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ELECTRONIC SUPPLEMENTARY INFORMATION

A Novel Catalytic Asymmetric Route towards Skipped Dienes with a Methyl-Substituted Central Stereogenic Carbon

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General Techniques

Starting materials were purchased from Aldrich, Alpha Aesar or Acros and used as received unless stated otherwise. All solvents were reagent grade and, if necessary, dried and distilled prior to use. All reactions were carried out under a nitrogen atmosphere using oven dried glassware and using standard Schlenk techniques. Column chromatography was performed on silica gel (Aldrich 60, 230-400 mesh). TLC was performed on silica gel 60/Kieselguhr F254.

$^1$H and $^{13}$C NMR spectra were recorded on a Varian VXR300 (299.97 MHz for $^1$H, 75.48 MHz for $^{13}$C) or a Varian AMX400 (399.93 MHz for $^1$H, 100.59 MHz for $^{13}$C) spectrometer in CDCl$_3$ unless stated otherwise. Chemical shifts are reported in $\delta$ values (ppm) relative to the residual solvent peak (CDCl$_3$, $^1$H = 7.24, $^{13}$C = 77.0). Carbon assignments are based on $^{13}$C and APT $^{13}$C experiments. Splitting patterns are indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad).

High resolution mass spectra (HRMS) were recorded on an AEI-MS-902 and FTMS orbitrap (Thermo Fisher Scientific) mass spectrometer. Optical rotations were measured on a Schmidt+ Haensch polarimeter (Polartronic MH8) with a 10 cm cell (c given in g/100 mL). Enantiomeric excesses were determined by HPLC analysis using a Shimadzu LC-10ADVP HPLC equipped with a Shimadzu SPD-M10AVP diode array detector (Chiralcel OD-H, 250*4.6, 10 $\mu$m) or by capillary GC analysis (HP 6890, CP-Chiralsil-Dex-CB column (25 m * 0.25 mm)) using a flame ionization detector.

Racemic products were synthesized by reaction of the allyl bromide and the corresponding organomagnesium reagent at –80 °C in dry dichloromethane in the presence of CuBr•SMe$_2$ (10 mol%) and PPh$_3$ (20 mol%).
Synthesis of allylic bromides

Synthesis of ((1\(E\),3\(E\))-5-bromopenta-1,3-dienyl)benzene (1a)\(^1\)

(2\(E\),4\(E\))-Methyl 5-phenylpenta-2,4-dienoate (8). To a stirred solution of 5-phenylpenta-2,4-dienoic acid 7 (3.91 g, 22.4 mmol) in 50 mL of methanol was added HCl (20 ml, 60 mmol, 3M in methanol) at room temperature. The solution was stirred for 16 h, concentrated and purified by flash chromatography (eluent pentane/ether = 10/1) to give 8\(^1\) as a white solid (4.07 g, 97% yield). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.45 – 7.21 (m, 6H), 6.87 – 6.73 (m, 2H), 5.93 (d, \(J = 15.3\) Hz, 1H), 3.70 (s, 3H); \(^13\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 167.5, 144.8, 140.5, 136.0, 129.0, 128.8, 127.2, 126.2, 120.8, 51.6.

(2\(E\),4\(E\))-5-Phenylpenta-2,4-dien-1-ol (9). To a stirred solution of the methyl ester 8 (4.0 g, 21.2 mmol) in 50 mL of dry DCM was added DIBAL-H (63.8 ml, 1 M in DCM, 63.8 mmol, 3 eq) over 0.5 h at –78 °C. The reaction mixture was stirred for 4 h when TLC showed full conversion. The mixture was quenched with 60 mL of saturated aqueous Rochelle salt (potassium sodium tartrate) and stirred for 30 min. The phases were separated and the aqueous layer was extracted with DCM (3 x 50 mL). The combined organic phases were dried over Na\(_2\)SO\(_4\), filtered, concentrated and purified by flash chromatography (eluent pentane/ether = 4/1) to give 9\(^1\) as a white solid (3.0 g, 88% yield). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.38 – 7.05 (m, 5H), 6.72 (dd, \(J = 15.6, 10.5\) Hz, 1H), 6.49 (d, \(J = 15.6\) Hz, 1H), 6.36 (dd, \(J = 15.1, 10.5\) Hz, 1H), 5.90 (dt, \(J = 15.1, 5.9\) Hz, 1H), 4.19 (d, \(J = 5.9\) Hz, 2H), 1.31 (br, 1H); \(^13\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 137.1, 132.8, 132.4, 131.6, 128.6, 128.1, 127.6, 126.4, 63.5.

((1\(E\),3\(E\))-5-Bromopenta-1,3-dienyl)benzene (1a). To a stirred solution of NBS (4.17 g, 23.4 mmol, 1.3 eq) in DCM (40 mL) at –20 °C was added Me\(_2\)S (0.98 g, 1.2 mL, 28.9 mmol, 1.83 eq) slowly over 5 min. The reaction mixture was stirred for 15 min before a solution of allylic alcohol 9 (2.5 g, 15.6 mmol) in 10 mL of DCM was added dropwise over 10 min. The mixture was quenched with a saturated aqueous NH\(_4\)Cl solution (50 mL) when TLC showed full conversion and after the mixture was warmed up to room temperature, the layers were separated. The organic layer was washed with water (3 x 20 mL), dried over Na\(_2\)SO\(_4\), filtered and concentrated to give crude 1a as a white solid (2.83 g, 81%) which was used in the next step (asymmetric allylic alkylation) immediately due to instability.
1H NMR (400 MHz, CDCl3) δ 7.54 – 7.15 (m, 5H), 6.77 (dd, J = 15.6, 10.4 Hz, 1H), 6.60 (d, J = 15.6 Hz, 1H), 6.46 (dd, J = 14.8, 10.4 Hz, 1H), 6.08 – 5.90 (m, 1H), 4.11 (d, J = 8.0 Hz, 2H); 13C NMR (101 MHz, CDCl3) δ 136.7, 135.2, 134.5, 128.9, 128.7, 128.0, 127.3, 126.6, 33.4.

Synthesis of (2E,4E)-1-bromo-7-methylocta-2,4-diene (1b)

(2E,4E)-Ethyl 7-methylocta-2,4-dienoate (12). To a stirred solution of compound 11 (mixture of E/Z isomers, 5.0 g, 20 mmol) in 30 mL of dry THF was added LiHDMS (20 mL, 20 mmol, 1M in THF) at –78 °C under nitrogen. The mixture was stirred for about 30 min when a THF solution (5 mL) of aldehyde 10 (1.72 g, 20 mmol, 1 eq) was added dropwise over 10 min. The resulting solution was stirred overnight and quenched with a saturated aqueous NH4Cl solution (50 mL) at –78 °C. The mixture was warmed up to room temperature and the layers were separated. The aqueous layer was washed with ether (3 x 30 mL) and the organic layers were dried over Na2SO4, filtered and concentrated and purified by flash chromatography (eluent pentane/ether = 10/1) to give 12 as a colorless oil (2.3 g, 62% yield). 1H NMR (400 MHz, CDCl3) δ 7.25 – 7.12 (m, 1H), 6.17 – 5.94 (m, 2H), 5.72 (d, J = 15.5 Hz, 1H), 4.13 (q, J = 7.1 Hz, 2H), 2.01 – 1.97 (m, 2H), 1.66 – 1.63 (m, 1H), 1.23 (t, J = 7.1 Hz, 3H), 0.84 (d, J = 6.7 Hz, 6H); 13C NMR (101 MHz, CDCl3) δ 167.3, 145.0, 143.5, 129.4, 119.2, 60.2, 42.3, 28.3, 22.3, 14.3.

(2E,4E)-7-Methylocta-2,4-dien-1-ol (13). To a stirred solution of the ethyl ester 12 (2.0 g, 11 mmol) in 30 mL of dry DCM was added DIBAL-H (33 ml, 1 M in DCM, 33 mmol, 3 eq) over 0.5 h at –78 °C. The reaction mixture was stirred for 4 h when TLC showed full conversion. The reaction mixture was quenched with 30 mL saturated aqueous Rochelle salt (potassium sodium tartrate) and stirred for 30 min. The phases were separated and the aqueous layer was extracted with DCM (3 x 30 mL). The combined organic phases were dried over Na2SO4, filtered, concentrated and purified by flash chromatography (eluent pentane/ether = 4/1) to give 13 as a colorless oil (1.5 g, 95% yield). 1H NMR (400 MHz, CDCl3) δ 6.23 (dd, J = 15.1, 10.4 Hz, 1H), 6.03 (dd, J = 15.1, 10.4 Hz, 1H), 5.81 – 5.63 (m, 2H), 4.16 (dd, J = 6.1, 0.9 Hz, 2H), 2.02 – 1.92 (m, 2H), 1.65 – 1.62 (m, 1H), 1.38 (br, 1H), 0.89 (d, J = 6.7 Hz, 6H); 13C NMR (101 MHz, CDCl3) δ 134.5, 132.1, 130.4, 129.3, 63.5, 42.0, 28.5, 22.3. HRMS (APCI+) calculated for C9H15[M–OH]+: 123.1174, found: 123.1116.

(2E,4E)-1-Bromo-7-methylocta-2,4-diene (1b). To a stirred solution of NBS (1.07 g, 6 mmol, 1.3 eq) in DCM (20 mL) at –20 °C was slowly added Me2S (460 mg, 0.54 mL, 7.4 mmol, 1.83 eq) over a 5 min
period. The reaction mixture was stirred for 15 min before a solution of allylic alcohol 13 (560 mg, 4 mmol) in 10 mL of DCM was added dropwise over 10 min. The mixture was quenched with a saturated aqueous NH₄Cl solution (50 mL) when TLC showed full conversion and after the mixture was warmed up to room temperature, the layers were separated. The organic layer was washed with water (3 x 20 mL), dried over Na₂SO₄, filtered and the solvent was concentrated to give crude 1b as colorless oil (0.69 g, 85%) used in the next step immediately due to instability.

1H NMR (400 MHz, CDCl₃) δ 6.32 – 6.07 (m, 1H), 5.99 – 5.88 (m, 1H), 5.78 – 5.63 (m, 2H), 4.02 – 3.85 (m, 2H), 1.96 – 1.87 (m, 2H), 1.60 – 1.57 (m, 1H), 0.82 (d, J = 6.7 Hz, 6H); 13C NMR (101 MHz, CDCl₃) δ 136.5, 135.4, 129.8, 126.1, 42.0, 33.9, 28.4, 22.3.

Synthesis of (2E,4E)-methyl 6-bromohexa-2,4-dienoate (1c)

(2E,4E)-Methyl hexa-2,4-dienoate (15). To a stirred solution of acid 14 (4 g, 36 mmol, 1 eq) in 50 mL of methanol was added HCl (24 mL, 72 mmol, 3M in methanol, 2 eq) at room temperature. The resulting solution was stirred for 16 h, concentrated and purified by flash chromatography (eluent pentane/ether = 10/1) to give 15 as colorless oil (4.22 g, 93% yield). 1H NMR (400 MHz, CDCl₃) δ 7.25 – 7.10 (m, 1H), 6.19 – 5.98 (m, 2H), 5.71 (d, J = 15.4 Hz, 1H), 3.67 (s, 3H), 1.78 (d, J = 5.6 Hz, 3H); 13C NMR (101 MHz, CDCl₃) δ 167.8, 145.2, 139.4, 129.7, 118.5, 51.4, 18.6.

(2E,4E)-Methyl 6-bromohexa-2,4-dienoate (1c). To a solution of methyl sorbate 15 (1.0 g, 8 mmol) and allyl bromide 16 (4.84 g, 40 mmol, 5 eq) in 80 mL of CH₂Cl₂ (c = 0.1 M) was added the Hoveyda-Grubbs-II catalyst (C₁₁H₃₈Cl₂N₂ORu, 50 mg, 0.08 mmol, 0.01 equiv) at room temperature. After stirring for 24 h, silica was added to the reaction mixture and after evaporation of the solvent, the pad of silica was loaded on top of a silica gel column and the product was quickly purified by a flash chromatography (eluent pentane/ether = 4/1) to give 1c as a colorless oil (483 mg, 30% yield). 1H NMR (400 MHz, CDCl₃) δ 7.32 – 7.21 (m, 1H), 6.39 (dd, J = 15.0, 10.9 Hz, 1H), 6.24 (dd, J = 15.4, 10.9 Hz, 1H), 5.94 (d, J = 15.4 Hz, 1H), 4.06 – 3.99 (m, 2H), 3.75 (s, 3H); 13C NMR (101 MHz, CDCl₃) δ 166.9, 142.8, 136.7, 131.8, 122.7, 51.7, 31.2.
Synthesis of \((2E,4E)\)-6-bromohexa-2,4-dienyloxy)(tert-butyl) dimethylsilane (1d)

\((2E,4E)\)-Dimethyl hexa-2,4-dienedioate (18). To a stirred solution of acid 17 (4.0 g, 28.1 mmol) in 50 mL of methanol was added HCl (19 mL, 57 mmol, 3M in methanol, 2 eq) at room temperature. The resulting solution was stirred for 16 h, concentrated and purified by crystallization from ether to give 18 as a white solid (4.13 g, 86% yield). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.33 – 7.21 (m, 2H), 6.21 – 6.07 (m, 2H), 3.72 (s, 6H); \(^1^3\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 166.3, 140.9, 128.0, 51.9.

\((2E,4E)\)-Hexa-2,4-diene-1,6-diol (19). To a stirred solution of the methyl ester 18 (1.0 g, 5.94 mmol) in 30 mL of dry DCM was added DIBAL-H (36 ml, 1 M in DCM, 36 mmol, 6 eq) over 0.5 h at –78 °C. The reaction mixture was stirred for 8 h when TLC showed full conversion. The reaction mixture was quenched with 30 mL saturated aqueous Rochelle salt (potassium sodium tartrate) followed by stirring for 30 min. The phases were separated and the aqueous layer was extracted with DCM (3 x 30 mL). The combined organic phases were dried over Na\(_2\)SO\(_4\), filtered, concentrated and purified by flash chromatography (eluent pentane/EtOAc = 2/1) to give 19 as a white solid (560 mg, 83% yield). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 6.30 – 6.08 (m, 2H), 5.91 – 5.66 (m, 2H), 4.14 (t, \(J\) = 5.4 Hz, 4H), 1.29 (t, \(J\) = 5.4 Hz, 2H); \(^1^3\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 132.4, 130.4, 63.2.

\((2E,4E)\)-6-((tert-Butyldimethylsilyl)oxy)hexa-2,4-dien-1-ol (20). To a solution of 19 (300 mg, 2.63 mmol) in dry dichloromethane (20 mL) was added imidazole (269 mg, 3.95 mmol, 1.5 eq) followed by tert-butyl-dimethylsilyl chloride (436 mg, 2.89 mmol, 1.1 eq), and the resulting white suspension was stirred at room temperature for 12 h. The reaction mixture was quenched with 20 mL of water and extracted with ether (3 x 20 mL). The combined organic layers were dried over Na\(_2\)SO\(_4\), filtered, concentrated and purified by flash chromatography (eluent pentane/EtOAc = 4/1) to give 20 as a colorless oil (319 mg, 53%). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 6.24 – 6.11 (m, 2H), 5.81 – 5.65 (m, 2H), 4.15 (d, \(J\) = 4.5 Hz, 2H), 4.11 (t, \(J\) = 5.6 Hz, 2H), 1.50 (br, 1H), 0.84 (s, 9H), 0.00 (s, 6H); \(^1^3\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 133.3, 131.4, 131.0, 128.8, 63.4, 63.3, 25.9, 18.4, –5.2.
((2E,4E)-6-Bromohexa-2,4-dienyloxy)(tert-butyl) dimethylsilane (1d). To a stirred solution of NBS (267 mg, 1.5 mmol, 1.5 eq) in DCM (20 mL) at –20 °C was slowly added Me2S (115 mg, 0.14 mL, 1.85 mmol, 1.85 eq) over a 5 min period. The reaction mixture was stirred for 15 min before a solution of allylic alcohol 20 (228 mg, 1 mmol) in 5 mL of DCM was added dropwise over 10 min. The mixture was quenched with a saturated aqueous NH4Cl solution (20 mL) when TLC showed full conversion and subsequently the mixture was warmed up to room temperature and the layers separated. The organic layer was washed with water (3 x 10 mL), dried over Na2SO4, filtered and concentrated to give the crude 1d as colorless oil (248 mg, 85%) immediately used in the next step due to instability. 1H NMR (400 MHz, CDCl3) δ 6.29 – 6.10 (m, 2H), 5.77 (m, 2H), 4.16 (dd, J = 5.0, 1.1 Hz, 2H), 3.96 (d, J = 7.9 Hz, 2H), 0.84 (s, 9H), 0.00 (s, 6H); 13C NMR (101 MHz, CDCl3) δ 135.2, 134.4, 127.9, 127.9, 63.1, 33.3, 25.9, 18.1, –5.3.

Synthesis of (2E,4E)-ethyl 6-bromo-2-methylhexa-2,4-dienoate (1e)

(E)-But-2-ene-1,4-diol (22). To a stirred solution of diol 21 (2.6 g, 30 mmol) in dry THF (40 mL) was added solid LiAlH4 (1.44 g, 36 mmol, 1.2 eq) at 0 °C under nitrogen. The mixture was heated to reflux for 4 h, followed by quenching with a saturated aqueous NH4Cl solution (20 mL) at 0 °C. The mixture was allowed to warm to room temperature and the phases were separated. The aqueous layer was extracted with EtOAc (3 x 30 mL). The combined organic phases were dried over Na2SO4, filtered, concentrated and purified by flash chromatography (eluent pentane/EtOAc = 1/1) to give 222 as colourless oil (660 mg, 20% yield, soluble in water). 1H NMR (400 MHz, CDCl3) δ 5.89 – 5.79 (m, 2H), 4.17 – 4.05 (m, 4H), 1.38 (br, 2H); 13C NMR (101 MHz, CDCl3) δ 130.5, 62.9.

(E)-4-Hydroxybut-2-en-1-yl acetate (23). To a stirred solution of but-2-ene-1,4-diol 22 (1.0 g, 11 mmol) in dry THF (20 mL) was added solid NaH (440 mg, 60% in mineral oil, 11 mmol, 1 eq) at 0 °C. The mixture was stirred at room temperature for 1 h followed by the addition of a THF solution (5 mL) of acetyl chloride (863 mg, 0.81 mL, 1 eq). The reaction mixture was stirred for 3 h after which time TLC (diethyl ether) showed a mixture of starting compound, monoacetate and diacetate. H2O (10 mL) was added, and the mixture was extracted with diethyl ether (3 x 30 mL). The combined organic phases were dried over Na2SO4, filtered, concentrated and purified by flash chromatography (eluent pentane/EtOAc = 4/1) to give 239 as colourless oil (930 mg, 65% yield). 1H NMR (400 MHz, CDCl3) δ 5.93 – 5.81 (m, 1H),
5.80 – 5.73 (m, 1H), 4.52 (dd, \( J = 5.8, 1.2 \) Hz, 2H), 4.12 (dd, \( J = 5.0, 1.2 \) Hz, 2H), 2.01 (s, 3H), 1.63 (br, 1H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 171.6, 133.5, 125.1, 64.2, 62.7, 20.9.

\((2E,4E)-Ethyl\ 6\text{-acetoxy-2-methylhexa-2,4-dienoate (25})\). 4-Acetoxy- 2-buten-1-ol \( \text{23 (0.91 g, 7 mmol)} \) was added to a suspension of pyridinium chlorochromate (1.81 g, 8.4 mmol) in 20 mL of DCM at 0 °C. The mixture was stirred at room temperature until TLC showed full conversion. The solids were removed by flash chromatography, washed with diethyl ether and the organic solvents were removed in vacuo to give 4-acetoxy-crotonaldehyde used immediately in the next step.

The aldehyde was dissolved in 10 mL of DCM followed by the addition of phosphorane \( \text{24 (2.54 g, 7.0 mmol)} \) at room temperature. The solution was stirred for 30 min until TLC showed full conversion. The solvent was removed in vacuo. The product was purified by flash chromatography (eluent pentane/ether = 4/1) to give \( \text{25}^9 \) as colourless oil (945 mg, 64% yield over 2 steps). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.10 (d, \( J = 11.4 \) Hz, 1H), 6.58 – 6.45 (m, 1H), 6.02 (dt, \( J = 15.2, 6.1 \) Hz, 1H), 4.62 (d, \( J = 6.1 \) Hz, 2H), 4.15 (q, \( J = 7.1 \) Hz, 2H), 2.03 (s, 3H), 1.88 (d, \( J = 0.7 \) Hz, 3H), 1.24 (t, \( J = 7.1 \) Hz, 3H).

\((2E,4E)-Ethyl\ 6\text{-hydroxy-2-methylhexa-2,4-dienoate (26})\). K\(_2\)CO\(_3\) (1.23 g, 8.9 mmol) was added to a solution of \( \text{25 (945 mg, 4.45 mmol)} \) in 15 mL of ethanol at room temperature. The resulting mixture was stirred about 2 h when TLC showed full conversion. The reaction was quenched with an aqueous saturated NaCl solution (20 mL). The phases were separated and the aqueous layer was extracted with EtOAc (3 x 30 mL). The combined organic phases were dried over Na\(_2\)SO\(_4\), filtered, concentrated and purified by flash chromatography (eluent pentane/EtOAc = 4/1) to give \( \text{26}^9 \) as colourless oil (707 mg, 93% yield). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.13 (d, \( J = 11.4 \) Hz, 1H), 6.53 (dd, \( J = 15.2, 11.4 \) Hz, 1H), 6.11 (dt, \( J = 15.2, 5.2 \) Hz, 1H), 4.28 – 4.20 (m, 2H), 4.15 (q, \( J = 7.1 \) Hz, 2H), 1.89 (d, \( J = 0.7 \) Hz, 3H), 1.45 (br, 1H), 1.24 (t, \( J = 7.1 \) Hz, 3H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 168.4, 139.2, 137.1, 127.8, 125.7, 63.1, 60.6, 14.3, 12.7.

\((2E,4E)-Ethyl\ 6\text{-bromo-2-methylhexa-2,4-dienoate (1e})\). To a stirred solution of NBS (470 mg, 2.64 mmol, 1.3 eq) in DCM (20 mL) at \(-20 \) °C was slowly added Me\(_2\)S (197 mg, 0.23 mL, 3.17 mmol, 1.83 eq) over a 5 min period. The reaction mixture was stirred for 15 min before a solution of allylic alcohol \( \text{26 (300 mg, 1.76 mmol)} \) in 5 mL of DCM was added dropwise over 10 min. The mixture was quenched with a saturated aqueous NH\(_4\)Cl solution (50 mL) when TLC showed full conversion and after the mixture was warmed to room temperature, the layers were separated. The organic layer was washed with water (3 x 10 mL), dried over Na\(_2\)SO\(_4\), filtered and concentrated to give the crude \( \text{1e} \) as colorless oil (323 mg, 79%) used in the next step immediately due to instability. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.09 (dd, \( J = 11.4, 0.9 \) Hz, 1H).
Hz, 1H), 6.59 – 6.44 (m, 1H), 6.13 (dt, $J = 15.4, 7.8$ Hz, 1H), 4.15 (q, $J = 7.1$ Hz, 2H), 4.01 (d, $J = 7.8$ Hz, 2H), 1.90 (d, $J = 1.3$ Hz, 3H), 1.24 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 167.9, 136.0, 135.1, 129.6, 129.5, 60.8, 32.0, 14.3, 12.8.

Synthesis of (2$E$,4$E$)-ethyl 6-bromo-3-methylhexa-2,4-dienoate (1f)

Ethyl 4,4-dimethoxy-3-methylbut-2-enoate (29). A mixture of 1,1-dimethoxyacetone 27 (5.91 g, 50 mmol) and ethyl 2-(diethoxyphosphoryl)acetate 28 (13.45 g, 60 mmol) was added dropwise to a suspension of K$_2$CO$_3$ (17.28 g) in 10 mL of water at room temperature. The reaction mixture was stirred for 16 h. The insoluble material was then removed by filtration and washed with ether. The organic phase was separated and washed with brine (50 mL). The organic layer was dried over Na$_2$SO$_4$, filtered, concentrated and purified by flash chromatography (eluent pentane/ether) to give product 29$^{10}$ as colorless oil (8.0 g, 85%, mixture of E and Z acetal esters).

(2$E$,4$E$)-Ethyl 6-hydroxy-3-methylhexa-2,4-dienoate (31). HCl (3 N, 3.5 mL of an aq. solution) was added dropwise to a stirred solution of the above obtained esters 29 (2.0 g, 10.6 mmol) in 15 mL DCM at 0 °C. The resulting mixture was stirred for 2 h. The organic layer was separated and washed with a saturated aqueous solution of NaHCO$_3$ (30 mL) and brine (20 mL), dried over Na$_2$SO$_4$, filtered and concentrated. The crude product was purified by vacuum distillation to yield the aldehyde which was used directly for the next step.

Compound 30 (3.2 g, 10.6 mmol) was added to a stirred solution of the aldehyde in DCM (10 mL) at room temperature. The reaction mixture was stirred for 15 h and subsequently concentrated. The resulting mixture was dissolved in pentane and the solids were filtered. The solution was concentrated to give the crude aldehyde which was used in the next step.

A solution of the aldehyde in 5 mL of ethanol was added to a solution of sodium borohydride (1.0 g, 25 mmol) in EtOH/H$_2$O (1:1, 20 mL) at 0 °C. The reaction mixture was stirred at room temperature for 20 min followed by quenching with aqueous saturated NaCl. The aqueous layer was separated and extracted with Et$_2$O (5 x 20 mL). The combined organic layers were dried over Na$_2$SO$_4$, filtered, concentrated and
purified by flash chromatography (eluent pentane/ether = 1/1) to give product $31^{11}$ as colorless oil (0.87 g, 50% yield over three steps). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 6.26 (d, $J = 15.8$ Hz, 1H), 6.17 (m, 1H), 5.71 (s, 1H), 4.24 (d, $J = 5.2$ Hz, 2H), 4.11 (q, $J = 7.1$ Hz, 2H), 2.22 (s, 3H), 1.51 (br, 1H), 1.22 (t, $J = 7.1$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 167.0, 151.3, 134.3, 133.8, 119.7, 63.1, 59.8, 14.3, 13.8.

$(2E,4E)$-Ethyl 6-bromo-3-methylhexa-2,4-dienoate ($1f$). To a stirred solution of NBS (470 mg, 2.64 mmol, 1.3 eq) in DCM (20 mL) at $-20^\circ$C was slowly added Me$_2$S (197 mg, 0.23 mL, 3.17 mmol, 1.83 eq) over a 5 min period. The reaction mixture was stirred for 15 min before a solution of allylic alcohol $31$ (300 mg, 1.76 mmol) in 5 mL of DCM was added dropwise over 10 min. The mixture was quenched with a saturated aqueous NH$_4$Cl solution (50 mL) when TLC showed full conversion and subsequently the mixture was warmed up to room temperature and the layers were separated. The organic layer was washed with water (3 x 10 mL), dried over Na$_2$SO$_4$, filtered and concentrated to give the crude $1f$ as colorless oil (354 mg, 86%) used in the next step immediately due to instability. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 6.29 – 6.13 (m, 2H), 5.73 (s, 1H), 4.11 (q, $J = 7.1$ Hz, 2H), 3.99 (d, $J = 7.1$ Hz, 2H), 2.20 (d, $J = 1.2$ Hz, 3H), 1.22 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 166.6, 150.3, 137.6, 130.7, 121.1, 59.9, 32.0, 14.3, 13.8.

**Synthesis of $(2Z,4E)$-ethyl 6-bromo-3-methylhexa-2,4-dienoate ($1g$)**

$(Z)$-Ethyl 3-iodobut-2-enoate ($33$). To a mixture of ethyl but-2-ynoate $32$ (2.34 g, 20 mmol) and lithium iodide (4.4 g, 32 mmol, 1.6 eq) was added acetic acid (6 mL) at room temperature. The reaction mixture was heated to 70 $^\circ$C and stirred for 16 h followed by dilution with ether (50 mL). The organic phase was washed with water (20 mL), saturated aqueous NaHCO$_3$ (20 mL), and saturated aqueous Na$_2$S$_2$O$_3$ (20 mL), dried over Na$_2$SO$_4$, filtered and concentrated and purified by flash chromatography (eluent pentane/ether = 10/1) to give product $33^{12}$ as a colorless oil (2.1 g, 88% yield). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 6.29 (q, $J = 1.4$ Hz, 1H), 4.22 (q, $J = 7.1$ Hz, 2H), 2.73 (d, $J = 1.4$ Hz, 3H), 1.29 (t, $J = 7.1$ Hz, 3H).
(2Z,4E)-Ethyl 6-hydroxy-3-methylhexa-2,4-dienoate (35). A solution of Pd$_2$(dba)$_3$ (45 mg, 0.005 mmol) in 20 mL of NMP was treated with triphenyl arsine (59 mg, 0.2 mmol) at room temperature. The solution was stirred for 10 min followed by the addition of a solution of iodide 33 (466 mg, 1.94 mmol) in 5 mL of NMP. The solution was further stirred for 10 min followed by the addition of a solution of stannane 34 (674 mg, 1.94 mmol) in 5 mL of NMP. The reaction mixture was stirred for 16 h followed by quenching with saturated aqueous potassium fluoride solution (20 mL). The reaction mixture was diluted with diethyl ether (20 mL). The organic layer was separated and washed with saturated aqueous potassium fluoride solution (10 mL), dried over Na$_2$SO$_4$, filtered and concentrated. The product was purified by column chromatography (eluent pentane/ether = 2/1) to give 35 as a colourless oil (252 mg, 76%). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.75 (dd, $J = 16.0, 0.7$ Hz, 1H), 6.23 (dt, $J = 16.0, 5.6$ Hz, 1H), 5.71 (s, 1H), 4.32 (td, $J = 5.6, 1.4$ Hz, 2H), 4.16 (q, $J = 7.1$ Hz, 2H), 2.02 (d, $J = 1.3$ Hz, 3H), 1.63 (br, 1H), 1.28 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 166.2, 150.0, 135.8, 127.8, 117.9, 63.6, 59.8, 21.0, 14.3. HRMS (APCI+) calculated for C$_9$H$_{13}$O$_2$[M–OH]$: 153.0910$, found:153.0909.

(2Z,4E)-Ethyl 6-bromo-3-methylhexa-2,4-dienoate (1g). To a stirred solution of NBS (313 mg, 1.76 mmol, 1.3 eq) in DCM (20 mL) at –20 $^\circ$C was slowly added Me$_2$S (132 mg, 0.16 mL, 2.12 mmol, 1.83 eq) over a 5 min period. The reaction mixture was stirred for 15 min before a solution of allylic alcohol 35 (200 mg, 1.18 mmol) in 5 mL of DCM was added dropwise over 10 min. The mixture was quenched with a saturated aqueous NH$_4$Cl solution (50 mL) after TLC showed full conversion and subsequently the mixture was warmed up to room temperature and the layers were separated. The organic layer was washed with water (3 x 10 mL), dried over anhydrous Na$_2$SO$_4$, filtered and concentrated to give the crude 1g as colorless oil (214 mg, 78%) used in the next step immediately due to instability. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.80 (dd, $J = 15.6, 0.9$ Hz, 1H), 6.23 (dt, $J = 15.6, 7.8$ Hz, 1H), 5.72 (s, 1H), 4.16 (q, $J = 7.1$ Hz, 2H), 4.10 (dd, $J = 7.8, 0.9$ Hz, 2H), 2.00 (d, $J = 1.3$ Hz, 3H), 1.28 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 165.9, 149.0, 132.0, 131.1, 119.2, 59.9, 32.6, 20.8, 14.3.
**General procedure for the copper-catalyzed allylic alkylation of an allylic bromide with organomagnesium reagents**

A Schlenk tube equipped with septum and stirring bar was charged with CuBr•SMe$_2$ (0.0125 mmol, 2.6 mg, 5 mol%) and the appropriate ligand (0.015 mmol, 6 mol%). Dry dichloromethane (3 mL) was added and the solution was stirred under nitrogen at room temperature for 15 min and cooled to –80 °C. Then, the corresponding organomagnesium reagent (0.3 mmol, 1.2 eq) was added under nitrogen. Allylic bromide (0.25 mmol) was dissolved in 1 mL of DCM and added dropwise to the reaction mixture over 1 h using a syringe pump. The reaction was quenched after overnight with a saturated aqueous NH$_4$Cl solution (2 mL) and the mixture was warmed up to room temperature, diluted with ether and the layers were separated. The aqueous layer was extracted with dichloromethane (3 x 5 mL) and the combined organic layers were dried over anhydrous Na$_2$SO$_4$, filtered and carefully concentrated (note: several products are highly volatile). The crude product was purified by flash chromatography on silica gel using different mixtures of n-pentane: Et$_2$O as the eluent.

**Note:** Gas chromatography analysis was carried out to determine the S$_{N2}$':S$_{N2}$ ratio’s and ee’s on a sample obtained after aqueous extraction with dichloromethane, which has been passed through a short plug of silica gel to remove transition metal residues.

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**(R,E)-(3-Methylpenta-1,4-dienyl)benzene (2a)**

The title compound was prepared from 1a (55 mg, 0.25 mmol) following the general procedure for the copper-catalyzed asymmetric allylic alkylation. Purification by column chromatography (SiO$_2$, Pentane) afforded product (26 mg, 66% yield, 99% ee) as a colourless oil as a mixture of two regioisomers 2a/3a (S$_{N2}$'/S$_{N2}$) in 95:5 ratio (determined by $^1$H NMR at 20 °C and GC). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.40 – 7.14 (m, 5H), 6.39 (d, $J = 16.0$ Hz, 1H), 6.18 (dd, $J = 16.0$, 7.0 Hz, 1H), 5.88 (ddd, $J = 17.0$, 10.3, 6.5 Hz, 1H), 5.05 (m, 2H), 3.11 – 2.99 (m, 1H), 1.21 (d, $J = 6.9$ Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 142.4, 137.6, 134.3, 128.6, 128.5, 127.0, 126.1, 113.3, 40.6, 19.8. HRMS (APCI+) calculated for C$_{12}$H$_{15}$:159.1168, found: 159.1157. [$a]_D^{20} = –56.5$ (c = 2.3, CHCl$_3$), [Lit. $^{14}$ (S isomer, er = 96:4) [$a]_D^{20} = +55$ (c = 0.87, CHCl$_3$)]. Enantiomeric excess was determined by chiral GC analysis, CP-Chiralsil-Dex-CB (25 m x 0.25 mm), initial temperature 80 °C for 80 min, then 1°C/min to 140°C (hold for 5 min), then 10°C/min to 180°C (final temp), retention times (min.): 25.8 (major) and 26.9 (minor); retention time 3a: 72.0 min.

In analogy to this result, the absolute configuration of the other products is assumed to be (R).
(R,E)-3,7-Dimethylocta-1,4-diene (2b)

The title compound was prepared from 1b (50 mg, 0.25 mmol) following the general procedure for the copper-catalyzed asymmetric allylic alkylation. Purification by column chromatography (SiO₂, Pentane) afforded product (11 mg, 32% yield, 99% ee) as a colourless oil as a mixture of two regioisomers 2b/3b (SN₂'/SN₂) in 96:4 ratio (determined by ¹H NMR at 20 °C and GC). ¹H NMR (400 MHz, CDCl₃) δ 5.80 – 5.66 (m, 1H), 5.38 – 5.23 (m, 2H), 4.97 – 4.81 (m, 2H), 2.77 – 2.73 (m, 1H), 1.82 (dd, J = 9.7, 3.6 Hz, 2H), 1.55 – 1.50 (m, 1H), 1.01 (d, J = 6.9 Hz, 3H), 0.80 (d, J = 6.6 Hz, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 143.4, 135.0, 128.0, 112.4, 41.9, 40.3, 28.4, 22.2, 20.0. HRMS (APCI+) calculated for C₇H₁₁[M–iso-propyl]⁺: 95.0861, found: 95.0814. [α]D₂₀ = +4.8 (c = 0.25, CHCl₃). Enantiomeric excess was determined by chiral GC analysis, CP-Chiralsil-Dex-CB (25 m x 0.25 mm), initial temperature 60 ºC for 20 min, then 0.5°C/min to 100°C (hold for 10 min), then 1°C/min to 140°C (final temp), retention times (min.): 15.1 (major) and 15.5 (minor); retention time 3b: 34.6 min.

(R,E)-Methyl 4-methylhexa-2,5-dienoate (2c)₁⁵

The title compound was prepared from 1c (51 mg, 0.25 mmol) following the general procedure for the copper-catalyzed asymmetric allylic alkylation. Purification by column chromatography (SiO₂, Pentane/Et₂O = 10/1) afforded product (15 mg, 43% yield, 97% ee) as a colorless oil as a mixture of two regioisomers 2c/3c (SN₂'/SN₂) in 94:6 ratio (determined by ¹H NMR at 20 °C and GC). ¹H NMR (400 MHz, CDCl₃) δ 6.86 (dd, J = 15.7, 6.9 Hz, 1H), 5.79 – 5.63 (m, 2H), 5.05 – 4.94 (m, 2H), 3.66 (s, 3H), 3.02 – 2.87 (m, 1H), 1.10 (d, J = 6.9 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 167.1, 152.1, 140.0, 119.7, 114.8, 51.4, 40.0, 18.8. [α]D₂₀ = –20 (c = 0.65, CHCl₃). Enantiomeric excess was determined by chiral GC analysis, CP-Chiralsil-Dex-CB (25 m x 0.25 mm), initial temperature 60 ºC for 20 min, then 0.5°C/min to 100°C (hold for 10 min), then 1°C/min to 140°C (final temp), retention times (min.): 35.9 (major) and 37.6 (minor); retention time 3c: 64.0 min.

(R,E)-tert-Butyldimethyl(4-methylhexa-2,5-dienyloxy)silane (2d)

The title compound was prepared from 1d (73 mg, 0.25 mmol) following the general procedure for the copper-catalyzed asymmetric allylic alkylation. Purification by column chromatography (SiO₂, Pentane/Et₂O = 10/1) afforded product (52 mg, 92% yield, 99% ee) as a colorless oil as a mixture of two regioisomers 2d/3d (SN₂'/SN₂) in 91:9 ratio (determined by ¹H NMR at 20 °C and GC). ¹H NMR (400 MHz, CDCl₃) δ 7.13 – 6.86 (m, 1H), 5.72 – 5.46 (m, 2H), 4.93 – 4.67 (m, 2H), 2.82 – 2.68 (m, 1H), 1.22 (d, J = 6.9 Hz, 3H), 1.07 (d, J = 6.8 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 167.2, 151.5, 140.1, 119.6, 114.7, 50.9, 40.0, 18.8. [α]D₂₀ = –20 (c = 0.65, CHCl₃). Enantiomeric excess was determined by chiral GC analysis, CP-Chiralsil-Dex-CB (25 m x 0.25 mm), initial temperature 60 ºC for 20 min, then 0.5°C/min to 100°C (hold for 10 min), then 1°C/min to 140°C (final temp), retention times (min.): 35.9 (major) and 37.6 (minor); retention time 3d: 164.0 min.
MHz, CDCl₃) δ 5.72 (ddd, J = 17.1, 10.3, 6.6 Hz, 1H), 5.58 – 5.39 (m, 2H), 4.91 (m, 2H), 4.08 (dt, J = 4.7, 1.0 Hz, 2H), 2.87 – 2.72 (m, 1H), 1.03 (d, J = 6.9 Hz, 3H), 0.84 (s, 9H), 0.00 (s, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 142.6, 134.5, 128.2, 112.9, 64.0, 39.9, 26.0, 19.6, 18.4, –5.1. HRMS (ESI+) calculated for C₁₄H₂₇OSi:227.1826, found: 227.1820. \[\alpha\]D²⁰ = –4.4 (c = 2.5, CHCl₃). Enantiomeric excess was determined by chiral GC analysis, CP-Chiralsil-Dex-CB (25 m x 0.25 mm), initial temperature 80 ºC for 80 min, then 1ºC/min to 140ºC (hold for 5 min), then 10ºC/min to 180ºC (final temp), retention times (min.): 23.6 (major) and 24.4 (minor); retention time 3d: 48.2 min.

\[\alpha\]D²⁰ = –2.8 (c = 1.85, CHCl₃). Enantiomeric excess was determined by chiral GC analysis, CP-Chiralsil-Dex-CB (25 m x 0.25 mm), initial temperature 60 ºC for 20 min, then 0.5ºC/min to 100ºC (hold for 10 min), then 1ºC/min to 140ºC (final temp), retention times (min.): 54.6 (major) and 55.8 (minor); retention time 3e: 86.3 min.

\[\alpha\]D²⁰ = +19.0 (c = 0.6, CHCl₃). Enantiomeric excess was determined by chiral GC analysis, CP-Chiralsil-Dex-CB (25 m x 0.25 mm), initial temperature 60 ºC for 20 min, then 0.5ºC/min to 100ºC (hold for 10 min), then 1ºC/min to 140ºC (final temp), retention times (min.): 54.6 (major) and 55.8 (minor); retention time 3e: 86.3 min.
determined by HPLC analysis (Chiralpak OD-H: 0.5 mL/min, n-heptane, 40 °C isotherm, 214 nm), retention times: 54.2 min (major), 57.9 min (minor).

(R,Z)-Ethyl 3,4-dimethylhexa-2,5-dienoate (2g)
The title compound was prepared from 1g (58 mg, 0.25 mmol) following the general procedure for the copper-catalyzed asymmetric allylic alkylation. Purification by column chromatography (SiO₂, Pentane/Et₂O = 10/1) afforded product (32 mg, 74% yield with trace of ether, 99% ee) as a colorless oil as a mixture of two regioisomers 2g/3g (SN₂'/SN₂) in 96:4 ratio (determined by ¹H NMR at 20 °C and GC). ¹H NMR (400 MHz, CDCl₃) δ 5.77 (ddd, J = 16.4, 10.4, 6.0 Hz, 1H), 5.58 (s, 1H), 5.10 – 4.92 (m, 2H), 4.63 – 4.50 (m, 1H), 4.08 (q, J = 7.1 Hz, 2H), 1.71 (d, J = 1.0 Hz, 3H), 1.21 (t, J = 7.1 Hz, 3H), 1.08 (d, J = 7.0 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 166.1, 162.0, 140.4, 116.1, 114.3, 59.5, 37.9, 20.0, 17.1, 14.3. HRMS (APCI+) calculated for C₁₀H₁₇O₂:169.1223, found: 169.1222. [α]D²⁰ = +130.1 (c = 1.5, CH₂Cl₂). Enantiomeric excess was determined by chiral GC analysis, CP-Chiralsil-Dex-CB (25 m x 0.25 mm), initial temperature 60 °C for 20 min, then 0.5°C/min to 100°C (hold for 10 min), then 1°C/min to 140°C (final temp), retention times (min): 56.1 (major) and 56.5 (minor); retention time 3g: 80.6 min.

Cross metathesis between 2d and 4

(S,2E,5E)-Ethyl 7-((tert-butyldimethylsilyl)oxy)-4-methylhepta-2,5-dienoate (5). To a stirred solution of compound 2d/3d (20 mg, 0.088 mmol, 91/9) in 4 mL of dry DCM was added ethyl acrylate 4 (9 mg, 0.09 mmol) and Hoveyda–Grubbs second-generation catalyst¹⁶ (0.6 mg, 0.00088 mmol, 1 mol%) under a nitrogen atmosphere at room temperature. The reaction mixture was stirred for 2 d and the product was purified by flash chromatography (pentane/Et₂O = 10/1) to give 5 as a colorless oil (15 mg, 57%) which was contaminated by trace of compound 6. ¹H NMR (400 MHz, CDCl₃) δ 6.84 (dd, J = 15.7, 6.9 Hz, 1H), 5.72 (dd, J = 15.7, 1.4 Hz, 1H), 5.55 – 5.44 (m, 2H), 4.14 – 4.07 (m, 4H), 2.99 – 2.94 (m, 1H), 1.22 (t, J = 7.1 Hz, 3H), 1.10 (d, J = 6.9 Hz, 3H), 0.84 (s, 9H), 0.00 (s, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 166.8, 152.1, 132.0, 129.8, 119.9, 63.6, 60.2, 38.7, 26.0, 19.1, 18.4, 14.3, -5.2. HRMS (APCI+) calculated for C₁₆H₃₁O₃Si:299.2042, found: 299.2037. [α]D²⁰ = +8.2 (c = 0.7, CH₂Cl₂).
References
Electronic Supplementary Material (ESI) for Chemical Communications
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Optically active 2a:

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Optically active 2b:
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Optically active 2c:

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Racemic 2f:

Optically active 2f:
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Optically active 2g:

Main Pe  Main Pe  Meas. RT
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