



Supporting Information

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Enantioselective Chromium-Catalyzed Carbonyl-ene Cyclizations

Melissa L. Grachan, Matthew T. Tudge, Eric N. Jacobsen*

*Department of Chemistry and Chemical Biology, Harvard University, 12 Oxford Street,
Cambridge, Massachusetts 02138*

General protocol. Unless noted otherwise, all reactions were performed in flame dried round bottom flasks fitted with rubber septa, under a nitrogen atmosphere. All air or moisture sensitive liquids were transferred by syringe or stainless steel cannulae. In addition, all air or moisture sensitive solids were handled in a nitrogen-filled glovebox. Flash chromatography was conducted using 60 silica (mesh 230-400) from EM Science.

Reagents. All reagents were purchased from Lancaster, Sigma-Aldrich, Alfa-Aesar, or Fluka Chemicals and were used as received unless otherwise stated. Anhydrous THF and ether were obtained via distillation from sodium benzophenone at 760 Torr. Anhydrous dichloromethane was obtained via distillation from CaH₂ at 760 Torr and toluene was distilled from sodium metal at 760 Torr.

Instrumentation. Proton and carbon nuclear magnetic resonance (¹H & ¹³C NMR) spectra were recorded on Varian-Mercury 400 (400 MHz), Inova-500 (500 MHz) or Inova-600 (600 MHz) spectrometers. Chemical shifts for protons are reported in parts per million (ppm) downfield from tetramethylsilane and are referenced against the chloroform lock signal (¹H, 7.26; ¹³C, 77.0 ppm). Data is reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, m = multiplet) coupling constants (Hz) and proton assignment. Infrared spectra (IR) were recorded on a Mattson-Galaxy Series FTIR 3000 spectrophotometer referenced to a polystyrene standard. Absorbancies are reported in wave numbers (cm⁻¹) and their relative intensities assigned as strong (s), medium (m), or weak (w). Optical rotations were measured using a 2 mL cell on a Jasco DIP 370 digital polarimeter. Mass spectra were obtained from the Harvard University mass spectrometry service. Chiral HPLC analysis was performed on a Shimadzu VP-series instrument; chiral GC analysis was performed on a Hewlett-Packard 5890 gas chromatograph using a Chiraldex γ-TA (30 m x 0.25 mm) column or an Alltech Cyclodex β (30 m x 0.25 mm) column.

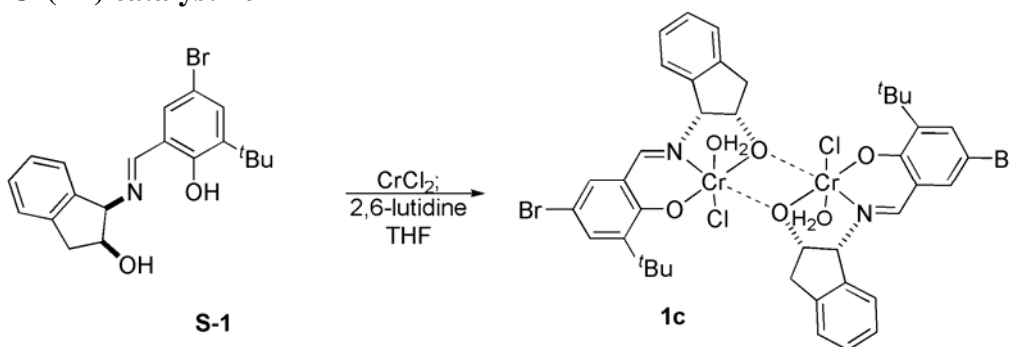
Experimental Procedures.

- 1) Catalyst Preparation
- 2) Substrate Preparation
- 3) Enantioselective Ene Cyclizations
- 4) Crystallographic Data

1) Preparation of catalyst 1c

Ligand **S-1** was prepared in accordance with the published procedure.¹

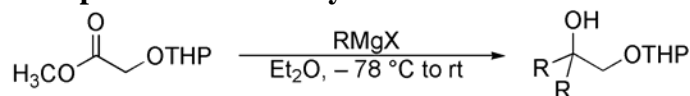
(1R, 2S)-Cr(III) catalyst **1c**



To a stirred solution of ligand **S-1** (1.0g, 2.58 mmol) in THF (30 mL) was added anhydrous chromium-(II)-chloride under a gentle flow of nitrogen. The mixture was stirred for 1 h, 2,6-lutidine (1.62 mL, 13.9 mmol) was added, and stirring was continued for an additional 1.5 h. The reaction mixture was then diluted with TBME (60 mL) and washed sequentially with 0.5 N HCl (2 x 100 mL) and brine (200 mL). The organic phase was then separated, dried over anhydrous Na₂SO₄, and concentrated to give a brown solid. Finally, the solid was dried azeotropically three times with anhydrous benzene to afford the desired catalyst **1c** (980 mg, 77%) which was used without further purification. Characterization of **1c** by X-ray crystallography and CD spectroscopy has been described previously.^{1,2}

2) Substrate Preparation

General procedure A: Preparation of tertiary alcohols



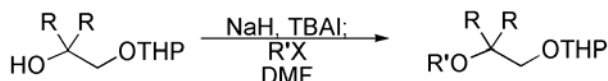
THP = 2-tetrahydropyranyl

To a cold (-78 °C), stirred solution of methyl 2-(tetrahydro-2H-pyran-2-yloxy)acetate (7.0 g, 6.1 mL, 40.2 mmol) in ether (100 mL) was added the required alkyl magnesium halide (121 mmol) dropwise over 20 minutes. The reaction mixture was allowed to warm to room temperature and stirring continued for 1 – 24 h. After complete consumption of the starting ester, the reaction mixture was carefully poured onto cold (0 °C) saturated aqueous NH₄Cl solution (200 mL). Additional Et₂O (100 mL) was added and the organic phase separated. The aqueous phase was extracted with Et₂O (2 x 100 mL) and the combined organic extracts washed with brine (200 mL). The organic phase was separated, dried over Na₂SO₄, and concentrated *in vacuo* to afford the crude product. Purification by column chromatography eluting with 10 – 20% ether / hexanes afforded the desired products.

General procedure B: Alkylation of tertiary alcohols

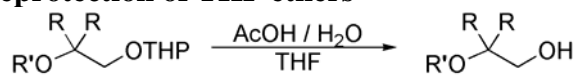
¹ Ruck, R. T.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 2882.

² Ruck, R. T. PhD. Dissertation, Harvard University, 2003.



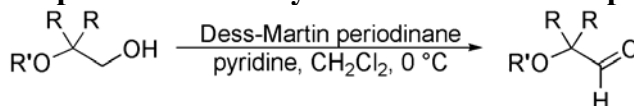
To a cooled (10 °C), stirred solution of the tertiary alcohol (35.9 mmol) in *N,N*-dimethylformamide (50 mL) was added tetrabutylammonium iodide (2.6 g, 7.2 mmol). The solution was then cautiously treated with sodium hydride (951 mg, 39.5 mmol) and allowed to warm to room temperature over 30 min during which time the solution had turned yellow. The reaction mixture was then treated with the alkyl halide (43.8 mmol) and stirred until no starting material remained by TLC. The solution was then cooled to 0 °C, carefully quenched by the addition of water (ca. 0.5 ml / mmol of NaH) and diluted with ether (60 mL). The ethereal solution was washed with water (2 x 300 mL) and then brine (300 mL) before being separated and dried (Na₂SO₄). Finally the solvent was removed *in vacuo* to afford the crude product. Purification by flash chromatography (3 – 5% Et₂O / hexanes) afforded the desired products as colorless oils.

General procedure C: Deprotection of THP ethers



The THP ether (25.6 mmol) was dissolved in 4 : 1 : 2 AcOH / H₂O / THF (100 mL) and stirred at room temperature until no starting material remained by TLC (ca. 24 – 48 h). The reaction mixture was poured onto cold (4 °C) NaOH before being extracted with ether (3 x 30 mL). The combined organic extracts were washed with brine (100 mL), dried (Na₂SO₄), and concentrated *in vacuo* to afford the crude product. Purification by flash chromatography, eluting with 8 – 15% Et₂O / hexanes, provided the desired primary alcohols as colorless oils.

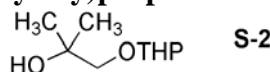
General procedure D: Preparation of aldehydes with Dess-Martin periodinane



To a cold (0 °C) stirred solution of the alcohol (2.0 g, 12.7 mmol) in reagent grade CH₂Cl₂ (50 mL) was added pyridine (1.0 mL, 67.8 mmol) followed by Dess-Martin periodinane (6.4 g, 15.2 mmol). The reaction was stirred until no starting material remained by TLC (ca. 2 – 4 h) at which point hexanes (50 mL) was added. The organic solution was then poured onto a 1:1 mixture of saturated aqueous NaHCO₃ (75 mL) and 10% Na₂S₂O₃. The biphasic solution was stirred for 15 minutes, separated, and the aqueous extracted with 1:1 Et₂O / hexanes (2 x 50 mL). The combined organic extracts were washed with brine (100 mL), dried (Na₂SO₄) and concentrated *in vacuo* to give the crude product. Purification by flash column chromatography, eluting with 5 – 10 % Et₂O / hexanes, afforded the desired aldehydes which, unless otherwise noted, could be stored for several months at – 78 °C without deterioration.

Preparation of aldehyde 2b.

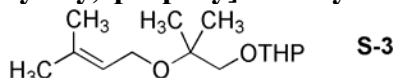
2-methyl-1-(tetrahydro-2H-pyran-2-yloxy)propan-2-ol (S-2)



In accordance with general procedure A, methyl 2-(tetrahydro-2H-pyran-2-yloxy)acetate (7.0g, 6.1 mL, 40.2 mmol) was converted to tertiary alcohol **S-2** (6.30 g, 89%) as a colorless oil. **R_f** = 0.08 (10% Et₂O / hexanes); **v_{max}** / cm⁻¹ (film) 3443 (s), 2943 (s), 2871 (s), 1383 (m); **¹H NMR**

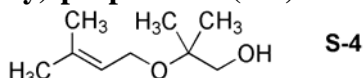
(500 MHz, CDCl₃) δ 4.53 (1H, dd, J = 4.5, 3, OCH₂O), 3.84 – 3.80 (1H, m, OCH₂CH₂), 3.51 (1H, d, J = 10, OCHC), 3.47 – 3.45 (1H, m, OCH₂CH₂), 3.25 (1H, d, J = 10.5, OCHC), 2.86 (1H, br. s, OH), 1.79 – 1.77 (1H, m, CH₂CH), 1.71 – 1.67 (1H, m, CH₂CH), 1.56 – 1.46 (4H, m, 2 x CH₂), 1.16 (6H, s, 2 x CH₃); ¹³C NMR (125.6 MHz, CDCl₃) δ 76.9, 69.8, 62.6, 30.5, 26.0, 25.9, 25.1, 19.6; m/z (ES+) 175 ([M+H]), 192 ([M+NH₄]).

2-[2-methyl-2-(3-methylbut-2-enyloxy)-propoxy]-tetrahydro-2H-pyran (S-3)



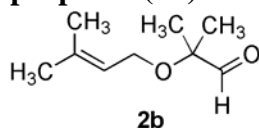
In accordance with general procedure B, tertiary alcohol **S-2** (6.25 g, 35.9 mmol) was treated with prenyl bromide (5.1 mL, 43.8 mmol, 90%) to afford prenyl ether **S-3** (6.45 g, 74%) as a colorless oil. R_f = 0.45 (10% EtOAc / hexanes); ν_{\max} / cm⁻¹ (film) 2969 (s), 2938 (s), 2871 (s), 1677 (w), 1453 (m); ¹H NMR (500 MHz, CDCl₃) δ 5.29 (1H, app. tt, J = 1.5, 7, CH=C(CH₃)₂), 4.59 (1H, app. t, J = 3.5, OCH₂O), 3.94 (2H, d, J = 7, OCH₂), 3.85 – 3.80 (1H, m, OCH₂CH₂), 3.61 (1H, d, J = 10, OCHC), 3.47 – 3.45 (1H, m, OCH₂CH₂), 3.27 (1H, d, J = 9.5, OCHC), 1.85 – 1.78 (1H, m, CH), 1.69 (3H, s, CH₃), 1.69 – 1.63 (1H, m, CH), 1.62 (3H, s, CH₃), 1.59 – 1.53 (1H, m, CH), 1.53 – 1.48 (3H, m, CH + CH₂), 1.23 (3H, s, CH₃), 1.19 (3H, s, CH₃); ¹³C NMR (125.6 MHz, CDCl₃) δ 135.4, 122.2, 98.9, 74.4, 73.3, 61.8, 58.8, 30.5, 25.8, 25.4, 23.4, 23.3, 19.2, 17.9; m/z (ES+) 243 ([M+H]), 260 ([M+NH₄]).

2-methyl-2-(3-methylbut-2-enyloxy)-propan-1-ol (S-4)



In accordance with general procedure C, prenyl ether **S-3** (6.2 g, 25.6 mmol) was deprotected to afford primary alcohol **S-4** (3.1 g, 78%) as a colorless oil. R_f = 0.12 (10% EtOAc / hexanes); ν_{\max} / cm⁻¹ (film) 3443 (s), 2927 (s), 2973 (s), 2930 (s), 2874 (s), 1677 (w), 1447 (m); ¹H NMR (400 MHz, CDCl₃) δ 5.28 (1H, br. t, J = 7, CH=C(CH₃)₂), 3.81 (2H, d, J = 7, CCH₂O), 3.40 (2H, d, J = 6.5, CCH₂OH), 2.18 (1H, t, J = 6.5, OH), 1.71 (3H, s, CH₃), 1.64 (3H, s, CH₃), 1.17 (6H, s, 2 x CH₃); ¹³C NMR (100.6 MHz, CDCl₃) δ 136.4, 121.9, 75.3, 69.6, 58.6, 26.0, 22.3, 18.2; m/z (CI, NH₄⁺) 159 ([M+H]), 176 ([M+NH₄]).

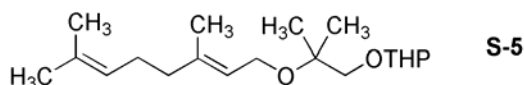
2-methyl-2-(3-methylbut-2-enyloxy)-propanal (2b)



In accordance with general procedure D, alcohol **S-4** (2.0 g, 12.7 mmol) was oxidized to afford aldehyde **2b** (1.8 g, 93%) as a colorless oil. R_f = 0.45 (10% EtOAc / hexanes); ν_{\max} / cm⁻¹ (film) 2980 (s), 2933 (s), 2870 (s), 1736 (s), 1646 (w), 1450 (m); ¹H NMR (400 MHz, CDCl₃) δ 9.58 (1H, s, CHO), 5.34 (1H, br. t, J = 7, CH=C(CH₃)₂), 3.90 (2H, d, J = 7, CH₂O), 1.74 (3H, s, CH₃), 1.65 (3H, s, CH₃), 1.28 (6H, s, 2 x CH₃); ¹³C NMR (100.6 MHz, CDCl₃) δ 204.8, 137.7, 121.2, 80.1, 61.4, 26.1, 21.1, 18.2; m/z (CI, NH₄⁺) 174 ([M+NH₄]).

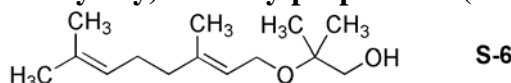
Preparation of aldehyde 2c.

(E)-2-[2-(3,7-dimethylocta-2,6-dienyloxy)-2-methylpropoxy]-tetrahydro-2H-pyran (S-5)



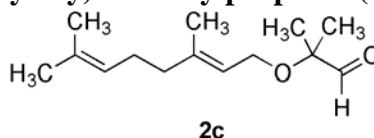
In accordance with general procedure B, tertiary alcohol **S-2** (4.0 g, 22.9 mmol) was treated with geranyl bromide (5.3 mL, 27.5 mmol) to afford geranyl ether **S-5** (5.2 g, 73%) as a colorless oil. $R_f = 0.62$ (20% EtOAc / hexanes); $\nu_{\max} / \text{cm}^{-1}$ (film) 2969 (s), 2938 (s), 2871 (s), 1677 (w), 1453 (m); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 5.31 (1H, app. t, $J = 7.5$, $\text{C}=\text{CH}$), 5.08 (1H, app. t, $J = 7$, $\text{C}=\text{CH}$), 4.61 (1H, app. t, $J = 3$, OCH), 3.98 (2H, d, $J = 6.5$, OCH_2), 3.87 – 3.82 (1H, m, OCHCH_2), 3.64 (1H, d, $J = 10$, OCHC), 3.52 – 3.48 (1H, m, OCHCH_2), 3.29 (1H, d, $J = 10$, OCHC), 2.08 (2H, app. q, $J = 7$, CH_2), 1.99 (2H, t, $J = 7.5$, CH_2), 1.85 – 1.80 (1H, m, CH), 1.73 – 1.68 (1H, m, CH), 1.66 (3H, s, CH_3), 1.65 – 1.63 (1H, m, CH), 1.63 (3H, s, CH_3), 1.58 (3H, s, CH_3), 1.53 – 1.49 (3H, m, $\text{CH} + \text{CH}_2$), 1.24 (3H, s, CH_3), 1.21 (3H, s, CH_3); $^{13}\text{C NMR}$ (125.6 MHz, CDCl_3) δ 138.7, 131.7, 124.4, 122.3, 99.2, 74.7, 73.6, 62.2, 59.3, 39.9, 30.8, 26.6, 25.9, 25.7, 23.7, 23.6, 19.5, 17.9, 16.7; m/z (ES^+) 311 ($[\text{M}+\text{H}]$), 328 ($[\text{M}+\text{NH}_4]$), 333 ($[\text{M}+\text{Na}]$).

(E)-2-(3,7-dimethylocta-2,6-dienyloxy)-2-methylpropan-1-ol (S-6)



In accordance with general procedure C, geranyl ether **S-5** (5.1 g, 25.6 mmol) was deprotected to afford primary alcohol **S-6** (3.3 g, 88%) as a colorless oil. $R_f = 0.30$ (20% EtOAc / hexanes); $\nu_{\max} / \text{cm}^{-1}$ (film) 3451 (s), 2970 (s), 2973 (s), 2926 (s), 2877 (s), 1671 (w), 1449 (m); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 5.30 (1H, br. t, $J = 6.5$, $\text{CH}=\text{C}(\text{CH}_3)_2$), 5.08 (1H, br. t, $J = 7$, $\text{CH}=\text{CCH}_3$), 3.91 (2H, d, $J = 6$, CCH_2O), 3.42 (2H, d, $J = 6$, CCH_2OH), 2.12 – 2.06 (2H, m, CH_2), 2.04 – 2.00 (2H, m, CH_2), 1.67 (3H, s, CH_3), 1.65 (3H, s, CH_3), 1.19 (3H, s, 2 x CH_3); $^{13}\text{C NMR}$ (100.6 MHz, CDCl_3) δ 139.5, 131.9, 124.2, 121.7, 75.3, 69.7, 58.8, 39.8, 26.6, 25.9, 22.3, 17.9, 16.7; m/z (CI , NH_4^+) 227 ($[\text{M}+\text{H}]$), 244 ($[\text{M}+\text{NH}_4]$).

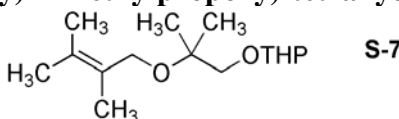
(E)-2-(3,7-dimethylocta-2,6-dienyloxy)-2-methylpropanal (2c)



In accordance with general procedure D, alcohol **S-6** (1.5 g, 6.6 mmol) was oxidized to afford aldehyde **2c** (1.1 g, 90%) as a colorless oil. $R_f = 0.45$ (10% EtOAc / hexanes); $\nu_{\max} / \text{cm}^{-1}$ (film) 2979 (s), 2928 (s), 2859 (s), 1735 (s), 1451 (m); $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 9.62 (1H, s, CHO), 5.38 (1H, br. t, $J = 6.5$, $\text{CH}=\text{C}(\text{CH}_3)_2$), 5.11 (1H, br. t, $J = 7$, $\text{CH}=\text{CCH}_3$), 3.97 (2H, d, $J = 6.5$, CH_2O), 2.13 (2H, app. q, $J = 6.5$, CH_2), 2.06 (2H, t, $J = 6.5$, CH_2), 1.71, (3H, s, CH_3), 1.68 (3H, s, CH_3), 1.63 (3H, s, CH_3), 1.32 (6H, s, 2 x CH_3); $^{13}\text{C NMR}$ (100.6 MHz, CDCl_3) δ 204.9, 140.8, 132.0, 124.1, 120.9, 80.1, 61.5, 39.8, 26.5, 25.9, 21.2, 17.9, 16.7; m/z (CI , NH_4^+) 242 ($[\text{M}+\text{NH}_4]$).

Preparation of aldehyde 2d.

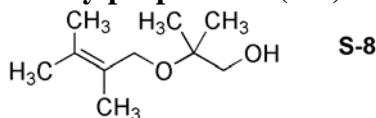
2-(2-(2,3-dimethylbut-2-enyloxy)-2-methylpropoxy)-tetrahydro-2H-pyran (S-7)



In accordance with general procedure B, tertiary alcohol **S-2** (0.88 g, 5.00 mmol) was treated

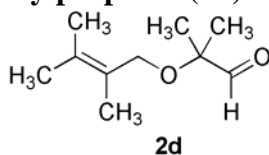
with 1-bromo-2,3-dimethylbut-2-ene³ (805 μ L, 6.00 mmol) to afford ether **S-7** (1.029g, 80%) as a pale yellow oil. R_f = 0.74 (15% EtOAc / hexanes); ν_{\max} / cm^{-1} (film) 2941 (s), 2871 (m), 1726 (w), 1377 (m), 1125 (s), 1068 (s), 1036 (s); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 4.62 (1H, app. t, J = 3.6, OCH_2O), 3.92 (2H, s, OCH_2), 3.87 – 3.82 (1H, m, OCHCH_2), 3.64 (1H, d, J = 10, OCHC), 3.50 (1H app. dtd, J = 1.6, 4, 11.2, OCHCH_2), 3.30 (1H, d, J = 10, OCHC), 1.87 – 1.79 (1H, m, CH), 1.73 – 1.63 (1H, m, CH), 1.71 (3H, app. d, J = 1.2, CH_3), 1.69 (3H, app. td, J = 1.2, 2), 1.66 (3H, s, CH_3), 1.63 – 1.55 (1H, m, CH), 1.53 – 1.49 (3H, m, $\text{CH} + \text{CH}_2$), 1.25 (3H, s, CH_3), 1.21 (3H, s, CH_3); $^{13}\text{C-NMR}$ (100.6 MHz, CDCl_3) δ 129.2, 125.9, 99.2, 74.5, 73.8, 63.3, 62.1, 30.8, 25.8, 23.7, 21.2, 20.3, 19.5, 17.2; m/z (FAB+) 257 ($[\text{M}+\text{H}]$), 279 ($[\text{M}+\text{Na}]$).

2-(2,3-dimethylbut-2-enyloxy)-2-methylpropan-1-ol (**S-8**)



In accordance with general procedure C, ether **S-7** (1.50 g, 5.86 mmol) was deprotected to afford primary alcohol **S-8** (0.645 g, 63%) as a pale yellow oil. R_f = 0.35 (20% EtOAc / hexanes); ν_{\max} / cm^{-1} (film) 3421 (br, m), 2976 (s), 1725 (w), 1466 (w), 1376 (m), 1072 (s); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 3.87 (2H, s, CH_2), 3.44 (2H, s, CH_2), 2.08 (1H, s, OH), 1.72 (3H, s, CH_3), 1.71 (3H, app. d, J = 0.8), 1.69 (3H, s, CH_3), 1.20 (6H, s, 2 x CH_3); $^{13}\text{C-NMR}$ (100.6 MHz, CDCl_3) δ 129.9, 125.4, 75.1, 70.0, 63.0, 22.2, 21.1, 20.3, 17.3; m/z (ES+) 173 ($[\text{M}+\text{H}]$).

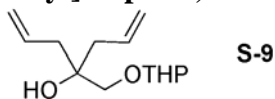
2-(2,3-dimethylbut-2-enyloxy)-2-methylpropanal (**2d**)



In accordance with general procedure D, alcohol **S-8** (0.600 g, 3.45 mmol) was oxidized to afford aldehyde **2d** (0.545 g, 92%) as a colorless oil. R_f = 0.65 (20% EtOAc / hexanes); ν_{\max} / cm^{-1} (film) 2984 (m), 2923 (m), 1734 (s), 1458 (w), 1383 (m), 1172 (s), 1041 (s); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 9.60 (1H, s, CHO), 3.88 (2H, s, CH_2O), 1.75 (3H, app. t, J = 1.6, CH_3), 1.71 (3H, app. t, J = 1.6, CH_3), 1.69 (3H, s, CH_3), 1.29 (6H, s, 2 x CH_3); $^{13}\text{C-NMR}$ (100.6 MHz, CDCl_3) δ 204.9, 130.9, 124.9, 79.9, 65.7, 21.2, 21.1, 20.4, 17.3; m/z (ES+) 171 ($[\text{M}+\text{H}]$).

Preparation of aldehyde **2e**.

4-[(tetrahydro-2H-pyran-2-yloxy)methyl]-hepta-1,6-dien-4-ol (**S-9**)

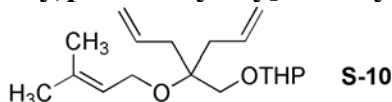


In accordance with general procedure A, methyl 2-(tetrahydro-2H-pyran-2-yloxy)acetate (6.0g, 5.2 mL, 34.5 mmol) was converted to tertiary alcohol **S-9** (7.5 g, 96%) as a yellow oil. R_f = 0.08 (10% Et_2O / hexanes); ν_{\max} / cm^{-1} (film) 3450 (m), 2942 (s), 2871 (m), 1640 (w), 1440 (w); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 5.91 – 5.83 (2H, m, 2 x $\text{CH}=\text{CH}_2$), 5.12 – 5.08 (4H, m, 2 x $\text{CH}=\text{CH}_2$), 4.57 (1H, dd, J = 4.5, 3, OCH_2O), 3.89 – 3.85 (1H, m, OCHCH_2), 3.59 (1H, d, J = 10.5, OCHC), 3.55 – 3.51 (1H, m, OCHCH_2), 3.35 (1H, d, J = 10.5, OCHC), 2.75 (1H, br. s,

³ Murray, R. W.; Agarwal, S. K. *J. Org. Chem.* **1985**, *50*, 4698-4702.

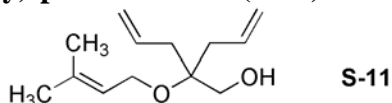
OH), 2.33 – 2.43 (4H, m, 2 x $\text{CH}_2\text{C}=\text{CH}_2$), 1.84 – 1.80 (1H, m, CH_2CH), 1.76 – 1.70 (1H, m, CH_2CH), 1.64 – 1.51 (4H, m, 2 x CH_2); ^{13}C NMR (125.6 MHz, CDCl_3) δ 133.9, 118.5, 118.4, 100.2, 74.0, 73.2, 62.9, 41.7, 41.5, 30.1, 25.5, 19.3; m/z (ES^+) 227 ($[\text{M}+\text{H}]$).

2-[2-allyl-2-(3-methylbut-2-enyloxy)pent-4-enyloxy]-tetrahydro-2H-pyran (S-10)



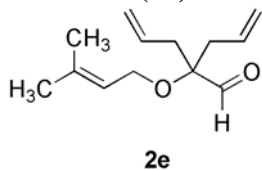
In accordance with general procedure B, ether **S-9** (2.2 mL, 9.5 mmol) was treated with prenyl bromide (1.9 mL, 14.3 mmol, 90%) to afford prenyl ether **S-10** (2.3 g, 83%) as a colorless oil. R_f = 0.61 (20% EtOAc / hexanes); ν_{max} / cm^{-1} (film) 2940 (s), 2872 (s), 1677 (w), 1640 (m), 1441 (m); ^1H NMR (600 MHz, CDCl_3) δ 5.93 – 5.86 (2H, m, 2 x $\text{CH}=\text{CH}_2$), 5.35 (1H, app. tt, J = 7, 1, $\text{CH}=\text{C}(\text{CH}_3)_2$), 5.14 (2H, br. dd, J = 7, 1, $\text{CH}=\text{CH}_2$), 5.12 (2H, br. dd, J = 5, 0.5, $\text{CH}=\text{CH}_2$), 4.64 (1H, app. t, J = 3.5, OCH_2), 4.05 (2H, d, J = 6.5, OCH_2), 3.89 – 3.85 (1H, m, OCH_2CH_2), 3.75 (1H, d, J = 11, OCH_2CH), 3.57 – 3.54 (1H, m, OCH_2CH_2), 3.32 (1H, d, J = 10.5, OCH_2CH), 2.43 – 2.37 (4H, m, 2 x $\text{CH}_2\text{C}=\text{CH}_2$), 1.89 – 1.83 (1H, m, CH), 1.76 (3H, s, CH_3), 1.75 – 1.69 (1H, m, CH), 1.69 (3H, s, CH_3), 1.69 – 1.54 (4H, m, 2 x CH_2); ^{13}C NMR (125.6 MHz, CDCl_3) δ 135.8, 134.1, 134.0, 122.1, 117.9, 117.8, 99.2, 77.9, 69.9, 61.9, 58.8, 38.4, 38.3, 30.8, 26.1, 25.7, 19.4, 18.2; m/z (ES^+) 295 ($[\text{M}+\text{H}]$), 312 ($[\text{M}+\text{NH}_4]$).

2-allyl-2-(3-methylbut-2-enyloxy)-pent-4-en-1-ol (S-11)



In accordance with general procedure C, primary alcohol **S-10** (2.2 g, 7.5 mmol) was deprotected to afford primary alcohol **S-11** (1.2 g, 76%) as a colorless oil. R_f = 0.40 (15% EtOAc / hexanes); ν_{max} / cm^{-1} (film) 3450 (s), 2977 (s), 2926 (s), 2882 (s), 1640 (m), 1440 (m); ^1H NMR (600 MHz, CDCl_3) δ 5.91 – 5.84 (2H, m, 2 x $\text{CH}=\text{CH}_2$), 5.35 (1H, br. t, J = 6.5, $\text{CH}=\text{C}(\text{CH}_3)_2$), 5.18 – 5.14 (4H, m, 2 x $\text{CH}=\text{CH}_2$), 4.00 (2H, d, J = 7, CCH_2O), 3.55 (2H, d, J = 5, CCH_2OH), 2.40 (2H, dd, J = 14.5, 7, CH_2), 2.29 (2H, dd, J = 14.5, 7, CH_2), 1.86 (1H, br. s, OH), 1.78 (3H, s, CH_3), 1.71 (3H, s, CH_3); ^{13}C NMR (125.6 MHz, CDCl_3) δ 136.6, 133.6, 121.5, 118.4, 78.7, 64.8, 58.3, 37.6, 26.1, 18.3; m/z (ES^+) 211 ($[\text{M}+\text{H}]$).

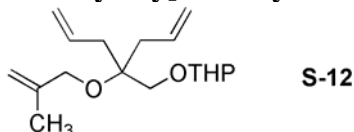
2-allyl-2-(3-methylbut-2-enyloxy)-pent-4-enal (2e)



In accordance with general procedure D, alcohol **S-11** (1.2 g, 5.6 mmol) was oxidized to afford aldehyde **2e** (1.1 g, 91%) as a colorless gum. R_f = 0.40 (10% EtOAc / hexanes); ν_{max} / cm^{-1} (film) 2980 (m), 2916 (m), 2861 (m), 1734 (s), 1441 (m); ^1H NMR (500 MHz, CDCl_3) δ 9.59 (1H, s, CHO), 5.78 – 5.67 (2H, m, 2 x $\text{CH}=\text{CH}_2$), 5.36 (1H, br. t, J = 7, $\text{CH}=\text{C}(\text{CH}_3)_2$), 5.14 – 5.11 (4H, m, 2 x $\text{CH}=\text{CH}_2$), 3.98 (2H, d, J = 7, CH_2O), 2.47 (4H, br. d, J = 7, 2 x CH_2), 1.75 (3H, s, CH_3), 1.66 (3H, s, CH_3); ^{13}C NMR (100.6 MHz, CDCl_3) δ 204.9, 137.4, 131.4, 120.6, 119.1, 83.3, 60.7, 36.4, 25.8, 18.0; m/z (CI , NH_4^+) 226 ($[\text{M}+\text{NH}_4]$).

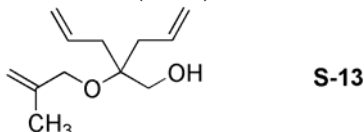
Preparation of aldehyde 2f.

2-[2-allyl-2-(2-methylallyloxy)pent-4-enyloxy]-tetrahydro-2H-pyran (S-12)



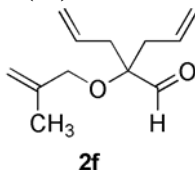
In accordance with general procedure B, tertiary alcohol **S-9** (2.2 mL, 9.5 mmol) was treated with methallyl bromide (1.9 g, 14.3 mmol, 90%) to yield methallyl ether **S-12** (2.3 g, 83%) as a colorless oil. $R_f = 0.54$ (15% EtOAc / hexanes); $\nu_{\max} / \text{cm}^{-1}$ (film) 2942 (s), 2871 (s), 1655 (w), 1640 (m), 1441 (m); $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 5.94 – 5.86 (2H, m, 2 x $\text{CH}=\text{CH}_2$), 5.14 – 5.11 (4H, m, 2 x $\text{CH}=\text{CH}_2$), 5.03 (1H, br. s, $\text{C}=\text{CH}$), 4.86 (1H, br. d, $J = 0.5$, $\text{C}=\text{CH}$), 4.63 (1H, app. t, $J = 3.5$, OCH_2), 3.97 (2H, br. s, OCH_2), 3.89 – 3.85 (1H, m, OCH_2CH_2), 3.75 (1H, d, $J = 11$, OCH_2CH), 3.57 – 3.54 (1H, m, OCH_2CH_2), 3.33 (1H, d, $J = 11$, OCH_2CH), 2.43 – 2.41 (4H, app. t, $J = 8$, 2 x $\text{CH}_2\text{C}=\text{CH}_2$), 1.88 – 1.82 (1H, m, CH_2), 1.77 (3H, s, CH_3), 1.75 – 1.70 (1H, m, CH_2), 1.67 – 1.60 (1H, m, CH_2), 1.58 – 1.54 (3H, m, $\text{CH}_2 + \text{CH}_3$); $^{13}\text{C NMR}$ (125.6 MHz, CDCl_3) δ 143.3, 134.2, 134.0, 117.9, 117.9, 111.0, 99.2, 78.1, 70.3, 66.0, 61.9, 38.5, 38.4, 30.8, 25.7, 20.0, 19.4; m/z (ES^+) 281 ($[\text{M}+\text{H}]$), 298 ($[\text{M}+\text{NH}_4]$).

2-allyl-2-(2-methylallyloxy)pent-4-en-1-ol (S-13)



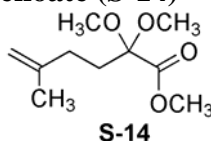
In accordance with general procedure C, ether **S-12** (2.1 g, 7.5 mmol) was deprotected to afford primary alcohol **S-13** (1.2 g, 82%) as a colorless oil. $R_f = 0.38$ (15% EtOAc / hexanes); $\nu_{\max} / \text{cm}^{-1}$ (film) 3451 (s), 2978 (s), 2921 (s), 2873 (s), 1640 (m), 1440 (m); $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 5.91 – 5.84 (2H, m, 2 x $\text{CH}=\text{CH}_2$), 5.18 – 5.14 (4H, m, 2 x $\text{CH}=\text{CH}_2$), 5.05 (1H, s, $\text{C}=\text{CH}$), 4.90 (1H, s, $\text{C}=\text{CH}$), 3.91 (2H, s, OCH_2), 3.57 (2H, s, OCH_2), 2.40 (2H, dd, $J = 14.5$, 7, CH_2), 2.34 (2H, dd, $J = 14.5$, 7, CH_2), 1.85 (1H, br. s, OH), 1.79 (3H, s, CH_3); $^{13}\text{C NMR}$ (125.6 MHz, CDCl_3) δ 142.9, 133.5, 118.4, 111.4, 78.9, 65.4, 65.0, 37.8, 20.0; m/z (CI , NH_4^+) 214 ($[\text{M}+\text{NH}_4]$).

2-allyl-2-(2-methylallyloxy)-pent-4-enal (2f)

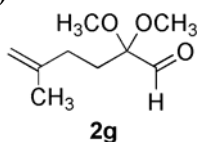


In accordance with general procedure D, alcohol **S-13** (1.2 g, 6.1 mmol) was oxidized to afford aldehyde **2f** (1.1 g, 92%) as a colorless oil. $R_f = 0.40$ (10% EtOAc / hexanes); $\nu_{\max} / \text{cm}^{-1}$ (film) 2980 (m), 2916 (m), 2861 (m), 1734 (s), 1441 (m); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 9.61 (1H, s, CHO), 5.79 – 5.69 (2H, m, 2 x $\text{CH}=\text{CH}_2$), 5.13 – 5.09 (4H, m, 2 x $\text{CH}=\text{CH}_2$), 5.04 (1H, s, CH), 4.89 (1H, s, CH), 3.88 (2H, s, CH_2O), 2.47 (4H, d, $J = 7.5$, 2 x CH_2), 1.77 (3H, s, CH_3); $^{13}\text{C NMR}$ (100.6 MHz, CDCl_3) δ 205.4, 142.0, 131.6, 119.4, 112.3, 83.8, 67.9, 36.9, 19.9; m/z (CI , NH_4^+) 212 ($[\text{M}+\text{NH}_4]$).

Preparation of aldehyde 2g.

methyl 2,2-dimethoxy-5-methylhex-5-enoate (S-14)

Under a gentle flow of nitrogen, a round bottom flask was charged with tetrahydrofuran (30 mL), hexamethylphosphoramide (20 mL), and diisopropylamine (5.69 mL, 40.7 mmol). The mixture was cooled to -78 °C with stirring. To this solution, butyllithium (24 mL, 1.6 M in hexanes) was added dropwise. The reaction vessel was transferred to a 0 °C bath for 15 minutes. The solution was cooled to -78 °C and methyl dimethoxyacetate (4.55 mL, 37.0 mmol) was added to it dropwise. After stirring for 10 minutes at -78 °C, the reaction mixture was transferred to a 0 °C bath for 30 minutes. The solution was then cooled to -78 °C and 4-iodo-2-methylbut-1-ene⁴ (3.63 mL, 18.5 mmol) was added dropwise. The -78 °C bath was allowed to warm to 4 °C and the reaction mixture was stirred for an additional 12 hours. The reaction mixture was partitioned between 0.25M HCl_(aq) (200 mL) and 1:1 diethyl ether / hexanes (200 mL). The organic layer was then washed with saturated aqueous sodium bicarbonate, water, and saturated sodium chloride (250 mL / ea). The organic layer was dried with sodium sulfate, filtered, and concentrated. Following purification via flash chromatography on silica gel (elute 5% Et₂O / hex), title compound **S-14** (1.66 g, 44%) was isolated as a colorless oil. *R*_f = 0.26 (20% EtOAc / hexanes); *ν*_{max} / cm⁻¹ (film) 2949 (w), 1758 (m), 1450 (w), 1101 (s); ¹H NMR (500 MHz, CDCl₃) δ 4.69 (1H, s, C=CH), 4.65 (1H, s, C=CH), 3.79 (3H, s, OCH₃), 3.52 (6H, s, 2 x OCH₃), 2.00 (2H, m, CH₂), 1.89 (2H, m, CH₂), 1.69 (3H, s, CH₃); ¹³C NMR (125.8 MHz, CDCl₃) δ 169.8, 144.6, 110.3, 102.7, 52.7, 50.0, 32.0, 31.3, 22.8; *m/z* (ES+) 220 ([M+NH₄]).

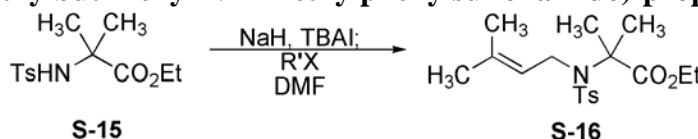
2,2-dimethoxy-5-methylhex-5-enal (2g)

Under a gentle flow of nitrogen, ester **S-14** (1.60 g, 7.92 mmol) was dissolved in anhydrous dichloromethane (16 mL) and cooled to -78 °C while stirring. To this solution, diisobutylaluminum hydride (9.50 mL; 1 M in hexanes) was added dropwise to avoid exotherm. The reaction progress was monitored via GC and after 1 h methanol (5 mL) was added carefully to avoid exotherm. An aqueous solution of 10% Rochelle's salt (10 mL) was immediately added in one portion and the reaction mixture diluted with diethyl ether (10 mL), removed from the cold bath, and allowed to warm to room temperature while stirring vigorously. The solution was filtered through celite, then partitioned between saturated aqueous sodium chloride and diethyl ether. The organic layer was dried with sodium sulfate. Following filtration and concentration, the title compound **2g** was purified by flash chromatography, eluting with 2% to 5% Et₂O / hexanes, and isolated as a colorless oil (0.864 g, 64%). *R*_f = 0.64 (25% EtOAc / hexanes); *ν*_{max} / cm⁻¹ (film) 2943 (m), 1749 (s), 1450 (m), 1053 (s); ¹H NMR (500 MHz, CDCl₃) δ 9.44 (1H, s, CHO), 4.70 (1H, s, C=CH), 4.66 (1H, s, C=CH), 3.27 (6H, s, 2 x OCH₃), 1.89 (4H, m, 2 x CH₂), 1.67 (3H, s, CH₃); ¹³C NMR (125.8 MHz, CDCl₃) δ 200.2, 144.7, 110.7, 102.4, 49.8, 30.7, 30.2, 22.7; *m/z* (APCI+) 141 ([M-OCH₃]), 100%; 173 ([M+H]), 20%.

⁴ Larock, R. C.; Yang, H.; *J. Org. Chem.* **1994**, *59*, 4172-4178.

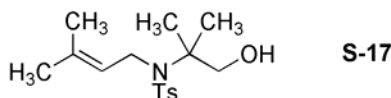
Preparation of aldehyde 2h.

2-methyl-2-*N*-(3-methylbut-2-enyl)-*N*-(4-methylphenyl)sulfonamido)-propionate (**S-16**)



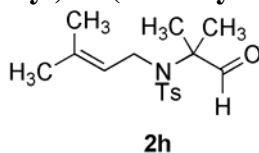
In accordance with general procedure B, tosyl amide **S-15**⁵ (2.0 g, 7.0 mmol) was reacted with prenyl bromide (1.8 mL, 4.0 mmol) to afford prenyl sulfonamide **S-16** (2.2 g, 89%) as a colorless gum. R_f = 0.57 (20% EtOAc / hexanes); ν_{\max} / cm^{-1} (film) 2984 (m), 2932 (s), 2871 (m), 1738 (s), 1603 (w), 1324 (s); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.87 (2H, d, J = 8, ArH), 7.27 (2H, d, J = 8, ArH), 5.25 (1H, app. tt, J = 6, 3, $\text{C}=\text{CH}$), 4.24 (2H, q, J = 7, OCH_2), 3.78 (2H, br. d, J = 6, NCH_2), 2.41 (3H, s, ArCH_3), 1.63 (3H, s, CH_3), 1.57 (6H, s, 2 x CH_3), 1.54 (3H, s, CH_3), 1.32 (3H, t, J = 6.5, CH_3); $^{13}\text{C NMR}$ (125.6 MHz, CDCl_3) δ 174.8, 143.1, 138.1, 133.4, 129.3, 128.1, 122.5, 63.6, 61.5, 43.5, 26.0, 25.6, 21.5, 17.6, 14.0; m/z (ES^+) 354 ($[\text{M}+\text{H}]$), 371 ($[\text{M}+\text{NH}_4]$).

N-(1-hydroxy-2-methylpropan-2-yl)-4-methyl-*N*-(3-methylbut-2-enyl)benzenesulfonamide (**S-17**)



To a cold (-78 °C) suspension of LiAlH_4 (284 mg, 7.5 mmol) in THF (30 mL) was added ester **S-16** (2.2 g, 6.22 mmol) in THF (5 mL + 5 mL washings). The reaction mixture was then warmed to -10 °C and allowed to proceed for 2 h until no starting material remained by TLC. At this point, the reaction was cautiously treated with water (0.32 mL) followed by 15% aqueous NaOH (0.91 mL). After 20 minutes, the resultant solid was removed via filtration, the filter cake washed with Et_2O (2 x 50 mL) and the organic filtrate concentrated to give the crude product. Purification by flash column chromatography eluting with 15% Et_2O / hexanes afforded alcohol **S-17** (1.9 g, 98%) as a colorless gum. R_f = 0.20 (50% EtOAc / hexanes); ν_{\max} / cm^{-1} (film) 3529 (m), 2973 (m), 2928 (m), 1448 (m); $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.73 (2H, d, J = 8, 2 x ArCH), 7.28 (2H, d, J = 8, 2 x ArCH), 5.29 (1H, br. t, J = 6, $\text{CH}=\text{C}(\text{CH}_3)_2$), 3.99 (2H, d, J = 6.5, CH_2OH), 3.65 (2H, d, J = 7, CH_2N), 2.64 (1H, t, J = 6.5, OH), 2.42 (3H, s, ArCH_3), 1.71 (3H, s, CH_3), 1.63 (3H, s, CH_3), 1.23 (6H, s, 2 x CH_3); $^{13}\text{C NMR}$ (125.6 MHz, CDCl_3) δ 143.0, 140.0, 133.2, 129.6, 127.1, 123.9, 69.9, 63.5, 45.0, 25.7, 24.9, 21.5, 17.8; m/z (ES^+) 312 ($[\text{M}+\text{H}]$), 329 ($[\text{M}+\text{NH}_4]$).

4-methyl-*N*-(2-methyl-1-oxopropan-2-yl)-*N*-(3-methylbut-2-enyl)benzenesulfonamide (**2h**)



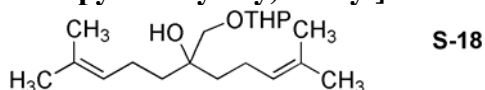
In accordance with general procedure D, alcohol **S-17** (1.8 g, 5.8 mmol) was oxidized to afford aldehyde **2h** (1.7 g, 96%) as a colorless gum. Note that aldehyde **2h** was used in the enantioselective cyclization reaction within 30 minutes of purification due to spontaneous ene

⁵ Gensler, W. J.; Frank, F. J.; Dheer, S. K.; Lauher, J. W. *J. Org. Chem.* **1971**, 4102.

cyclization of this aldehyde. R_f = 0.40 (50% EtOAc / hexanes); ν_{\max} / cm^{-1} (film) 2984 (m), 2929 (m), 2863 (m), 1738 (s), 1448 (m); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 9.63 (1H, s, CHO), 7.73 (2H, d, J = 8.5, 2 x ArCH), 7.27 (2H, d, J = 7.5, 2 x ArCH), 5.11 (1H, br. t, J = 6, $\text{CH}=\text{C}(\text{CH}_3)_2$), 3.78 (2H, d, J = 6, CH_2N), 2.40 (3H, s, ArCH₃), 1.61 (3H, s, CH_3), 1.53 (3H, s, CH_3), 1.34 (6H, s, 2 x CH_3); $^{13}\text{C NMR}$ (125.6 MHz, CDCl_3) δ 198.5, 143.7, 137.2, 134.0, 129.5, 127.9, 121.8, 66.7, 43.2, 25.5, 22.1, 21.4, 17.6; m/z (ES^+) 310 ($[\text{M}+\text{H}]$), 327 ($[\text{M}+\text{NH}_4]$).

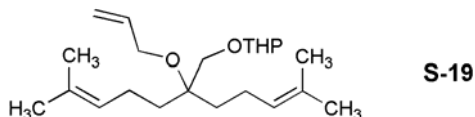
Preparation of aldehyde 4a.

2,10-dimethyl-6-[(tetrahydro-2H-pyran-2-yloxy)methyl]-undeca-2,9-dien-6-ol (S-18)



To a stirred suspension of magnesium (85 mg, 24.3 mmol) in ether (5 mL) was added homoprenyl bromide⁶ (60 μL , 0.23 mmol). The suspension was gently heated to initiate Grignard formation before adding additional homoprenyl bromide (600 μL , 2.25 mmol) at such a rate as to maintain auto reflux. After the initial exotherm subsided, the reaction mixture was diluted with ether (2 mL) and heated at reflux for 2 h. The solution was then cooled to -78°C and treated with methyl 2-(tetrahydro-2H-pyran-2-yloxy)acetate (304 μL , 2 mmol) before warming to room temperature over 3 h. The reaction mixture was quenched with saturated aqueous NH_4Cl solution (20 mL), diluted with Et_2O (10 mL), and the organic phase separated. The aqueous phase was extracted with Et_2O (2 x 10 mL) and the combined organic extracts were washed with brine (20 mL). The organic phase was separated, dried (Na_2SO_4), and concentrated *in vacuo* to give the crude product. Purification by column chromatography, eluting with 10% ether / hexane, afforded tertiary alcohol **S-18** (556 mg, 89%) as a colorless oil. R_f = 0.32 (10% Et_2O / hexanes); ν_{\max} / cm^{-1} (film) 3461 (s), 2938 (s), 2870 (s), 1744 (w), 1452 (m); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 5.10 (2H, app. t, J = 7, 2 x $(\text{CH}_3)_2\text{C}=\text{CH}$), 4.57 (1H, dd, J = 4.5, 3, OCH_2O), 3.89 – 3.83 (1H, m, OCH_2CH_2), 3.61 (1H, d, J = 10, OCH_2C), 3.55 – 3.49 (1H, m, OCH_2CH_2), 3.34 (1H, d, J = 10, OCH_2C), 2.61 (1H, s, OH), 2.06 – 1.97 (4H, m, 2 x CH_2), 1.86 – 1.69 (2H, m, CH_2), 1.67 (6H, s, 2 x CH_3), 1.58 (6H, s, 2 x CH_3), 1.58 – 1.49 (8H, m, 4 x CH_2); $^{13}\text{C NMR}$ (100.6 MHz, CDCl_3) δ 131.7, 124.8, 124.7, 100.1, 98.5, 74.3, 73.7, 62.8, 62.5, 36.7, 36.6, 30.9, 25.9, 25.5, 22.5, 22.4, 19.9, 17.8; m/z (ES^+) 311 ($[\text{M}+\text{H}]$).

2-[2-(allyloxy)-6-methyl-2-(4-methylpent-3-enyl)hept-5-enyloxy]-tetrahydro-2H-pyran (S-19)

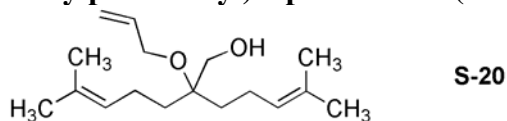


In accordance with general procedure B, tertiary alcohol **S-18** (3.06 g, 9.5 mmol) was treated with allyl iodide (1.35 mL, 11.8 mmol, 90%) to provide allyl ether **S-19** (2.8 g, 81%) as a colorless oil. R_f = 0.59 (10% EtOAc / hexanes); ν_{\max} / cm^{-1} (film) 2927 (s), 2870 (s), 1713 (w), 1645 (w), 1640 (m), 1442 (m); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 5.95 – 5.86 (1H, m, $\text{CH}=\text{CH}_2$), 5.27 (1H, app. dq, J = 17, 1.5, $\text{CH}=\text{CH}_2$), 5.12 – 4.97 (3H, m, $\text{CH}=\text{CH}_2$ + 2 x $\text{CH}=\text{C}(\text{CH}_3)_2$), 4.59 (1H, app. t, J = 3, OCH_2O), 3.93 (2H, dt, J = 5, 1.5 OCH_2), 3.85 – 3.79 (1H, m, OCH_2CH_2), 3.72 (1H, d, J = 10, OCH_2C), 3.53 – 3.48 (1H, m, OCH_2CH_2), 3.28 (1H, d, J = 10.5, OCH_2C), 2.01

⁶ Biernacki, W.; Gdula, A. *Synthesis* **1979**, 37.

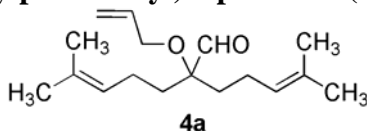
– 1.97 (4H, m, 2 x CH_2), 1.88 – 1.76 (1H, m, CH), 1.67 (6H, s, 2 x CH_3), 1.65 – 1.61 (1H, m, CH), 1.59 (6H, s, 2 x CH_3), 1.58 – 1.48 (8H, m, 4 x CH_2); ^{13}C NMR (100.6 MHz, CDCl_3) δ 135.8, 131.2, 124.6, 124.5, 115.3, 98.9, 78.0, 69.7, 62.4, 61.7, 33.4, 30.5, 25.6, 25.5, 21.8, 21.7, 19.1, 17.5; m/z (ES^+) 351 ($[\text{M}+\text{H}]$), 368 ($[\text{M}+\text{NH}_4]$).

2-(allyloxy)-6-methyl-2-(4-methylpent-3-enyl)hept-5-en-1-ol (**S-20**)



In accordance with general procedure C, ether **S-19** (2.8 g, 7.9 mmol) was deprotected to afford primary alcohol **S-20** (1.2 g, 57%) as a colorless oil. R_f = 0.44 (20% EtOAc / hexanes); ν_{max} / cm^{-1} (film) 3450 (m), 2967 (s), 2925 (s), 2860 (s), 1646 (w), 1452 (m); ^1H NMR (600 MHz, CDCl_3) δ 5.99 – 5.93 (1H, m, $\text{CH}=\text{CH}_2$), 5.34 (1H, br. d, J = 17, $t\text{CH}=\text{CH}_2$), 5.18 (1H, br. d, J = 10, $c\text{CH}=\text{CH}_2$), 5.35 (2H, br. t, J = 7, 2 x $\text{CH}=\text{C}(\text{CH}_3)_2$), 3.94 (2H, br. d, J = 5.5, CH_2O) 3.56 (2H, br. s, CH_2OH), 2.02 (4H, q, J = 8, 2 x CH_2), 1.72 (6H, s, 2 x CH_3), 1.65 (6H, s, 2 x CH_3), 1.62 – 1.52 (4H, m, 2 x CH_2); ^{13}C NMR (125.6 MHz, CDCl_3) δ 135.3, 131.6, 124.1, 115.9, 79.1, 64.3, 61.9, 32.7, 25.7, 21.9, 17.6; m/z (CI , NH_4^+) 284 ($[\text{M}+\text{NH}_4]$).

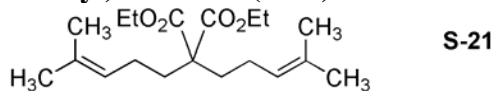
2-(allyloxy)-6-methyl-2-(4-methylpent-3-enyl)hept-5-enal (**4a**)



In accordance with general procedure D, alcohol **S-20** (1.2 g, 4.5 mmol) was oxidized to afford aldehyde **4a** (1.2 g, 97%) as a colorless oil. R_f = 0.39 (10% EtOAc / hexanes); ν_{max} / cm^{-1} (film) 2969 (s), 2925 (s), 2859 (s), 1735 (s), 1648 (w), 1451 (s); ^1H NMR (400 MHz, CDCl_3) δ 9.59 (1H, s, CHO), 6.01 – 5.92 (1H, m, $\text{CH}=\text{CH}_2$), 5.34 (1H, br. d, J = 17, $t\text{CH}=\text{CH}_2$), 5.18 (1H, br. d, J = 10, $c\text{CH}=\text{CH}_2$), 5.02 (2H, br. t, J = 7, 2 x $\text{CH}=\text{C}(\text{CH}_3)_2$), 3.93 (2H, dt, J = 5.5, 1, OCH_2), 2.03 – 1.84 (4H, m, 2 x CH_2), 1.69 (4H, t, J = 8.5, 2 x CH_2), 1.65 (6H, s, 2 x CH_3), 1.57 (6H, s, 2 x CH_3); ^{13}C NMR (100.6 MHz, CDCl_3) δ 206.3, 134.8, 132.7, 123.9, 116.8, 84.8, 63.9, 33.2, 25.9, 21.8, 17.8; m/z (CI , NH_4^+) 265 ($[\text{M}+\text{H}]$), 282 ($[\text{M}+\text{NH}_4]$).

Preparation of aldehyde **4b**.

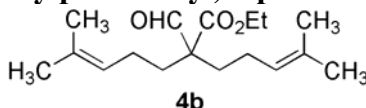
diethyl 2,2-bis(4-methylpent-3-enyl)malonate (**S-21**)



Under a gentle flow of nitrogen, diethyl malonate (0.758 mL, 5 mmol) was dissolved in *N,N*-dimethylformamide (5 mL) and treated carefully with sodium hydride (0.362 g, 15 mmol). After 30 minutes, homoprenyl bromide⁵ (1.99 mL, 15 mmol) was added to the solution dropwise. After 18 hours, the reaction mixture was carefully quenched with 50 mL of saturated aqueous NH_4Cl and diluted with 50 mL of diethyl ether. The aqueous layer was treated with an additional 50 mL of diethyl ether and the combined organic extracts were washed with 75 mL of saturated aqueous CaCl_2 , dried (Na_2SO_4), and concentrated *in vacuo* to afford the crude product. Purification by flash chromatography, eluting with 2 – 4% Et_2O / hexanes, provided the product malonate **S-21** (1.07 g, 66%) as a pale yellow oil. R_f = 0.55 (15% EtOAc / hexanes); ν_{max} / cm^{-1} (film) 2975 (w), 1731 (s), 1262 (w), 1219 (w), 1164 (m), 1112 (m), 1031 (w); ^1H NMR (500

MHz, CDCl₃) δ 5.09 (2H, app. t, $J = 7.5$, 2 x CH=C(CH₃)₂), 4.18 (4H, q, $J = 7$, 2 x OCH₂CH₃), 1.93 – 1.85 (8H, m, 2 x CH₂CH₂ + 2 x CH₂CH₂), 1.67 (6H, s, 2 x CH₃), 1.58 (6H, s, 2 x CH₃), 1.25 (6H, t, $J = 7$, 2 x OCH₂CH₃); ¹³C NMR (125.8 MHz, CDCl₃) δ 172.0, 132.5, 123.6, 61.2, 57.4, 32.6, 25.9, 23.1, 17.8, 14.4; m/z (ES+) 325 ([M+H]).

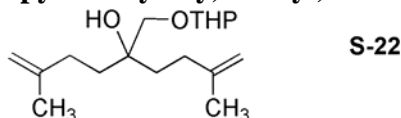
ethyl 2-formyl-6-methyl-2-(4-methylpent-3-enyl)hept-5-enoate (4b)



Under a gentle flow of nitrogen, malonate **S-21** (1.00 g, 3.09 mmol) was dissolved in anhydrous dichloromethane (5 mL) and cooled to -78 °C while stirring. To this solution, diisobutylaluminum hydride (3.43 mL; 1 M in hexanes) was added dropwise to avoid exotherm. The reaction progress was monitored via GC and after 1 h the mixture was quenched by careful addition of methanol (3 mL), avoiding exotherm. An aqueous solution of 10% Rochelle's salt (10 mL) was immediately added in one portion and the reaction mixture was diluted with diethyl ether (5 mL) and allowed to warm to room temperature with vigorous stirring. The solution was filtered through celite, then partitioned between saturated aqueous sodium chloride and diethyl ether. The organic layer was dried with sodium sulfate, filtered, and concentrated. Although the crude product was determined 94% pure by GC, the title compound **4b** was purified by flash chromatography, eluting with 2% Et₂O / hexanes, and isolated as a pale yellow oil (0.521 g, 60%). $R_f = 0.75$ (33% EtOAc / hexanes); ν_{\max} / cm⁻¹ (film) 2969 (w), 2918 (w), 1745 (w), 1720 (s), 1447 (w), 1218 (w), 1178 (w), 1096 (m); ¹H NMR (500 MHz, CDCl₃) δ 9.88 (1H, s, CHO), 5.04 (2H, app. tt, $J = 1.5, 5.5$, 2 x CH=C(CH₃)₂), 4.24 (2H, q, $J = 7.5$, OCH₂CH₃), 1.95 – 1.75 (8H, m, 2 x CH₂CH₂ + 2 x CH₂CH₂), 1.66 (6H, s, 2 x CH₃), 1.56 (6H, s, 2 x CH₃), 1.30 (3H, 1.30, t, $J = 7$); ¹³C NMR (125.8 MHz, CDCl₃) δ 201.6, 172.5, 133.0, 123.4, 61.4, 60.8, 33.7, 25.9, 23.4, 17.8, 14.5; m/z (ES+) 281 ([M+H]).

Preparation of aldehyde 4c.

2,8-dimethyl-5-((tetrahydro-2H-pyran-2-yloxy)methyl)nona-1,8-dien-5-ol (S-22)

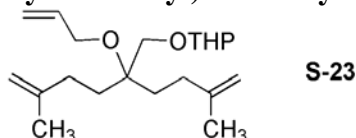


To a stirred suspension of magnesium (8.51 g, 350 mmol) in diethyl ether (10 mL) was added 4-bromo-2-methylbut-1-ene⁷ (0.51 mL, 3.90 mmol) dropwise. The suspension was gently heated to initiate Grignard formation before adding additional 4-bromo-2-methylbut-1-ene (4.50 mL, 30.6 mmol) as a solution in diethyl ether (25 mL) at such a rate as to maintain auto reflux. After the initial exotherm subsided, the reaction mixture was heated at reflux for 2 h. The reaction was then cooled to -78 °C and treated with methyl 2-(tetrahydro-2H-pyran-2-yloxy)acetate (2.0 g, 11.5 mmol) before warming to room temperature over 3 h. The reaction mixture was quenched with saturated aqueous NH₄Cl solution (200 mL), diluted with Et₂O (150 mL), and the organic phase separated. The aqueous phase was extracted with Et₂O (2 x 100 mL) and the combined organic extracts then washed with brine (200 mL). The organic phase was separated and dried (Na₂SO₄) before being concentrated to give the crude product. Purification by column chromatography eluting with 10% ether / hexane afforded tertiary alcohol **S-22** (1.631 g, 50%) as

⁷ Berkowitz, W. F.; Wu, Y. *J. Org. Chem.* **1997**, *62*, 1536.

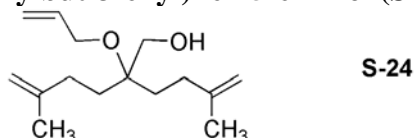
a colorless oil. R_f = 0.32 (20% EtOAc / hexanes); ν_{\max} / cm^{-1} (film) 2942 (s), 2868 (w), 1452 (w), 1124 (m), 1034 (s), 885 (m); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 4.70 (4H, app. d, J = 1.2, 4 x $\text{C}=\text{CH}$), 4.58 (1H, dd, J = 2.8, 4.4, OCH), 3.89 – 3.84 (1H, m, OCHCH_2), 3.64 (1H, d, J = 10, OCHC), 3.56 – 3.51 (1H, m, OCHCH_2), 3.39 (1H, d, J = 10, OCHC), 2.91 (1H, app. dd, J = 0.8, 29.6, OH), 2.08 – 2.02 (4H, m, 2 x CH_2CH_2), 1.86 – 1.78 (1H, m, CH_2CH), 1.74 (6H, s, 2 x CH_3), 1.68 – 1.63 (5H, m, 4 x $\text{CH}_2\text{CH} + \text{CH}$), 1.58 – 1.53 (4H, m, 2 x $\text{CH} + \text{CH}_2$); $^{13}\text{C NMR}$ (100.6 MHz, CDCl_3) δ 146.4, 109.8, 100.2, 74.4, 73.5, 63.0, 34.74, 34.70, 31.87, 31.81, 30.9, 25.5, 22.9, 19.4; m/z (ES+) 283 ($[\text{M}+\text{H}]$).

2-(2-(allyloxy)-5-methyl-2-(3-methylbut-3-enyl)hex-5-enyloxy)-tetrahydro-2H-pyran (S-23)



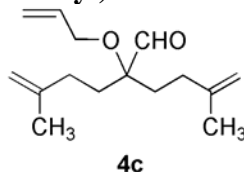
In accordance with general procedure B, tertiary alcohol **S-22** (1.55 g, 5.45 mmol) was treated with allyl bromide (0.69 mL, 8.18 mmol) to afford allyl ether **S-23** (1.14g, 65%) as a pale yellow oil. R_f = 0.56 (20% EtOAc / hexanes); ν_{\max} / cm^{-1} (film) 2941 (s), 1126 (s), 1075 (s), 1036 (s), 886 (m); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 5.92 (1H, app. tdd, J = 5.2, 10.8, 17.2 $\text{CH}=\text{CH}_2$), 5.28 (1H, app. dtd, J = 2, 2, 17.2, $\text{CH}=\text{CH}$), 5.11 (1H, app. dtd, J = 2, 2, 10.4, $\text{CH}=\text{CH}$), 4.69 (4H, s, 4 x $\text{C}=\text{CH}$), 4.61 (1H, app. t, J = 0.8, OCHO), 3.95 (2H, app. td, J = 1.6, 5.2, $\text{CH}_2\text{CH}=\text{CH}_2$), 3.83 (1H, m, OCHCH_2), 3.74 (1H, d, J = 10, OCHC), 3.53 (1H, app. dtd, J = 2, 4, 10.8, OCHCH_2), 3.31 (1H, d, J = 10, OCHC), 2.08 – 1.98 (4H, m, 2 x CH_2CH_2), 1.85 – 1.77 (1H, m, CH), 1.74 (6H, s, 2 x CH_3), 1.72 – 1.67 (5H, m, 2 x $\text{CH}_2\text{CH}_2 + \text{CH}$), 1.67 – 1.50 (4H, m, 2 x CH_2); $^{13}\text{C NMR}$ (100.6 MHz, CDCl_3) δ 146.5, 136.0, 115.8, 109.7, 99.2, 78.3, 69.9, 62.7, 62.0, 31.9, 31.5, 31.4, 30.8, 26.7, 22.9, 19.4; m/z (CI+) 323 ($[\text{M}+\text{H}]$).

2-(allyloxy)-5-methyl-2-(3-methylbut-3-enyl)hex-5-en-1-ol (S-24)



In accordance with general procedure C, THP ether **S-23** (1.10 g, 3.42 mmol) was deprotected to afford primary alcohol **S-24** (0.42 g, 55%) as a pale yellow oil. R_f = 0.37 (20% EtOAc / hexanes); ν_{\max} / cm^{-1} (film) 3451 (w), 2938 (m), 2858 (w), 1648 (m), 1453 (m), 1063 (m), 886 (s); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 5.93 (1H, tdd, J = 5.2, 10, 17.6, $\text{CH}=\text{CH}_2$), 5.30 (1H, dtd, J = 1.6, 2, 17.2, $\text{CH}=\text{CH}$), 5.16 (1H, dtd, J = 1.6, 1.6, 10, $\text{CH}=\text{CH}$), 4.70 (4H, s, 4 x $\text{C}=\text{CH}$), 3.91 (2H, td, J = 1.6, 5.6, $\text{CH}_2\text{CH}=\text{CH}_2$), 3.53 (2H, s, CH_2OH), 2.01 (4H, app. t, J = 8.4, 2 x CH_2CH_2), 1.74 (6H, s, 2 x CH_3), 1.71 – 1.62 (4H, m, 2 x CH_2CH_2); $^{13}\text{C NMR}$ (100.6 MHz, CDCl_3) δ 146.0, 135.4, 116.4, 110.0, 79.3, 64.4, 62.2, 31.5, 31.1, 22.9; m/z (CI+) 239 ($[\text{M}+\text{H}]$).

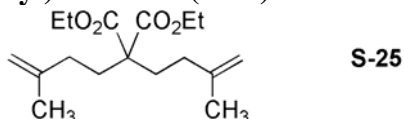
2-(allyloxy)-5-methyl-2-(3-methylbut-3-enyl)hex-5-enal (4c)



In accordance with general procedure D, primary alcohol **S-24** (0.40 g, 1.68 mmol) was oxidized to afford aldehyde **4c** (0.22 g, 55%) as a colorless oil. $R_f = 0.82$ (10% EtOAc / hexanes); $\nu_{\max} / \text{cm}^{-1}$ (film) 3073 (w), 2934 (m), 1734 (s), 1648 (m), 1452 (m), 1102 (m), 1056 (m), 888 (s); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 9.64 (1H, s, CHO), 5.97 (1H, tdd, $J = 5.2, 10.4, 17.2$, $\text{CH}=\text{CH}_2$), 5.36 (1H, app. dtd, $J = 1.6, 2, 17.2$, $\text{CH}=\text{CH}$), 5.21 (1H, app. tdd, $J = 1.4, 1.6, 10.4$, $\text{CH}=\text{CH}$), 4.71 (2H, s, 2 x $\text{C}=\text{CH}$), 4.69 (2H, s, 2 x $\text{C}=\text{CH}$), 3.94 (2H, app. td, $J = 1.6, 5.2$, $\text{CH}_2\text{CH}=\text{CH}_2$), 2.03 – 1.96 (2H, m, 2 x CHCH_2), 1.97 – 1.88 (2H, m, 2 x CHCH_2), 1.87 – 1.81 (4H, m, 2 x CH_2CH_2), 1.71 (6H, s, 2 x CH_3); $^{13}\text{C NMR}$ (100.6 MHz, CDCl_3) δ 206.0, 145.3, 134.6, 117.0, 110.5, 84.7, 64.1, 31.2, 31.0, 22.7; m/z (CI^+) XX ($[\text{M}+\text{H}]$).

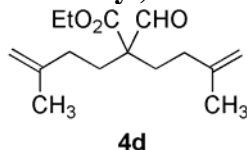
Preparation of aldehyde **4d**.

diethyl 2,2-bis(3-methylbut-3-enyl)malonate (**S-25**)



Under a gentle flow of nitrogen, diethyl malonate (0.61 mL, 4.0 mmol) was dissolved in *N,N*-dimethylformamide (4 mL) and treated carefully with sodium hydride (0.12 g, 5.0 mmol). After 30 minutes, 4-bromo-2-methylbut-1-ene⁶ (0.69 mL, 6.0 mmol) was added to the solution dropwise. After stirring at room temperature for 3 hours, the solution was treated with another portion of sodium hydride (0.12 g, 5.0 mmol). After 30 minutes, 4-bromo-2-methylbut-1-ene⁶ (0.69 mL, 6.0 mmol) was added to the solution dropwise. After 18 hours, the reaction mixture was carefully quenched with 50 mL of saturated aqueous NH_4Cl and diluted with 50 mL of diethyl ether. The aqueous layer was treated with an additional 50 mL of diethyl ether and the combined organic extracts were washed with 75 mL of saturated aqueous CaCl_2 , dried (Na_2SO_4), and concentrated *in vacuo* to afford the crude product. Purification by flash chromatography, eluting with 2 – 4% Et_2O / hexanes, provided the product malonate **S-25** (0.54 g, 46%) as a pale yellow oil. $R_f = 0.55$ (25% EtOAc / hexanes); $\nu_{\max} / \text{cm}^{-1}$ (film) 2979 (m), 1732 (s), 1650 (m), 1450 (m), 1180 (s), 1029 (m); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 4.70 (2H, app. d, $J = 1.5$, 2 x $\text{C}=\text{CH}$), 4.69 (2H, s, 2 x $\text{C}=\text{CH}$), 4.17 (4H, q, 2 x OCH_2CH_3), 2.04 – 2.00 (4H, m, 2 x CH_2), 1.88 – 1.84 (4H, m, 2 x CH_2), 1.71 (6H, s, 2 x CH_3), 1.23 (6H, t, $J = \text{OCH}_2\text{CH}_3$); $^{13}\text{C NMR}$ (125.8 MHz, CDCl_3) δ 171.8, 145.1, 110.5, 61.31, 57.3, 32.3, 30.8, 22.7, 14.3; m/z (ES^+) 297 ($[\text{M}+\text{H}]$).

ethyl 2-formyl-5-methyl-2-(3-methylbut-3-enyl)hex-5-enoate (**4d**)

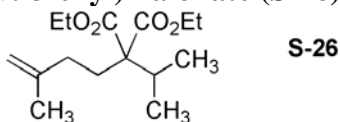


Under a gentle flow of nitrogen, malonate **S-25** (0.50 g, 1.69 mmol) was dissolved in anhydrous dichloromethane (5 mL) and cooled to -78°C while stirring. To this solution, diisobutylaluminum hydride (3.54 mL; 1 M in hexanes) was added dropwise to avoid exotherm. The reaction progress was monitored via GC and after 3 h the mixture was quenched by careful addition of methanol (0.6 mL), avoiding exotherm. An aqueous solution of 10% Rochelle's salt (2 mL) was immediately added in one portion and the solution diluted with diethyl ether (2 mL) and allowed to warm to room temperature with vigorous stirring. The reaction mixture was filtered through celite, then partitioned between saturated aqueous sodium chloride and diethyl

ether. The organic layer was dried with sodium sulfate, filtered, and concentrated. The title compound **4d** was isolated, after flash chromatography, eluting with 2% Et₂O / hexanes, as a pale yellow oil (0.240 g, 56%). R_f = 0.60 (20% EtOAc / hexanes); ν_{\max} / cm⁻¹ (film) 2979 (w), 1745 (w), 1721 (s), 1450 (w), 1185 (m), 889 (m); ¹H NMR (500 MHz, CDCl₃) δ 9.86 (1H, s, CHO), 4.70 (2H, s, 2 x C=CH), 4.66 (2H, s, 2 x C=CH), 4.24 (2H, q, J = 7, OCH₂), 2.01 – 1.83 (8H, m, 2 x CH₂CH₂ + 2 x CH₂CH₂), 1.69 (6H, s, 2 x CH₃), 1.29 (3H, t, J = 7, CH₂CH₃); ¹³C NMR (125.8 MHz, CDCl₃) δ 200.1, 172.2, 144.9, 110.9, 61.5, 60.6, 32.6, 31.6, 22.5, 14.4; m/z (ES+) 253 ([M+H]).

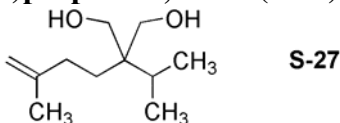
Preparation of aldehyde 6a.

diethyl 2-isopropyl-2-(3-methylbut-3-enyl)malonate (**S-26**)



Under a gentle flow of nitrogen, diethyl isopropylmalonate (1.02 mL, 5.0 mmol) was dissolved in *N,N*-dimethylformamide (5 mL) and treated carefully with sodium hydride (0.181 g, 7.5 mmol). After 30 minutes, 4-bromo-2-methylbut-1-ene⁶ (1.2 mL, 10 mmol) was added to the solution dropwise. After 18 hours, the reaction mixture was carefully quenched with 50 mL of saturated aqueous NH₄Cl and diluted with 50 mL of diethyl ether. The aqueous layer was treated with an additional 50 mL of diethyl ether and the combined organic extracts were washed with 75 mL of saturated aqueous CaCl₂, dried (Na₂SO₄), and concentrated *in vacuo* to afford the crude product. Purification by flash chromatography, eluting with 2 – 4% Et₂O / hexanes, provided the product malonate **S-26** (0.45 g, 33%) as a colorless oil. R_f = 0.56 (15% EtOAc / hexanes); ν_{\max} / cm⁻¹ (film) 2979 (s), 1727 (s), 1447 (m), 1370 (m), 1184 (s), 1031 (m), 889 (w); ¹H NMR (500 MHz, CDCl₃) δ 4.68 (1H, s, C=CH), 4.67 (1H, s, C=CH), 4.18 (4H, q, J = 7, 2 x OCH₂CH₃), 2.32 (1H, septet, J = 6.5, CH(CH₃)₂), 2.01 – 1.98 (2H, m, CH₂CH₂), 1.91 – 1.88 (2H, m, CH₂CH₂), 1.70 (3H, s, CH₃), 1.25 (6H, t, J = 7, 2 x OCH₂CH₃), 0.97 (6H, d, J = 7, CH(CH₃)₂); ¹³C NMR (125.8 MHz, CDCl₃) δ 171.3, 145.5, 110.3, 61.6, 60.9, 33.0, 32.4, 32.1, 22.7, 18.8, 14.4; m/z (ES+) 271 ([M+H]).

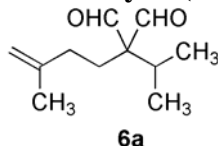
2-isopropyl-2-(3-methylbut-3-enyl)propane-1,3-diol (**S-27**)



Under a gentle flow of nitrogen gas, solid lithium aluminum hydride (0.123 g, 3.22 mmol) was added carefully to a stirring solution of malonate **S-26** (0.290 g, 1.07 mmol) in anhydrous THF (7 mL) cooled to 0 °C. The reaction mixture was allowed to warm to room temperature. After 2 hours, the suspension was cooled to 0 °C and carefully quenched by dropwise addition of 0.12 mL water followed by 0.12 mL 15% aqueous NaOH and an additional 0.36 mL of water. The mixture was filtered through a silica plug which was washed with diethyl ether. The filtrate was concentrated *in vacuo* to obtain the crude product. Diol **S-27** was obtained as a colorless oil (0.181 g, 91%) following purification of the crude product via flash chromatography, eluting with 25 – 75% Et₂O / hexanes. R_f = 0.41 (33% EtOAc / hexanes); ν_{\max} / cm⁻¹ (film) 3340 (br, s), 2962 (s), 1649 (w), 1451 (m), 1028 (s), 885 (m); ¹H NMR (500 MHz, CDCl₃) δ 4.70 (2H, app. t, J = 1, 2 x C=CH), 3.80 (2H, dd, J = 6, 13, 2 x CHOH), 3.65 (2H, dd, J = 7, 13, 2 x CHOH), 2.40

(2H, app. t, $J = 6$, 2 x OH), 1.98 – 1.88 (3H, m, $\text{CH}(\text{CH}_3)_2 + \text{CH}_2\text{CH}_2$), 1.74 (3H, s, CH_3), 1.54 – 1.49 (2H, m, CH_2CH_2), 0.89 (6H, d, $J = 7$, $\text{CH}(\text{CH}_3)_2$); ^{13}C NMR (100.5 MHz, CDCl_3) δ 146.8, 109.8, 68.3, 42.6, 31.5, 28.7, 27.9, 22.9, 17.4; m/z (ES+) 187 ([M+H]).

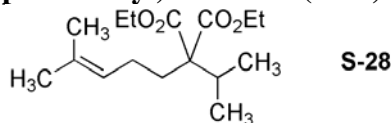
2-isopropyl-2-(3-methylbut-3-enyl)malonaldehyde (6a)



Under a gentle flow of nitrogen, a solution of oxalyl chloride (0.211 mL, 2.43 mmol) in anhydrous dichloromethane (1 mL) was cooled to -78°C while stirring vigorously. To this solution, dimethyl sulfoxide (0.346 mL, 4.87 mmol) in anhydrous dichloromethane (1 mL) was added dropwise as to avoid exotherm. Immediately, diol **S-27** (0.215 g, 1.16 mmol) in anhydrous dichloromethane (1 mL) was added dropwise to the solution. The reaction mixture was stirred at -78°C for 30 min before carefully adding triethylamine (1.16 mL, 8.35 mmol) and allowing the solution to warm to room temperature. The reaction mixture was then partitioned between 50 mL of water and 75 mL of diethyl ether, the organic layer retained and extracted with 2 x 75 mL of saturated aqueous CuSO_4 followed by 75 mL each of saturated aqueous NH_4Cl and saturated aqueous CaCl_2 . The organic layer was dried with solid K_2CO_3 , filtered through a plug of silica, and concentrated *in vacuo* to yield the dial **6a** (0.209 g, 99%) in 98% purity by ^1H -NMR and GC. Note that this compound partially decomposes during prolonged exposure to silica gel. $R_f = 0.52$ (20% EtOAc / hexanes); ν_{max} / cm^{-1} (film) 2969 (m), 1728 (s), 1713 (s), 1447 (w), 1376 (w), 891 (m); ^1H NMR (500 MHz, CDCl_3) δ 9.86 (2H, s, 2 x CHO), 4.72 (1H, app. t, $J = 2$, $\text{C}=\text{CH}$), 4.67 (1H, d, $J = 1.5$, $\text{C}=\text{CH}$), 2.27 (1H, septet, $J = 7$, $\text{CH}(\text{CH}_3)_2$), 1.96 – 1.92 (2H, m, CH_2CH_2), 1.89 – 1.85 (2H, m, CH_2CH_2), 1.69 (3H, s, CH_3), 1.01 (6H, d, $J = 7$, $\text{CH}(\text{CH}_3)_2$); ^{13}C NMR (100.5 MHz, CDCl_3) δ 203.4, 145.0, 111.0, 66.4, 32.53, 32.49, 27.7, 22.5, 17.9.; m/z (ES+) 183 ([M+H]).

Preparation of dialdehyde 6b.

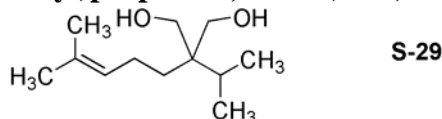
diethyl 2-isopropyl-2-(4-methylpent-3-enyl)malonate (S-28)



Under a gentle flow of nitrogen, diethyl isopropylmalonate (1.02 mL, 5 mmol) was dissolved in *N,N*-dimethylformamide (5 mL) and treated carefully with sodium hydride (0.181 g, 7.5 mmol). After 30 minutes, homoprenyl bromide⁵ (0.80 mL, 6.0 mmol) was added to the solution dropwise. After 18 hours, the reaction mixture was carefully quenched with 50 mL of saturated aqueous NH_4Cl and diluted with 50 mL of diethyl ether. The aqueous layer was treated with an additional 50 mL of diethyl ether and the combined organic extracts were washed with 75 mL of saturated aqueous CaCl_2 , dried (Na_2SO_4), and concentrated *in vacuo* to afford the crude product. Purification by flash chromatography, eluting with 2 – 5% Et_2O / hexanes, provided the product malonate **S-28** (1.42 g, 55%) as a pale yellow oil. $R_f = 0.60$ (15% EtOAc / hexanes); ν_{max} / cm^{-1} (film) 2979 (m), 2881 (w), 1726 (s), 1446 (w), 1371 (w), 1226 (s), 1063 (w); ^1H NMR (500 MHz, CDCl_3) δ 5.09 (1H, app. tt, $J = 1.5$, 5, $\text{CH}=\text{C}(\text{CH}_3)_2$), 4.19 (4H, q, $J = 7$, 2 x OCH_2CH_3), 2.34 (1H, septet, $J = 7$, $\text{CH}(\text{CH}_3)_2$), 1.92 – 1.85 (4H, m, $\text{CH}_2\text{CH}_2 + \text{CH}_2\text{CH}_2$), 1.67 (3H, s, CH_3),

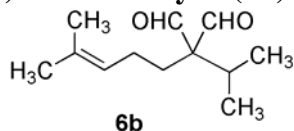
1.59 (3H, s, CH_3), 1.27 (6H, t, $J = 7$, 2 x OCH_2CH_3), 0.98 (6H, d, $J = 7$, $\text{CH}(\text{CH}_3)_2$); ^{13}C NMR (125.8 MHz, CDCl_3) δ 171.4, 132.4, 123.8, 61.7, 60.9, 34.1, 32.2, 25.9, 23.7, 18.8, 17.8, 14.4; m/z (ES+) 285 ($[\text{M}+\text{H}]$).

2-isopropyl-2-(4-methylpent-3-enyl)propane-1,3-diol (S-29).



Under a gentle flow of nitrogen gas, solid lithium aluminum hydride (0.188 g, 4.93 mmol) was added carefully to a stirring solution of malonate **S-28** (0.700 g, 2.46 mmol) in anhydrous THF (16 mL) cooled to 0 °C. The reaction mixture was allowed to warm to room temperature. After two hours, the solution was cooled to 0 °C and carefully quenched by dropwise addition of 0.2 mL water followed by 0.2 mL 15% aqueous NaOH and an additional 0.55 mL of water. The mixture was filtered through a silica plug which was washed with diethyl ether. The filtrate was concentrated *in vacuo* to obtain the crude product. Diol **S-29** was obtained as a pale yellow oil (0.360 g, 73%) following purification of the crude product via flash chromatography, eluting with 25 – 75% Et_2O / hexanes. $R_f = 0.40$ (50% EtOAc / hexanes); ν_{max} / cm^{-1} (film) 3379 (br, m), 2963 (s), 2928 (s), 2882 (m), 1446 (m), 1376 (m), 1027 (s); ^1H NMR (500 MHz, CDCl_3) δ 5.10 (1H, app. tt, $J = 1.5, 7$, $\text{CH}=\text{C}(\text{CH}_3)_2$), 3.81 (2H, app. dd, $J = 2.5, 11$, 2 x CHOH), 3.67 (2H, app. dd, $J = 2.5, 11$, 2 x CHOH), 2.45 (2H, br. s, 2 x OH), 1.98 – 1.90 (3H, m, $\text{CH}_2\text{CH}_2 + \text{CH}(\text{CH}_3)_2$), 1.68 (3H, app. d, $J = 1$, CH_3), 1.61 (3H, s, CH_3), 1.36 (2H, m, CH_2CH_2), 0.90 (6H, d, $J = 6.5$, $\text{CH}(\text{CH}_3)_2$); ^{13}C NMR (125.8 MHz, CDCl_3) δ 131.8, 125.1, 68.4, 42.7, 29.7, 28.5, 25.9, 22.1, 17.9, 17.4; m/z (ES+) 201 ($[\text{M}+\text{H}]$).

2-isopropyl-2-(4-methylpent-3-enyl)malonaldehyde (6b)

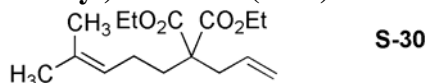


Under a gentle flow of nitrogen, a solution of oxalyl chloride (0.245 mL, 2.82 mmol) in anhydrous dichloromethane (1 mL) was cooled to -78 °C while stirring vigorously. To this solution, dimethyl sulfoxide (0.400 mL, 5.65 mmol) in anhydrous dichloromethane (1 mL) was added dropwise as to avoid exotherm. Immediately, diol **S-29** (0.269 g, 1.35 mmol) in anhydrous dichloromethane (1 mL) was added dropwise to the solution. The reaction was stirred at -78 °C for 30 min before carefully adding triethylamine (1.38 mL, 9.95 mmol) and allowing the reaction mixture to warm to room temperature. To the solution was added 5 mL of an aqueous solution of 10% LiCl. The solution was then partitioned between 50 mL of water and 75 mL of diethyl ether, the organic layer retained and extracted with 2 x 75 mL of saturated aqueous CuSO_4 , then 75 mL each of saturated aqueous NH_4Cl and saturated aqueous CaCl_2 . The organic layer was dried with solid K_2CO_3 , filtered through a plug of davisil, and concentrated *in vacuo* to yield the dial **6b** (0.219 g, 82%) in >99% purity by ^1H -NMR and GC. Note that this compound partially decomposes during prolonged exposure to silica gel. $R_f = 0.85$ (33% EtOAc / hexanes); ν_{max} / cm^{-1} (film) 2969 (m), 2937 (w), 1713 (s), 1455 (w), 1377 (w), 1170 (w), 1114 (m); ^1H NMR (500 MHz, CDCl_3) δ 9.87 (2H, s, 2 x CHO), 5.04 (1H, app. dt, $J = 1, 6$, $\text{CH}=\text{C}(\text{CH}_3)_2$), 2.24 (1H, septet, $J = 7$, $\text{CH}(\text{CH}_3)_2$), 1.90 – 1.83 (4H, m, $\text{CH}_2\text{CH}_2 + \text{CH}_2\text{CH}_2$) 1.67

(3H, s, CH_3), 1.55 (3H, s, CH_3), 1.01 (6H, d, $J = 7$, $\text{CH}(\text{CH}_3)_2$); ^{13}C NMR (125.8 MHz, CDCl_3) δ 203.6, 133.6, 123.4, 66.4, 32.7, 29.7, 25.9, 23.4, 17.9 (2C); m/z (ES+) 201 ($[\text{M}+\text{H}]$).

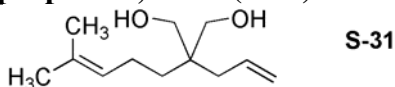
Preparation of dialdehyde 6c.

diethyl 2-allyl-2-(4-methylpent-3-enyl)malonate (S-30)



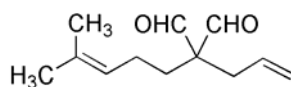
Under a gentle flow of nitrogen gas, diethyl allylmalonate (5.00 mL, 25.2 mmol) was dissolved in *N,N*-dimethylformamide (25 mL) and treated carefully with sodium hydride (0.912 g, 37.8 mmol). After stirring for 30 minutes, homoprenyl bromide⁵ (4.02 mL, 30.2 mmol) was added to the solution dropwise. After 18 hours, the reaction mixture was carefully quenched with 250 mL of saturated aqueous NH_4Cl and diluted with 200 mL of diethyl ether. The aqueous layer was treated with an additional 200 mL of diethyl ether and the combined organic extracts were washed with 300 mL of saturated aqueous CaCl_2 , dried (Na_2SO_4), and concentrated *in vacuo* to afford the malonate **S-30** (5.98 g, 84%) as a pale yellow oil in 95% purity as determined by ^1H -NMR and GC. $R_f = 0.63$ (20% EtOAc / hexanes); ν_{max} / cm^{-1} (film) 2981 (w), 1732 (s), 1446 (w), 1271 (w), 1219 (m), 1176 (m), 1028 (w), 920 (w), 861 (w); ^1H NMR (500 MHz, CDCl_3) δ 5.65 (1H app. tdd, $J = 7.5, 10, 16.5$, $\text{CH}=\text{CH}_2$), 5.12 (1H, app. t, $J = 1.5$, $\text{HC}=\text{C}(\text{CH}_3)_2$), 5.08 (1H, s, $\text{CCH}=\text{CH}$), 5.06 (1H, app. t, $J = 1$, $\text{CCH}=\text{CH}$), 4.17 (4H, q, $J = 7$, $2 \times \text{OCH}_2\text{CH}_3$), 2.66 (2H, app. dd, $J = 1, 6.5$, $\text{CH}_2\text{CH}=\text{CH}_2$), 1.87 (4H, m, $2 \times \text{CH}_2$), 1.66 (3H, s, CH_3), 1.56 (3H, s, CH_3), 1.24 (6H, t, $J = 7$, $2 \times \text{OCH}_2\text{CH}_3$); ^{13}C NMR (125.8 MHz, CDCl_3) δ 171.5, 132.8, 132.5, 123.5, 119.0, 61.3, 57.4, 37.2, 32.4, 25.8, 22.9, 17.7, 14.3; m/z (ES+) 283 ($[\text{M}+\text{H}]$).

2-allyl-2-(4-methylpent-3-enyl)propane-1,3-diol (S-31)



Under a gentle flow of nitrogen gas, solid lithium aluminum hydride (1.62 g, 42.4 mmol) was added carefully to a stirring solution of malonate **S-30** (5.98 g, 21.2 mmol) in anhydrous THF (140 mL) cooled to 0 °C. The reaction mixture was allowed to warm to room temperature. After two hours, the solution was cooled to 0 °C and carefully quenched by dropwise addition of 1.6 mL water followed by 1.6 mL 15% aqueous NaOH and an additional 4.9 mL of water. The mixture was filtered through a silica plug which was then washed with diethyl ether. The filtrate was concentrated *in vacuo* to obtain diol **S-31** as a colorless oil (3.86 g, 92%). $R_f = 0.25$ (50% EtOAc / hexanes); ν_{max} / cm^{-1} (film) 3372 (br, s), 2922 (s), 1443 (m), 1037 (s), 914 (m); ^1H NMR (500 MHz, CDCl_3) δ 5.82 (1H, m, $\text{CH}=\text{CH}_2$), 5.13 (1H, app. t, $J = 2$, $\text{HC}=\text{C}(\text{CH}_3)_2$), 5.10 (1H, m, $\text{CCH}=\text{CH}$), 5.08 (1H, app. td, $J = 1, 2.5$, $\text{CCH}=\text{CH}$), 3.58 (4H, s, $2 \times \text{CH}_2\text{OH}$), 2.64 (1H, br s, OH), 2.50 (1H, br s, OH), 2.11 (2H, app. dd, $J = 1, 7.5$, $\text{CH}_2\text{CH}=\text{CH}_2$), 1.95 (2H, dt, $J = 5, 7.5$, CH_2CH_2), 1.67 (3H, s, CH_3), 1.60 (3H, s, CH_3), 1.28 (2H, m, CH_2CH_2); ^{13}C -NMR (125.8 MHz, CDCl_3) δ 134.3, 132.0, 124.7, 118.1, 68.9, 41.8, 36.0, 31.4, 25.9, 21.8, 17.9; m/z (ES+) 199 ($[\text{M}+\text{H}]$).

2-allyl-2-(4-methylpent-3-enyl)malonaldehyde (6c)

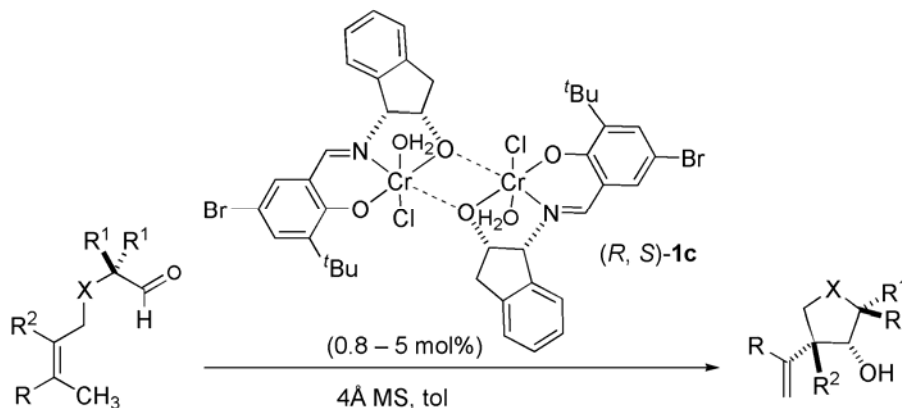


6c

Under nitrogen, a solution of oxalyl chloride (0.365 mL, 4.20 mmol) in anhydrous dichloromethane (3 mL) was cooled to $-78\text{ }^{\circ}\text{C}$ while stirring vigorously. To this solution, dimethyl sulfoxide (0.596 mL, 8.40 mmol) in anhydrous dichloromethane (1 mL) was added dropwise to avoid exotherm. Immediately, diol **S-31** (0.396 g, 2.00 mmol) in anhydrous dichloromethane (1 mL) was added dropwise to the solution. The reaction mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 30 min before carefully adding triethylamine (2.06 mL, 14.8 mmol) and allowing the reaction to warm to room temperature. To the reaction was added 10 mL of an aqueous solution of 10% LiCl. The solution was then partitioned between 75 mL of water and 100 mL of diethyl ether, the organic layer retained and extracted with 2 x 100 mL of saturated aqueous CuSO_4 followed by 100 mL each of saturated aqueous NH_4Cl and saturated aqueous CaCl_2 . The organic layer was dried with solid K_2CO_3 , filtered through a plug of davisil, and concentrated *in vacuo* to yield the dial **16a** (0.355 g, 92%) in 92% purity by $^1\text{H-NMR}$ and GC. Note that this compound partially decomposes during prolonged exposure to silica gel. $R_f = 0.85$ (20% EtOAc / hexanes); $\nu_{\text{max}} / \text{cm}^{-1}$ (film) 2972 (w), 2916 (m), 2854 (m), 1711 (s), 1444 (m), 923 (m); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 9.71 (2H, s, 2 x CHO), 5.67 (1H, dtd, $J = 7.5, 10, 17$, $\text{CH}=\text{CH}_2$), 5.17 (1H, app. td, $J = 1.5, 10$, $\text{CCH}=\text{CH}$), 5.14 (1H, app. t, $J = 1.5$, $\text{CCH}=\text{CH}$), 5.03 (1H, app. tt, $J = 1.5, 6.5$, $\text{HC}=\text{C}(\text{CH}_3)_2$), 2.59 (2H, d, $J = 7.5$, $\text{CH}_2\text{CH}=\text{CH}_2$), 1.96 (2H, app. td, $J = 7.5, 15$, CH_2CH_2), 1.88 (2H, m, CH_2CH_2), 1.66 (3H, s, CH_3), 1.56 (3H, s, CH_3); $^{13}\text{C-NMR}$ (125.8 MHz, CDCl_3) δ 201.4, 133.9, 131.3, 123.0, 120.2, 64.9, 35.2, 31.4, 25.8, 22.8, 17.9; m/z (ES+) 195 ($[\text{M}+\text{H}]$).

3. Enantioselective Chromium-catalyzed carbonyl-ene cyclizations

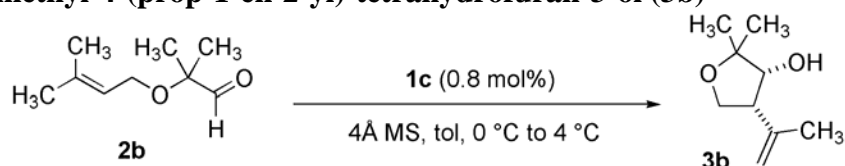
General procedure E:



To a cold ($0\text{ }^{\circ}\text{C}$), stirred mixture of 4Å molecular sieves (40 mg) and catalyst **1c** (1.6 mg, 1.6 μmol), contained in a flame dried 0.5 dram reaction vial, under a N_2 atmosphere, was added toluene (25 μL) and aldehyde **3a** (0.2 mmol). The reaction mixture was then warmed to $4\text{ }^{\circ}\text{C}$ and allowed to stir until complete by TLC (ca. 30 h). The reaction mixture was diluted with 50% Et_2O / hexanes (0.5 mL), loaded onto a column and purified by silica flash column

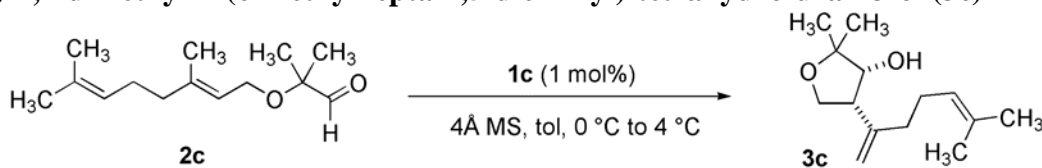
chromatography eluting with 10% Et₂O / hexanes (unless otherwise stated) to afford the title compound as a colorless oil.

(3R,4R)-2,2-dimethyl-4-(prop-1-en-2-yl)-tetrahydrofuran-3-ol (3b)



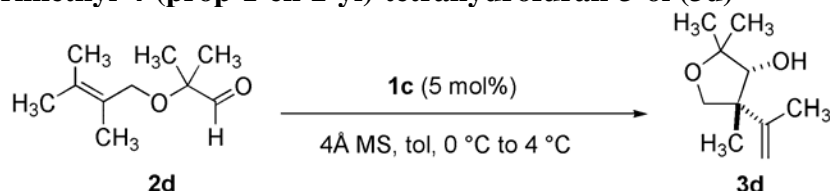
In accordance with general procedure E, aldehyde **2b** (35 μ L, 0.2 mmol) was treated with catalyst **1c** (1.6 mg, 1.6 μ mol) to afford tetrahydrofuran **3b** (24 mg, 77%) as a volatile, colorless oil in >30:1 dr by ¹H NMR and 93% ee by chiral GC (γ -TA, 85 °C isothermal, t_r (minor) 19.5 min, t_r (major) 27.1). R_f = 0.15 (10% EtOAc / hexanes); $[\alpha]_D^{20}$ = -11.3 (c. 0.36, CH₂Cl₂); ν_{\max} / cm⁻¹ (film) 3429 (s), 2972 (s), 2934 (m), 2884 (w), 1650 (w), 1451 (w); ¹H NMR (500 MHz, CDCl₃) δ 5.07 (1H, br. s, CH), 4.77 (1H, br. s, CH), 3.98 – 3.92 (2H, m, OCH₂), 3.83 (1H, app. t, J = 4, HOCH), 3.09 – 3.05 (1H, m, CH), 1.84 (3H, s, CH₃), 1.62 (1H, d, J = 4, OH), 1.31 (3H, s, CH₃), 1.22 (3H, s, CH₃); ¹³C NMR (125.6 MHz, CDCl₃) δ 141.1, 113.8, 84.7, 76.6, 67.6, 51.1, 27.7, 23.9, 22.7; m/z (CI, NH₄⁺) 174 ([M+NH₄]).

(3R,4R)-2,2-dimethyl-4-(6-methylhepta-1,5-dien-2-yl)-tetrahydrofuran-3-ol (3c)



In accordance with general procedure E, aldehyde **2c** (51 μ L, 0.2 mmol) was treated with catalyst **1c** (2 mg, 2 μ mol) to afford tetrahydrofuran **3c** (42 mg, 94%) as a colorless oil in 20:1 dr by ¹H NMR and 96% ee by chiral GC (γ -TA, 123 °C isothermal, t_r (minor) 29.3 min, t_r (major) 33.0). R_f = 0.15 (10% EtOAc / hexanes); $[\alpha]_D^{20}$ = -3.9 (c. 1.25, CH₂Cl₂); ν_{\max} / cm⁻¹ (film) 3415 (s), 2972 (s), 2933 (s), 1645 (w), 1441 (w); ¹H NMR (500 MHz, CDCl₃) δ 5.12 – 5.09 (2H, m, C=CH + CH=C(CH₃)₂), 4.85 (1H, br. s, CH), 3.94 – 3.90 (2H, m, OCH₂), 3.83 (1H, app. t, J = 3.5, HOCH), 3.12 – 3.08 (1H, m, CH), 2.19 – 2.09 (4H, m, 2 x CH₂), 1.68 (3H, s, CH₃), 1.63 (1H, d, J = 6, OH), 1.61 (3H, s, CH₃), 1.31 (3H, s, CH₃), 1.22 (3H, s, CH₃); ¹³C NMR (125.6 MHz, CDCl₃) δ 144.8, 132.6, 123.7, 113.2, 84.7, 76.4, 68.0, 50.0, 37.4, 27.9, 26.5, 25.9, 22.7, 17.9; m/z (CI, NH₄⁺) 225 ([M+H]), 242 ([M+NH₄]).

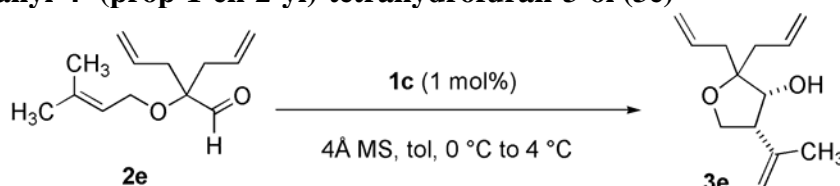
(3R,4R)-2,2,4-trimethyl-4-(prop-1-en-2-yl)-tetrahydrofuran-3-ol (3d)



In accordance with general procedure E, aldehyde **2d** (75 μ L, 0.40 mmol) was treated with catalyst **1c** (8 mg, 8 μ mol), and the reaction mixture stirred for 48h, to afford tetrahydrofuran **3d** (50 mg, 78%) as a colorless oil in >30:1 dr by ¹H NMR and 75% ee by chiral GC (γ -TA, 70 °C isothermal, t_r (major) 46.9 min, t_r (minor) 48.2 min). R_f = 0.25 (20% EtOAc / hexanes); $[\alpha]_D^{20}$ =

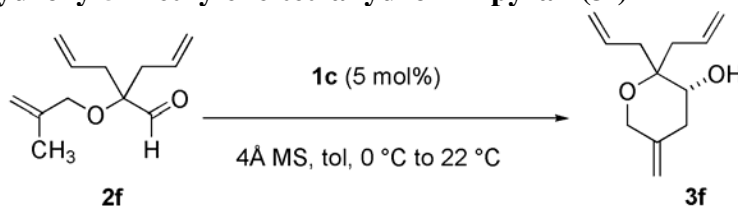
14.8 (c. 2.25, CH₂Cl₂); ν_{\max} / cm⁻¹ (film) 3410 (s), 2975 (m), 2870 (m), 2644 (m), 1644 (m), 1377 (m), 1075 (s), 1038 (s), 886 (m); ¹H NMR (400 MHz, CDCl₃) δ 5.00 (1H, app. t, J = 1.2, CH), 4.72 (1H, s, CH), 3.96 (1H, d, J = 8.8, OCH), 3.58 (1H, d, J = 4, CHOH), 3.52 (1H, d, J = 8.8, OCH), 1.84 (3H, s, CH₃), 1.69 (1H, d, J = 4, OH), 1.35 (3H, s, CH₃), 1.29 (3H, s, CH₃), 1.19 (3H, s, CH₃); ¹³C-NMR (100.6 MHz, CDCl₃) δ 147.3, 113.1, 84.2, 83.7, 72.7, 53.7, 29.3, 24.5, 22.9, 21.3; *m/z* (ES+) 171 ([M+H]).

(3R,4R)-2,2-diallyl-4- (prop-1-en-2-yl)-tetrahydrofuran-3-ol (3e)



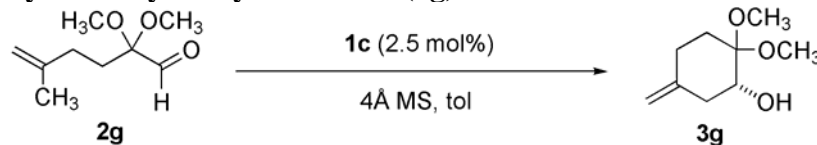
In accordance with general procedure E, aldehyde **2e** (46 μ L, 0.2 mmol) was treated with catalyst **1c** (2 mg, 2 μ mol) to afford tetrahydrofuran **3e** (40 mg, 96%) as a colorless oil in >30:1 dr by ¹H NMR and 96% ee by chiral GC (γ -TA, 115 °C isothermal, *t_r* (minor) 22.3 min., *t_r* (major) 24.4). *R_f* = 0.18 (10% EtOAc / hexanes); $[\alpha]_D^{20}$ = -28.0 (c. 0.4, CH₂Cl₂); ν_{\max} / cm⁻¹ (film) 3453 (s), 2977 (s), 2938 (m), 1640 (w), 1437 (w); ¹H NMR (600 MHz, CDCl₃) δ 5.99 – 5.84 (2H, m, 2 x CH=CH₂), 5.20 – 5.12 (5H, m, 2 x CH=CH₂ + CH), 4.80 (1H, br. s, CH), 4.03 – 3.99 (3H, m, OCH₂ + CHOH), 3.08 – 3.04 (1H, m, CH), 2.54 – 2.50 (2H, m, CH₂), 2.32 – 2.26 (2H, m, CH₂), 1.87 (3H, s, CH₃), 1.66 (1H, d, J = 3.5, OH); ¹³C NMR (125.6 MHz, CDCl₃) δ 140.8, 135.1, 133.9, 118.3, 118.1, 113.9, 87.9, 74.9, 67.8, 50.9, 42.0, 38.3, 23.8; *m/z* (CI, NH₄⁺) 209 ([M+H]), 226 ([M+NH₄]).

(R)-2,2-diallyl-3-hydroxy-5-methylene-tetrahydro-2H-pyran (3f)



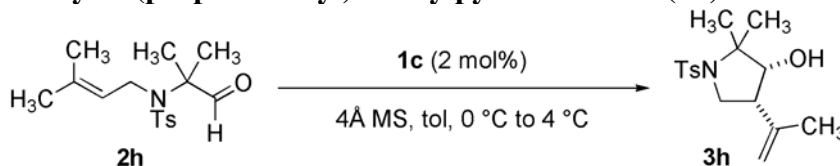
To a cold (0 °C), stirred mixture of 4Å molecular sieves (20 mg), catalyst **1c** (19.6 mg, 20 μ mol), and toluene (50 μ L) contained in a flame dried 0.5 dram reaction vial, under a N₂ atmosphere, was added aldehyde **2f** (86 μ L, 0.4 mmol). The reaction mixture was warmed to room temperature and allowed to stir for 76 h until complete by TLC. The reaction mixture was then diluted with 50% Et₂O / hexanes (0.5 mL), loaded onto a column and purified by silica gel flash column chromatography, eluting with 10% Et₂O / hexanes, to afford alcohol **3f** (56 mg, 72%) as a colorless oil in >30:1 dr by ¹H NMR and 93% ee by chiral GC of the corresponding trifluoroacetate ester derivative (γ -TA, 75 °C isothermal, *t_r* (minor) 49.0 min, *t_r* (major) 51.4). *R_f* = 0.15 (10% EtOAc / hexanes); $[\alpha]_D^{20}$ = -2.1 (c. 1.0, CH₂Cl₂); ν_{\max} / cm⁻¹ (film) 3450 (m), 2979 (m), 2935 (m), 2884 (w), 1639 (m), 1434 (m); ¹H NMR (500 MHz, CDCl₃) δ 5.92 – 5.81 (2H, m, 2 x CH=CH₂), 5.18 – 5.13 (4H, m, 2 x CH=CH₂), 4.95 (1H, br. s, C=CH), 4.89 (1H, br. s, C=CH), 4.12 (1H, d, J = 13, OCH), 4.12 (1H, d, J = 13, OCH), 3.67 – 3.64 (1H, m, CHOH), 2.67 (1H, dd, J = 14, 2.5, CH), 2.57 (1H, dd, J = 15, 6.5, CH), 2.49 (1H, dd, J = 14.5, 7, CH), 2.39 – 2.30 (3H, m, 3 x CH), 1.92 (1H, d, J = 8.5, OH); ¹³C NMR (125.6 MHz, CDCl₃) δ 140.5, 133.4, 118.7, 118.5, 112.9, 77.8, 70.5, 65.8, 36.8, 36.3, 36.1; *m/z* (ES+) 195 ([M+H]), 212 ([M+NH₄]).

(R)-2,2-dimethoxy-5-methylenecyclohexanol (3g)



In accordance with general procedure E, aldehyde **2g** (34 mg, 0.20 mmol) was treated with catalyst **1c** (5 mg, 5 μ mol) at room temperature, stirring for 24h, to afford alcohol **3b** (30 mg, 88%) as a colorless oil in 94% ee by chiral GC (γ -TA, 75 °C isothermal, t_r (minor) 56.6 min, t_r (major) 58.8 min). R_f = 0.24 (25% EtOAc / hexanes); $[\alpha]_D^{20}$ = -1.6 (*c.* 1.3, CH₂Cl₂); ν_{\max} / cm⁻¹ (film) 3475 (w), 2946 (m), 1118 (s), 1058 (s); ¹H NMR (500 MHz, CDCl₃) δ 4.79 (1H, d, *J* = 1, C=CH), 4.75 (1H, d, *J* = 1, C=CH), 3.88 (1H, s, CHOH), 3.24 (3H, s, OCH₃), 3.23 (3H, s, OCH₃), 2.46 (1H, dd, *J* = 1, 14, CH), 2.32 (1H, ddd, *J* = 1.5, 4, 14, CH), 2.12 (2H, m, 2 x CHCH₂), 1.90 (1H, s, OH), 1.83 (1H, m, CH₂CH), 1.67 (1H, m, CH₂CH); ¹³C-NMR (125.8 MHz, CDCl₃) δ 143.7, 111.6, 100.6, 68.7, 48.4, 48.0, 38.0, 30.7, 28.6; *m/z* (ApCI+) 141 ([M-OCH₃]), 100%; 173 ([M+H]), 13%.

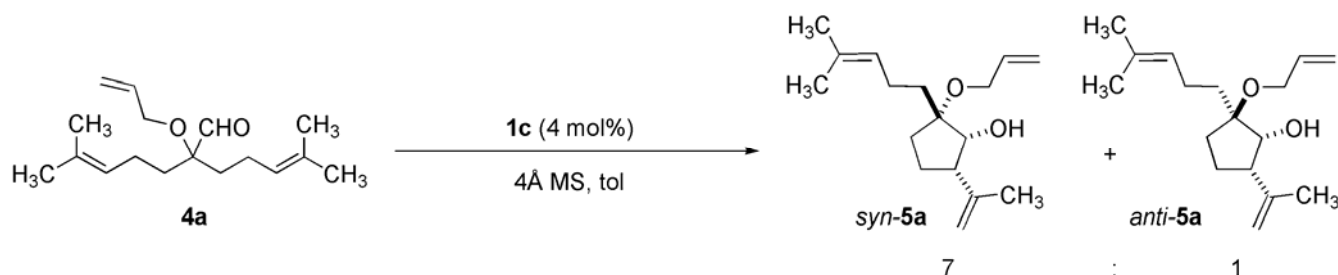
(3R,4R)-2,2-dimethyl-4-(prop-1-en-2-yl)-1-tosylpyrrolidin-3-ol (3h)



To a cold (0 °C), stirred solution of freshly prepared aldehyde **2h**⁸ (170 mg, 0.55 mmol) in toluene (55 μ L), was added a mixture of 4 Å molecular sieves (55 mg) and catalyst **1c** (11 mg, 11 μ mol). The solution was then warmed to 4 °C and stirred at this temperature for 35 h until no starting material remained by TLC. The reaction mixture was diluted with 50% Et₂O / hexanes (0.5 mL) and loaded onto a silica gel column. Purification by flash column chromatography, eluting with 30% Et₂O / hexanes, afforded **3h** (166 mg, 98%) as a colorless, waxy solid in >30:1 dr by ¹H NMR and 95% ee by chiral HPLC (Chiralcel AD, 5.5% IPA / hexanes, 1 mL / min. t_r (major) 23.9 min. t_r (minor) 34.4 min). R_f = 0.15 (10% EtOAc / hexanes); $[\alpha]_D^{20}$ = -25.5 (*c.* 0.2, CH₂Cl₂); ν_{\max} / cm⁻¹ (film) 3515 (m), 2974 (m), 2942 (m), 1649 (w), 1451 (w); ¹H NMR (600 MHz, CDCl₃) δ 7.78 (2H, d, *J* = 8.5, 2 x ArCH), 7.31 (2H, d, *J* = 8, 2 x ArCH), 5.10 (1H, br. s, CH), 4.79 (1H, br. s, CH), 3.81 (1H, app. t, *J* = 3, HOCH), 3.72 (1H, dd, *J* = 9, 8, NCH), 3.48 (1H, dd, *J* = 11, 8.5, NCH), 3.09 – 3.05 (1H, m, CH), 2.45 (3H, s, ArCH₃), 1.84 (3H, s, CH₃), 1.54 (1H, d, *J* = 2, OH), 1.52 (3H, s, CH₃), 1.51 (3H, s, CH₃); ¹³C NMR (125.6 MHz, CDCl₃) δ 142.9, 140.6, 138.9, 129.7, 127.2, 113.9, 79.4, 69.5, 49.2, 46.9, 28.6, 23.1, 21.9, 21.7; *m/z* (ES+) 310 ([M+H]), 327 ([M+NH₄]).

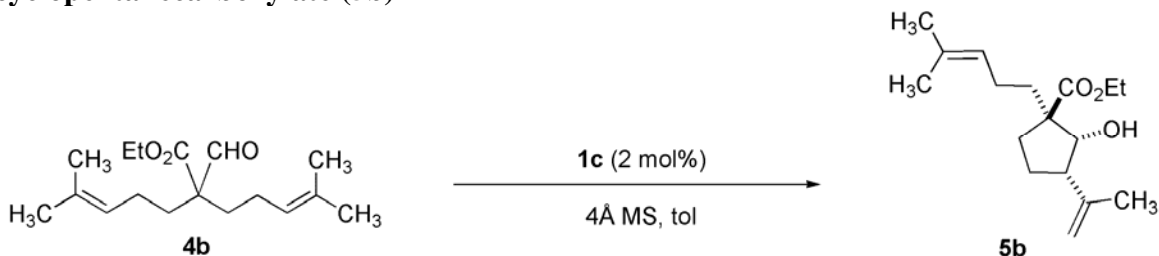
(1R,2S,5S)-2-(allyloxy)-2-(4-methylpent-3-enyl)-5-(prop-1-en-2-yl)cyclopentanol (5a)

⁸ Upon storage, this aldehyde underwent cyclization leading to racemic product and therefore diminished enantioselectivities. This problem was eliminated by freshly preparing aldehyde **9a** and using it within 0.5 hours after purification.



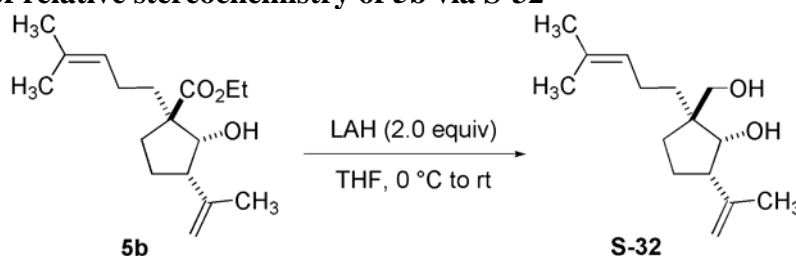
In accordance with general procedure E, aldehyde **4a** (30 μ L, 0.1 mmol) was treated with catalyst **1c** (4 mg, 4 μ mol) at room temperature to afford cyclopentanol *syn*-**5a** (23 mg, 87%) and *anti*-**5a** (3.4 mg, 13%) as colorless oils. The major diastereoisomer *syn*-**5a** was isolated in >30:1 dr, as determined by ^1H NMR, and 99% ee, as measured by chiral GC (β -cyclodextr, 138 $^\circ\text{C}$ isothermal, t_r (major) 35.3 min, t_r (minor) 36.0). R_f = 0.35 (5% EtOAc / hexanes); $[\alpha]_D^{20}$ = -12.6 (c. 0.42, CH_2Cl_2); ν_{max} / cm^{-1} (film) 3541 (s), 2967 (s), 2918 (m), 1645 (w), 1449 (w); ^1H NMR (600 MHz, CDCl_3) δ 5.99 – 5.93 (1H, m, $\text{CH}=\text{CH}_2$), 5.32 (1H, dd, 17, 2, $\text{tCH}=\text{CH}$), 5.21 (1H, br. t, J = 7, $\text{CH}=\text{C}(\text{CH}_3)_2$), 5.32 (1H, dd, 10, 2, $\text{cCH}=\text{CH}_2$), 5.07 (1H, d, J = 1, $\text{C}=\text{CH}$), 4.92 (1H, br. s, J = 1, $\text{C}=\text{CH}$), 3.96 – 3.91 (2H, m, OCH_2), 3.90 – 3.89 (1H, m, CHOH), 3.06 – 3.03 (1H, m, CH), 2.17 – 2.06 (2H, m, 2 x CH), 1.93 – 1.88 (1H, m, CH), 1.86 (3H, s, CH_3), 1.88 – 1.82 (1H, m, CH), 1.80 – 1.74 (3H, m, 3 x CH), 1.74 (3H, s, CH_3), 1.73 – 1.67 (1H, m, CH), 1.66 (3H, s, CH_3), 1.47 (1H, d, J = 2, OH); ^{13}C NMR (125.6 MHz, CDCl_3) δ 144.8, 135.9, 131.7, 124.9, 115.9, 112.4, 89.5, 75.6, 62.9, 50.0, 32.4, 31.5, 25.9, 24.3, 24.1, 22.9, 17.9; m/z (CI , NH_4^+) 282 ($[\text{M}+\text{NH}_4]^+$).

(1R,2S,3R)-ethyl 2-hydroxy-1-(4-methylpent-3-enyl)-3-(prop-1-en-2-yl)cyclopentanecarboxylate (5b**)**



According to general procedure E, aldehyde **4b** (0.140 g, 0.5 mmol) was treated with catalyst **1c** (9.8 mg, 0.01 mmol) at room temperature for 48 h, to afford cyclopentanol **5b** (0.133 g, 95%) as a colorless oil in >30:1 dr by ^1H -NMR and 98% ee by chiral GC (β -cyclodextr, 140 $^\circ\text{C}$ isothermal, t_r (major) 54.9 min, t_r (minor) 56.3 min). R_f = 0.65 (33% EtOAc / hexanes); $[\alpha]_D^{20}$ = -2.6 (c. 1.65, CH_2Cl_2); ν_{max} / cm^{-1} (film) 3510 (w), 2989 (m), 1725 (s), 1446 (w), 1181 (m), 1067 (m), 889 (w); ^1H NMR (400 MHz, CDCl_3) δ 5.10, (1H, app. tt, J = 1.2, 5.8, $\text{CH}=\text{C}(\text{CH}_3)_2$), 5.01 (1H, app. d, J = 1.2, $\text{C}=\text{CH}$), 4.85 (1H, s, $\text{C}=\text{CH}$), 4.30 (1H, app. t, J = 2.8, CHOH), 4.17 (1H, dq, J = 14.8, 7.1 OCH_2CH_3), 4.14 (1H, dq, J = 14.4, 7.1, OCH_2CH_3), 2.55 (1H, app. dt, J = 3.2, 9.6, tCH), 2.32 (1H, m, CHCH_2), 1.95 – 1.83 (4H, m, CH_2CH_2 + 2 x CHCH_2), 1.81 (3H, s, CH_3), 1.76 – 1.67 (3H, m, CH_2CH_2 + CHCH_2), 1.66 (3H, s, CH_3), 1.58 (3H, s, CH_3), 1.40 (1H, d, J = 2.8, OH), 1.27 (3H, app. t, J = 6.4, OCH_2CH_3); ^{13}C -NMR (100.6 MHz, CDCl_3) δ 176.7, 144.1, 132.1, 124.3, 112.5, 75.4, 60.8, 59.5, 51.4, 34.6, 32.2, 25.9, 24.8, 24.6, 23.8, 17.8, 14.5; m/z (ES^+) 298 ($[\text{M}+\text{NH}_4]^+$).

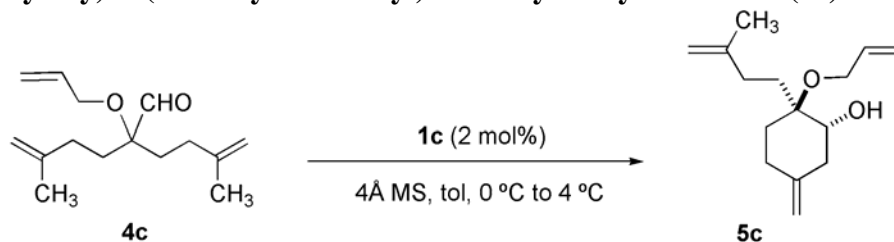
Determination of relative stereochemistry of 5b via S-32



Diol **S-32** was prepared via a procedure analogous to that for **S-27** (see preparation of aldehyde **6a** in Section 2). Diol **S-32** (0.047 g) was recovered as a white powder in quantitative yield following purification by flash chromatography (elute with 10 – 25% Et₂O / hexanes). A crystal structure of **S-32** was obtained and confirmed the relative stereochemistry shown (see Section 4b).

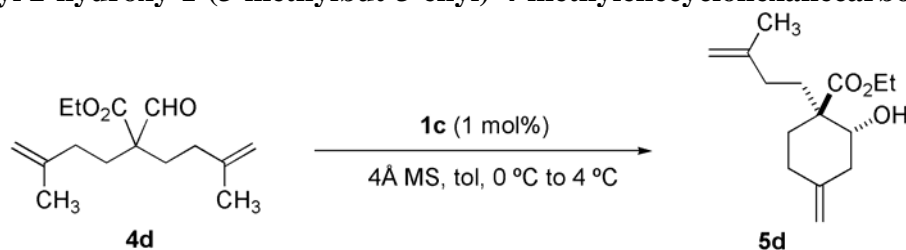
R_f = 0.21 (25% EtOAc / hexanes); ν_{max} / cm⁻¹ (film) 3309 (s), 2929 (m), 1085 (m), 1053 (m); ¹H NMR (500 MHz, CDCl₃) δ 5.18 (1H, app. tt, J = 1.5, 7, CH=C(CH₃)₂), 5.02 (1H, app. dd, J = 1.5, 3, C=CH), 4.85 (1H, s, C=CH), 3.91 (1H, d, J = 4, CHOH), 3.45 (2H, app. q, J = 11, 2 x CH₂OH), 2.63 (1H, td, J = 7, 10, tCH), 2.08 – 2.00 (1H, m, CHCH₂), 1.99 – 1.94 (1H, m, CHCH₂), 1.89 (1H, tt, J = 2.5, 10, CHCH₂), 1.82 (3H, s, CH₃), 1.72 – 1.63 (2H, buried m, 2 x CHCH₂), 1.68 (3H, s, CH₃), 1.62 (3H, s, CH₃), 1.58 (1H, td, J = 3, 13, CHCH₂), 1.42 – 1.35 (1H, m, CHCH₂); ¹³C-NMR (125.8 MHz, CDCl₃) δ 144.3, 131.8, 125.3, 112.7, 75.5, 67.0, 51.51, 51.49, 32.3, 31.9, 25.9, 25.3, 23.8, 23.7, 17.9; m/z (ES⁺) 239 ([M+H]).

(1S,2R)-2-(allyloxy)-2-(3-methylbut-3-enyl)-5-methylenecyclohexanol (**5c**)



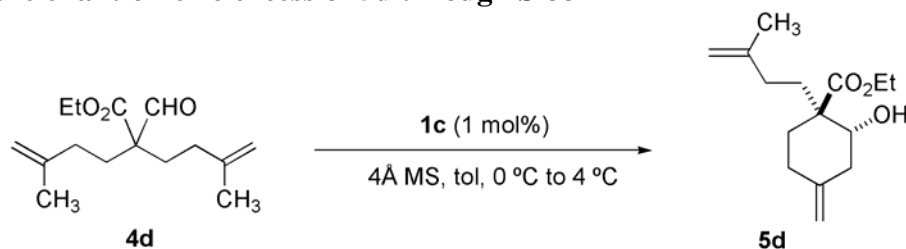
In accordance with general procedure E, aldehyde **4c** (47 mg, 0.2 mmol) was treated with catalyst **1c** (4 mg, 4 μ mol) for 48h to afford cyclohexanol **5c** (42 mg, 89%) as a colorless oil in >30:1 dr by ¹H-NMR and 97% ee by chiral GC (γ -TA, 90 $^\circ$ C isothermal, t_r (minor) 186.6 min. t_r (major) 202.4 min.). R_f = 0.60 (10% EtOAc / hexanes); $[\alpha]_D^{20}$ = -14.0 (c. 1.70, CH₂Cl₂); ν_{max} / cm⁻¹ (film) 3478 (br, w), 2934 (s), 2857 (m), 1649 (m), 1453 (m), 1072 (s), 885 (s); ¹H NMR (400 MHz, CDCl₃) δ 5.93 (1H, app. tdd, J = 5, 10, 15, CH=CH₂), 5.30 (1H, m, CH=CH), 5.14 (1H, dd, J = 1, 10.5, CH=CH), 4.83 (1H, s, C=CH), 4.75 (1H, s, C=CH), 4.69 (2H, s, 2 x C=CH), 3.88 (2H, app. dq, J = 5.5, 12.5, OCH₂), 3.80 (1H, br. s, CHOH), 2.82 (1H, dd, J = 1, 13.5, CHCHOH), 2.23 (1H, app. dt, J = 4, 13, CHCHOH), 2.18 – 1.98 (4H, m, 4 x CHCH₂), 1.81 – 1.76 (2H, m, 2 x CHCH₂), 1.74 (3H, s, CH₃), 1.65 – 1.59 (2H, m, 2 x CHCH₂), 1.48 (1H, dt, J = 5, 13, CHCH₂), 1.25 (1H, s, OH); ¹³C-NMR (100.6 MHz, CDCl₃) δ 146.6, 145.0, 135.5, 115.9, 111.4, 109.6, 77.4, 70.6, 61.8, 38.4, 30.7, 30.5, 30.3 (2C), 23.0; m/z (CI⁺) 254 ([M+NH₄]).

(1R,2R)-ethyl 2-hydroxy-1-(3-methylbut-3-enyl)-4-methylenecyclohexanecarboxylate (5d)



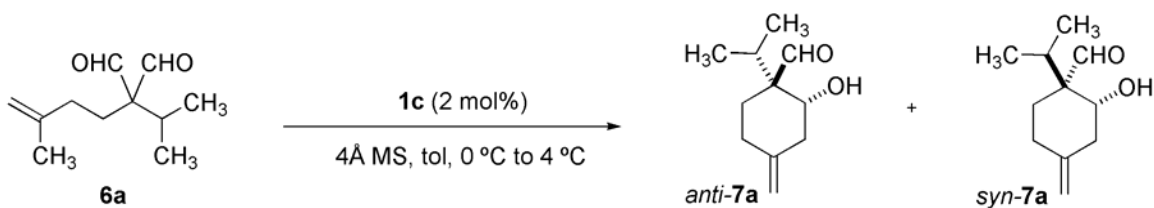
In accordance with general procedure E, aldehyde **4d** (101 mg, 0.4 mmol) was treated with catalyst **1c** (4 mg, 4 μ mol) for 15 h to afford cyclohexanol **5d** (100 mg, 99%) as a colorless oil in >30:1 dr by $^1\text{H-NMR}$. Ester **5d** was converted to **S-33** in order to analyze enantiomeric excess, which was determined to be 99%. R_f = 0.42 (20% EtOAc / hexanes); $[\alpha]_D^{20}$ = -15.0 (c. 0.85, CH_2Cl_2); ν_{max} / cm^{-1} (film) 3515 (br), 3072 (w), 2939 (m), 1723 (s), 1650 (m), 1450 (m), 1183 (s), 887 (m); $^1\text{H-NMR}$ (600 MHz, CDCl_3) δ 4.81 (1H, s, $\text{C}=\text{CH}$), 4.74 (1H, s, $\text{C}=\text{CH}$), 4.67 (1H, s, $\text{C}=\text{CH}$), 4.65 (1H, s, $\text{C}=\text{CH}$), 4.18 (2H, q, J = 7.2, OCH_2CH_3), 4.09 (1H, dd, J = 3, 6.6, CHOH), 2.42 (1H, dd, J = 2, 14, CHCH), 2.29 (1H, dd, J = 6, 14, CHCH), 2.17 – 2.06 (2H, m, 2 x CH_2CH), 2.07 (1H, d, J = 7, OH), 1.97 – 1.85 (4H, m, 4 x CH_2CH), 1.71 – 1.66 (1H, buried m, CH_2CH), 1.69 (3H, s, CH_3), 1.60 – 1.55 (1H, CH_2CH), 1.26 (3H, t, J = 8.4, OCH_2CH_3); $^{13}\text{C-NMR}$ (100.6 MHz, CDCl_3) δ 175.8, 145.8, 144.4, 111.7, 110.1, 71.0, 60.8, 50.7, 39.7, 32.6, 32.4, 31.3, 30.3, 22.8, 14.5; m/z (CI+) 253 ($[\text{M}+\text{H}]$).

Analysis of the enantiomeric excess of 5d through S-33



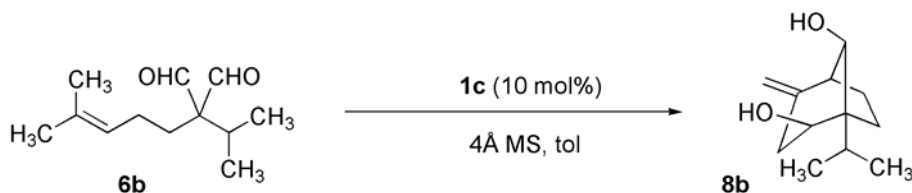
Ester **5d** was reduced and bis-benzoylated, as shown, to yield **S-33**. The enantiomeric excess of **S-33** was measured as 99% by chiral HPLC (AD-H, 1% isopropanol / hexanes, t_r (major) 24.7 min. t_r (minor) 28.1 min.). R_f = 0.57 (15% EtOAc / hexanes); $[\alpha]_D^{20}$ = -35.4 (c. 0.85, CH_2Cl_2); ν_{max} / cm^{-1} (film) 2940 (w), 1720 (s), 1451 (w), 1270 (s), 1110 (m), 709 (s); $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 7.99 (4H, m, 2 x CH_{Ar} + 2 x CH_{Ar}), 7.56 (1H, tt, J = 1.5, 7.5, CH_{Ar}), 7.53 (1H, tt, J = 1.5, 7.5, CH_{Ar}), 7.42 (2H, t, J = 8, 2 x CH_{Ar}), 7.39 (2H, t, J = 8, 2 x CH_{Ar}), 5.34 (1H, dd, J = 4.5, 9, $\text{C}_\beta\text{HOCOPh}$), 4.81 (1H, s, $\text{C}=\text{CH}$), 4.75 (1H, s, $\text{C}=\text{CH}$), 4.71 (2H, s, 2 x $\text{C}=\text{CH}$), 4.42 (1H, d, J = 11.5, $\text{C}_\beta\text{HOCOPh}$), 4.31 (1H, d, J = 11.5, $\text{C}_\beta\text{HOCOPh}$), 2.64 (1H, dd, J = 4, 14, CHCH), 2.53 (1H, dd, J = 9, 14, CHCH), 2.28 (2H, app. t, CH_2CH_2), 2.10 (2H, dd, J = 7.5, 10, CH_2CH_2), 1.94 – 1.83 (3H, m, 3 x CH_2CH), 1.73 (3H, s, CH_3), 1.63 (1H, td, J = 7, 13.5, CH_2CH); $^{13}\text{C-NMR}$ (100.6 MHz, CDCl_3) δ 166.7, 165.9, 146.1, 143.9, 133.2, 133.2, 129.8, 128.2, 111.2, 110.4, 133.24, 133.18, 129.8, 128.6, 75.0, 67.1, 40.5, 35.9, 31.5, 30.5, 29.7, 28.8, 22.8; m/z (ApCI+) 419 ($[\text{M}+\text{H}]$).

(1S,2R)-2-hydroxy-1-isopropyl-4-methylenecyclohexanecarbaldehyde (7a)



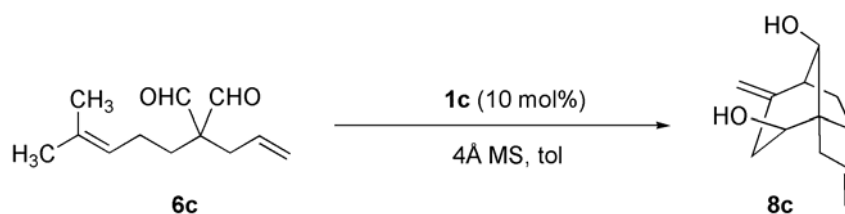
In accordance with general procedure E, aldehyde **6a** (91 mg, 0.5 mmol) was treated with catalyst **1c** (10 mg, 10 μ mol) for 20h to afford cyclohexanols *anti*-**7a** and *syn*-**7a** in a diastereomeric ratio of 2.2:1 (76 mg, 84%). After purification via flash chromatography, eluting with 5 – 20% Et₂O / hexanes, the major diastereoisomer, *anti*-**7a**, was isolated (52 mg, 57%) as a colorless oil in >30:1 dr by ¹H-NMR and 91% ee by chiral GC (β -cyclodex, 95 °C isothermal, *t_r* (minor) 66.3 min. *t_r* (major) 73.5 min.). *R_f* = 0.31 (20% EtOAc / hexanes); [α]_D²⁰ = –39.7 (c. 1.15, CH₂Cl₂); ν_{max} / cm^{–1} (film) 3480 (br, m), 2941 (s), 2709 (w), 1720 (s), 1390 (m), 1030 (m), 873 (m); ¹H-NMR (500 MHz, CDCl₃) δ 9.69 (1H, s, CHO), 4.87 (1H, s, C=CH), 4.76 (1H, s, C=CH), 4.42 (1H, dd, *J* = 3.5, 3.5, CHOH), 2.36 – 2.24 (3H, m, 2 x OHCHCH + CHCH₂), 2.02 (1H, septet, *J* = 7, CH(CH₃)₂), 1.95 (1H, dt, *J* = 4.5, 14, CHCH₂), 1.48 – 1.42 (2H, m, 2 x CHCH₂), 1.04 (3H, d, *J* = 7, CHCH₃), 0.96 (3H, d, *J* = 7, CHCH₃); ¹³C-NMR (100.4 MHz, CDCl₃) δ 207.5, 143.6, 112.4, 67.8, 56.1, 40.5, 33.4, 31.8, 28.3, 17.6, 17.4; *m/z* (ES⁺) 183 ([M+H]), 200 (M+NH₄).

diol **8b**



To a stirring mixture of 4Å molecular sieves (50 mg), toluene (63 μ L), and catalyst **1c** (49 mg, 0.05 mmol), contained in a flame dried 0.5 dram reaction vial, under a N₂ atmosphere, was added aldehyde **6b** (98 mg, 0.5 mmol). The solution was allowed to stir at room temperature for 48 h, until starting material appeared consumed by TLC analysis. The reaction mixture was diluted with 50% Et₂O / hexanes (0.5 mL) and loaded onto a silica gel column. Purification via flash column chromatography, eluting with 25% Et₂O / hexanes, afforded diol **8b** (45 mg, 46%) as a pale yellow oil in >30:1 dr by ¹H-NMR and 92% ee by chiral GC (γ -TA, 140 °C isothermal, *t_r* (major) 26.6 min, *t_r* (minor) 28.0 min). *R_f* = 0.30 (33% EtOAc / hexanes); [α]_D²⁰ = –32.9 (c. 2.15, CH₂Cl₂); ν_{max} / cm^{–1} (film) 3302 (br, s), 2957 (s), 1473 (m), 1087 (s), 1034 (m), 868 (m); ¹H NMR (400 MHz, CDCl₃) δ 4.83 (1H, app. t, *J* = 2.5, C=CH), 4.80 (1H, app. t, *J* = 2.5, C=CH), 3.99 (1H, app. d, *J* = 4.5, *t*CCHOH), 3.93 (1H, app. d, *J* = 5.5, *q*CCHOH), 3.35 (2H, s, 2 x OH), 2.70 (1H, app. t, *J* = 7.0, *t*CHC=CH₂), 2.62 (1H, app. td, *J* = 3.0, 13.5, *s*CHC=CH₂), 2.35 – 2.28 (2H, m, CH(CH₃)₂ + *s*CHC=CH₂), 1.76 – 1.67 (1H, m, CHCH₂), 1.56 – 1.47 (2H, m, 2 x CHCH₂), 1.16 – 1.08 (1H, m, CHCH₂), 0.94 (3H, d, *J* = 6.8, CH₃), 0.89 (3H, d, *J* = 7.2, CH₃); ¹³C-NMR (100.6 MHz, CDCl₃) δ 145.9, 111.2, 77.9, 74.3, 49.8, 47.8, 38.1, 26.4, 23.9, 23.4, 18.1, 16.8; *m/z* (CI⁺) 214 ([M+NH₄]).

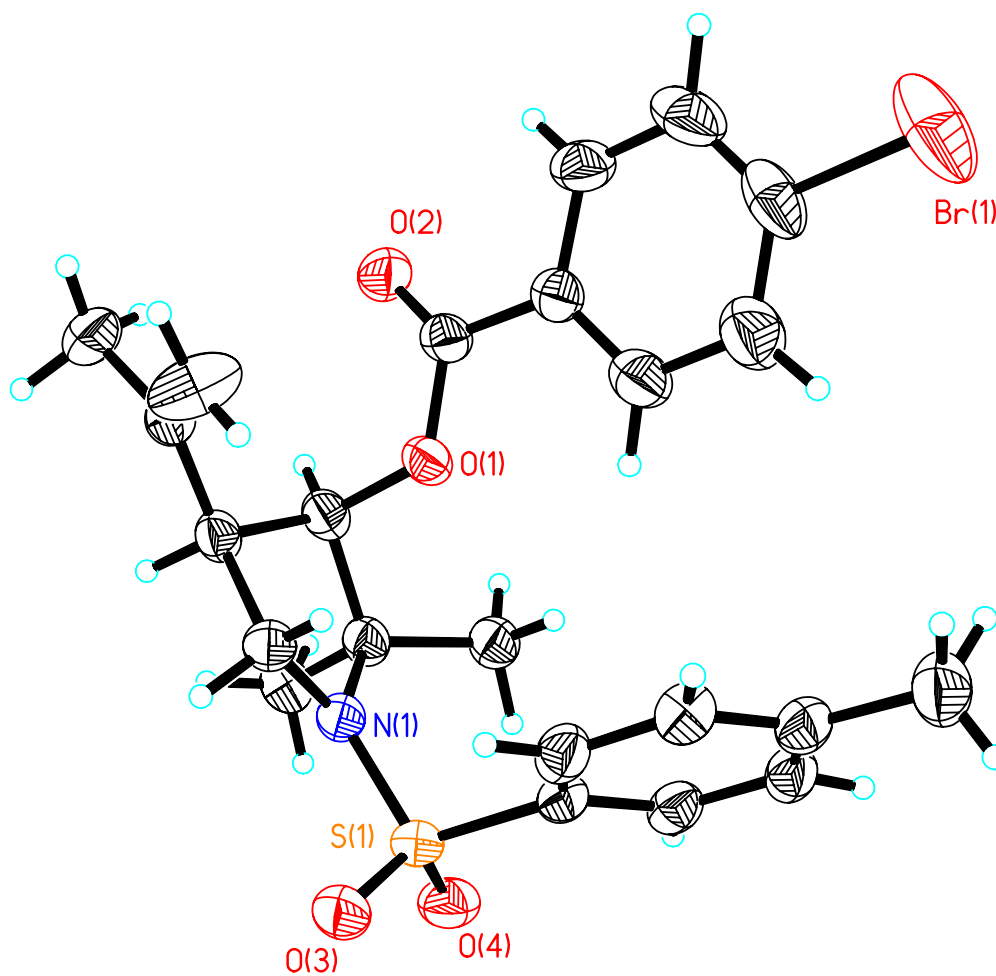
diol **8c**



To a stirring mixture of 4Å molecular sieves (50 mg), toluene (63 μ L), and catalyst **1c** (49 mg, 0.05 mmol), contained in a flame dried 0.5 dram reaction vial, under a N₂ atmosphere, was added aldehyde **6c** (96 mg, 0.5 mmol). The solution was allowed to stir at room temperature for 48 h until starting material appeared consumed by TLC analysis. The reaction mixture was diluted with 50% Et₂O / hexanes (0.5 mL) and loaded onto a silica gel column. Purification by flash column chromatography, eluting with 25% Et₂O / hexanes, afforded diol **8c** (40 mg, 42%) as a pale yellow oil in >30:1 dr by ¹H-NMR and 93% ee by chiral GC (γ -TA, 135 °C isothermal, t_r (major) 34.0 min, t_r (minor) 36.0 min). R_f = 0.30 (33% EtOAc / hexanes); $[\alpha]_D^{20}$ = -42.6 (c. 1.35, CH₂Cl₂); ν_{max} / cm⁻¹ (film) 3307 (br s), 2945 (s), 1555 (w), 1433 (m), 1085 (s); ¹H NMR (400 MHz, CDCl₃) δ 5.86 (1H, app. tdd, J = 8, 9, 17, CH=CH₂), 5.14 (1H, app. d, J = 17, CH=CH), 5.09 (1H, dd, J = 1.6, 9.6, CH=CH), 4.85 (1H, d, J = 2, C=CH), 4.83 (1H, d, J = 2, C=CH), 3.77 (1H, d, J = 3.6, *t*CCH₂OH), 3.74 (1H, d, J = 1, *q*CCH₂OH), 3.28 (1H, br s, OH), 3.24 (1H, br s, OH), 2.72 (1H, app. t, J = 5.2, *t*CH), 2.64 – 2.59 (2H, m, HCCCH=CH₂ + HCC=CH₂), 2.30 (1H, d, J = 15.6, HCC=CH₂), 2.16 (1H, dd, J = 6.8, 13.6, HCCH=CH₂), 1.77 (1H, m, CHCH₂*q*C), 1.59 – 1.48 (2H, m, CHCH₂*q*C + CHCH₂), 1.40 – 1.32 (1H, m, CHCH₂); ¹³C-NMR (100.6 MHz, CDCl₃) δ 145.5, 134.9, 117.0, 111.8, 80.8, 75.5, 49.5, 45.3, 38.9, 37.8, 28.9, 23.8; m/z (ES+) 195 ([M+H]).

4. Crystallographic data

a) *p*-bromobenzoyl **3h**: The crystal structure has been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number CCDC 665711.



b) diol S-32: The crystal structure has been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number CCDC 665710

