R*); 91 % *ee*.^[9]

$[\alpha]_D^{20}$ -5.3° (c 1.25, CH₂Cl₂).

¹H NMR (CDCl₃, 300 MHz): δ = 6.19 (m, 1H), 2.73-2.90 (m, 1H), 2.25-2.46 (m, 4H), 1.99-2.23 (m, 2H), 1.52-1.70 (m, 2H) ppm.

¹³C NMR (CDCl₃, 75 MHz): δ = 141.1, 119.5, 98.4, 51.0, 33.4, 30.2, 27.4, 14.3 ppm.

m/z (%): 247 (1, M⁺), 206 (2), 193 (10), 121 (10), 120 (100), 103 (3), 91 (7), 80 (11), 79 (72), 77 (17), 66 (39), 65 (12), 51 (5).

HRMS (EI): calcd. for C₈H₁₁IN [M+H⁺]: 247.9936, found: 247.9937.

IR (film): 2931 (vs), 2849 (s), 2245 (m), 1601 (m), 1447 (s), 1424 (s), 1328 (w), 958 (w), 802 (s), 752 (m), 508 (w).

anal. calcd. for C₈H₁₀IN (247.1): C 38.89, H 4.08, N 5.67; found: C 38.98, H 3.88, N 5.67.

(S)-3-(2-Iodo-2-cyclohexen-1-yl)propanenitrile (3m):

2-Cyanoethylzinc iodide^[8] was freshly prepared by treatment of 3-iodopropionitrile (0.543 g, 3.0 mmol, 1.0 equiv) with activated Zn foil (0.6 g, 9.0 mmol, 3.0 equiv) in THF (2 mL) at 25 °C for 3 h. After insertion of Zn was complete (monitored by GC analysis of hydrolyzed aliquots), the resulting solution was titrated with sodium thiosulfate.

The freshly prepared zinc iodide (1.5 M solution in THF, 0.7 mL, 1.0 mmol, 2.0 equiv) was added dropwise to a solution stirred at -30 °C of CuCN·2LiCl (1 M solution in THF; 1.0 mL, 1.0 mmol, 2.0 equiv). The resulting mixture was stirred 0.5 h at -30 °C, then 2-iodo-2-cyclohexen-1-yl diethylphosphate (**2a**) (0.180 g, 0.5 mmol, 1.0 equiv) in NMP (0.8 mL) was added dropwise. The reaction mixture was stirred overnight while warming up to 25 °C (~16 h). The vinylic iodide **3m** was isolated, after purification by column chromatography (SiO₂, pentane:Et₂O = 3:1) as a colourless oil (0.110 g, 0.42 mmol, 84 % yield).

GC (column A, method A): *t_R*/min = 35.1 (*R*), 35.9 (*S*); 95.3 % *ee*.

$[\alpha]_D^{20}$ +2.7° (c 1.32, CH₂Cl₂).

¹H NMR (CDCl₃, 300 MHz): δ = 6.46 (dt, *J* = 4.0, 1.3 Hz, 1H), 2.25-2.48 (m, 3H), 2.00-2.23 (m, 3H), 1.81-1.95 (m, 1H), 1.55-1.78 (m, 4H) ppm.

¹³C NMR (CDCl₃, 75 MHz): δ = 140.3, 119.3, 102.8, 43.6, 30.5, 29.3, 27.6, 18.4, 14.5 ppm.

m/z (%): 261 (M⁺, 5), 134 (94), 117 (20), 106 (4), 93 (100), 80 (11), 79 (34), 77 (31), 65 (9), 51 (8).

HRMS (EI): calcd. for C₉H₁₂IN [M⁺]: 261.0014, found: 261.0021.

IR (film): 2936 (vs), 2862 (s), 2246 (m), 1627 (m), 1449 (s), 1427 (s), 1328 (m), 1091 (w), 962 (m), 803 (w), 723 (m).

1-[(5*R*)-5-Methyl-1-cyclopenten-1-yl]ethanone (7):^[10]

To a solution of (*R*)-1-iodo-5-methyl-1-cyclopentene (0.165 g, 0.79 mmol) in dry THF (11 mL) cooled at -78 °C, *t*-BuLi (1.69 M in pentane, 935 μ L, 1.58 mmol, 2.0 equiv) was slowly added. The reaction mixture was stirred at -78 °C for 20 min and then, CuCN·2LiCl (1 M solution in THF; 0.79 mL, 0.79 mmol, 1.0 equiv) was added dropwise. The mixture was warmed up to 0 °C and stirred at this temperature for 10 min. Acetyl chloride (150 μ L, 2.1 mmol, 2.7 equiv) was added and the reaction mixture was stirred for further 30 min at 0 °C. Then, saturated aqueous NH₄Cl sol. (20 mL) was added followed by 25 % aqueous ammonia solution (1 mL), and the reaction mixture was stirred at 25 °C until the copper salts had dissolved. The mixture was extracted with pentane (2 x 10 mL). The combined extracts were washed with brine, dried over Na₂SO₄ and filtered through a pad of SiO₂. After the filtration, the SiO₂ was eluted with Et₂O: pentane = 1:6. Careful removal of solvents of the combined organic phase afforded **7** (0.093 g, 0.75 mmol, 95 % yield, 94 % *ee*^[11]) as a colourless liquid (volatile).

$[\alpha]_D^{20}$ -15° (c 1.37, CHCl₃).

¹H NMR (CDCl₃, 300 MHz): δ = 6.62 (m, 1H), 2.95-3.09 (m, 1H), 2.27-2.59 (m, 2H), 2.23 (s, 3H), 1.95-2.12 (m, 1H), 1.42-1.52 (m, 1H), 1.01 (d, *J* = 6.9 Hz, 3 H) ppm.

¹³C NMR (CDCl₃, 75 MHz): δ = 196.6, 150.3, 143.8, 38.1, 32.0, 31.7, 27.0, 19.6 ppm.

m/z (%): 124 (54, M⁺), 109 (100), 81 (72), 79 (45), 65 (8), 53 (18).

HRMS (EI): calcd. for C₈H₁₂O [M⁺]: 124.0888, found: 124.0872.

(4*aS*)-3,4,4*a*,5,6,7-Hexahydro-1(2*H*)-naphthalenone (8):

To a solution of (*S*)-4-(2-iodo-2-cyclohexen-1-yl) ethylbutanoate (**3g**) (0.129 g, 0.4 mmol) in dry THF (8 mL) cooled at -100 °C, TMSCl (76 μ L, 0.6 mmol, 1.5 equiv) was added dropwise. To the resulting mixture *t*-BuLi (1.69 M in pentane, 284 μ L, 0.48 mmol, 1.2 equiv) was slowly added. After the addition was complete, the reaction flask was transferred to a cooling bath at -70 °C and stirred for 2 h at this temperature and then, two more hours at 0 °C. Saturated aqueous NH₄Cl sol. (20 mL) was added to the cold reaction mixture and the phases were separated. After extraction with Et₂O (2 x 15 mL) the combined organic phase was dried over Na₂SO₄. The solvent was removed and the crude product purified by column chromatography (SiO₂, Et₂O: pentane = 1:20 to 1:6) to give **8** (0.045 g, 0.3 mmol, 75 % yield) as a colourless oil.

GC (column A, method E): *t_R*/min = 46.5 (*S*), 49.1(*R*); 93 % *ee*.

$[\alpha]_D^{20}$ -52.7° (c 0.565, CH₂Cl₂).

¹H NMR (CDCl₃, 300 MHz): δ = 6.73 (m, 1H), 2.43-2.60 (m, 1H), 1.15-2.40 (brm, 12H) ppm.

¹³C NMR (CDCl₃, 75 MHz): δ = 201.2, 139.9, 135.9, 40.2, 37.8, 31.6, 30.3, 26.2, 22.5, 21.4 ppm.

m/z (%): 150 (68, M⁺), 135 (15), 132 (23), 122 (41), 117 (11), 107 (17), 104 (20), 94 (74), 79 (100), 66 (9).

HRMS (EI): calcd. for C₁₀H₁₄O [M⁺]: 150.1045, found: 150.1055.

IR (film): 3357 (m), 2930 (vs), 2861 (s), 1686 (vs), 1618 (vs), 1453 (m), 1422 (m), 1264 (s), 1215 (m), 1181 (w), 1124 (w), 836 (w), 593 (w).

(3*aS*)-2,3,3*a*,4,5,6-Hexahydro-1*H*-inden-1-one (9):

To a solution of (*S*)-3-(2-iodo-2-cyclohexen-1-yl)propanenitrile (**3m**) (0.234 g, 0.90 mmol) in dry THF (19 mL) cooled at -100 °C, TMSCl (160 μ L, 1.26 mmol, 1.4 equiv) was added dropwise. To the resulting mixture *t*-BuLi (1.77 M in pentane, 610 μ L, 1.08 mmol, 1.2 equiv) was slowly added. Then, the reaction mixture was stirred at -70 °C for 2 h and at 0 °C for 5 h. HCO₂Et (1.0 equiv) was added to quench the excess of organolithium. The reaction mixture was treated with excess of HCl 37 % and stirred at 25 °C for 24 h. Saturated aqueous NH₄Cl sol. (20 mL) was added to the reaction mixture and the phases were separated. After extraction with Et₂O (2 x 15 mL) the combined organic phase was washed with saturated aqueous NaHCO₃ sol. (10 mL) and dried over Na₂SO₄. The solvent was removed

and the crude product purified by column chromatography (SiO₂, Et₂O: pentane = 1:6) to give **9** (0.064 g, 0.47 mmol, 52 % yield) as a colourless oil.

GC (column A, method E): t_R /min = 26.2 (*S*), 28.8 (*R*); 95 % *ee*.^[12]

$[\alpha]_D^{20}$ -91.4° (c 0.95, CH₂Cl₂).

¹H NMR (CDCl₃, 300 MHz): δ = 6.67 (m, 1H), 2.46-2.66 (m, 1H), 2.06-2.35 (m, 6H), 1.84-1.90 (m, 1H), 1.50-1.72 (m, 1H), 1.22-1.47 (m, 1H), 1.02-1.20 (m, 1H) ppm.

¹³C NMR (CDCl₃, 75 MHz): δ = 206.7, 141.2, 132.2, 38.3, 38.1, 29.0, 28.3, 25.5, 21.7 ppm.

m/z (%): 136 (45, M⁺), 121 (4), 108 (20), 94 (65), 93 (21), 91 (14), 80 (24), 79 (100), 77 (23), 65 (7), 51 (9).

HRMS (EI): calcd. for C₉H₁₂O [M⁺]: 136.0888, found: 136.0877.

IR (film): 3357 (m), 2930 (vs), 2861 (s), 1686 (vs), 1618 (vs), 1453 (m), 1422 (m), 1264 (s), 1215 (m), 1181 (w), 1124 (w), 836 (w), 593 (w).

[(6*R*)-Ethyl-1-cyclohexen-1-yl](phenyl)methanone (10**):**

To a solution of (6*R*)-ethyl-1-iodo-1-cyclohexene (**3c**) (0.118 g, 0.50 mmol) in dry THF (7 mL) cooled at -78 °C, *t*-BuLi (1.4 M in pentane, 714 μ L, 1.0 mmol, 2.0 equiv) was slowly added. The reaction mixture was stirred at -78 °C for 20 min and then, CuCN·2LiCl (1 M solution in THF; 0.5 mL, 0.5 mmol, 1.0 equiv) was added dropwise. The mixture was warmed up to 0 °C and stirred at this temperature for 10 min. Benzoyl chloride (116 μ L, 1.0 mmol, 2.0 equiv) was added and the reaction mixture was stirred for further 30 min at 0 °C. Then, saturated aqueous NH₄Cl sol. (20 mL) was added followed by 25 % aqueous ammonia solution (1 mL), and the reaction mixture was stirred at 25 °C until the copper salts had dissolved. The mixture was extracted with Et₂O (3 x 20 mL). The combined extracts were washed with brine and dried over Na₂SO₄. Evaporation of the solvents and purification by column chromatography (SiO₂, Et₂O: pentane = 1:20) afforded **10** (0.079 g, 0.37 mmol, 74 % yield) as a colourless oil.

GC (column A, method A): t_R /min = 29.9 (*S*), 30.7 (*R*); 93 % *ee*.

$[\alpha]_D^{20}$ -124.8° (c 0.585, CH₂Cl₂).

¹H NMR (CDCl₃, 300 MHz): δ = 7.58-7.64 (m, 2H), 7.40-7.45 (m, 1H), 7.31-7.34 (m, 2H), 6.32 (m, 1H), 2.70-2.82 (m, 1H), 2.00-2.26 (m, 2H), 1.41-1.71 (m, 5H), 1.13-1.35 (m, 1H), 0.83 (t, *J* = 7.3 Hz, 3H) ppm.

¹³C NMR (CDCl₃, 75 MHz): δ = 198.4, 143.4, 141.7, 138.8, 131.6, 129.4, 128.0, 34.3, 26.4, 26.1, 25.8, 18.3, 11.9 ppm.

m/z (%): 215 (12), 214 (75, M⁺), 213 (52), 199 (22), 185 (43), 172 (13), 171 (21), 157 (16), 145 (17), 129 (13), 115 (8), 105 (100), 91 (13), 77 (72), 67 (11), 51 (11).

HRMS (EI): calcd. for C₁₅H₁₈O [M⁺]: 214.1358, found: 214.1326.

IR (film): 2960 (s), 2933 (vs), 2872 (m), 1712 (m), 1648 (vs), 1447 (m), 1292 (m), 1268 (s), 1177 (w), 1115 (w), 900 (w), 717 (s), 665 (m).

(2*S*)-4-[(6*R*)-6-cyclohexyl-1-cyclohexen-1-yl]-3butyn-2-ol (11**):**

(6*R*)-Cyclohexyl-1-iodo-1-cyclohexene (**3d**) (0.151 g, 0.52 mmol) dissolved in piperidine (1 mL) was canulated over a mixture of CuI (0.020 g, 0.10 mmol, 0.2 equiv) and Pd(PPh₃)₄ (0.060 g, 0.05 mmol, 0.1 equiv) dissolved in dry piperidine (1.5 mL). To this mixture (*R*)-3-butyn-2-ol (115 μ L, 1.56 mmol, 3.0 equiv) was added and the reaction was stirred overnight at 25 °C. After evaporation of the solvent, the residue was redissolved in Et₂O (20 mL) and washed with HCl 2M (15 mL). The aqueous phase was extracted with Et₂O (2 x 20 mL). and washed with saturated aqueous NH₄Cl sol. (20 mL). The combined organic phase was washed with brine and dried over Na₂SO₄. Evaporation of the solvents and purification by column chromatography (SiO₂, Et₂O: pentane = 1:4) afforded **11** (0.093 g, 0.40 mmol, 77 % yield) as a colourless oil.

Diastereomeric ratio: 95.5 : 4.5 determined by quant. ^{13}C NMR on crude reaction mixture (e.g. 137.0 and 136.8 ppm).

^1H NMR (CDCl_3 , 300 MHz): δ = 6.14 (m, 1H), 4.57-4.66 (m, 1H), 1.97-2.14 (m, 4H), 0.88-1.88 (m, 15H) 1.46 (d, J = 6.6 Hz, 3H) ppm.

^{13}C NMR (CDCl_3 , 75 MHz): δ = 136.8, 124.2, 89.5, 85.0, 58.7, 42.6, 40.5, 31.2, 27.4, 27.1, 26.9, 26.7, 25.8, 24.6, 23.2, 21.2 ppm.

m/z (%): 232 (37, M^+), 214 (2), 203 (3), 199 (3), 189 (9), 174 (7), 159 (5), 150 (27), 149 (22), 145 (19), 135 (23), 133 (21), 132 (100), 131 (32), 122 (11), 121 (46), 117 (55), 115 (17), 107 (18), 106 (16), 105 (22), 92 (10), 91 (44), 83 (16), 79 (24), 78 (12), 77 (19), 67 (11), 55 (39).

HRMS (EI): calcd. for $\text{C}_{16}\text{H}_{24}\text{O}$ [M^+]: 232.1827, found: 232.1811.

IR (film): 3435 (vs), 2926 (vs), 2852 (m), 1636 (w), 1450 (w), 1094 (w), 1026 (w).

[(5*R*)-5-methyl-1-cyclopenten-1-yl](phenyl)methanone (**12**):

To a solution of (*R*)-1-iodo-5-methyl-1-cyclopentene (0.141 g, 0.68 mmol) in dry THF (10 mL) cooled at -78°C , *t*-BuLi (1.4 M in pentane, 970 μL , 1.36 mmol, 2.0 equiv) was slowly added. The reaction mixture was stirred at -78°C for 20 min and then, $\text{CuCN}\cdot 2\text{LiCl}$ (1 M solution in THF; 0.68 mL, 0.68 mmol, 1.0 equiv) was added dropwise. The mixture was warmed up to 0°C and stirred at this temperature for 10 min. Benzoyl chloride (160 μL , 1.36 mmol, 2.0 equiv) was added and the reaction mixture was stirred for further 30 min at 0°C . Then, saturated aqueous NH_4Cl sol. (20 mL) was added followed by 25 % aqueous ammonia solution (1 mL), and the reaction mixture was stirred at 25°C until the copper salts had dissolved. The mixture was extracted with Et_2O (2 x 10 mL). The combined extracts were washed with brine and dried over Na_2SO_4 and filtered through a pad of SiO_2 . Evaporation of the solvents and purification by column chromatography (SiO_2 , Et_2O : pentane = 1:20) afforded **12** (0.082 g, 0.44 mmol, 65 % yield) as a colourless oil.

GC (column A, method F): t_R/min = 33.3 (*R*), 34.1 (*S*); 94 % *ee*.

$[\alpha]_{\text{D}}^{20}$ -56.5° (c 1.12, CH_2Cl_2).

^1H NMR (CDCl_3 , 300 MHz): δ = 7.64-7.71 (m, 2H), 7.40-7.48 (m, 1H), 7.29-7.39 (m, 2H), 6.35 (m, 1H), 3.12-3.29 (m, 1H), 2.49-2.63 (m, 1H), 2.32-2.45 (m, 1H), 2.10-2.23 (m, 1H), 1.45-1.57 (m, 1H), 1.11 (d, J = 7.1 Hz, 3H) ppm.

^{13}C NMR (CDCl_3 , 75 MHz): δ = 194.4, 148.7, 145.6, 139.2, 131.8, 128.9, 128.1, 39.6, 32.4, 32.0, 19.4 ppm.

m/z (%): 186 (98, M^+), 185 (83), 171 (19), 158 (28), 157 (23), 143 (13), 128 (12), 105 (100), 77 (71), 65 (6), 51 (20).

HRMS (EI): calcd. for $\text{C}_{13}\text{H}_{14}\text{O}$ [M^+]: 186.1045, found: 186.1057.

IR (film): 3368 (m), 2956 (s), 2868 (w), 1642 (vs), 1598 (s), 1448 (s), 1350 (s), 1274 (m), 938 (w), 720 (s), 697 (m), 672 (w).

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- [4] See experimental data given for (6*R*-ethyl-1-cyclohexen-1-yl)(phenyl)methanone (**10**).
- [5] See experimental data given for (2*R*)-4-[(6*S*)-6-cyclohexyl-1-cyclohexen-1-yl]-3butyn-2-ol (**11**).
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- [7] The enantiomeric excess of the starting (*R*)-2-iodo-2-cyclohexen-1-yl diethylphosphate was 98 % *ee* in this case.
- [8] Yeh, M. C. P.; Knochel, P. *Tetrahedron Lett.* **1988**, 29, 2395.
- [9] The enantiomeric excess of the starting (*R*)-2-iodo-2-cyclopenten-1-yl diethylphosphate was 96 % *ee* in this case.
- [10] Graf, C.-D.; Knochel, P. *Tetrahedron* **1999**, 55, 8801
- [11] The enantiomeric excess was determined by capillary GC analysis on the corresponding benzoilated compound; see experimental data given for [(5*R*)-5-methyl-1-cyclopenten-1-yl](phenyl)methanone (**12**).
- [12] The enantiomeric excess of the starting nitrile was also 95 % *ee*.

3a

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