Highly Diastereoselective Pd-Catalyzed Carboetherification Reactions of Acyclic Internal Alkenes. Stereoselective Synthesis of Polysubstituted Tetrahydrofurans

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Supporting Information
Experimental procedures and characterization data for new compounds (30 pages).

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General. All reactions were carried out under a nitrogen atmosphere in oven or flame dried glassware. Tris(dibenzylideneacetone)dipalladium (0) and all phosphine ligands were purchased from Strem Chemical Co. and used without further purification. All aryl bromides were obtained from commercial sources (Aldrich Chemical CO or Acros Chemical CO) and were used as obtained. [3-(Ethoxycarbonyl)propyl]triphenylphosphonium bromide,1 (E)-ethyl 5-phenylpent-4-enolate,2 (Z)-ethyl 5-phenylpent-4-enolate,3 (E)-ethyl 5-(4-methoxyphenyl)pent-4-enolate,4 1-[4-
(trifluoromethyl)phenyl]prop-2-en-1-ol, 5-cyclohexylprop-2-en-1-ol, dodec-1-en-3-ol, 1-(but-3-enyl)cyclohexanol, \((E)\)-2-methylhept-5-en-2-ol, \((Z)\)-2-methylhept-5-en-2-ol, and \((E)\)-2,4-dimethylhept-5-en-2-ol were prepared according to literature procedures. Stereochemistry of tetrahydrofuran products was assigned by analogy to related compounds previously reported by our group through comparison of NMR spectra. Toluene and THF were purified using a GlassContour solvent purification system. Yields refer to isolated yields of compounds estimated to be \(\geq 95\%\) pure as determined by \(^1\)H NMR. The yields reported in the supporting information describe the result of a single experiment, whereas the yields reported in Tables 1–2 and eq 3–5 are average yields of two or more experiments. Thus, the yields reported in the supporting information may differ from those shown in Tables 1–2 and eq 3–5.

**Preparation of Substrates**

**General Procedure 1: Synthesis of \((E)\)-\(\gamma,\delta\)-Unsaturated Esters via Johnson Orthoester Claisen Rearrangements of Allylic Alcohols.** A round bottom flask equipped with a short path distillation head and a recovery flask was charged with an appropriate allylic alcohol (1.0 equiv), triethyl orthoacetate (5 equiv), and pivalic acid (0.05 equiv). The mixture was heated to 140 °C with stirring until the starting material had been completely consumed as judged by GC analysis. The reaction mixture was cooled to room temperature and diluted with ethyl acetate (1:1 v:v). A solution of 1 M HCl (1:1 v:v) was slowly added and the resulting biphasic mixture was stirred for 1 h at rt. The layers were separated and the organic layer was washed with water (2 x 50 mL) and saturated NaHCO\(_3\) (1 x 50 mL). The organic layer was then dried over
anhydrous Na$_2$SO$_4$, filtered, and concentrated in vacuo. The crude material was purified by flash chromatography on silica gel.

**General Procedure 2: Synthesis of (Z)-γ,δ-Unsaturated Esters via Wittig Olefinationsof Aldehydes With [3-(Ethoxycarbonyl)propyl]triphenylphosphonium Bromide.$^{12}$** An oven-dried flask equipped with a magnetic stirbar was cooled under a stream of nitrogen and charged with [3-(ethoxycarbonyl)propyl]triphenylphosphonium bromide$^1$ (1 equiv) and THF (1 M). The resulting suspension was cooled to –78 °C then a solution of NaHMDS (1 equiv) in THF (1 M), was added dropwise. The resulting mixture was stirred at –78 °C for one h, then a solution of the appropriate aldehyde (1 equiv) in THF (3 M) was added dropwise. The reaction mixture was stirred at –78 °C for 2 h then was warmed to rt, and stirred overnight (ca 12 h). A solution of brine (5 mL) was added, followed by with EtOAc (5 mL), and the mixture was transferred to a separatory funnel. The layers were separated and the aqueous layer was extracted with EtOAc (2 x 20 mL). The combined organic layers were then dried over anhydrous MgSO$_4$, filtered, and concentrated in vacuo. The crude material was purified by flash chromatography on silica gel.

**OEt**

![OEt](image)

**(E)-Ethyl 5-[4-(trifluoromethyl)phenyl]pent-4-enoate.** General procedure 1 was used for conversion of 1-[4-(trifluoromethyl)phenyl]prop-2-en-1-ol$^5$ (1.74 g, 0.86 mmol) to the title compound. This procedure afforded 2.6 g (92%) of the title compound as a colorless oil. This material was obtained with >20:1 $E$:$Z$ selectivity as judged by $^1$H NMR analysis. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.47 (d, $J = 8.2$ Hz, 2 H), 7.34 (d, $J = 8.2$ Hz, 2 H), 6.40 (d, $J = 15.8$ Hz, 1 H),
6.26 (dt, \(J = 6.2, 15.8 \text{ Hz}, 1 \text{ H}\)), 4.10 (q, \(J = 7.0 \text{ Hz}, 2 \text{ H}\)), 2.54–2.47 (m, 2 H), 2.46–2.41 (m, 2 H), 1.20 (t, \(J = 7.0 \text{ Hz}, 3 \text{ H}\)); \(^{13}\text{C NMR (100 MHz, CDCl}_3\)) \(\delta 172.6, 140.8, 131.33 \) (q, \(J = 234.2 \text{ Hz}\)), 129.0 (q, \(J = 32.1 \text{ Hz}\)), 128.8, 125.3 (q, \(J = 3.8 \text{ Hz}\)), 122.9, 60.3, 33.6, 28.2, 14.1; IR (film, cm\(^{-1}\)) 2984, 1734, 1327; MS(ESI): 272.1026 (272.1024 calcd for C\(_{14}\)H\(_{15}\)F\(_3\)O\(_2\), M\(^+\)).

\((Z)-\text{Ethyl 5-[4-(trifluoromethyl)phenyl]pent-4-enoate.}\) General Procedure 2 was used for conversion of 4-(trifluoromethyl)benzaldehyde (0.35 mL, 3.28 mmol) to the title compound. This procedure afforded 0.70 g (70\%) of the title compound as a colorless oil. This material was obtained as a 20:1 mixture of \(Z:E\) isomers as judged by \(^1\text{H NMR analysis}.\) Data are for the major isomer.\(^1\text{H NMR (400 MHz, CDCl}_3\)) \(\delta 7.55 \) (d, \(J = 8.3 \text{ Hz}, 2 \text{ H}\)), 7.34 (d, \(J = 8.3 \text{ Hz}, 2 \text{ H}\)), 6.44 (d, \(J = 11.7 \text{ Hz}, 1 \text{ H}\)), 5.72 (dt, \(J = 7.3, 11.7 \text{ Hz}, 1 \text{ H}\)), 4.10 (q, \(J = 7.1 \text{ Hz}, 2 \text{ H}\)), 2.65–2.59 (m, 2 H), 2.43–2.38 (m, 2 H), 1.20 (t, \(J = 7.1 \text{ Hz}, 3 \text{ H}\)); \(^{13}\text{C NMR (100 MHz, CDCl}_3\)) \(\delta 172.5, 140.9, 131.4 \) (q, \(J = 218.9\)), 129.0 (q, \(J = 47.2 \text{ Hz}\)), 128.9, 125.1 (q, \(J = 3.7 \text{ Hz}\)), 123.2, 60.3, 34.0, 23.9, 14.0; IR (film, cm\(^{-1}\)) 2984, 1734; MS(ESI): 272.1026 (272.1024 calcd for C\(_{14}\)H\(_{17}\)F\(_3\)O, M\(^+\)).
(Z)-Ethyl 5-(4-methoxyphenyl)pent-4-enoate. General Procedure 2 was used for the conversion of 4-methoxybenzaldehyde (0.4 g, 3.28 mmol) to the title compound. This procedure afforded 0.46 g (59%) of the title compound as a colorless oil. This material was obtained as a 10:1 mixture of Z:E isomers as judged by $^1$H NMR analysis. Data are for the major isomer. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.25–7.22 (m, 2 H), 6.90–6.87 (m, 2 H), 6.41 (d, $J$ = 11.7 Hz, 1 H), 5.54 (dt, $J$ = 7.1, 11.7 Hz, 1 H), 4.14 (q, $J$ = 7.1 Hz, 2 H), 3.80 (s, 3 H), 2.70–2.64 (m, 2 H), 2.46–2.42 (m, 2 H), 1.25 (t, $J$ = 7.1 Hz, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 172.9, 158.4, 129.9, 129.5, 128.8, 113.6, 60.4, 55.2, 34.5, 24.1, 14.2 (one carbon signal is absent due to incidental equivalence); IR (film, cm$^{-1}$) 2981, 1732; MS(ESI): 257.1152 (257.1154 calcd for C$_{14}$H$_{18}$O$_3$, M + Na$^+$).

(E)-Ethyl 5-cyclohexylpent-4-enoate. General Procedure 1 was used for the conversion of 1-cyclohexylprop-2-en-1-ol$^6$ (1.28 g, 9.13 mmol) to the title compound. This procedure afforded 1.92 g (81%) of the title compound as a colorless oil. This material was obtained with >20:1 $E$:Z selectivity as judged by $^1$H NMR analysis. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.45–5.32 (m, 2 H), 4.13 (q, $J$ = 7.3 Hz, 2 H), 2.38–2.26 (m, 4 H), 1.94–1.85 (m, 1 H), 1.74–1.60 (m, 5 H), 1.30–1.21 (m, 5 H), 1.19–1.10 (m, 1 H), 1.09–0.98 (m, 2 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 173.1, 137.6,
125.3, 60.1, 40.5, 34.4, 33.0, 28.0, 26.1, 25.9, 14.2; IR (film, cm\(^{-1}\)) 2924, 1738; MS(ESI): 233.1520 (233.1517 calcd for C\(_{14}\)H\(_{18}\)O\(_2\), M + Na\(^+\)).

(\textit{Z})-\textit{Ethyl 5-cyclohexylpent-4-enoate}. General Procedure 2 was used for the conversion of 1-cyclohexy1prop-2-en-1-ol\(^6\) (1.70 g, 3.70 mmol) to the title compound. This procedure afforded 0.65 g (51\%) of the title compound as a colorless oil. This material was obtained with 20:1 \(E:Z\) selectivity as judged by \(^1\)H NMR analysis. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 5.21–5.12 (m, 2 H), 4.06 (q, \(J = 7.0\) Hz, 2 H), 2.34–2.24 (m, 4 H), 2.23–2.17 (m, 1 H), 1.66–1.50 (m, 5 H), 1.27–1.17 (m, 5 H), 1.13–1.05 (m, 1 H), 1.03–0.94 (m, 2 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 173.0, 137.3, 125.4, 60.1, 36.2, 34.6, 33.2, 26.0, 25.8, 23.0, 14.2; IR (film, cm\(^{-1}\)) 2923, 1739; MS(ESI): 233.1521 (233.152 calcd for C\(_{14}\)H\(_{18}\)O\(_2\), M + Na\(^+\)).

(\textit{E})-\textit{Ethyl tetradec-4-enoate}. General Procedure 1 was used for the conversion of dodec-1-en-3-ol\(^7\) (1.3 g, 7.06 mmol) to the title compound. This procedure afforded 1.17 g (69\%) of the title compound as a colorless oil. This material was obtained with >20:1 \(E:Z\) selectivity as judged by \(^1\)H NMR analysis. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 5.50–5.35 (m, 2 H), 4.12 (q, \(J = 6.8\) Hz, 2 H), 2.37–2.26 (m, 4 H), 1.96 (q, \(J = 6.6\) Hz, 2H), 1.35–1.19 (m, 17 H), 0.88 (t, \(J = 6.8\) Hz, 3 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 173.2, 131.8, 127.9, 60.2, 34.4, 32.5, 32.0, 29.6, 29.5, 29.4, 29.3,
29.1, 27.9, 22.7, 14.2, 14.1; IR (film, cm\(^{-1}\)) 2924, 1739; MS(ESI): 277.2140 (277.2144 calcd for C\(_{16}\)H\(_{30}\)O\(_2\), M + Na\(^+\)).

(Z)-Ethyl tetradec-4-enoate. General Procedure 2 was used for the conversion of dodec-1-en-3-ol\(^7\) (1.50 g, 3.28 mmol) to the title compound. This procedure afforded 0.83 g (54%) of the title compound as a colorless oil. This material was obtained with 20:1 \(E:Z\) selectivity as judged by \(^1\)H NMR analysis. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 5.40–5.20 (m, 2 H), 4.05 (q, \(J = 7.0\) Hz, 2 H), 2.33–2.20 (m, 4 H), 2.00–1.92 (m, 2 H), 1.29–1.15 (m, 17 H), 0.80 (t, \(J = 7.0\) Hz, 3 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 173.0, 131.4, 127.2, 60.1, 34.3, 31.8, 29.6, 29.5, 29.4, 29.3, 27.1, 22.7, 22.6, 14.1, 14.0; IR (film, cm\(^{-1}\)) 2924, 1739; MS(ESI): 277.2135 (277.2144 calcd for C\(_{16}\)H\(_{30}\)O\(_2\), M + Na\(^+\)).

**General Procedure 3: Addition of MeMgBr to Esters.** An oven or flame dried flask equipped with a magnetic stirbar was cooled under a stream of nitrogen and charged with MeMgBr (3 equiv, 3.0 M in diethyl ether). Additional ether was added to provide a 1.0 M solution of MeMgBr, which was then cooled to 0 °C. The appropriate ester (1.0 equiv) was added dropwise via syringe and the resulting mixture was warmed to rt and stirred for 2–4 h until the starting material was completely consumed as judged by TLC analysis. A saturated solution of aqueous NH\(_4\)Cl (1:1 by volume with the reaction mixture) was added dropwise and the resulting mixture was then diluted with ethyl acetate (40 mL). The layers were separated and the aqueous layer was extracted with ethyl acetate (2 x 20 mL). The combined organic layers were dried over
anhydrous Na$_2$SO$_4$, filtered, and concentrated in vacuo. The crude product was then purified by flash chromatography on silica gel.

(E)-2-Methyl-6-phenylhex-5-en-2-ol (15). General Procedure 3 was used for the conversion of (E)-ethyl 5-phenylpent-4-enoate$^2$ (1.16 g, 5.6 mmol) to the title compound. This procedure afforded 0.76 g (71%) of the title compound as a white solid, m.p. 42 °C. This material was obtained as a >20:1 mixture of E:Z isomers as judged by $^1$H NMR analysis. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.32–7.22 (m, 4 H), 7.18–7.13 (m, 1 H), 6.38 (d, J = 15.8 Hz, 1 H), 6.21 (dt, J = 6.8 Hz, 15.8 Hz, 1 H), 2.31–2.24 (m, 2 H), 1.65–1.59 (m, 3 H), 1.21 (s, 6 H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 137.7, 130.8, 129.8, 128.4, 126.9, 125.9, 70.9, 43.2, 29.2, 28.0; IR (film, cm$^{-1}$) 3362, 2970; MS(ESI): 190.1355 (190.1358 calcd for C$_{13}$H$_{18}$O, M$^+$).

(Z)-2-Methyl-6-phenylhex-5-en-2-ol (16). General Procedure 3 was used for the conversion of (Z)-ethyl 5-phenylpent-4-enoate$^3$ (0.47 g, 2.3 mmol) to the title compound. This procedure afforded 0.39 g (90%) of the title compound as a colorless oil. This material was obtained as a >20:1 mixture of Z:E isomers as judged by $^1$H NMR analysis. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.35–7.26 (m, 4 H), 7.23–7.17 (m, 1 H), 6.44–6.40 (m, 1 H), 5.65 (dt, J = 7.2, 11.7 Hz, 1 H), 2.44–2.37 (m, 2 H), 1.64–1.58 (m, 3 H), 1.20 (s, 6 H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 137.6, 132.8, 129.0, 128.7, 128.2, 126.6, 70.8, 43.8, 29.2, 23.7; IR (film, cm$^{-1}$) 3370, 2970; MS(ESI): 190.1360 (190.1358 calcd for C$_{13}$H$_{18}$O, M$^+$).
(E)-2-Methyl-6-[4-(trifluoromethyl)phenyl]hex-5-en-2-ol (17). General Procedure 3 was used for the conversion of (E)-ethyl 5-[4-(trifluoromethyl)phenyl]pent-4-enoate (0.75 g, 2.75 mmol) to the title compound. This procedure afforded 0.71 g (96%) of the title compound as a white solid m.p. 58°C. This material was obtained as a >20:1 mixture of E:Z isomers as judged by \(^1\)H NMR analysis. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.54 (d, \(J = 8.1\) Hz, 2 H), 7.34 (d, \(J = 8.1\) Hz, 2 H), 6.40 (d, \(J = 11.5\) Hz, 1 H), 5.74 (dt, \(J = 7.4, 11.5\) Hz, 1 H), 2.41–2.32 (m, 2 H), 1.62–1.56 (m, 3 H), 1.18 (s, 6 H); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 141.1, 134.9, 128.8, 128.6 (q, \(J = 32.0\) Hz), 127.7 (q, \(J = 225.2\) Hz), 125.1 (q, \(J = 3.8\) Hz), 70.8, 43.4, 29.2, 23.6; IR (film, cm\(^{-1}\)) 3370, 2972, 1327. MS(EI): 240.1132 (240.1126 calcd for C\(_{14}\)H\(_{17}\)F\(_3\)O, M – H\(_2\)O).

(Z)-2-Methyl-6-[4-(trifluoromethyl)phenyl]hex-5-en-2-ol (18). General Procedure 3 was used for the conversion of (Z)-ethyl 5-[4-(trifluoromethyl)phenyl]pent-4-enoate (0.52 g, 1.91 mmol) to the title compound. This procedure afforded 0.49 g (80%) of the title compound as a colorless oil. This material was obtained as a >20:1 mixture of Z:E isomers as judged by \(^1\)H NMR analysis. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.54 (d, \(J = 8.1\) Hz, 2 H), 7.43 (d, \(J = 8.1\) Hz, 2 H), 6.46 (d, \(J = 15.9\) Hz, 1 H), 6.36 (dt, \(J = 6.6, 15.9\) Hz, 1 H), 2.39–2.33 (m, 2 H), 1.70–1.66 (m, 3 H), 1.28 (s, 6 H); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 141.2, 133.8, 128.8, 128.7 (q, \(J = 32.5\) Hz), 126.0 (q, \(J = 220.2\) Hz), 125.4 (q, \(J = 3.7\) Hz), 70.8, 42.9, 29.3, 28.1 (one signal is missing due to
incidental equivalence); IR (film, cm\(^{-1}\)) 3470, 2972; MS(EI): 240.1134 (240.1126 calcd for C\(_{14}\)H\(_{17}\)F\(_3\)O, M – H\(_2\)O).

\(\text{(E)-6-(4-Methoxyphenyl)-2-methylhex-5-en-2-ol (19).}\) General Procedure 3 was used for the conversion of \((E)\)-ethyl 5-(4-methoxyphenyl)pent-4-enoate\(^4\) (0.095 g, 0.04 mmol) to the title compound. This procedure afforded 0.059 g (66%) of the title compound as a white solid, m.p. 48 °C. This material was obtained as a >20:1 mixture of \(E:Z\) isomers as judged by \(^1\)H NMR analysis. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.24–7.21 (m, 2 H), 6.81–6.78 (m, 2 H), 6.32 (d, \(J = 15.8\) Hz, 1 H), 6.06 (dt, \(J = 6.8, 15.8\) Hz, 1 H), 3.76 (s, 3 H), 2.29–2.21 (m, 2 H), 1.63–1.57 (m, 2 H), 1.35 (s, 1 H), 1.22 (s, 6 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 158.7, 130.5, 129.2, 128.6, 126.9, 113.9, 70.9, 55.2, 43.3, 29.3, 27.9; IR (film, cm\(^{-1}\)) 3297, 2966, 1250; MS(ESI): 243.1372 (243.1361 calcd for C\(_{14}\)H\(_{20}\)O\(_2\), M + Na\(^+\)).

\(\text{(Z)-6-(4-Methoxyphenyl)-2-methylhex-5-en-2-ol (20).}\) General Procedure 3 was used for the conversion of \((Z)\)-ethyl 5-(4-methoxyphenyl)pent-4-enoate (0.45 g, 1.92 mmol) to the title compound. A second chromatoigraphic purification using silver impregnated silica gel provided the product as a >20:1 mixture of \(Z:E\) isomers as judged by \(^1\)H NMR analysis. This procedure afforded 0.42 g (86%) of the title compound as a colorless oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\)
7.22–7.17 (m, 2 H), 6.85–6.82 (m, 2 H), 6.34–6.30 (m, 1 H), 5.53 (dt, $J = 7.2$, 11.5 Hz, 1 H), 3.77 (s, 3 H), 2.42–2.34 (m, 2 H), 1.64–1.57 (m, 2 H), 1.41 (s, 1 H), 1.19 (s, 6 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 158.2, 131.0, 130.2, 129.8, 128.4, 113.6, 70.9, 55.2, 43.8, 29.2, 23.7; IR (film, cm$^{-1}$) 3364, 2968, 1250; MS(ESI): 243.1361 (243.1361 calcd for C$_{14}$H$_{20}$O$_2$, M + Na$^+$).

\[ \text{(E)-6-Cyclohexyl-2-methylhex-5-en-2-ol (21).} \]

General Procedure 3 was used for the conversion of (E)-ethyl 5-cyclohexylpent-4-enolate (0.26 g, 1.25 mmol) to the title compound. This procedure afforded 0.25 g (93%) of the title compound as a colorless oil. This material was obtained as a 20:1 mixture of E:Z isomers as judged by $^1$H NMR analysis. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.30–5.19 (m, 2 H), 2.32–2.24 (m, 1 H), 2.17–2.11 (m, 2 H), 1.74–1.59 (m, 6 H), 1.56–1.51 (m, 2 H), 1.35–1.12 (m, 9 H), 1.11–1.03 (m, 2 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 136.4, 127.7, 71.1, 44.0, 36.3, 33.3, 29.2, 26.0, 25.9, 22.5, 19.2; IR (film, cm$^{-1}$) 3362, 2923; MS(El): 178.1729 (178.1722 calcd for C$_{13}$H$_{24}$O, M – H$_2$O).

\[ \text{(Z)-6-Cyclohexyl-2-methylhex-5-en-2-ol (22).} \]

General Procedure 3 was used for the conversion of (Z)-ethyl 5-cyclohexylpent-4-enolate (1.46 g, 6.94 mmol) to the title compound. This procedure afforded 1.36 g (81%) of the title compound as a colorless oil. This material was obtained as a >20:1 mixture of E:Z isomers as judged by $^1$H NMR analysis. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.29–5.17 (m, 2 H), 2.31–2.22 (m, 1 H), 2.18–2.11 (m, 2 H), 1.73–1.58 (m, 6 H), 1.56–1.50 (m, 2 H), 1.34–1.12 (m, 9 H), 1.10–1.03 (m, 2 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 136.4, 127.7, 71.1, 44.0, 36.3, 33.3, 29.2, 26.0, 25.9, 22.5, 19.2; IR (film, cm$^{-1}$) 3362, 2923; MS(El): 178.1729 (178.1722 calcd for C$_{13}$H$_{24}$O, M – H$_2$O).
CDCl₃) δ 5.37–5.34 (m, 2 H), 2.07–2.00 (m, 2 H), 1.90–1.80 (m, 1 H), 1.71–1.59 (m, 5 H), 1.59–1.55 (m, 1 H), 1.52 (s, 1 H), 1.51–1.47 (m, 2 H), 1.28 (s, 1 H), 1.27–0.91 (m, 9 H); ^1^C NMR (100 MHz, CDCl₃) δ 136.7, 127.5, 71.1, 43.4, 40.6, 33.1, 29.2, 27.6, 27.5 26.2, 26.0; IR (film, cm⁻¹) 3358, 2924; MS(ESI): 197.1903 (197.1905 calcd for C₁₃H₂₄O, M + H⁺).

(E)-2-Methylpentadec-5-en-2-ol (23). General Procedure 3 was used for the conversion of (E)-ethyl tetradec-4-enoate (0.63 g, 2.46 mmol) to the title compound. This procedure afforded 0.44 g (75%) of the title compound as a colorless oil. This material was obtained as a >20:1 mixture of E:Z isomers as judged by ^1^H NMR analysis. ^1^H NMR (400 MHz, CDCl₃) δ 5.41–5.37 (m, 2 H), 2.08–2.01 (m, 2 H), 1.97–1.90 (m, 2 H), 1.66 (s, 1 H), 1.53–1.47 (m, 2 H), 1.34–1.20 (m, 14 H), 1.17 (s, 6 H), 0.85 (t, J = 6.6 Hz, 3 H); ^1^C NMR (100 MHz, CDCl₃) δ 130.6, 130.1, 70.9, 43.5, 32.5, 31.9, 29.6, 29.5, 29.3, 29.2, 29.1, 27.6, 22.6, 14.1 (one signal is missing due to incidental equivalence); IR (film, cm⁻¹) 3364, 2960; MS(ESI): 241.2521 (241.2531 calcd for C₁₆H₃₂O, M + H⁺).

(Z)-2-Methylpentadec-5-en-2-ol (24). General Procedure 3 was used for the conversion of (Z)-ethyl tetradec-4-enoate (0.29 g, 1.12 mmol) to the title compound. This procedure afforded 0.27 g (70%) of the title compound as a colorless oil. This material was obtained as a 20:1 mixture of E:Z isomers as judged by ^1^H NMR analysis. ^1^H NMR (400 MHz, CDCl₃) δ 5.36–5.28 (m, 2 H), 2.11–2.04 (m, 2 H), 2.03–1.94 (m, 2 H), 1.66 (s, br, 1 H), 1.50–1.44 (m, 2 H), 1.33–1.20 (m, 14
H), 1.18 (s, 6 H), 0.83 (t, J = 6.8 Hz, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 130.3, 129.4, 71.0, 43.6, 31.9, 29.6, 29.5, 29.4, 29.3, 29.2, 29.1, 27.1, 22.6, 22.3, 14.0; IR (film, cm$^{-1}$) 3367, 2924; MS(El): 222.2344 (222.2348 calcd for C$_{16}$H$_{32}$O, M – H$_2$O).

(E)-[6-(1,3-Dioxolan-2-yl)-2-methylhex-5-en-2-yloxy]trimethylsilane. An oven-dried flask equipped with a magnetic stirbar was cooled under a stream of nitrogen and charged with 2-vinyl-1,3-dioxolane (0.1 mL, 0.99 mmol), trimethyl(2-methylhex-5-en-2-yloxy)silane$^\text{vi}$ (0.186 g, 0.99 mmol), and CH$_2$Cl$_2$ (2.5 mL) was added. Solid 1,3-Bis(2,4,6-trimethylphenyl)-2-(imidazolidinylidene)(dichlorophenylmethylene)(tricyclohexylphosphine)ruthenium (Grubbs 2$^{\text{nd}}$ generation catalyst) (0.042 g, 0.05 mmol) was added and the mixture was heated to reflux overnight. The mixture was then cooled to rt and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel to afford 0.23 g (90%) of a yellow oil. This material was obtained as a 15:1 mixture of E:Z isomers as judged by $^1$H NMR analysis. Data are for the major isomer. $^1$H NMR (400 MHz, CDCl$_3$) δ 5.93 (dt, J = 6.7, 15.5 Hz, 1 H), 5.45 (tq, J = 1.6, 6.7 Hz, 1 H), 5.14 (d, J = 6.7 Hz, 1 H), 4.00–3.91 (m, 2 H), 3.89–3.83 (m, 2 H), 2.15–2.07 (m, 2 H), 1.52–1.45 (m, 2 H), 1.18 (s, 6 H), 0.05 (s, 9 H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 138.3, 125.8, 104.2, 73.5, 64.9, 43.4, 30.0, 27.0, 2.5; IR (film, cm$^{-1}$) 2970, 1249; MS(ESI): 281.1535 (281.1549 calcd for C$_{13}$H$_{26}$O$_3$Si, M + Na$^+$).
(E)-6-(1,3-Dioxolan-2-yl)-2-methylhex-5-en-2-ol (25). A flask equipped with a magnetic stirbar was purged with nitrogen and charged with (E)-[6-(1,3-dioxolan-2-yl)-2-methylhex-5-en-2-yloxy]trimethylsilane (0.27 g, 1 mmol) and THF (1 mL). The resulting solution was cooled to 0 °C then TBAF (3.18 mL, 3.18 mmol, 1M in THF) was added dropwise. The mixture was warmed to rt and stirred until the starting material had been completely consumed as judged by TLC analysis. The mixture was diluted with water (x mL) then extracted with ethyl acetate (2 x 20 mL). The combined organic layers were dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography on basic alumina to afford 0.197 g (81%) of the title compound as a colorless oil. This material was obtained as a 15:1 mixture of E:Z isomers as judged by ¹H NMR analysis. Data are for the major isomer. ¹H NMR (400 MHz, CDCl₃) δ 5.89 (dt, J = 6.7, 13.3 Hz, 1 H), 5.43 (tq, J = 0.4, 6.7 Hz, 1 H), 5.11 (d, J = 6.7 Hz, 1 H), 3.95–3.89 (m, 2 H), 3.85–3.77 (m, 2 H), 2.14–2.07 (m, 2 H), 1.54–1.47 (m, 4 H), 1.14 (s, 6 H); ¹³C NMR (100 MHz, CDCl₃) δ 137.7, 126.1, 104.0, 70.5, 64.8, 42.4, 29.2, 26.9; IR (film, cm⁻¹) 3391, 22968; MS(ESI): 209.1149 (209.1154 calcd for C₁₀H₁₈O₃, M + Na⁺).

(E)-Methyl 5-(1-hydroxycyclohexyl)pent-2-enoate. An oven-dried flask equipped with a magnetic stirbar was cooled under a stream of nitrogen and charged with methyl acrylate (0.29 mL, 3.24 mmol), 1-(but-3-enyl)cyclohexanol⁸ (0.1 g, 0.65 mmol), and CH₂Cl₂ (3.25 mL). Solid
1,3-Bis(2,4,6-trimethylphenyl)-2-(imidazolidinylidene)(dichlorophenylmethylene) (tricyclohexylphosphine)ruthenium (Grubbs 2nd generation catalyst) (28 mg, 0.032 mmol) was added and the reaction mixture was heated to reflux for 4 hours. The mixture was then cooled to rt and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel to afford 0.11 g (78%) of the title compound as a tan oil. This material was obtained as a 15:1 mixture of E:Z isomers as judged by $^1$H NMR analysis. Data are for the major isomer. $^1$H NMR (400 MHz, CDCl$_3$) δ 6.93 (dt, $J = 6.9, 15.7$ Hz, 1 H), 5.76 (dt, $J = 1.6, 15.7$ Hz, 1 H), 3.64 (s, 3 H), 2.27–2.20 (m, 2 H), 1.69–1.10 (m, 13 H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 167.1, 150.1, 120.5, 51.3, 40.3, 37.3, 26.0, 25.9, 25.7, 22.1; IR (film, cm$^{-1}$) 3482, 2931, 1725; MS(ESI): 235.1303 (235.1310 calcd for C$_{12}$H$_{20}$O$_3$, M + Na$^+$).

(E)-1-(5-Hydroxypent-3-en-1yl)cyclohexanol. An oven-dried flask equipped with a magnetic stirbar was cooled under a stream of nitrogen and charged with (E)-methyl 4-(1-hydroxycyclohexyl)pent-2-enoate (100 mg, 0.47 mmol) and THF (0.5 mL). The resulting solution was cooled to $-78$ °C, then DIBAL-H (1.97 mL, 1.97 mmol, 1M in THF) was added dropwise. The reaction mixture was stirred at $-78$ °C for one h, at which time TLC analysis indicated the starting material had been completely consumed. The reaction was quenched with 1M NaOH, and the solid precipitate was washed with EtOAc. The organic solutions were combined and washed with brine (1 x 5 mL), then dried over anhydrous Na$_2$SO$_4$, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel to yield 86 mg (73%) of the title compound as a colorless oil. This material was obtained as a 15:1
mixture of $E$:Z isomers. Data are for the major isomer. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.72–5.52 (m, 2 H), 4.02 (d, $J = 5.5$ Hz, 2 H), 2.14–2.05 (m, 2 H), 1.60–1.29 (m, 13 H), 1.27–1.15 (m, 1 H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 133.4, 128.9, 71.3, 63.6, 41.5, 37.4, 25.8, 25.7, 22.1; IR (film, cm$^{-1}$) 3350, 1456; MS(ESI): 207.1352 (207.1361 calcd for C$_{11}$H$_{20}$O$_2$, M + Na$^+$).

(\textit{E})-1-[5-(\textit{tert}-Butyldimethylsilyloxy)pent-3-en-1-yl]cyclohexanol (26). An oven-dried flask equipped with a magnetic stirbar was cooled under a stream of nitrogen and charged with (\textit{E})-1-\[4\text{-hydroxybut}-2\text{-enyl}]cyclohexanol (56 mg, 0.3 mmol) and DMF (0.3 mL). The solution was cooled to 0 °C then imidazole was added (25 mg, 0.3 mmol), followed by a solution of TBSCl (40 mg, 0.3 mmol) in DMF(0.3 mL). The mixture was warmed to rt and stirred overnight (ca 12 h). Water (x mL) was added to the reaction mixture, which was then extracted with ethyl acetate (2 x 20 mL). The combined organic layers were dried over anhydrous Na$_2$SO$_4$, filtered, and concentrated in vacuo. The product was then purified by flash chromatography on silica gel to yield 69 mg (79%) of the title compound as a colorless oil. This material was obtained as an 18:1 mixture of $E$:Z isomers. Data are for the major isomer. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.66–5.57 (m, 1 H), 5.56–5.44 (m, 1 H), 4.09–4.05 (m, 2 H), 2.12–2.04 (m, 2 H), 1.60–1.33 (m, 11 H), 1.28–1.15 (m, 2 H), 0.85 (s, 9 H), 0.02 (s, 6 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 131.4, 129.2, 71.3, 63.9, 42.6, 37.4, 25.9, 25.8, 22.2, 18.4, −5.1, (one signal is missing due to incidental equivalence); IR (film, cm$^{-1}$) 3392, 2930; MS(ESI): 321.2213 (321.2226 calcd for C$_{17}$H$_{34}$O$_2$Si, M + Na$^+$).
Synthesis of Tetrahydrofurans via Pd-Catalyzed Alkene Carboetherification

General Procedure 4: Palladium-Catalyzed Carboetherification Reactions for the Formation of Tetrahydrofurans. An oven or flame-dried Schlenk tube was cooled under a stream of nitrogen and charged with Pd$_2$(dba)$_3$ (2 mol% complex, 4 mol % Pd), S-Phos (4 mol %), NaOtBu (2.0 equiv), and the aryl bromide (2.0 equiv). The tube was purged with nitrogen and the alcohol substrate (1.0 equiv), and xylenes (0.25 M in substrate) were added. The mixture was heated to 140 °C with stirring until the starting material had been consumed as judged by GC or $^1$H NMR analysis. The mixture was cooled to room temperature, quenched with saturated aqueous NH$_4$Cl (2 mL), and diluted with ethyl acetate (10 mL). The layers were separated and the aqueous layer was extracted with ethyl acetate (3 X 10 mL). The combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The crude product was then purified by flash chromatography on silica gel.

(1'S*,5S*)-2,2-Dimethyl-5-(1-phenylethyl)tetrahydrofuran (13). The coupling of (Z)-2-methylhept-5-en-2-ol$^9$ (0.025 g, 0.20 mmol) with bromobenzene (0.041 mL, 0.4 mmol) was conducted following General Procedure 4. This procedure afforded 0.033 g (84%) of the title compound as an orange oil. This material was obtained as a 9:1 mixture of diastereomers as judged by $^1$H NMR analysis. Data are for the major isomer. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.32–7.27 (m, 3 H), 7.23–7.20 (m, 2 H), 4.08–4.02 (m, 1 H), 2.74 (p, $J = 7.1$ Hz, 1 H), 1.76–1.69 (m, 1 H), 1.66–1.54 (m, 3 H), 1.35 (d, $J = 7.2$ Hz, 3 H), 1.25 (s, 3 H), 1.22 (s, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 144.6, 128.1, 128.0, 126.2, 83.4, 80.6, 46.0, 38.2, 30.0, 29.1, 28.2, 18.8; IR (film, cm$^{-1}$) 2968, 1063; MS(ESI): 227.1408 (227.1412 calcd for C$_{14}$H$_{20}$O, M + Na$^+$).
(1'R*,5S*)-2,2-Dimethyl-5-(1-phenylethyl)tetrahydrofuran (14). The coupling of (E)-2-methylhept-5-en-2-ol\(^\theta\) (0.05 g, 0.39 mmol) with bromobenzene (0.082 mL, 0.78 mmol) was conducted following General Procedure 4. This procedure afforded 0.079 g (86%) of the title compound as an orange oil. This material was obtained as a 20:1 mixture of diastereomers as judged by \(^1\)H NMR analysis. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.33–7.25 (m, 4 H), 7.24–7.17 (m, 1 H), 4.19–4.13 (m, 1 H), 2.96–2.88 (m, 1 H), 1.90–1.81 (m, 1 H), 1.78–1.71 (m, 1 H), 1.70–1.61 (m, 1 H), 1.69–1.51 (m, 1 H), 1.30 (d, \(J = 7.2\) Hz, 3 H), 1.25 (s, 3 H), 1.21 (s, 3 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 144.1, 128.2, 128.0, 126.1, 82.6, 80.5, 44.0, 38.5, 28.7, 28.3, 28.0, 19.2; IR (film, cm\(^{-1}\)) 2968, 1046; MS(ESI): 227.1408 (227.1412 calcd for C\(_{14}\)H\(_{20}\)O, M + Na\(^+\)).

(1'R*,5S*)-2,2-Dimethyl-5-phenyl[(o-tolyl)methyl]tetrahydrofuran (27). The coupling of (E)-2-methyl-6-phenylhex-5-en-2-ol (0.025 g, 0.13 mmol) with 1-bromo-2-methylbenzene (0.031 mL, 0.26 mmol) was conducted following General Procedure 4. This procedure afforded 0.037 g (95%) of the title compound as a yellow oil. This material was obtained as a >20:1 mixture of diastereomers as judged by \(^1\)H NMR analysis. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.51 (d, \(J = 7.6\) Hz, 1 H), 7.27–7.16 (m, 6 H), 7.15–7.07 (m, 2 H), 4.72–4.66 (m, 1 H), 4.18 (d, \(J = 7.6\) Hz, 1 H), 2.20 (s, 3 H), 1.91–1.81 (m, 1 H), 1.79–1.73 (m, 1 H), 1.72–1.63 (m, 1 H), 1.57–1.49 (m, 1 H), 1.25 (s, 3 H), 1.20 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 141.9, 140.8, 136.8, 130.5, 129.2, 128.0, 127.3, 126.1, 126.0, 125.7, 80.7, 80.3, 53.0, 38.4, 30.9, 29.0, 28.1, 20.1; IR (film, cm\(^{-1}\)) 2967, 1489; MS(ESI): 303.1722 (303.1725 calcd for C\(_{20}\)H\(_{24}\)O, M + Na\(^+\)).
(1'R*,5S*)-2,2-Dimethyl-5-{phenyl[4-(trifluoromethyl)phenyl]methyl}tetrahydrofuran (28).

The coupling of (E)-2-methyl-6-phenylhex-5-en-2-ol (0.05 g, 0.26 mmol) with 1-bromo-4-(trifluoromethyl)benzene (0.074 mL, 0.52 mmol) was conducted following General Procedure 4. This procedure afforded 0.077 g (87%) of the title compound as a clear oil. This material was obtained as a >20:1 mixture of diastereomers as judged by $^1$H NMR analysis. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.56 (d, $J = 8.3$ Hz, 2 H), 7.50 (d, $J = 8.3$ Hz, 2 H), 7.34–7.22 (m, 5 H), 4.77–4.71 (m, 1 H), 4.02 (d, $J = 8.2$ Hz, 1 H), 1.95–1.88 (m, 1 H), 1.78–1.64 (m, 3 H), 1.30 (s, 3 H), 1.24 (s, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 147.0, 142.4, 129.3, (q, $J = 241.5$ Hz), 128.6, 128.45 (q, $J = 32.5$ Hz), 128.2, 126.7, 125.1 (q, $J = 3.9$ Hz), 81.5, 80.1, 57.3, 38.2, 31.3, 29.1, 28.3; IR (film, cm$^{-1}$) 2969, 1325; MS(ESI): 357.1438 (357.1442 calcd for C$_{20}$H$_{21}$F$_3$O, M + Na$^+$).

(1'S*,5S*)-2,2-Dimethyl-5-{phenyl[4-(trifluoromethyl)phenyl]methyl}tetrahydrofuran (29).

The coupling of (Z)-2-methyl-6-phenylhex-5-en-2-ol (0.025 g, 0.13 mmol) with 1-bromo-4-(trifluoromethyl)benzene (0.037 mL, 0.26 mmol) was conducted following General Procedure 4. This procedure afforded 0.035 g (80%) of the title compound as a clear oil. This material was obtained as a 9:1 mixture of diastereomers as judged by $^1$H NMR analysis. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.50 (d, $J = 8.4$ Hz, 2 H), 7.38 (d, $J = 8.4$ Hz, 2 H), 7.31–7.23 (m, 4 H), 7.21–7.16 (m,
1 H), 4.68 (q, $J = 7.2$ Hz, 1 H), 4.02 (d, $J = 7.2$ Hz, 1 H), 1.92–1.84 (m, 1 H), 1.70–1.59 (m, 2 H), 1.56–1.46 (m, 1 H), 1.24 (s, 3 H), 1.14 (s, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 147.4, 141.5, 129.1 (q, $J = 262.7$ Hz), 128.6, 128.3 (q, $J = 36.0$ Hz), 128.2, 126.5, 125.2 (q, $J = 3.8$ Hz), 81.3, 79.7, 56.6, 38.2, 30.9, 29.1, 28.9, 28.2, 28.1; IR (film, cm$^{-1}$) 2973, 1328; MS(ESI): 357.1431 (357.1442 calcd for C$_{20}$H$_{21}$F$_3$O, M + Na$^+$).

(1'R*,5S*)-2,2-Dimethyl-5-{naphthalen-2-yl[4-(trifluoromethyl)phenyl]methyl} tetrahydrofuran (30). The coupling of (E)-2-methyl-6-[4-(trifluoromethyl)phenyl]hex-5-en-2-ol (0.03 g, 0.12 mmol) with 2-bromonaphthalene (0.048 g, 0.23 mmol) was conducted following General Procedure 4. This procedure afforded 0.037 g (84%) of the title compound as a clear oil. This material was obtained as a >20:1 mixture of diastereomers as judged by $^1$H NMR analysis, but contained ca 2% of an unidentified impurity. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.84–7.78 (m, 3 H), 7.75 (d, $J = 8.5$ Hz, 1 H), 7.54 (d, $J = 8.5$ Hz, 2 H), 7.49–7.39 (m, 5 H), 4.83 (q, $J = 6.3$ Hz, 1 H), 4.22 (d, $J = 6.3$ Hz, 1 H), 2.01–1.93 (m, 1 H), 1.78–1.67 (m, 2 H), 1.59–1.52 (m, 1 H), 1.29 (s, 3 H), 1.18 (s, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 147.0, 139.0, 133.4, 132.3, 130.1, 129.2 (q, $J = 52.0$ Hz), 127.9, 127.8 (q, $J = 225.2$), 127.7, 127.6, 127.5, 125.9, 125.6, 125.2 (q, $J = 3.8$ Hz), 81.4, 79.7, 56.7, 38.2, 31.0, 28.9, 28.1; IR (film, cm$^{-1}$) 2969, 1325; MS(ESI): 407.1600 (407.1599 calcd for C$_{24}$H$_{23}$F$_3$O, M + Na$^+$).
(1'S*,5R*)-2,2-Dimethyl-5-{2-phenyl-1-[4-(trifluoromethyl)phenyl]allyl}tetrahydrofuran (31). The coupling of (E)-2-methyl-6-[4-(trifluoromethyl)phenyl]hex-5-en-2-ol (0.03 g, 0.12 mmol) with α-bromostyrene (0.035 mL, 0.23 mmol) was conducted following General Procedure 4. This procedure afforded 0.025 g (62%) of the title compound as an amber oil. This material was obtained as a >20:1 mixture of diastereomers as judged by $^1$H NMR analysis. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.47 (d, $J = 8.1$ Hz, 2 H), 7.35 (d, $J = 8.1$ Hz, 2 H), 7.29–7.27 (m, 2 H), 7.24–7.18 (m, 3 H), 5.55 (s, 1 H), 5.45 (s, 1 H), 4.55 (q, $J = 7.3$ Hz, 1 H), 4.02 (d, $J = 7.3$ Hz, 1 H), 1.81–1.74 (m, 1 H), 1.69–1.60 (m, 2 H), 1.50–1.44 (m, 1 H), 1.28 (s, 3 H), 1.23 (s, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 148.5, 133.9, 129.3, 128.1 (q, $J = 253.1$ Hz), 128.9, 127.4, 127.2 (q, $J = 65$ Hz), 126.8, 124.9 (q, $J = 3.8$ Hz), 114.7, 79.7, 69.0, 55.7, 38.3, 30.3, 28.9, 28.0, 19.3; IR (film, cm$^{-1}$) 2968, 1324; MS(EI): 360.1709 (360.1701 calcd for C$_{22}$H$_{23}$F$_3$O, M$^+$).

(1'S*,5S*)-2,2-Dimethyl-5-{naphalen-2-yl[4-(trifluoromethyl)phenyl]methyl}tetrahydrofuran (32). The coupling of (Z)-2-methyl-6-[4-(trifluoromethyl)phenyl]hex-5-en-2-ol (0.03 g, 0.12 mmol) with 2-bromonaphthalene (0.048 g, 0.23 mmol) was conducted following
General Procedure 4. This procedure afforded 0.042 g (94%) of the title compound as a clear oil. This material was obtained as a >20:1 mixture of diastereomers as judged by $^1$H NMR analysis. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.83–7.77 (m, 2 H), 7.76 (d, $J = 8.3$ Hz, 2 H), 7.55–7.50 (m, 2 H), 7.50–7.43 (m, 3 H), 7.31 (dd, $J = 1.9$, 8.3 Hz, 1 H), 4.85–4.80 (m, 1 H), 4.15 (d, $J = 8.1$ Hz, 1 H), 1.94–1.86 (m, 1 H), 1.80–1.62 (m, 3 H), 1.30 (s, 3 H), 1.24 (s, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 146.8, 139.9, 133.4, 132.3, 129.3 (q, $J = 49.6$ Hz), 128.3, 127.8 (q, $J = 230.1$ Hz), 127.6, 127.1, 126.9, 126.2, 125.8, 125.1 (q, $J = 3.7$ Hz), 81.6, 80.0, 57.3, 38.3, 31.4, 29.2, 19.0, 18.9 (one carbon signal is absent due to incidental equivalence; IR (film, cm$^{-1}$) 2969, 1326; MS(ESI): 407.1597 (407.1599 calcd for C$_{24}$H$_{23}$F$_{3}$O, M + Na$^+$).

(1'R*,5S*)-5-(3,5-Dichlorophenyl)(4-methoxyphenyl)methyl-2,2-dimethyltetrahydrofuran (33). The coupling of (E)-6-(4-methoxyphenyl)-2-methylhex-5-en-2-ol (0.02 g, 0.09 mmol) with 1-bromo-3,5 dichlorobenzene (0.041 g, 0.18 mmol) was conducted following General Procedure 4. This procedure afforded 0.017 g (52%) of the title compound as a clear oil. This material was obtained as a >20:1 mixture of diastereomers as judged by $^1$H NMR analysis. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.16 (d, $J = 1.7$ Hz, 2 H), 7.12 (t, $J = 2.4$ Hz, 1 H), 7.11–7.07 (m, 2 H), 6.81–6.76 (m, 2 H), 4.53 (q, $J = 7.2$ Hz, 1 H), 3.77–3.73 (m, 4 H), 1.88–1.76 (m, 1 H), 1.67–1.52 (m, 3 H), 1.21 (s, 3 H), 1.15 (s, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 158.3, 146.4, 134.3, 134.0, 129.4,
127.5, 126.2, 113.9, 81.5, 80.0, 56.0, 55.2, 38.1, 31.2, 29.0, 28.1; IR (film, cm$^{-1}$) 2968, 1511;
MS(ESI): 387.0906 (387.0895 calcd for C$_{20}$H$_{22}$Cl$_2$O$_2$ M + Na$^+$).

(1'S*,5'S*)-5-(3,5-Dichlorophenyl)(4-methoxyphenyl)methyl-2,2-dimethyltetrahydrofuran (34). The coupling of (Z)-6-(4-methoxyphenyl)-2-methylhex-5-en-2-ol (0.027 g, 0.123 mmol) with 1-bromo-3,5 dichlorobenzene (0.055 g, 0.24 mmol) was conducted following General Procedure 4. This procedure afforded 0.037 g (69%) of the title compound as a clear oil. This material was obtained as a $\geq$20:1 mixture of diastereomers as judged by $^1$H NMR analysis. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.17–7.11 (m, 5 H), 6.82–6.78 (m, 2 H), 4.53 (q, $J$ = 7.4 Hz, 1 H), 3.83 (d, $J$ = 7.4 Hz, 1 H), 3.74 (s, 3 H), 1.93–1.82 (m, 1 H), 1.67–1.54 (m, 2 H), 1.49–1.38 (m, 1 H), 1.20 (s, 3 H), 1.11 (s, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 158.2, 147.0, 134.5, 132.8, 130.0, 127.2, 126.3, 113.6, 81.3, 79.6, 55.3, 55.1, 38.1, 30.7, 28.8, 28.0; IR (film, cm$^{-1}$) 2969, 1512; MS(ESI): 387.1600 (387.0901 calcd for C$_{20}$H$_{22}$Cl$_2$O$_2$, M + Na$^+$).
(1'R*,5S*)-5-[Cyclohexyl(m-tolyl)methyl]-2,2-dimethyltetrahydrofuran (35). The coupling of (E)-6-cyclohexyl-2-methylhex-5-en-2-ol (0.025 g, 0.127 mmol) with 3-bromotoluene (0.031 mL, 0.26 mmol) was conducted following General Procedure 4. This procedure afforded 0.034 g (94%) of the title compound as a clear oil. This material was obtained as a >20:1 mixture of diastereomers as judged by 1H NMR analysis. 1H NMR (400 MHz, CDCl3) δ 7.08 (t, J = 7.4 Hz, 1 H), 7.05–7.03 (m, 1 H), 7.00–6.93 (m, 2 H), 4.42–4.36 (m, 1 H), 2.28 (s, 3 H), 2.18–2.12 (m, 1 H), 2.11–2.03 (m, 1 H), 1.85–1.66 (m, 3 H), 1.60–1.42 (m, 4 H), 1.38–1.26 (m, 3 H), 1.17–1.04 (m, 8 H), 0.98–0.87 (m, 1 H), 0.72–0.60 (m, 1 H); 13C NMR (100 MHz, CDCl3) δ 141.3, 136.5, 131.1, 127.5, 127.0, 126.5, 80.2, 77.3, 56.3, 39.3, 38.1, 32.2, 31.4, 29.8, 28.4, 27.8, 26.7, 26.3, 26.2, 21.5; IR (film, cm⁻¹) 2923, 1738; MS(ESI): 309.2193 (309.2194 calcd for C20H30O, M + Na⁺).

(1'S*,5S*)-5-[Cyclohexyl(m-tolyl)methyl]-2,2-dimethyltetrahydrofuran (36). The coupling of (Z)-6-cyclohexyl-2-methylhex-5-en-2-ol (0.05 g, 0.26 mmol) with 3-bromotoluene (0.062 mL, 0.50 mmol) was conducted following General Procedure 4. This procedure afforded 0.016 g (22%) of the title compound as an amber oil. This material was obtained as a 2:1 mixture of diastereomers as judged by 1H NMR analysis, and was contaminated with ca. 15% of an unidentified side product. Carbon NMR data are not reported due to the complexity of the
mixture. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.15–7.00 (m, 2 H), 6.96–6.85 (m, 2 H), 4.38–4.33 (m, 1 H), 2.88–2.79 (m, 1 H), 2.24 (s, 3 H), 2.20–2.14 (m, 2 H), 2.14–2.05 (m, 2 H), 1.74–1.59 (m, 3 H), 1.59–1.45 (m, 2 H), 1.31–1.21 (m, 6 H), 1.14–1.00 (m, 6 H); IR (film, cm$^{-1}$) 2921, 1446; MS(ESI): 309.2196 (309.2194 calcd for C$_{20}$H$_{30}$O, M + Na$^+$).

(1$^{R*}$,5$^{S*}$)-5-[1-(3-Methoxyphenyl)decyl]-2,2-dimethyltetrahydrofuran (37). The coupling of (E)-2-methylpentadec-5-en-2-ol (0.025 g, 0.104 mmol) with 3-bromoanisole (0.026 mL, 0.21 mmol) was conducted following General Procedure 4. This procedure afforded 0.036 g (92%) of the title compound as a clear oil. This material was obtained as a >20:1 mixture of diastereomers as judged by $^1$H NMR analysis. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.20 (t, $J$ = 8.3 Hz, 1 H), 6.85–6.81 (m, 2 H), 6.77–6.74 (m, 1 H), 4.18–4.13 (m, 1 H), 3.81 (s, 3 H), 2.68–2.62 (m, 1 H), 1.90–1.82 (m, 1 H), 1.76–1.64 (m, 3 H), 1.63–1.56 (m, 1 H), 1.47–1.41 (m, 1 H), 1.34–1.10 (m, 20 H), 0.88 (t, $J$ = 6.8 Hz, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 159.2, 114.1, 128.7, 121.8, 115.0, 111.2, 82.0, 80.4, 55.1, 50.5, 38.4, 31.9, 31.3, 29.8, 29.6, 29.5, 29.3, 28.9, 28.7, 28.0, 27.7, 22.7, 14.1; IR (film, cm$^{-1}$) 2968, 1512; MS(ESI): 369.2757 (369.2770 calcd for C$_{23}$H$_{38}$O$_2$, M + Na$^+$).

(1$^{S*}$,5$^{S*}$)-5-[1-(3-Methoxyphenyl)decyl]-2,2-dimethyltetrahydrofuran (38). The coupling of (Z)-2-methylpentadec-5-en-2-ol (0.029 g, 0.120 mmol) with 3-bromoanisole (0.030 mL, 0.24
mmol) was conducted following General Procedure 4. This procedure afforded 0.018 g (43%) of the title compound as an orange oil. This material was obtained as a 4:1 mixture of diastereomers as judged by $^1$H NMR analysis. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.18 (t, $J = 7.8$ Hz, 1 H), 6.76–6.68 (m, 3 H), 4.05–3.97 (m, 1 H), 3.81–3.76 (m, 4 H), 2.52–2.44 (m, 1 H), 2.03–1.91 (m, 1 H), 1.70–1.45 (m, 6 H), 1.26–1.15 (m, 18 H), 0.89–0.83 (m, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 159.4, 144.6, 128.9, 114.5, 111.0, 82.8, 80.8, 55.1, 52.6, 38.2, 32.8, 31.9, 30.3, 29.3, 29.6, 29.5, 29.3, 29.2, 28.3, 27.5, 22.6, 14.1; IR (film, cm$^{-1}$) 2924, 1456; MS(ESI): 369.2769 (369.2770 calcd for C$_{23}$H$_{38}$O$_2$, M + Na$^+$).

(1'R*,5S*)-2-[(5,5-Dimethyltetrahydrofuran-2-yl)(6-methoxynaphthalen-2-yl)methyl]-1,3-dioxolane (39). The coupling of (E)-6-(1,3-dioxolan-2-yl)-2-methylhex-5-en-2-ol (0.025 g, 0.13 mmol) with 2-bromo-6-methoxy-naphthalene (0.064 g, 0.27 mmol) was conducted following General Procedure 4. This procedure afforded 0.023 g (50%) of the title compound as an orange solid. m.p. 92 °C. This material was obtained as a >20:1 mixture of diastereomers as judged by $^1$H NMR analysis. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.73–7.64 (m, 3 H), 7.47 (dd, $J = 2.2$, 8.3 Hz, 1 H), 7.11–7.07 (m, 2 H), 5.40 (d, $J = 8.6$ Hz, 1 H), 4.62–4.56 (m, 1 H), 3.98–3.84 (m, 6 H), 3.82–3.72 (m, 1 H), 2.88 (dd, $J = 2.2$, 8.3 Hz, 1 H), 2.04–1.92 (m, 1 H), 1.65–1.56 (m, 1 H), 1.55–1.46 (m, 1 H), 1.18 (s, 3 H), 1.171–1.10 (m, 1 H), 1.06 (s, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 157.3, 133.7, 132.7, 129.4, 129.2, 129.0, 128.7, 126.0, 118.5, 105.5, 105.2, 81.2, 77.8, 65.1, 55.3, 54.6,
38.0, 29.7, 28.4, 27.8, 19.1; IR (film, cm$^{-1}$) 2965, 1646, 1540; MS(ES): 365.1718 (365.1729 calcd for C$_{21}$H$_{26}$O$_4$, M + Na$^+$).

(1'R*,2S*)-2-[(Biphenyl-3-yl)-2-(-1-oxaspiro[4.5]decan-2-yl)ethoxy](tert-butyl)dimethylsilane (40). The coupling of (E)-1-(4-(tert-butyldimethylsilyloxy)but-2-enyl)cyclohexanol (0.028 g, 0.10 mmol) with 3-bromo-biphenyl (0.046 mL, 0.20 mmol) was conducted following General Procedure 4. This procedure afforded 0.040 g (90%) of the title compound as a clear oil. This material was obtained as a 12:1 mixture of diastereomers as judged by $^1$H NMR analysis. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.59–7.55 (m, 2 H), 7.53–7.50 (m, 1 H), 7.44–7.37 (m, 3 H), 7.33–7.24 (m, 3 H), 4.40–4.34 (m, 1 H), 4.03 (dd, $J$ = 7.8, 9.8 Hz, 1 H), 3.83 (dd, $J$ = 6.1, 12.2 Hz, 1 H), 2.89–2.78 (m, 1 H), 1.88–1.80 (m, 1 H), 1.66–1.50 (m, 6 H), 1.46–1.35 (m, 3 H), 1.34–1.20 (m, 4 H), 0.83 (s, 9 H), 0.00 (s, 3 H), -0.05 (s, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 141.6, 140.8, 140.3, 128.8, 128.6, 128.5, 127.9, 127.1, 126.9, 125.1, 82.0, 77.3, 65.2, 52.8, 38.1, 37.4, 29.1, 25.9, 25.8, 24.0, 23.7, 18.3, -5.4, -5.5; IR (film, cm$^{-1}$) 2928, 1093; MS(ESI): 473.2862 (473.2852 calcd for C$_{29}$H$_{42}$O$_2$Si, M + Na$^+$).

(E)-(1'R*,4S*,5S*)-2,2,4-Trimethyl-5-(4-phenylbut-3-en-2-yl)tetrahydrofuran (42). The coupling of (E)-2,4-dimethylhept-5-en-2-ol$^{10}$ (0.025 g, 0.18 mmol) with β-bromostyrene (0.045 mL, 0.35 mmol) was conducted following General Procedure 4. This procedure afforded 0.043 g
(92%) of the title compound as an orange oil. This was obtained as a 12:1 mixture of diastereomers, as judged by $^1$H NMR analysis. Characterization data were identical to those previously reported in the literature.$^{10}$

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\text{(1'R*,2S*,5S*)-2-Methyl-2-phenyl-5-{[4-(trifluoromethyl)phenyl]ethyl}tetrahydrofuran (46).}
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The coupling of (E)-2-phenylhept-5-en-2-ol$^{10}$ (0.03 g, 0.16 mmol) with 4-bromobenzotrifluoride (0.044 mL, 0.32 mmol) was conducted following General Procedure 4. This procedure afforded 0.05 g (93%) of the title compound as a clear oil. This material was obtained as a 20:1 mixture of diastereomers as judged by $^1$H NMR analysis. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.60 (s, 1 H), 7.47 (d, $J = 7.2$ Hz, 2 H), 7.42–7.37 (m, 1 H), 7.31–7.24 (m, 4 H), 7.20–7.14 (m, 1 H), 4.14–4.07 (m, 1 H), 3.00–2.91 (m, 1 H), 2.18–2.09 (m, 1 H), 1.85–1.74 (m, 2 H), 1.70–1.58 (m, 1 H), 1.38 (s, 3 H), 1.35 (d, $J = 7.2$ Hz, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 148.6, 145.1, 132.0 (q, $J = 32.6$ Hz), 128.3, 128.1 (q, $J = 252.4$ Hz), 125.0 (q, $J = 3.7$ Hz), 124.6, 123.0, 84.4, 82.3, 67.0, 44.5, 39.1, 29.3, 18.0; IR (film) 2957, 1327; MS(ESI): 357.1434 (357.1442 calcd for C$_{20}$H$_{21}$F$_3$O, M + Na$^+$).

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\text{(1'S*,2S*,5S*)-2-methyl-2-phenyl-5-{[4-(trifluoromethyl)phenyl]ethyl}tetrahydrofuran (47).}
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The coupling of (Z)-2-phenylhept-5-en-2-ol$^{10}$ (0.03 g, 0.16 mmol) with 4-bromo-
benzotrifluoride (0.044 mL, 0.32 mmol) was conducted following General Procedure 4. This procedure afforded 0.05 g (94%) of the title compound as a clear oil. This material was obtained as a 7:1 mixture of diastereomers as judged by $^1$H NMR analysis. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.58 (s, 1 H), 7.54–7.47 (m, 2 H), 7.46–7.41 (m, 3 H), 7.38–7.33, (m, 2 H), 7.28–7.22 (m, 1 H), 4.13 (q, $J = 6.8$ Hz, 1 H), 3.03 (p, $J = 7.1$ Hz, 1 H), 2.17–2.11 (m, 1 H), 1.86–1.79 (m, 1 H), 1.70–1.59 (m, 2 H), 1.48 (s, 3 H), 1.47 (d, $J = 7.1$ Hz, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 148.6, 145.2, 131.4 (q, $J = 31.5$ Hz), 128.7, 128.8 (q, $J = 225.0$ Hz), 125.0 (q, $J = 3.9$ Hz), 124.7, 123.1, 84.7, 82.9, 45.0, 39.1, 30.6, 29.3, 18.1; IR (film, cm$^{-1}$) 2971, 1326; MS(ESI): 357.1456 (357.1442 calcd for C$_{20}$H$_{21}$F$_3$O, M + Na$^+$).

(1'R*,3S*,2S*)-Phenyl-{4-[1-(3,5,5-trimethyltetrahydrofuran-2-yl)ethyl]phenyl}methanone (48). The coupling of (E)-2,4-dimethylhept-5-en-2-ol$^{10}$ (0.03 g, 0.21 mmol) with 4-bromo-benzophenone (0.11 g, 0.42 mmol) was conducted following General Procedure 4. This procedure afforded 0.059 g (86%) of the title compound as a clear oil. This material was obtained as a 20:1 mixture of diastereomers as judged by $^1$H NMR analysis material. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.79–7.75 (m, 2 H), 7.74–7.70 (m, 2 H), 7.58–7.52 (m, 1 H), 7.48–7.42 (m, 2 H), 7.40–7.36 (m, 2 H), 3.66–3.62 (m, 1 H), 2.99–2.91 (m, 1 H), 1.80–1.72 (m, 2 H), 1.42–1.36 (m, 4 H), 1.24 (s, 3 H), 0.95 (s, 3 H), 0.91 (d, $J = 6.1$ Hz, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 148.7, 137.9, 135.4, 132.0, 129.9, 129.7, 128.9, 128.1, 88.8, 79.2, 48.1, 48.0, 42.2, 36.2, 29.4, 29.2, 18.5, 16.8; IR (film, cm$^{-1}$) 2930, 1653; MS(ESI): 345.1826 (345.1830 calcd for C$_{22}$H$_{26}$O$_2$, M + Na$^+$).
(1’R*,3S*,5S*)-2,2,3-Trimethyl-5-(1-p-tolyethyl)tetrahydrofuran (49). The coupling of (E)-2,4-dimethylhept-5-en-2-ol\textsuperscript{10} (0.025 g, 0.18 mmol) with 4-bromotoluene (0.043 mL, 0.35 mmol) was conducted following General Procedure 4. This procedure afforded 0.033 g (85%) of the title compound as a clear oil. This material was obtained as a 4:1 mixture of diastereomers (epimeric at C3) as judged by \textsuperscript{1}H NMR analysis. \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 7.13–7.04 (m, 4 H), 3.98 (p, \(J = 5.9\) Hz, 1 H), 2.86–2.76 (m, 1 H), 2.28 (s, 3 H), 1.98–1.89 (m, 1 H), 1.58–1.50 (m, 1 H), 1.46–1.36 (m, 1 H), 1.19 (d, \(J = 7.0\) Hz, 3 H), 1.16 (s, 3 H), 0.93 (s, 3 H), 0.87 (d, \(J = 6.8\) Hz, 3 H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\) 135.6, 135.4, 129.5, 128.7, 85.4, 79.3, 48.2, 40.2, 38.6, 29.6, 29.4, 21.0, 18.9, 16.7; IR (film, cm\textsuperscript{-1}) 2967, 1064; MS(ESI): 241.1565 (241.1568 calcd for C\textsubscript{16}H\textsubscript{24}O, M + Na\textsuperscript{+}).

(1’R*,3S*,5S*)-3,5,5-Trimethyltetrahydrofuran-2-yl(ethyl)pyridine (50). The coupling of (E)-2,4-dimethylhept-5-en-2-ol\textsuperscript{10} (0.02 g, 0.14 mmol) with 4-bromopyridine HCl (0.55 g, 0.28 mmol) was conducted following General Procedure 4 except using 4 equiv of NaOrBu. This procedure afforded 22 mg (71%) of the title compound as an amber oil. This was obtained as a 15:1 mixture of diastereomers (epimeric at C3) as judged by \textsuperscript{1}H NMR analysis material. \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 8.40 (d, \(J = 5.3\) Hz, 2 H), 7.17–7.15 (m, 2 H), 3.57 (dd, \(J = 3.7, 9.0\) Hz, 1 H), 2.84–2.76 (m, 1 H), 1.77–1.63 (m, 2 H), 1.40–1.35 (m, 1 H), 1.32 (d, \(J = 7.3\) Hz, 3 H), 1.20 (s, 3 H), 0.91 (s, 3 H), 0.88 (d, \(J = 6.4\) Hz, 3 H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\) 149.1,
149.0, 124.4, 88.2, 47.9, 41.8, 36.3, 29.3, 29.2, 18.1, 16.7; IR (film, cm\(^{-1}\)) 2965, 1598; MS(ESI): 220.1707 (220.1701 calcd for C\(_{14}\)H\(_{21}\)NO, M + H\(^{+}\)).

References