Aldol Synthesis by anti-Markovnikov Hydration of Propargyloxy Substrates: Feasibility, Stereospecificity, and Reiterative Alkynylation/Hydration

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General

Abbreviations

aq = aqueous solution; Arl = aryl group; CC = column chromatography (performed on SiO₂); Cp = \( \eta^5-C_5H_5 \); dppm = 1,1-bis(diphenylphosphinomethane; Ind = indenyl, \( C_9H_7 \); \( ^{2,4,6} \text{Ph}_3C_6H_2PyPPh_2 \) = 6-(2,4,6-triphenylphenyl)-2-diphenylphosphinopyridine; sat. = saturated; \( p \text{Ts} \) = para-toluenesulfonyl.

Characterization

NMR: All chemical shifts are given in \( \delta/\text{ppm} \) (coupling constants \( J/\text{Hz} \)) referenced relative to tetramethylsilane = 0 ppm, either internally or via solvent signals.

IR: Wavenumbers are given in \( \text{cm}^{-1} \), relative intensity of signals given (s = strong, m = medium, w = weak).

M.p. “Corrected values” (digital thermometer reading, metal block heating).

Materials

CpRuCl(dppm), \(^1 \) \( \eta^5 \text{-IndRuCl(PPh}_3)_2 \), \(^2 \) \( ^{2,4,6} \text{Ph}_3C_6H_2PyPPh_2 \). \(^3 \) The complexes CpRu\((L)_2(\text{MeCN})\)PF\(_6\) were prepared in situ as earlier described, followed by washing with hexanes and drying. \(^3 \)

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1. Ruthenium-catalyzed hydrative decarbonylation of a propargyl acetate

4-Acetoxy-3-methoxy-benzaldehyde: In a dried round-bottom flask, a solution of vanilline (305 mg, 2.0 mmol), Ac₂O (348 mg, 3.4 mmol) and DMAP (49 mg, 0.4 mmol) in EtOAc (3 mL) was stirred at room temperature for 1 h. After completion (TLC control), the reaction was quenched by addition of tBuOMe (5 mL) and H₂O (3 mL). The organic phase was washed with water (5 mL), aq HCl (2 M, 3 mL) and sat. aq NaHCO₃ (5 mL). The organic layer was dried over MgSO₄. Removal of the solvent under reduced pressure afforded the product (320 mg, 83% yield) as white crystals.

M.p. 85–86 °C. ¹H NMR (300 MHz, CDCl₃): 1.19 (s, 3 H, Me), 2.34 (s, 3 H, MeO), 7.18–7.26 (m, 1 H Arl), 7.43–7.53 (m 2 H Arl), 9.94 (s, 1 H, CHO). ¹³C NMR (75 MHz, CDCl₃): 20.6, 56.0, 110.8, 123.4, 124.6, 135.2, 144.9, 151.9, 168.3, 191.0. IR (KBr): ν = 2967w, 2944w, 2846m, 1754s, 1689s, 1597s, 1508s, 1497s, 1378s, 1208s, 1211s, 1152s, 737s cm⁻¹. MS (EI, 70 eV): m/z (%) = 194 (6) M⁺, 177 (4), 152 (100), 136 (3), 123 (6), 108 (7), 91 (90). Anal calcd for C₁₀H₁₀O₄ (194.18): C 61.85, H 5.19; found C 61.69, H 5.29.

3-(4-Acetoxy-3-methoxyphenyl)-1-propyn-3-ol: In a dried round-bottom Schlenk flask under an inert atmosphere of argon, ethynylmagnesium chloride⁴ (30 mmol, 0.72 M in THF) was added dropwise to a solution of 4-acetoxy-3-methoxy-benzaldehyde (1.94 g, 10.0 mmol) in anhydrous THF (15 mL) at −10 °C with stirring. The mixture was stirred for 1 h and quenched with sat. aq NH₄Cl (20 mL) and extracted with tBuOMe (2×30 mL). The combined organic layers were washed with H₂O (40 mL) and dried over MgSO₄. Removal of the solvent under reduced pressure and purification by CC (tBuOMe/hexanes 1:4) gave yellowish oil (1.84 g, 84%).

1H NMR (300 MHz, CDCl3): 2.33 (s, 3 H, OAc), 2.70 (d, J = 2.3, 1 H_alkyne), 3.28 (br s, 1 H, OH), 3.84 (s, 3 H, OMe), 5.41 (br s, 1 H-3), 7.04 (d, J = 8.1 Hz, 1 H_Ar), 7.12 (dd, J = 8.1, 2.0 Hz, 1 H_Ar), 7.19 (d, J = 2.0 Hz, 1 H_Ar). 13C NMR (75 MHz, CDCl3): 20.7, 26.9, 55.9, 63.8, 74.9, 83.4, 110.8, 118.9, 122.7, 139.2, 151.1, 169.4. IR (KBr): 3282s, 3013s, 2942s, 2879m, 1762s, 1509s, 1420s, 1373s, 1150s, 1029s, 863s, 673s. MS (EI, 70 eV): m/z (%) = 220 (14) M^+, 178 (100), 161 (21), 146 (25), 135 (4), 125 (11), 118 (5), 107 (3), 93 (3).

3-Acetoxy-3-(4-acetoxy-3-methoxyphenyl)-1-propyne (1): In a dried round-bottom flask, a solution of 3-(4-acetoxy-3-methoxyphenyl)-1-propyn-3-ol (220 mg, 1.0 mmol), Ac_2O (189 mg, 1.85 mmol) and pyridine (0.3 mL) in EtOAc (1.5 mL) was stirred at room temperature for 4 h. After completion (TLC control), the reaction was quenched with tBuOMe (5 mL) and H_2O (3 mL). The organic phase was washed with water (5 mL), aq 2 M HCl (3 mL) and sat. aq NaHCO_3 (5 mL). The organic layer was dried over MgSO_4. Removal of the solvent under reduced pressure afforded the product (255 mg, 98%) as light brown solid. M.p. 92–93 °C. 1H NMR (400 MHz, CDCl3): 2.11 (s, 3 H, OAc), 2.31 (s, 3 H, OAc), 2.67 (d, J = 2.3 Hz, 1 H_alkyne), 3.86 (s, 3 H, OMe), 6.43 (d, J = 2.3 Hz, 1 H-3), 7.04 (d, J = 8.0 Hz, 1 H_Ar), 7.10–7.15 (m, 2 H_Ar). 13C NMR (100 MHz, CDCl3): 20.6, 20.9, 55.8, 64.8, 75.4, 79.9, 111.8, 120.1, 122.7, 134.9, 140.0, 150.9, 168.5, 169.3. IR (KBr): 3232s, 2943m, 2120w, 1735s, 1606m, 1514m, 1369s, 1291s, 1233s, 1156s, 1014s, 779s. MS (EI, 70 eV): m/z (%) = 262 (16) M^+, 220 (67), 178 (30), 160 (100), 146 (8), 118 (3), 89 (4). Anal calcd for C_{14}H_{14}O_5 (262.26): C 64.12, H 5.38; found: C 63.97, H 5.40.

4-Acetoxy-3-methoxy-styrene (2): A dried round-bottom Schlenk flask was charged with CpRuCl(dppm) (5 mol %) under argon. To this was added 1 (131 mg, 0.50 mmol), H_2O (0.4 mL) and acetone (1.5 mL). The mixture was heated to 70 °C for 36 h. After completion of the reaction (TLC control), the solution was allowed to cool to room
temperature and 1BuOMe (2 mL) and H2O (2 mL) were added. The organic layer was washed with water (2 mL), brine (3 mL), and dried over MgSO4. After evaporation of the solvent, purification by CC (1BuOMe/hexanes 1:4) gave a slightly brown solid (79 mg, 83% yield). For results obtained with other solvents, see Table S1.

Known compound, CAS: 46316-15-8. 1H NMR (300 MHz, CDCl3): 2.30 (s, 3 H, OAc), 3.83 (s, 3 H, OMe), 5.23 (dd, J = 10.8, 0.8 Hz, 1 HAlkene), 5.68 (dd, J = 17.5, 0.8 Hz, 1 HAlkene), 6.67 (dd, J = 17.5, 10.9 Hz, 1 HAlkene), 6.95–7.02 (m, 3 HAr). 13C NMR (75 MHz, CDCl3): 20.7, 55.8, 109.9, 114.1, 118.9, 122.8, 136.3, 136.7, 139.4, 151.1, 169.1. IR (KBr): 3232s, 2943m, 2120w, 1735s, 1606m, 1514m, 1369s, 1291s, 1233s, 1156s, 1014s, 779s. Analytical data agree with literature values.5

Table S1  Solvent screening for the ruthenium-catalyzed hydrative decarbonylation

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<th>Yield [%]</th>
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2. Catalytic hydration of secondary propargyl alcohols

*Representative procedure*: (±)-1-Octyn-3-ol (17 mg, 0.135 mmol) and 12 µL H₂O (0.67 mmol, 5 equiv) were added to a solution of [CpRu(2,4,6-Ph₃C₆H₂PyPPh₂)₂(MeCN)]PF₆ (20 mg, 0.0134 mmol, 10 mol %)³ in acetone-ｄ₆ (1 mL) in a glass vial. The yellow solution was transferred into an NMR tube and degassed by bubbling argon through the solution. The sample was set aside at the desired temperature and analyzed by NMR spectroscopy:

¹H NMR (400 MHz, acetone-ｄ₆):

1-Butyn-3-ol (3a): 1.36 (d, J = 6.6 Hz, 3 H, Me), 2.79 (d, J = 2.1 Hz, 1 Hₐₗkyn), 4.36 (d, J = 5.5 Hz, 1 H, OH), 4.44 (qdd, J = 6.6, 5.5, 2.1 Hz, 1 H₃).

3-Hydroxybutanal (4a): 1.21 (d, J = 6.3, 3 H, Me), 2.46 (dd, J = 16.0, 7.1, 2.7, 1 H-2), 2.51 (dd, J = 16.0, 5.4, 2.0 Hz, 1 H-2), 4.32 (regular m, 1 H₃), 9.76 (dd, J = 2.7, 2.0 Hz, 1 H-1).

*Crotonaldehyde* (5a): 2.01 (dd, J = 6.9, 1.6 Hz, 3 H, Me), 6.10 (ddq, J = 15.5, 8.0, 1.6 Hz, 1 H-2), H₃ obscured, 9.49 (d, J = 7.9 Hz, 1 H-1).

1-Octyn-3-ol (3b/6), selected signals: 2.77 (d, J = 2.1 Hz, 1 Hₐₗkyn), 4.24 (td, J = 6.7, 2.1 Hz, 1 H₃).

3-Hydroxy-octanal (4b) selected signals: 2.40 (dd, J = 16.0, 8.2, 3.0 Hz, 1 H-2), 2.48 (dd, J = 16.0, 4.3, 1.8 Hz, 1 H-2), 4.09 (regular m, 1 H₃), 9.72 (dd, J = 3.0, 1.8 Hz, 1 H-1).

2-Octenal (5b), selected signals: 2.30 (qd, J = 7.0, 1.5 Hz, 2 H-4), 6.04 (ddq, J = 15.5, 7.9, 1.5 Hz, 1 H-2), 9.45 (d, J = 7.9 Hz, 1 H-1).
3. Synthesis of O-protected 1-octyn-3-ol derivatives for hydration experiments

3-(Methoxymethyloxy)-1-octyne (7a): Prepared following the general method from ref. 6: A solution of 1-octyn-3-ol (2.92 mL, 20 mmol), LiBr (434 mg, 5 mmol) and pTsOH (305 mg, 1.6 mmol) in toluene (10 mL) and dimethoxymethane (10 mL) was stirred for 48 h at r.t. The reaction was quenched by addition of 25% aq NH₃ (5 mL), water (20 mL) und ¹BuOMe (20 mL). The organic phase was washed with water (2×15 mL) and the aqueous phase reextracted with ¹BuOMe. The combined organic phase was dried (MgSO₄), filtered and evaporated. Purification by CC (¹BuOMe/hexanes 1:10) gave a colorless liquid (2.50 g, 74%).

\[ R_f = 0.61 \ (¹BuOMe/hexanes 1:20). \]

¹H NMR (CDCl₃, 300 MHz): 0.91 (t, \( J = 7.0 \) Hz, 3 H, Me), 1.26–1.56 (m, 6 H), 1.68–1.81 (m, 2 H), 2.40 (d, \( J = 2.1 \) Hz, 1 H_{alkyne}), 3.38 (s, 3 H, OMe), 4.32 (td, \( J = 6.6, 2.1 \) Hz, 1 H), 4.60 (d, \( J = 6.8 \) Hz, 1 H, OCH₂OMe), 4.94 (d, \( J = 6.8 \) Hz, 1 H, OCH₂OMe). ¹³C NMR (CDCl₃, 75 MHz): 14.0 (CH₃), 22.5 (CH₂), 24.9 (CH₂), 31.5 (CH₂), 35.6 (CH₂), 55.7 (CH₃), 65.4 (CH), 73.3 (CH), 82.7 (C), 94.1 (CH₂). Spectral data agree with those reported. 7

3-(2-Tetrahydropyranloxy)-1-octyne (7b): Prepared following a related procedure in ref. 8: To a cooled (0 °C) solution of 1-octyn-3-ol (2.92 mL, 20 mmol) and 3,4-dihydro-2H-pyran (3.65 mL, 40 mmol) in CH₂Cl₂ (30 mL), solid dry pTsOH (38 mg, 0.2 mmol, 1 mol %) was added and the mixture stirred for 2 h at 0 °C. The reaction was quenched by addition of sat. aq NaHCO₃ (50 mL) and diluted with ¹BuOMe (100 mL). The organic phase was washed with sat. aq NaHCO₃ (50 mL) and water (100 mL), dried (Na₂SO₄), filtered, and evaporated. Purification by CC (¹BuOMe/hexanes 1:20) gave a faint yellow liquid (4.04 g, 96%).

$R_f = 0.33–0.41$ (\textsuperscript{t}BuOMe/hexanes 1:20). \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 300 MHz), mixture of diastereomers A (71\%) and B (29\%): 0.86–0.90 (t, $J = 7.0$ Hz, 3 H, Me), 1.26–1.3 (m, 4 H), 1.38–1.90 (m, 10 H), 2.37 (d, $J = 2.0$ Hz, 1 H\textsubscript{alkyne}, A), 2.43 (d, $J = 2.1$ Hz, 1 H\textsubscript{alkyne}, B), 3.49–3.58 (m, 1 H), 3.81 (ddd, $J = 11.4$, 8.3, 3.3 Hz, 1 H\textsubscript{A}), 4.02 (ddd, $J = 11.6$, 8.8, 3.8 Hz, 1 H\textsubscript{B}), 4.28 (td, $J = 6.7$, 2.1 Hz, 1 H\textsubscript{B}), 4.41 (dt, $J = 6.8$, 2.0 Hz, 1 H\textsubscript{A}), 4.75 (t, $J = 3.3$ Hz, 1 H\textsubscript{B}), 4.98 (t, $J = 3.7$ Hz, 1 H\textsubscript{A}). \textsuperscript{13}C NMR (CDCl\textsubscript{3}, 75 MHz), diastereomers A>B: 14.0/14.0 (CH\textsubscript{3}), 19.1/19.4 (B/A; CH\textsubscript{2}), 22.5 (CH\textsubscript{2}), 24.8/25.0 (B/A; CH\textsubscript{2}), 25.4/25.5 (B/A; CH\textsubscript{2}), 30.5 (CH\textsubscript{2}), 31.5/31.5 (B/A; CH\textsubscript{2}), 35.5/35.6 (B/A; CH\textsubscript{2}), 62.3/62.3 (B/A; CH\textsubscript{2}), 64.8/67.1 (B/A; CH), 72.5/73.1 (B/A; CH), 83.0/84.0 (A/B; C), 95.5/98.2 (A/B; CH). Spectral data agree with those reported.\textsuperscript{9}

3-\textit{tert}-Butyldimethylsilyloxy-1-octyne (7c): A solution of 1-octyn-3-ol (2.9 mL, 20 mmol), TBSCI (40 mmol) and imidazole (60 mmol) in N,N-dimethyl formamide (40 mL) was stirred at r.t. After completion (TLC control, ca 24 h), the reaction was quenched by addition of aq HCl (2.4 M, 60 mL). The aqueous phase was extracted with \textsuperscript{t}BuOMe (2×60 mL) and the combined organic phase washed with water (100 mL), sat. aq NaHCO\textsubscript{3} (100 mL) and water (100 mL). After drying (MgSO\textsubscript{4}) and evaporation of the organic phase, the residue was purified by CC (tBuOMe/hexanes 1:5) to give slightly yellow liquid (4.32 g, 90%).

$R_f = 0.82$ (\textsuperscript{t}BuOMe/hexanes 1:30). \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): 0.11 (s, 3 H, SiMe), 0.13 (s, 3 H, SiMe), 0.88 (t, $J = 7.1$ Hz, 3 H, Me), 0.91 (s, 9 H, Si\textsuperscript{t}Bu), 1.14–1.49 (m, 6 H), 1.61–1.71 (m, 2 H), 2.37 (d, $J = 2.1$ Hz, 1 H\textsubscript{alkyne}), 4.33 (td, $J = 6.5$, 2.1 Hz, 1 H-3). \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): −4.9 (CH\textsubscript{3}), −4.4 (CH\textsubscript{3}), 14.1 (CH\textsubscript{3}), 18.4 (C), 22.7 (CH\textsubscript{3}), 24.9 (CH\textsubscript{3}), 25.9 (CH\textsubscript{3}), 31.5 (CH\textsubscript{2}), 38.6 (CH\textsubscript{2}), 62.8 (CH), 71.9 (CH), 85.8 (C). IR (film): 3310, 2934, 2859, 1466, 1342, 1254, 1090, 838, 928.

3-Methoxy-1-octyne (7d): Prepared by a literature method. A solution of 1-octyn-3-ol (0.15 mL, 1.0 mmol), MeI (0.13 mL, 2.0 mmol) and KOH (0.224 g, 3.4 mmol) in DMSO (2 mL) was stirred for 1 h at r.t. The reaction was quenched by addition of sat. aq NaHCO₃ (10 mL) and tBuOMe (20 mL). The organic phase was washed with sat. aq NaHCO₃ (10 mL) and water (20 mL). The aqueous phase was extracted with tBuOMe. The combined organic phase was dried (MgSO₄), filtered, and evaporated. Purification by CC (tBuOMe/hexanes 1:30) gave a faint yellow liquid (123 mg, 87%).

\[ R_f = 0.65 \ (\text{tBuOMe/hexanes 1:20}). \]

\[ ^1H \text{ NMR (CDCl₃, 400 MHz): 0.89 (t, } J = 6.9 \text{ Hz, 3 H, Me), 1.24–1.50 (m, 4 H, } 2 \times \text{CH}_2, \text{ 1.63–1.79 (m, 2 H, CH}_2, \text{ 2.43 (d, } J = 2.1 \text{ Hz, 1 H}_{\text{alkyne}}, \text{ 3.41 (s, 3 H, OMe), 3.93 (td, } J = 6.5, 2.0 \text{ Hz, 1H, CH}). \]

\[ ^13C \text{ NMR (CDCl₃, 100 MHz): 14.1 (CH}_3, \text{ 22.7 (CH}_2, \text{ 24.9 (CH}_2, \text{ 31.6 (CH}_2, \text{ 35.6 (CH}_2, \text{ 56.5 (OCH}_3, \text{ 71.2 (CH), 73.7 (CH), 82.8 (C; assignment insecure because of weak signal). Spectral data agree with those reported.} \]

3-Benzylxy-1-octyne (7e): A solution of 1-octyn-3-ol (1.43 mL, 10 mmol), benzyl bromide (1.91 mL, 16 mmol) and tetrabutylammonium chloride (0.45 g, 1.6 mmol) in CH₂Cl₂ (10 mL) was vigorously stirred, while aq 50% NaOH (3.0 g, 37.5 mmol) was added dropwise. After completion of the addition, the reaction mixture was refluxed for 24 h. The reaction was quenched by addition of sat. aq NaHCO₃ (50 mL) and diluted with tBuOMe (100 mL). The organic phase was washed with sat. aq NaHCO₃ (2×50 mL) and water (2×50 mL). The aqueous

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phase was re-extracted with tBuOMe and the combined organic phase dried (MgSO₄), filtered and evaporated. Purification by CC (tBuOMe/hexanes 1:30) gave a faint yellow liquid (2.10 g, 97%).

\[ R_f = 0.60 \ (\text{tBuOMe/hexanes 1:20}). \]

\[^1H\] NMR (300 MHz, CDCl₃): 0.88 (t, \(J = 6.7\) Hz, 3 H, Me), 1.21–1.37 (m, 4 H), 1.41–1.54 (m, 2 H), 1.66–1.85 (m, 2 H), 2.46 (d, \(J = 2.1\) Hz, 1 H), 4.08 (td, \(J = 6.6, 2.0\) Hz, 1 H), 4.51 (d, \(J = 11.8\) Hz, 1 H, PhCH₂), 4.81 (d, \(J = 11.8\) Hz, 1 H, PhCH₂), 7.20–7.40 (m, 5 H Ph).

\[^{13}C\] NMR (CDCl₃, 75 MHz): 14.0 (CH₃), 22.5 (CH₂), 24.9 (CH₂), 31.5 (CH₂), 35.6 (CH₂), 68.5 (CH), 70.5 (CH₂), 73.7 (CH), 83.1 (C), 127.7 (CH), 128.0 (CH), 128.4 (CH), 137.9 (C).

Spectral data agree with those reported.

3-Benzyloxy-1-octyne (7f): To a solution of 1-octyn-3-ol (1.43 mL, 10 mmol), triethylamine (2.5 mL, 18 mmol) and 4-dimethylaminopyridine (61 mg, 0.5 mmol) in CH₂Cl₂ (10 mL), benzoyl chloride (1.6 mL, 14 mmol) was added dropwise with stirring. After stirring for 3 h at r.t. the reaction was quenched by addition of water (20 mL) and tBuOMe (60 mL). The organic phase was washed with aq NaOH (2 M, 20 mL) and water (20 mL). The organic phase was dried (MgSO₄), filtered and evaporated. Purification by CC (tBuOMe/hexanes 1:25) gave faint yellow oil (2.20 g, 95%).

\[ R_f = 0.29 \ (\text{tBuOMe/hexanes 1:25}). \]

\[^1H\] NMR (CDCl₃, 300 MHz): 0.90 (t, \(J = 7.0\) Hz, 3 H, Me), 1.30–1.42 (m, 4 H, 2×CH₂), 1.48–1.59 (m, 2 H, CH₂), 1.84–2.00 (m, 2 H, CH₂), 2.48 (d, \(J = 2.1\) Hz, 1 H, CH), 5.60 (dt, \(J = 6.6, 2.1\) Hz, 1 H), 7.41–7.48 (m, 2 H\text{Ad}), 7.53–7.61 (m, 1 H\text{Ad}), 8.03–8.11 (m, 2 H\text{Ad}).

\[^{13}C\] NMR (CDCl₃, 75 MHz): 14.0 (CH₃), 22.5 (CH₂), 24.6 (CH₂), 31.3 (CH₂), 34.7 (CH₂), 64.4 (CH), 73.6 (CH), 81.3 (C), 128.4 (CH), 129.8 (CH), 129.9 (C), 133.2 (C), 165.5 (C). Spectral data agree with those reported.

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4. Hydration of propargyloxy derivatives with [CpRu(L)₂(MeCN)]PF₆ catalysts

Analytical experiments (Table 2)

Representative procedure: A solution of 3-methoxymethyloxy-1-octyne (100 mg, 0.587 mmol), [CpRu(2,4,6Ph₃C₆H₂PyPPh₂)₂(MeCN)]PF₆ (43.7 mg, 0.0294 mmol, 5 mol %) and H₂O (53 mg, 2.94 mmol, 5 equiv) in acetone (1.2 mL) was stirred under argon at 50 °C for the required time interval. Samples were removed and evaporated in vacuum (12 mbar) and the residue dissolved in CDCl₃ for analysis (¹H NMR, ³¹P NMR), using the signal for the terminal methyl group as internal standard.

Note: 3-Benzoyloxy-1-octyne exclusively rearranged to 2-octenal (not mentioned in the main text).

Preparative experiments:

3-(Methoxymethyloxy)-octanal (8a): Prepared by stirring of 3-methoxymethyloxy-1-octyne (7a; 170.3 mg, 1.00 mmol) and [CpRu(2,4,6Ph₃C₆H₂PyPPh₂)₂(MeCN)]PF₆ (149 mg, 0.10 mmol, 10 mol %) in acetone (2 mL) and water (90 mg, 5.0 mmol) for 17.5 h at 50 °C. After evaporation and CC-purification (tBuOMe/hexanes 1:10), the aldehyd was obtained as colorless oil (119 mg, 63%).

Known compound. CAS 108383-17-1. Rf = 0.17 (tBuOMe/hexanes 1:10). ¹H NMR (CDCl₃, 400 MHz): 0.89 (t, J = 6.7 Hz, 3 H, Me), 1.27–1.39 (m, 6 H), 1.49–1.70 (m, 2 H), 2.56 (ddd, J = 16.3, 4.8, 1.8 Hz, 1 H, CH₂CHO), 2.64 (ddd, J = 16.3, 7.0, 2.8 Hz, 1 H, CH₂CHO), 3.35 (s, 3 H, OMe), 4.08 (quint, J ≈ 6.3 Hz, 1 H), 4.66 (d, J = 7.0, 1 H, OCH₂OMe), 4.69 (d, J = 7.0, 1 H, OCH₂OMe), 9.81 (dd, J = 2.8, 1.8 Hz, 1 H, CHO). ¹³C NMR (CDCl₃, 100 MHz): 14.1 (CH₃), 22.7 (CH₂), 25.0 (CH₃), 31.8 (CH₂), 35.0 (CH₂), 48.8 (CH₂), 55.7 (CH₃), 73.2 (CH), 95.8 (CH₂), 201.3 (CH).

Spectral data agree with those reported.¹⁵

3-(2-Tetrahydropyranloxy)-octanal (8b): A solution of 3-(2-tetrahydro-
pyranloxy)-1-octyne (7b; 210 mg, 1.0 mmol) and [CpRu(2,4,6-
Ph3C6H2Py-
PPh2)2(MeCN)]PF6 (149 mg, 0.1 mmol, 10 mol %) in acetone (2 mL) and water (90 mg, 5 mmol)
was stirred at 50 °C for 17.5 h. Evaporation and purification of the residue by CC (tBuOMe/hexanes
1:10) gave a colorless oil (101 mg, 44%).

Known compound, CAS 111633-54-6. Rf = 0.2 (tBuOMe/hexanes 1:10). 1H NMR (CDCl3, 400
MHz): mixture of diastereomers A (80%) and B (20%): 0.89 (t, J = 6.9 Hz, 3 H, Me), 1.21–1.87 (m,
14 H), 2.50–2.72 (m, 2 H-2), 3.43–3.56 (m, 1 H), 3.79–3.86/3.86–3.94 (m, 1 H, B/A), 4.15 (dq, J =
6.3, 5.3 Hz, 1 H), 4.64–4.67/4.68–4.71 (m, 1 H, B/A), 9.81/9.82 (t, J = 2.3 Hz, 1 H, CHO, A/B). 13C
NMR (CDCl3, 100 MHz): diastereomer A: 14.3 (CH3), 20.0 (CH2), 22.8 (CH2), 25.4 (CH2), 25.6
(CH2), 31.2 (CH2), 32.0 (CH2), 35.9 (CH2), 48.3 (CH2), 63.0 (CH2), 72.5 (CH), 97.9 (CH), 201.7
(CH); diastereomer B: 14.3 (CH3), 20.2 (CH2), 22.8 (CH2), 25.1 (CH2), 25.6 (CH2), 31.2 (CH2),
32.0 (CH2), 34.8 (CH2), 49.5 (CH2), 63.2 (CH2), 73.1 (CH), 98.9 (CH), 202.2 (CH). Spectral data
agree with those reported.16

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5. Experiments concerning catalyst deactivation

The lifetime of the hydration catalysts \([\text{CpRu(L)}_2(\text{MeCN})]\)PF\(_6\) is limited. When 4-acetoxy-4-phenyl-1-butyne\(^{17}\) was hydrated with only 0.5 mol % of \([\text{CpRu}(^{2,4,6}\text{Ph}_3\text{C}_6\text{H}_2\text{PyPPh}_2)_2(\text{MeCN})]\)PF\(_6\) as catalyst, the reaction came to a halt after 40–50% of conversion. Analysis of such reaction mixtures by \(^{31}\)P NMR spectroscopy revealed that the ruthenium-catalyst (\(\delta 43.6\) ppm) had been converted to a new species with a signal at \(\delta 46.8\) ppm. After the signal for the active catalyst had fully disappeared, the hydration reaction stopped. The new species was identified as the cationic ruthenium(II)-carbonyl complex \([\text{CpRu(CO)(}^{2,4,6}\text{Ph}_3\text{C}_6\text{H}_2\text{PyPPh}_2)_2]\)PF\(_6\).\(^{18}\) This was proven by an independent in situ synthesis of the same complex from \([\text{CpRu}(^{2,4,6}\text{Ph}_3\text{C}_6\text{H}_2\text{PyPPh}_2)_2(\text{MeCN})]\)PF\(_6\) and gaseous CO in acetone-\(d_6\). The new species, which formed only slowly, gave the expected signal at \(\delta 46.8\) ppm. The cause of catalyst deactivation thus appears to be irreversible generation of this coordinatively saturated ruthenium(II)-carbonyl complex.

\[\text{cat. (0.5 %)} \quad \text{Me}_2\text{CO, H}_2\text{O,} \quad 60 \, ^\circ\text{C, 12 h} \quad \text{cat.} \]

\[
\begin{align*}
\text{Ph} & \quad \text{OAc} \\
\text{Ph} & \quad \text{OAc} \\
\text{Me}_2\text{CO, H}_2\text{O,} & \quad 60 \, ^\circ\text{C, 12 h} \\
\text{40–50\%} & \quad (40–50\%)
\end{align*}
\]

\(\delta (^{31}\text{P}) = 43.6\) ppm

\(\delta (^{31}\text{P}) = 46.8\) ppm

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\(^{17}\) T. Kribber, A. Labonne, L. Hintermann, Synthesis 2007, 2809.

\(^{18}\) We are indebted to Prof. GROTJAHN, University of San Diego, CA, for pointing our attention to this point. According to GROTJAHN, decarbonylation with catalyst poisoning was observed in an attempted hydration of \(p\)-nitrophenylacetylene.
6. Stereospecificity of the anti-MARKOVNIKOV hydration

Structure correlation: 1,3-Dibenzoyloxy-octane (9) from acetal-protected 1-octyn-3-ol (7)

The correlation sequence was carried out in several instances with substrate bearing either THP or MOM protecting group, starting with either racemic, R- or S-enantiomer of 1-octyn-3-ol, with essentially identical results. The acetals of R- and S-1-octyn-3-ol were prepared as described above for the racemic material.

6.1 Conversion of O-THP (7b) or O-MOM-protected 1-octyn-3-ol (7a) to 1,3-dibenzoyloxy-octane (9) via anti-Markovnikov hydration and post-hydrative derivatization:

**Step 1 (hydration):** The 3-OTHP-1-octyne (7b; 100 mg, 0.475 mmol) was hydrated in degassed acetone (0.95 mL) and water (43 mg, 2.4 mmol, 5 equiv) by action of the catalyst [CpRu(2,4,6-Ph3C6H2PyPPh2)2(MeCN)]PF6 (35 mg, 5 mol %) at 50 °C for 22 h. **Step 2 (reduction):** The crude reaction mixture from step 1 was evaporated and the residue dissolved in MeOH (4.5 mL). At 0 °C, NaBH4 (46.7 mg, 1.235 mmol) was added and the mixture stirred for 15 min. Addition of tBuOMe (30 mL) was followed by washing with sat. aq NaCl (2×30 mL). The aqueous phase was extracted with tBuOMe (30 mL). The combined organic phase was dried (Na2SO4), filtered, and evaporated to dryness. **Step 3 (Acetal deprotection):** To the crude from Step 2 in
MeOH (5 mL), HCl aq (2.4 M, 2.5 mL) was added and the mixture stirred at r.t. After 20 min, 1BuOMe (20 mL) was added and the mixture transferred into a separatory funnel. The organic phase was washed with sat. aq NaHCO₃ (2×20 mL). The aqueous phases were re-extracted with 1BuOMe (2×20 mL). The combined organic phase was dried (MgSO₄), filtered, and evaporated to dryness. The residue was taken up twice in toluene (10 mL) and evaporated to remove any MeOH. **Step 4 (benzoylation):**¹⁹ Benzoyl chloride (0.552 mL, 4.75 mmol, 10eq.) was added dropwise to the crude from step 3, NEt₃ (0.99 mL, 7.125 mmol, 15 eq.) and dimethylaminopyridine (116.1 mg, 0.95 mmol, 2 eq.) were dissolved in CH₂Cl₂ (4.5 mL). After stirring for 70 min at r.t., the reaction was quenched by addition of aq NH₃ (25%; 10 mL) and 1BuOMe (30 mL). The organic phase was washed with aq HCl (2.4 M; 10 mL) and sat. aq NaHCO₃ (30 mL) and water (30 mL), dried over MgSO₄, filtered, and evaporated to dryness. Drying in HV gave colorless oil (41 mg, 24 %).

*Data for 1,3-dibenzoyloxy-octane (9):* Rᵣ = 0.81 (1BuOMe/hexanes 1:3). ¹H NMR (CDCl₃, 300 MHz): 0.83–0.93 (m, 3 H, Me), 1.25–1.97 (m, 8 H), 2.18 (ψ-q, J = 6.4 Hz, 2 H), 4.34–4.53 (m, 2 H), 5.36 (dq, J = 6.9, 6.0 Hz, 1 H), 7.34–7.59 (m, 6 Hₐr), 7.97–8.09 (m, 4 Hₐr). ¹³C NMR (CDCl₃, 75 MHz): 14.0 (CH₃), 22.5 (CH₂), 24.9 (CH₃), 31.7 (CH₂), 33.2 (CH₂), 34.3 (CH₂), 61.6 (CH₂), 72.2 (CH), 128.3 (CH), 128.3 (CH), 129.6 (CH), 129.6 (CH), 130.1 (C), 130.4 (C), 132.9 (2×CH), 166.2 (C), 166.5 (C). IR (film): 2931, 2861, 1719, 1602, 1451, 1313, 1272, 1107, 1070, 1026, 711. MS (EI, 70 eV): m/z (%) = 249 (3) M⁺, 232 (10), 127 (6), 110 (23), 105 (100), 107 (75), 91 (55), 77 (40).

HPLC (Chiralcel-OD, 20 °C, λ = 230 nm, heptane/i-PrOH = 95:5, 1.0 mL/min): tᵣ = 10.4 min (S), 14.6 min (R). Spectroscopic data agree with those reported in the literature.²⁰

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When starting from \((R)\)-3-(2-tetrahydropyranyloxy)-1-octyne, the HPLC retention time of the single peak was found at \(t_R = 14.55\) min \((R)\). Starting from \((S)\)-3-methoxymethyloxy-1-octyne, the above sequence was carried out analogously to give a product with \(t_R = 10.4\) min \((S)\). The same sequence was repeated starting from commercially available, enantiomerically enriched (\(\geq 95\%\) ee) \((R)\)-1-octyn-3-ol. The HPLC-traces of racemic, \(R\) obtained from \((R)\)-1-octyn-3-ol are displayed in Figure S1:

**Figure S1**  HPLC chromatograms of 1,3-dibenzoyloxy-octane measured on *Chiralcel OD*, \(^1\text{PrOH}/n\)-heptane = 5:95, flow = 0.5 mL/min, \(\lambda = 230\) nm. a) Racemic sample. b) Enriched sample made from \((R)\)-1-octyn-1-ol. ee \(\geq 95\%\). c) Sample derived from \((S)\)-1-octyn-1-ol. Peaks prior to 10 min are due to “aged HPLC solvent” impurities.
6.2 Correlation of 3-O-MOM-1-octyne (7a) with methyl (S)-3-hydroxyoctanoate (10)

Methyl (S)-3-hydroxyoctanoate: A solution of (S)-3-methoxymethyl-oxy-1-octyne (85.2 mg, 0.5 mmol) and [CpRu(2,4,6Ph₃C₆H₂PyPPh₂)₂(MeCN)]PF₆ (37.2 mg, 0.025 mmol, 5 mol %) in acetone (0.95 mL) and water (45 mg, 2.5 mmol, 5 equiv) was stirred for 6 h at 50 °C. The reaction mixture was evaporated and the residue dissolved in tert-butanol (3 mL). Aqueous solutions of NaH₂PO₄ (1.25 M, 2 mL) and KMnO₄ (1 M, 3 mL) were added and the mixture stirred for 70 min at r.t. The reaction was quenched by addition of sat. aq Na₂SO₃ (6 mL) and the mixture acidified to pH = 3 by adding aq 2.4 M HCl. After extraction with ¹BuOMe (30 mL) the organic phase was dried (Na₂SO₄), filtered, and evaporated. The residue was taken up in MeOH (10 mL) and conc. H₂SO₄ (0.5 mL) was carefully added. After stirring for 45 min at 75 °C, the cooled reaction mixture was diluted with sat. aq NaHCO₃ (30 mL) and ¹BuOMe (50 mL). The organic phase was washed with water (2×30 mL). The aqueous phase was extracted with ¹BuOMe and the combined organic phase dried (MgSO₄), filtered, and evaporated. Purification by CC (¹BuOMe/hexanes 1:3) gave a colorless liquid (40 mg, 46 %).

[α]D²⁰ = +22.9 (c = 1, CHCl₃). Rf = 0.55 (¹BuOMe/hexanes 1:1). ¹H NMR (300 MHz, CDCl₃): 0.89 (t, J = 6.5 Hz, 3 H, CH₃), 1.22–1.57 (m, 8 H), 2.41 (dd, J = 16.4, 9.0 Hz, 1 H-2), 2.52 (dd, J = 16.4, 3.1 Hz, 1 H-2), 2.85 (d, J = 4.0 Hz, 1 H, OH), 3.72 (s, 3 H, OCH₃), 4.00 (octet, J ≈ 4 Hz, 1 H-3). ¹³C NMR (101 MHz, CDCl₃): 14.0 (CH₃), 22.6 (CH₂), 25.1 (CH₂), 31.7 (CH₂), 36.4 (CH₂), 41.0 (CH₂), 51.7 (CH₃), 67.9 (CH), 173.2 (C). Spectral data agree with those reported.


Note: Oxidation of aldehyde to carboxylic acid with KMnO₄ follows literature ref.²¹

The measured optical rotation value ([α]D²⁰ = +22.9, c = 1, CHCl₃) is in accord with the literature value for the (S)-enantiomer of [α]D²⁰ = +24 (c = 1, CHCl₃).²²

7. Synthesis of massoialactone (12)

**tert-Butyl 5-methoxymethyloxy-3-hydroxy-decanoate (11):** In a Schlenk vessel under argon, 3-methoxymethyloxy-1-octyne (85 mg, 0.50 mmol) and [CpRu(²,₄,₆Ph₃C₆H₂PyPPh₂)₂(MeCN)]PF₆ (37 mg, 0.025 mmol, 5 mol %) was stirred in a mixture of acetone (1 mL) and water (45 mg, 2.5 mmol, 5 equiv) at 50 °C for 6 h. After evaporation and drying in a medium vacuum (12 mbar), the residue was dissolved in dry THF (1 mL). In a separate vessel, the following reagent was prepared: n-Butyllithium (1.57 mL, 2.5 mmol) was added dropwise to a solution diisopropylamine (0.354 mL, 2.5 mmol) in dry THF (10 mL) at 0 °C, the mixture stirred for 15 min, then cooled to −78 °C, and tert-butylacetate (0.34 mL, 2.5 mmol) slowly added and the mixture stirred for 30 min. This reagent was added to the solution of the aldehyde at −78°C and the mixture stirred for 10 min. The reaction was quenched at −78°C by addition of sat. aq NH₄Cl (5 mL), water (20 mL) and ¹BuOMe (25 mL). The aqueous phase was extracted with ¹BuOMe (10 mL) and the combined organic phase washed with water (20 mL) and dried (MgSO₄). After filtration and evaporation, the residue was purified by CC (¹BuOMe/hexanes 1:5) to give colorless oil (104 mg, 68%).

R_f = 0.33/0.26 (2 diastereomers; ¹BuOMe/hexanes 1:3). ¹H NMR (CDCl₃, 300 MHz), diastereomers A/B: 0.89 (t, J = 6.6 Hz, 3 H, Me), 1.24–1.36 (m, 6 H, 3×CH₂), 1.46 (s, 9 H, ¹Bu) 1.47–1.84 (m, 4 H + 0.5 OH, A or B), 2.34–2.49 (m, 2 H), 3.39/3.41 (s, 3 H, MeO), 3.42/3.45 (d, J = 2.9 Hz, 0.5 H, OH, A or B), 3.72–3.87 (m, 1 H), 4.08–4.29 (m, 1 H), 4.64 (d, J = 6.8 Hz, 0.5 H, OCH₂OMe, A), 4.70 (d, J = 6.8 Hz, 0.5 H, OCH₂OMe, A), 4.68–4.70 (m, 2×0.5 H, OCH₂OMe, B). ¹³C NMR (CDCl₃, 75 MHz): 14.0 (CH₃), 22.6 (CH₂), 24.6/24.9 (CH₂), 28.1 (CH₃), 32.0 (CH₂), 34.2/34.9
(CH$_2$), 40.8/41.1 (CH$_2$), 42.7/42.9 (CH$_2$), 55.8/55.8 (CH$_2$), 64.9/66.8 (CH), 75.4/76.3 (CH), 81.0/81.0 (C), 95.2/96.3 (CH$_2$), 171.9/172.0 (C). IR (film): 3472, 2932, 2349, 1729, 1463, 1369, 1256, 1154, 954, 917, 844, 761, 608, 529.

MS (EI, 70 eV): $m/z$ (%) = 231.4 (5) [$M-O$Bu$^+$], 217.3 (11), 203.3 (11), 177.2 (23), 145.2 (89), 127.2 (22), 115.2 (62), 57.3 (86), 45.3 (100).

Anal calcd for C$_{16}$H$_{32}$O$_5$: C 63.13, H 10.60; found C 62.91, H 10.57.

6-Pentyl-5,6-dihydro-2-pyrone, massoialactone (12): A solution of tert-butyl 5-methoxymethyloxy-3-hydroxy-decanoate (11; 55 mg, 0.18 mmol) in CF$_3$CO$_2$H (5 mL) was stirred for 7 days at r.t. The reaction was quenched by addition of aq NaOH 50% (3.0 g, 37.5 mmol), tBuOMe (20 mL) and water (20 mL). The organic phase was pooled and the aqueous phase extracted with tBuOMe. The combined organic phase was dried (MgSO$_4$), filtered and evaporated. Purification by CC (tBuOMe/hexanes 1:3) gave the lactone (24 mg, 71%) as colorless oil.

$R_f$ = 0.24 (tBuOMe/hexanes 1:3). $^1$H NMR (CDCl$_3$, 300 MHz): 0.90 (t, $J = 6.9$ Hz, 3 H, Me), 1.25–1.70 (m, 7 H), 1.74–1.87 (m, 1 H), 2.30–2.36 (m, 2 H), 4.36–4.47 (m, 1 H), 6.02 (ddd, $J = 9.7$, 2.2, 1.5 Hz, 1 H$_{\text{alkene}}$), 6.87 (ddd, $J = 9.7$, 5.0, 3.7 Hz, 1 H$_{\text{alkene}}$). $^{13}$C NMR (75 MHz, CDCl$_3$): 14.0 (CH$_3$), 22.5 (CH$_2$), 24.5 (CH$_2$), 29.4 (CH$_2$), 31.5 (CH$_2$), 34.8 (CH$_2$), 78.0 (CH), 121.5 (CH), 145.0 (CH), 164.6 (C). Spectral data agree with those reported.$^{23}$

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8. Synthesis of a pyranone via reiterative alkynylation/hydration

5-Methoxymethyloxy-3-hydroxy-1-decyn (13): A solution of (±)-3-methoxymethyloxy-1-octyne (170.2 mg, 1 mmol) and [CpRu(2,4,6\textsubscript{Ph}3\textsubscript{C6H2}PyPPh\textsubscript{2})(MeCN)]PF\textsubscript{6} (74.4 mg, 0.05 mmol, 5 mol %) in degassed acetone/water (3+1 mL) was stirred for 3.5 h at 50 °C. After evaporation and drying in high vacuum, the residue was dissolved in dry THF (4 mL) and the solution cooled to 0 °C. Ethinylmagnesium chloride (0.5 M in THF, 10 mL, 5 mmol, 5 equiv) was slowly added and the mixture stirred for 40 min. The reaction was quenched by addition of sat. aq NH\textsubscript{4}Cl (25 mL) and \textsuperscript{t}BuOMe (50 mL). The aqueous phase was extracted with \textsuperscript{t}BuOMe. The combined organic phase washed with sat. aq NaHCO\textsubscript{3} (25 mL) and water (2\times25 mL), dried (MgSO\textsubscript{4}), filtered, and evaporated. Purification of the residue by CC (\textsuperscript{t}BuOMe/hexanes 1:10→1:3→1:0) gave bright yellow oil (120.1 mg, 74%).

R\textsubscript{f} = 0.32 (\textsuperscript{t}BuOMe/hexanes 1:3). \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 300 MHz), diastereomers A (60%), B (40%):

- 0.89 (t, J = 6.8 Hz, 3 H, Me), 1.23–1.39 (m, 6 H), 1.45–1.68 (m, 2 H), 1.83–2.06 (m, 2 H), 2.46 (d, J = 2.2 Hz, 1 H\textsubscript{alkyne}, B)/2.49 (d, J = 2.1 Hz, 1 H\textsubscript{alkyne}, A), 2.82 (br s, 1 H, OH), 3.40/3.42 (s, 3 H, MeO), 3.77–3.99 (m, 1 H), 4.54–4.73 (m, 3 H).

\textsuperscript{13}C NMR (CDCl\textsubscript{3}, 75 MHz), diastereomers A,B:

- 14.0 (CH\textsubscript{3}), 22.6 (CH\textsubscript{2}), 24.5/24.7 (CH\textsubscript{2}), 31.9 (CH\textsubscript{2}), 34.4/34.5 (CH\textsubscript{2}), 41.6/42.4 (CH\textsubscript{2}), 55.8/56.0 (CH\textsubscript{3}), 59.5/60.9 (CH), 72.6/72.9 (CH), 75.6/76.1 (CH), 84.6/84.7 (C), 95.5/96.2 (CH\textsubscript{2}). IR (film):

- 3308, 2931, 2859, 2114, 1716, 1577, 1541, 1465, 1380, 1307, 1217, 1151, 1098, 1037, 918, 758, 664, 632, 561. MS (EI, 70 eV): m/z (%) = 183.3 (2) [M–OMe]\textsuperscript{+}, 169.3 (1), 145.3 (13), 111.2 (100), 99.2 (21), 83.2 (14), 55.3 (42), 45.3 (90). Anal calcd for C\textsubscript{12}H\textsubscript{22}O\textsubscript{3}: C 67.26, H 10.35; found C 67.24, H 10.34.
3,5-Methylenedioxy-1-decyne (14): A solution of 5-methoxymethyloxy-3-hydroxy-1-decyne (13; 630 mg, 2.94 mmol) in dimethoxymethane (10 mL) was acidified by addition of CF<sub>3</sub>SO<sub>3</sub>H (52 µL, 0.59 mmol). After 5 min of stirring at r.t., the reaction was quenched by addition of aq 25% NH<sub>3</sub> (10 mL), water (30 mL) and tBuOMe (50 mL). The organic phase was washed with water (2×50 mL) and the aqueous phase extracted with tBuOMe. The combined organic phase was dried (MgSO<sub>4</sub>), filtered and evaporated. Purification of the residue by CC (tBuOMe/hexanes 1:10) gave colorless oil (475 mg, 89%).

R<sub>f</sub> = 0.59, 0.50 (diastereomers; tBuOMe/hexanes 1:10). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), diastereomers A (62%), B (38%): 0.89 (t, J = 6.5 Hz, 3 H, Me), 1.22–2.02 (m, 10 H), 2.52 (d, J = 2.2 Hz, 1 H<sub>alkyne</sub>, A), 2.57 (d, J = 2.2 Hz, 1 H<sub>alkyne</sub>, B), 3.48–3.59 (m, 1 H<sub>A</sub>/3.86–3.96 (m, 1 H<sub>B</sub>), 4.31–4.40 (m, 1 H<sub>A</sub>), 4.69 (d, J = 6.6 Hz, 1 H<sub>A</sub>, OCH<sub>2</sub>O), 4.82–4.86 (m, 1 H<sub>B</sub>), 4.89 (d, J = 6.5 Hz, 1 H<sub>B</sub>, OCH<sub>2</sub>O), 5.08 (d, J = 6.6 Hz, 1 H<sub>A</sub>, OCH<sub>2</sub>O), 5.22 (d, J = 6.5 Hz, 1 H<sub>B</sub>, OCH<sub>2</sub>O). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz), diastereomers A>B: 14.0 (CH<sub>3</sub>), 22.5/22.5 (CH<sub>2</sub>), 24.4/24.5 (CH<sub>2</sub>; A/B), 31.7/31.7 (CH<sub>2</sub>), 35.5/35.6 (CH<sub>2</sub>; A/B), 36.2/37.9 (CH<sub>2</sub>; B/A), 63.4/66.4 (CH; B/A), 72.5/76.2 (CH; B/A), 73.4/75.8 (CH; A/B), 81.0/81.6 (C; B/A), 88.7/93.4 (CH<sub>2</sub>; B/A). IR (film): 2930, 2858, 2770, 2127, 1587, 1542, 1465, 1402, 1379, 1362, 1257, 1235, 1215, 1183, 1138, 1111, 1032, 982, 945, 901, 843, 809, 758, 667, 633, 569, 517. MS (EI, 70 eV): m/z (%) = 181.4 (26) M<sup>+</sup>, 145.3 (25), 111.3 (44), 99.2 (21), 71.4 (14), 55.3 (43), 45.4 (100). Anal calcd for C<sub>11</sub>H<sub>18</sub>O<sub>2</sub>: C 72.49, H 9.95; found: C 72.35, H 9.91.

6,8-Methylenedioxy-4-hydroxy-1-tridecene (15): A solution of 3,5-methylenedioxy-1-decyne (14; 300 mg, 1.65 mmol) and [CpRu(2,4,6-Ph<sub>3</sub>C<sub>6</sub>H<sub>2</sub>PyPPh<sub>2</sub>)(MeCN)]PF<sub>6</sub> (97.9 mg, 0.066 mmol, 4 mol %) in a degassed mixture of acetone (5 mL) and water (1.5 mL) was stirred for 5 h at 50 °C. Degassed CH<sub>2</sub>Cl<sub>2</sub> (15 mL) was added and the organic phase removed via canula. The aqueous phase was extracted twice with CH<sub>2</sub>Cl<sub>2</sub> (5 mL). The combined organic phase was collected in a Schlenk vessel under argon. After
evaporation, the residue was dissolved in dry Et₂O (6.6 mL) and MgSO₄ (0.3 g) was added. To the suspension stirred at 0 °C, a solution of freshly prepared allylmagnesium bromide (0.8 M in Et₂O, 11.2 mL, 8.9 mmol, 5 equiv)²⁴ was added at 0 °C and the mixture stirred for 1 h. The reaction was quenched by careful addition of sat. aq NH₄Cl (10 mL), water (10 mL) and tBuOMe (30 mL). The organic phase was washed with sat. aq NaHCO₃ (20 mL) and water (2×25 mL). The aqueous phase was extracted with tBuOMe. The combined organic phase was dried (MgSO₄), filtered, and evaporated. Purification by CC (tBuOMe/hexanes 1:10) gave the homoallyl alcohol as colorless oil (292 mg, 73%).

Rₛ = 0.23 (tBuOMe/hexanes 1:10). ¹H NMR (CDCl₃, 300 MHz), several diastereomers: 0.86–0.93 (m, 3 H, Me), 1.23–1.97 (m, 12 H+0.7 OH), 2.15–2.35 (m, 2 H, CH₂), 2.90–3.10 (br s, 0.3 H, OH), 3.51–3.62 (m, 0.7 H), 3.78–4.01 (m, 2 H), 4.09–4.26 (m, 0.3 H), 4.69–5.20 (several m, 4 H), 5.75–5.92 (m, 1 H alkene). ¹³C NMR (CDCl₃, 75 MHz), signals of up to 4 diastereomers: 14.0 (CH₃), 22.6 (CH₂), 24.5/24.6/25.1/25.2 (CH₂), 31.7/31.7/32.2/32.3 (CH₂), 34.9/35.0/35.8/35.9 (CH₂), 37.6/37.8/39.7/40.0 (CH₂), 41.8/41.9/41.9 (CH₂), 42.1/42.2/42.3 (CH₂), 66.9/67.0/68.6/70.3/70.5/71.8/71.8/72.1/73.7/76.5/76.6/76.9 (3×CH), 86.9/87.0/93.2/93.4 (CH₂), 117.6/117.7/118.0/118.1 (CH₂), 134.6/134.6/134.7/134.7 (CH). IR (film): 3450, 3076, 2929, 2857, 2775, 2676, 1641, 1463, 1434, 1407, 1383, 1355, 1238, 1177, 1133, 1080, 1027, 914, 802. MS (EI, 70 eV): m/z (%) = 241.4 (2) M⁺, 201.4 (62), 171.3 (82), 153.3 (79), 127.3 (94), 109.3 (100), 97.2 (33), 83.3 (69), 71.3 (78), 55.3 (84), 45.3 (17). Anal calcd for C₁₄H₂₆O₃: C 69.38, H 10.81; found C 69.27, H 10.63.

6,8-Methylenedioxy-4-acryloyloxy-1-tridecene: To a solution of 6,8-methylenedioxy-4-hydroxy-1-tridecene (15; 260 mg, 1.073 mmol) in CH₂Cl₂ (2 mL), acryloyl chloride (0.13 mL, 1.6 mmol), NEt₃ (0.45 mL, 3.2 mmol) and DMAP (26 mg, 0.21 mmol, 20 mol %) was added with stirring. After 10 min of stirring at r.t., the

reaction was quenched by adding sat. aq NaHCO$_3$ (15 mL), water (10 mL) and CH$_2$Cl$_2$ (50 mL). The organic phase was washed with water (20 mL) and the aqueous phase extracted with tBuOMe. The combined organic phase was dried (MgSO$_4$), filtered, and evaporated. Purification by CC (tBuOMe/hexanes 1:5) gave the ester as colorless liquid (234 mg, 74%).

$R_f = 0.68/0.80$ (diastereomers; tBuOMe/hexanes 1:3). $^1$H NMR (CDCl$_3$, 400 MHz), several diastereomers: 0.84–0.92 (m, 3 H, Me), 1.22–1.85 (m, 11.3 H), 1.92–2.24 (m, 0.7 H), 2.31–2.50 (m, 2 H), 3.46–4.06 (several m, 2 H, H-6+H-8), 4.61–5.29 (several m, 5 H, H-4+ OCH$_2$O+2 H-1), 5.69–5.82 (m, 1 H-2), 5.82 (d×m, $J = 10.4$ Hz, 1 H$_{\text{acyrloyl}}$), 6.09/6.13 (d×m, $J = 10.4$ Hz, 1 H$_{\text{acyrloyl}}$), 6.36–6.39/6.41–6.44 (m, 1 H$_{\text{acyrloyl}}$). $^{13}$C NMR (CDCl$_3$, 100 MHz), 4 diastereomers: 14.1 (CH$_3$), 22.7 (CH$_2$), 24.9/24.7/25.1/25.2 (CH$_2$), 31.8/31.8/31.8/31.9 (CH$_2$), 32.8/33.2/34.6/35.1/36.0/36.0/36.5/37.4/37.6/38.0/38.4/38.9/39.2/39.3/39.9/40.3 (4×CH$_2$), 68.2/68.7/70.1/70.2/70.4/70.6/71.7/71.7/73.0/73.6/76.4/76.4/3×CH), 87.1/87.2/93.4/93.5 (CH$_2$), 118.0/118.1 (CH$_2$), 128.5/128.6/128.6/128.6 (CH), 130.5/130.6/130.6/130.6 (CH$_2$), 133.1/133.1/133.2/133.2 (CH), 165.5/165.6/165.6/165.6 (C). IR (film): 3433, 3078, 2930, 2857, 2774, 1724, 1639, 1463, 1435, 1406, 1295, 1271, 1194, 1136, 1033, 988, 917, 808. MS (EI, 70 eV): $m/z$ (%) = 295.4 (3) $M^+$, 255.4 (13), 225.4 (40), 195.3 (20), 183.3 (32), 157.3 (56), 153.3 (81), 135.3 (44), 123.3 (53), 109.3 (75), 97.3 (44), 79.3 (49), 67.3 (58), 55.3 (100). Anal calcd for C$_{17}$H$_{28}$O$_4$: C 68.89, H 9.52; found C 68.77, H 9.24.

**$5,6$-Dihydro-$6$-(2,4-methylenedioxyxonyl)-pyran-2-one (16):** A solution of 6,8-methylenedioxy-4-acyrloyloxy-1-tridecene (100 mg, 0.337 mmol) and Grubbs catalyst I ([Ru(=CHPh)Cl$_2$(PCy$_3$)$_2$]; 27.8 mg, 0.0338 mmol, 10 mol %) in degassed CH$_2$Cl$_2$ (50 mL) was refluxed for 4 h. After evaporation, the residue was purified by CC (tBuOMe/hexanes 1:1) to give two fractions of diastereomeric pyranones (A: 52.6 mg, B: 24.6 mg, total 77.2 mg 85%) as colorless liquids.

Data for diastereomer fraction A: $R_f = 0.33$ (tBuOMe/hexanes 1:1). $^1$H NMR (CDCl$_3$, 300 MHz), 2 diastereomers: 0.89 (t, $J = 6.7$ Hz, 3 H, Me), 1.23–1.66 (m, 10 H), 1.71–2.20 (2×m, 2 H), 2.25–2.55
(m, 2 H), 3.51–3.62 (m, 1 H), 3.83–4.02 (m, 1 H), 4.58–4.77 (m, 1 H), 4.69/4.73 (d, $J = 6.4$ Hz, 1 H, OCH$_2$O) 5.04 (d, $J = 6.4$ Hz, 1 H, OCH$_2$O), 5.99–6.06 (m, 1 H$_{\text{alkene}}$), 6.85–6.95 (m, 1 H$_{\text{alkene}}$). $^{13}$C NMR (CDCl$_3$, 75 MHz), 2 diastereomers: 14.0 (CH$_3$), 22.5 (CH$_2$), 24.5 (CH$_2$), 29.2/29.9 (CH$_2$), 31.7/31.7 (CH$_2$), 35.8 (CH$_2$), 37.2/37.9 (CH$_2$), 40.3/41.6 (CH$_2$), 71.7/72.2 (CH), 73.9/74.5 (CH), 76.4/76.4 (CH), 93.3/93.4 (CH$_2$), 121.2/121.3 (CH), 145.2/145.3 (CH), 164.3/164.3 (C). IR (film): 2930, 2858, 2774, 1725, 1465, 1426, 1385, 1249, 1195, 1142, 1029, 958, 819, 731, 664, 553. MS (EI, 70 eV): $m/z$ (%) = 269.4 (20) $M^+$, 250.3 (3), 238.4 (3), 221.4 (4), 197.3 (67), 183.3 (25), 167.2 (95), 139.3 (82), 109.3 (27), 97.2 (100). 68.3 (62), 55.3 (68). Anal calcd for C$_{15}$H$_{24}$O$_4$: C 67.14, H 9.01; found C 66.98, H 8.84.

Data for diastereomer fraction B: $R_f$ = 0.23 (tBuOMe/hexanes 1:1). $^1$H NMR (CDCl$_3$, 300 MHz), 2 diastereomers: 0.82–0.96 (m, 3 H, Me), 1.23–2.00 (m, 12 H), 2.26–2.50 (m, 2 H), 3.83–4.00 (m, 1 H), 4.10–4.29 (m, 1 H), 4.54–4.78 (m, 1 H), 4.78–4.97 (m, 2 H), 5.98–6.07 (m, 1 H$_{\text{alkene}}$), 6.85–6.95 (m, 1 H$_{\text{alkene}}$). $^{13}$C NMR (CDCl$_3$, 75 MHz): 14.0 (CH$_3$), 22.6/22.6 (CH$_2$), 25.1/25.3 (CH$_2$), 28.9/29.9 (CH$_2$), 31.5/32.5 (CH$_2$), 31.6 (CH$_2$), 34.5/34.9 (CH$_2$), 37.9/40.1 (CH$_2$), 67.1/67.4 (CH), 71.7/71.7 (CH), 74.1/74.8 (CH), 86.9/87.0 (CH$_2$), 121.3/121.4 (CH), 145.1/145.2 (CH), 164.2/164.3 (C). IR (film): 2930, 2859, 2782, 1723, 1462, 1430, 1387, 1247, 1183, 1135, 1018, 952, 818, 755, 726, 663, 554. MS (EI, 70 eV): $m/z$ (%) = 269.4 (26) $M^+$, 250.3 (2), 239.3 (12), 221.3 (5), 197.2 (73), 183.3 (27), 167.2 (96), 149.2 (40), 139.3 (79), 109.3 (48), 97.2 (100). 68.3 (71), 55.3 (81). Anal calcd for C$_{15}$H$_{24}$O$_4$: C 67.14, H 9.01; found C 66.90, H 8.80.