Rhodium-catalyzed redox allylation reactions of ketones

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A. General Information

All reactions were carried out using flame-dried glassware. Toluene was dried by passage through activated alumina using a GlassContour solvent purification system. Allyl acetate was purified by distillation and stored under N₂ over solid sodium sulfate. Acetophenone was distilled prior to use. All other ketones were used without distillation, but had been stored under a dry inert atmosphere for several months prior to use. [Rh(cod)Cl₂], bis(pinacolato)diboron ((Bpin)₂), dimethylphosphinoethane (dmpe), and 1,2-bis([2S,5S]-2,5-dimethylphospholano)benzene [(S,S)-MeDuphos] were stored in a N₂ atmosphere glovebox, with (Bpin)₂ being stored in a freezer within the glovebox. All reactions were run in sealed vials. Bis(pinacolato)diboron was donated by Frontier Chemicals and [Rh(cod)Cl₂] was donated by Hareaus.

¹H NMR, and ¹³C NMR, Bruker GN-500 (500 MHz ¹H, 125.7 MHz ¹³C), Bruker CRYO-500 (500 MHz ¹H, 125.7 MHz ¹³C), Bruker DRX-400 (400 MHz ¹H, 100 MHz ¹³C), or Bruker Avance-600 (600 MHz ¹H, 150 MHz ¹³C) NMR spectra are reported as δ values in ppm. Coupling constants are reported in Hz. The term br refers to “broad” and the term app refers to “apparent”. The term dddd refers to a doublet of doublet of doublet of doublets. Infrared (IR) spectra were obtained using a Galaxy Series FTIR 5000 spectrometer. Low-resolution mass spectra (LRMS) and high resolution mass spectra (HRMS) were obtained using a Waters-MicroMass Analytical LCT (ESI) spectrometer. Melting points were obtained on an Electrothermal melting point apparatus and are uncorrected. Analytical thin-layer chromatography (TLC) was performed using Silica Gel 60 F254 precoated plates (0.25 mm thickness). Flash chromatography was performed using Silica Gel 60A (170-400 mesh) from Fisher Scientific. Silver impregnated silica gel was prepared according to literature procedure,¹² and was used to isolate compounds 1c, 1d, and 5. PAA stands for p-anisaldehyde stain.

Spectral data of compound 6 can be found in the literature.³

B. Allylation Reactions

i. Experimental procedures for general allylation method.

In a glovebox [Rh(cod)Cl₂] (5 mg, 0.01 mmol, 0.03 equiv), ligand (0.02 mmol, 0.05 equiv), and bisboron pinacol ester (306 mg, 1.20 mmol, 3.00 equiv) were added to a vial with stirbar. Outside of the glovebox the vial was briefly opened to air and allyl acetate (130 µL, 1.2 mmol, 3.0 equiv), ketone (0.4 mmol, 1 equiv), and toluene (1mL) were added to the vial after which it was sealed with a cap. The reaction was allowed to stir in a 50 °C oil bath for 18h, after which it was allowed to cool to room temperature. Unless otherwise indicated, the reaction material was loaded directly onto a column for chromatographic separation (5–15% EtOAc/Hex using Davisil® when indicated to avoid streaking), followed by a second column (15–30% Et₂O/pentane) when necessary.

ii. Characterization data for 4a–4i

[2-phenylpent-4-en-2-ol (4a): Davisil® was used for isolation. 46 mg isolated as a pale yellow oil (71%): Rf = 0.6 (25% EtOAc/Hex; stains purple with PAA); ¹H NMR (400 MHz, CDCl₃) δ 7.44 (d, J = 7.5, 2H), 7.34 (t, J = 7.3, 2H), 7.23 (app t, J = 7.2, 1H), 5.62...
(dd, J = 1.70, 10.2, 8.5, 6.5, 1H), 5.13 (d, J = 18.9, 1H), 5.12 (d, J = 7.0, 1H), 2.69 (dd, J = 13.5, 6.8, 1H) 2.50 (dd, J = 13.8, 8.5, 1H), 2.08 (br s, 1H), 1.55 (s, 3H).

**2-(4-chlorophenyl)pent-4-en-2-ol (4b):** Davisil® was used for isolation. 65 mg isolated as a colorless oil (83%): Rf = 0.6 (25% EtOAc/Hex; stains purple-blue with PAA); 1H NMR (400 MHz, CDCl3) δ 7.37 (d, J = 8.5, 2H), 7.29 (d, J = 8.6, 2H), 5.60 (dd, J = 14.7, 9.4, 8.1, 6.7, 1H), 5.13 (br d, J = 12.7, 2H), 2.64 (dd, J = 13.6, 6.5, 1H), 2.48 (dd, J = 13.8, 8.3, 1H), 2.10 (br s, 1H), 1.52 (s, 3H).

**2-(4-methoxyphenyl)pent-4-en-2-ol (4c):** Silver impregnated silica was used for isolation (40% Et2O/pentane then 25–40% EtOAc/Hex). 47 mg isolated as a colorless oil (61%): Rf = 0.5 (EtOAc/Hex; stains purple-blue with PAA); 1H NMR (400 MHz, CDCl3) δ 7.36 (app d, J = 8.9, 2H), 6.88 (app d, J = 8.9, 1H), 5.63 (dd, J = 17.0, 10.8, 8.5, 6.1, 1H), 5.13 (br d, J = 8.7, 1H), 5.12 (br d, J = 17.3, 1H), 3.81 (s, 3H), 2.66 (dd, J = 13.9, 6.6, 1H), 2.49 (dd, J = 13.6, 8.2, 1H), 2.01 (br s, 1H), 1.53 (s, 3H).

**2-(3,4-dimethoxyphenyl)pent-4-en-2-ol (4d):** Silver impregnated silica was used for isolation (90% Et2O/pentane then 80% EtOAc/Hex) followed by a silica plug with 20% Et2O/pentane then 35% EtOAc/Hex). 48 mg isolated as a colorless solid (54%): Rf = 0.4 (25% EtOAc/Hex, stains blue with PAA); 1H NMR (400 MHz, CDCl3) δ 7.03 (d, J = 2.2, 1H), 6.93 (dd, J = 8.4, 2.0, 1H), 6.83 (d, J = 8.3, 1H), 5.64 (dd, J = 16.7, 10.2, 8.2, 6.5, 1H), 5.15 (br d, J = 7.6, 1H), 5.14 (br d, J = 17.4, 1H), 3.90 (s, 3H), 3.88 (s, 3H), 2.67 (dd, J = 13.8, 6.6, 1H), 2.49 (dd, J = 13.8, 8.3, 1H), 2.01 (s, 3H).

**2-(naphthalen-2-yl)pent-4-en-2-ol (4e):** Davisil® was used for isolation. 55 mg isolated as a colorless oil (65%): Rf = 0.6 (25% EtOAc/Hex, stains purple with PAA); 1H NMR (400 MHz, CDCl3) δ 7.93 (s, 1H), 7.84 (m, 3H), 7.55 (dd, J = 8.7, 1.9, 1H), 7.48 (m, 3H) 5.64 (dd, J = 16.7, 10.1, 8.4, 6.6, 1H), 5.17 (d, J = 17.3, 1H), 5.13 (d, J = 10.3, 1H), 2.82 (dd, J = 13.9, 6.3, 1H), 2.60 (dd, J = 13.8, 8.5, 1H), 2.22 (br s, 1H), 1.65 (s, 3H).

**3-phenylhex-5-en-3-ol (4f):** Davisil® was used for isolation. 32 mg isolated as a colorless oil (46%): Rf = 0.6 (25% EtOAc/Hex), stains purple with PAA); 1H NMR (400 MHz, CDCl3) δ 7.39 (d, J = 7.1, 2H), 7.34 (t, J = 7.2, 2H), 7.23 (t, J = 7.0, 1H), 5.58 (dd, J = 16.7, 10.0, 8.6, 6.1, 1H), 5.13 (d, J = 17.0, 1H), 5.10 (d, J = 10.0, 1H), 2.72 (dd, J = 13.6, 6.0, 1H), 2.50 (dd, J = 13.8, 8.7, 1H), 2.00 (s, 3H) 1.92–1.77 (m, 2H), 1.57 (s, 3H), 0.77 (t, J = 7.4, 3H).

**2-cyclohexylpent-4-en-2-ol (4g):** 55 mg isolated as a colorless oil (82%): Rf = 0.6 (25% EtOAc/Hex, stains purple with PAA); 1H NMR (400 MHz, CDCl3) δ 5.88 (ddt, J = 17.6, 10.2, 7.4, 1H), 5.14 (app dd, J = 10.4, 1.3, 1H), 5.11 (app ddt, J = 17.0, 2.1, 1.3, 1H), 2.25 (dd, J = 13.7, 7.5, 1H), 2.19 (ddt, J = 13.8, 7.5, 1.3, 1H), 1.89–1.62 (m, 6H), 1.31 (tt, J = 11.9, 2.9, 1H), 1.27–0.96 (m, 10H).
iii. Experimental procedures for pregnenolone acetate and compound 6.

The general procedures in part i used with 12 equivalents of allyl acetate (4.8 mmol). A septa cap was used rather than a vial cap in order to monitor reaction progress by TLC. Upon starting material consumption as determined by TLC, the reaction was allowed to cool and was isolated by column chromatography (5–15% EtOAc/Hex).

iv. Characterization data for compounds 5 and 7.

**Allylated pregnenolone acetate (5)**: Silver impregnated silica used for isolation (5–15% EtOAc/Hex). 133 mg isolated as a clear crystalline solid in 10:1 diastereomeric ratio epimeric at the tertiary alcohol (83%): Rf = 0.7 (25% EtOAc/Hex, stains blue-purple with PAA); 1H NMR (400 MHz, CDCl3, major reported) δ 5.80 (ddt, J = 17.5, 10.4, 7.5, 1H), 5.36 (d, J = 4.8, 1H), 5.08 (dd, J = 10.8, 2.0, 1H), 5.06 (dd, J = 16.8, 2.0, 1H), 4.63–4.54 (m, 1H), 2.33–2.27 (m, 2H), 2.16 (app dd, J = 7.7, 3.1, 2H), 2.15 (s, 1H), 2.07 (dt, J = 12.5, 3.4, 1H), 2.01 (s, 3H), 1.96 (dt, J = 17.7, 5.5, 1H), 1.84 (br d, J = 11.1, 2H), 1.77 (app tt, J = 11.4, 2.0, 1H), 1.73–1.51 (m, 5H), 1.51–1.40 (m, 5H), 1.27 (s, 3H), 1.25–1.07 (m, 4H), 1.02–0.98 (m, 4H), 0.97–0.89 (m, 1H), 0.85 (s, 3H).

**Compound 7**: 241 mg isolated as a colorless oil (97%): Rf = 0.6 (25% EtOAc/Hex, stains purple with PAA); 1H NMR (500 MHz, CDCl3, major reported) δ 7.65 (d, J = 7.6, 4H), 7.41 (t, J = 7.5, 2H), 7.36 (t, J = 7.1, 5H) 7.24 (app d, J = 7.8, 1H), 6.92 (t, J = 7.5, 1H), 6.88 (d, J = 8.1, 2H), 5.84 (ddt, J = 17.5, 10.2, 7.5, 1H), 5.14 (dd, J = 10.2, 1.7, 1H), 5.08 (dd, J = 17.2, 1.2, 1H), 4.05 (t, J = 8.6, 1H), 3.83 (dd, J = 8.8, 7.3, 1H), 3.61 (t, J = 6.4, 2H), 3.27 (br q, J = 10.0, 1H), 3.04 (br t, J = 10.0, 1H), 2.45 (dd, J = 15.9, 6.7, 1H), 2.13 (app d, J = 16.7, 1H), 2.10 (app d, J = 17.6, 1H), 2.16–2.02 (m, 4H), 1.85 (dd, J = 16.0, 8.8, 1H), 1.78–1.69 (m, 1H), 1.63 (d, J = 13.5, 1H), 1.48–1.34 (m, 3H), 1.34 (app t, J = 13.1, 2H), 1.26 (app d, J = 11.1, 1H), 1.26 (s, 3H), 1.03 (br s, 9H), 0.95 (d, J = 6.6, 3H); 13C NMR (125 MHz, CDCl3, major reported) δ 159.1, 145.7, 135.8 (4C), 133.7, 133.2, 129.8 (2C), 129.7 (2C), 127.8 (4C), 120.8, 119.3, 114.9 (2C), 73.8, 70.4, 64.2, 50.5, 44.8, 43.4, 41.8, 39.3, 36.4, 35.9, 33.2, 33.0, 27.0 (3C), 25.2, 20.2, 19.4; IR
(thin film, cm\(^{-1}\)) 2931, 2860, 1242, 1111, 702; LRMS (ESI, m+Na) 631.2, HRMS (ESI, m+Na) calc. for 631.3583, found 631.3595.

2 Silica preparation was scaled up. For 200 g silica 30 g AgNO\(_3\) was used and the mixture was stirred for 2 hours. The silica was dried in an oven overnight, protected from light at all times including during column chromatography.
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1H spectrum

[Diagram of a chemical structure labeled 4a with a 1H spectrum graph below it.]
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13C spectrum with 1H decoupling

4a

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13C spectrum with 1H decoupling

4a
13C spectrum with 1H decoupling

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$^{13}$C spectrum with $^1$H decoupling
Z-restored spin-echo $^{13}$C spectrum with $^1$H decoupling

![Chemical structure](image)

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$^{13}$C spectrum with $^1$H decoupling

$^{13}$C spectrum with $^1$H decoupling
$^{13}$C spectrum with $^1$H decoupling
$^{13}C$ spectrum with $^1H$ decoupling

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13C spectrum with 1H decoupling
1H spectrum

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13C spectrum with 1H decoupling
13C spectrum with 1H decoupling

AcO
Z-restored spin-echo 13C spectrum with 1H decoupling

TBDPSO

PhO