Supporting Information for *Angew. Chem. Int. Ed.* Z18674

A Novel Rhodium-Catalyzed Reduction-Oxidation Process: Reaction of 4-Alkynals with Phenol to Provide c*is*-4-Alkenoates

Ken Tanaka and Gregory C. Fu*

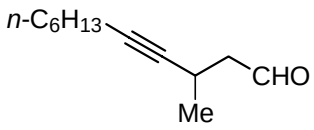
Department of Chemistry, Massachusetts Institute of Technology,
Cambridge, MA 02139

I. General

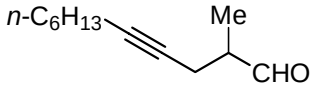
THF was distilled from sodium-benzophenone ketyl. CH_2Cl_2 was purified by passage through a neutral alumina column under argon. Acetone (99.9+%, Aldrich) was dried over Union Carbide 4Å molecular sieves (Fluka) prior to use. CuI (99.999%, Aldrich) and phenol (99+%, re-distilled, Aldrich; or, reagent grade) were used as received. $[Rh(dppe)]_2(BF_4)_2$ was prepared according to a literature procedure.[1] All other reagents and solvents were obtained from commercial sources and used as received.

All reactions were carried out under an atmosphere of nitrogen or argon in oven-dried glassware with magnetic stirring, unless otherwise indicated.

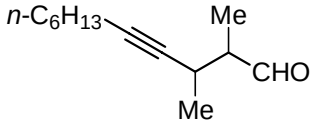
II. Preparation of 4-Alkynals



3-Methylundec-4-ynal. This was prepared according to a literature procedure.[2]



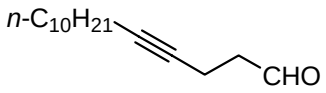
2-Methylundec-4-ynal. This was prepared according to a literature procedure.[2]



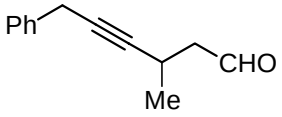
2,3-Dimethylundec-4-ynal. *n*-BuLi (1.6 M in hexane; 19 mL, 30 mmol) was added to a stirred solution of 1-octyne (4.5 mL, 30 mmol) in THF (80 mL) at 0 °C, and the resulting mixture was stirred at 0 °C for 20 min. CuI (99.999%; 6.3 g, 33 mmol) was added, and the reaction solution was stirred at 0 °C for 1 h. After cooling to –78 °C, TMSI (4.7 mL, 33 mmol) was added, and the resulting mixture was stirred at –78 °C for 10 min. 2-Methyl-2-butenal (2.0 mL, 21 mmol) was then added at –78 °C, and the solution was stirred at –45 °C for 2 h. The reaction was quenched by the addition of 4 M HCl (50 mL), and the crude mixture was extracted with Et_2O. The organic layer was dried over Na_2SO_4, concentrated, and purified by flash chromatography (pentane:Et_2O = 20:1), which furnished 2,3-dimethylundec-4-ynal (1.8 g, 9.3 mmol, 45%; not optimized) as a pale-yellow oil.

Mixture of diastereomers; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.75 (d, J = 2.4 Hz, 0.5H),

9.67 (d, J = 1.5 Hz, 0.5H), 2.86-2.96 (m, 0.5H), 2.65-2.76 (m, 0.5H), 2.26-2.34 (m, 1H), 2.09-2.15 (m, 2H), 1.22-1.50 (m, 8H), 1.169 (d, J = 7.2 Hz, 1.5H), 1.167 (d, J = 6.9 Hz, 1.5H), 1.143 (d, J = 7.2 Hz, 1.5H), 1.135 (d, J = 7.2 Hz, 1.5H), 0.87 (t, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 205.1, 204.7, 83.2, 81.5, 80.9, 51.1, 51.0, 31.5, 29.1, 28.70, 28.68, 27.6, 26.9, 22.8, 19.3, 19.0, 18.9, 18.8, 14.3, 11.7, 10.3. FTIR (neat) 2958, 2933, 2874, 2860, 1730, 1456 cm^{-1}; HRMS (EI) calcd for $C_{13}H_{22}O$ (M^+) 194.1665, found 194.1665.

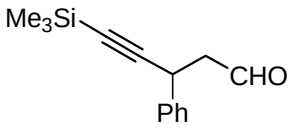


Pentadec-4-ynal. This was prepared according to a literature procedure.[2]



3-Methyl-6-phenylhex-4-ynal. This was prepared according to the procedure described for 2,3-dimethylundec-4-ynal, starting from 3-phenyl-1-propyne and crotonaldehyde (21% isolated yield; not optimized).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.83 (t, J = 2.0 Hz, 1H), 7.20-7.40 (m, 5H), 3.59 (d, J = 2.0 Hz, 2H), 3.05 (ttq, J = 7.0, 7.0, and 2.0 Hz, 1H), 2.61 (ddd, J = 16.5, 7.5, and 2.0 Hz, 1H), 2.53 (ddd, J = 16.5, 6.5, and 2.0 Hz, 1H), 1.28 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 202.2, 137.8, 129.2, 128.5, 127.2, 85.6, 79.8, 51.0, 25.7, 22.0, 21.5. FTIR (neat) 3030, 2972, 2825, 2727, 1728, 1495, 1454, 731, 697 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{15}O$ [$(M+H)^+$] 187.1123, found 187.1123.



3-Phenyl-5-trimethylsilylpent-4-ynal. This was prepared according to the procedure described for 2,3-dimethylundec-4-ynal, starting from (trimethylsilyl)acetylene and *trans*-cinnamaldehyde (7% isolated yield; not optimized).

^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.79 (t, J = 1.8 Hz, 1H), 7.23-7.41 (m, 5H), 4.23 (dd, J = 8.1 and 6.3 Hz, 1H), 2.89 (ddd, J = 16.8, 8.1, and 1.8 Hz, 1H), 2.80 (ddd, J = 16.8, 6.0, and 1.8 Hz, 1H), 0.18 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 200.4, 140.0, 129.0, 127.53, 127.47, 106.1, 89.0, 51.4, 33.0, 0.2. FTIR (neat) 2960, 2175, 1728, 1494, 1454, 1251, 844, 761, 699 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{18}OSi$ (M^+) 230.1121, found 230.1120.

III. Reaction of 4-Alkynals with Phenol to Provide *cis*-4-Alkenoates (eq 3 and Table 1)

General Procedure (eq 3). In a N_2-filled glove box, $[Rh(dppe)]_2(BF_4)_2$ (6.5 mg, 0.0055 mmol), PhOH (26 mg, 0.28 mmol), *n*-tridecane (10.0 μL), and 3-methylundec-4-ynal (10.0 mg, 0.055 mmol) were added to a Schlenk tube with the indicated solvent (1.0 mL). The vessel was removed from the glove box, and the mixture was stirred at r.t. for 24 h. The yields of the cyclopentenone and the *trans*-4-alkenoate were determined by GC.

General Procedure 1, Table 1 (without a glove box) (entry 1, first run). In the air, $[Rh(dppe)]_2(BF_4)_2$ (16 mg, 0.014 mmol) was placed into a Schlenk tube, which was then filled with argon. Under a positive pressure of argon, a solution of PhOH (260 mg, 2.76 mmol) and 3-methylundec-4-ynal (100 mg, 0.555 mmol) in $ClCH_2CH_2Cl$ (5 mL) was added. The vessel was closed, and the mixture was stirred at 80 °C for 40 hours. The resulting solution was concentrated and purified by column chromatography (pentane:Et_2O = 20:1), which furnished phenyl (*Z*)-3-methylundec-4-enoate (131 mg, 0.477 mmol, 86%) as a colorless oil.

General Procedure 2, Table 1 (with a glove box) (entry 1, second run). In a N_2-filled glove box, $[Rh(dppe)]_2(BF_4)_2$ (8.2 mg, 0.0070 mmol), PhOH (130 mg, 1.38 mmol), and 3-methylundec-4-ynal (50.0 mg, 0.277 mmol) were added to a Schlenk tube with $ClCH_2CH_2Cl$ (2.5 mL). The vessel was removed from the glove box, and the mixture was stirred at 80 °C for 40 h. It was then concentrated and purified by column chromatography (pentane:Et_2O = 20:1), which furnished phenyl (*Z*)-3-methylundec-4-enoate (66.2 mg, 0.241 mmol, 87%) as a colorless oil.

Phenyl (*Z*)-3-methylundec-4-enoate (Table 1, entry 1). Colorless oil; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.34-7.41 (m, 2H), 7.19-7.26 (m, 1H), 7.04-7.10 (m, 2H), 5.42 (dt, *J* = 10.8 and 7.5 Hz, 1H), 5.27 (dd, *J* = 10.8 and 9.6 Hz, 1H), 3.07-3.22 (m, 1H), 2.54 (dd, *J* = 14.7 and 6.9 Hz, 1H), 2.48 (dd, *J* = 14.7 and 7.5 Hz, 1H), 2.01-2.21 (m, 2H), 1.25-1.43 (m,

8H), 1.11 (d, J = 6.6 Hz, 3H) , 0.88 (t, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.3, 151.0, 133.6, 130.5, 129.6, 126.0, 121.9, 42.3, 32.0, 30.0, 29.5, 29.2, 27.7, 22.9, 21.4, 14.3. FTIR (neat) 2958, 2928, 2857, 2360, 2341, 1760, 1197, 688, 669 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{27}O_2$ [$(M+H)^+$] 275.2012, found 275.2012.

Phenyl (*Z*)-2-methylundec-4-enoate (Table 1, entry 2). A run was carried out according to Procedure 1, using 16 mg of $[Rh(dppe)]_2(BF_4)_2$, 260 mg of PhOH, and 100 mg of 2-methylundec-4-ynal. Reaction time: 65 h. Phenyl (*Z*)-2-methylundec-4-enoate was obtained in 68% yield.

A run was carried out according to Procedure 2, using 8.2 mg of $[Rh(dppe)]_2(BF_4)_2$, 130 mg of PhOH, and 50.0 mg of 2-methylundec-4-ynal. Reaction time: 41 h. Phenyl (*Z*)-2-methylundec-4-enoate was obtained in 71% yield.

Colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.34-7.41 (m, 2H), 7.19-7.26 (m, 1H), 7.04-7.08 (m, 2H), 5.53 (dt, J = 11.1 and 6.9 Hz, 1H), 5.41 (dt, J = 10.8 and 7.5 Hz, 1H), 2.67-2.79 (m, 1H), 2.49-2.64 (m, 1H), 2.30-2.40 (m, 1H), 2.00-2.13 (m, 2H), 1.25-1.38 (m, 8H), 1.30 (d, J = 6.9 Hz, 3H) , 0.85-0.92 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 175.1, 151.1, 132.9, 129.6, 125.93, 125.90, 121.8, 40.3, 32.0, 31.5, 29.8, 29.2, 27.6, 22.9, 16.8, 14.4. FTIR (neat) 2929, 2857, 1760, 1493, 1457, 1197, 1126, 747, 690 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{27}O_2$ [$(M+H)^+$] 275.2012, found 275.2011.

Phenyl (*Z*)-2,3-dimethylundec-4-enoate (Table 1, entry 3). A run was carried out according to Procedure 1, using 30 mg of $[Rh(dppe)]_2(BF_4)_2$, 242 mg of PhOH, and 100 mg of 2,3-dimethylundec-4-ynal. Reaction time: 65 h. Phenyl (*Z*)-2,3-dimethylundec-4-enoate was obtained in 81% yield.

A run was carried out according to Procedure 2, using 15.1 mg of $[Rh(dppe)]_2(BF_4)_2$, 121 mg of PhOH, and 50.0 mg of 2,3-dimethylundec-4-ynal. Reaction time: 63 h. Phenyl (*Z*)-2,3-dimethylundec-4-enoate was obtained in 71% yield.

Colorless oil (mixture of two diastereomers); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.33-7.42 (m, 2H), 7.19-7.26 (m, 1H), 7.02-7.10 (m, 2H), 5.32-5.52 (m, 1.5H), 5.19 (t, J = 10.5 Hz,

0.5H), 2.82-2.95 (m, 1H), 2.43-2.62 (m, 1H), 1.94-2.17 (m, 2H), 1.24-1.44 (m, 8H), 1.25 (d, *J* = 6.9 Hz, 1.5H), 1.20 (d, *J* = 7.2 Hz, 1.5H), 1.11 (d, *J* = 6.9 Hz, 1.5H), 1.08 (d, *J* = 6.9 Hz, 1.5H), 0.85-1.05 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 175.1, 174.6, 151.1, 151.0, 132.7, 132.2, 131.3, 130.8, 129.64, 129.56, 126.0, 125.9, 121.9, 121.8, 46.0, 45.6, 35.4, 35.2, 32.0, 30.0, 29.9, 29.3, 27.9, 27.7, 22.9, 19.9, 18.4, 15.5, 14.5, 14.4. FTIR (neat) 2960, 2928, 2856, 1759, 1494, 1457, 1197, 1161, 1122, 748, 689 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{29}O_2$ [$(M+H)^+$] 289.2162, found 289.2169.

Phenyl (*Z*)-pentadec-4-enoate (Table 1, entry 4). A run was carried out according to Procedure 1, using 26 mg of $[Rh(dppe)]_2(BF_4)_2$, 212 mg of PhOH, and 100 mg of pentadec-4-ynal. Reaction time: 65 h. Phenyl (*Z*)-pentadec-4-enoate was obtained in 63% yield.

A run was carried out according to Procedure 2, using 13.2 mg of $[Rh(dppe)]_2(BF_4)_2$, 106 mg of PhOH, and 50.0 mg of pentadec-4-ynal. Reaction time: 63 h. Phenyl (*Z*)-pentadec-4-enoate was obtained in 67% yield.

Colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.34-7.41 (m, 2H), 7.19-7.28 (m, 1H), 7.05-7.09 (m, 2H), 5.37-5.53 (m, 2H), 2.44-2.64 (m, 4H), 2.04-2.12 (m, 2H), 1.22-1.40 (m, 16H), 0.87 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.5, 151.4, 132.7, 130.1, 127.6, 126.5, 122.3, 35.2, 32.6, 30.35, 30.27, 30.1, 30.0, 28.0, 23.5, 23.4, 14.9. FTIR (neat) 2925, 2854, 1763, 1594, 1492, 1197, 1162, 689 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{33}O_2$ [$(M+H)^+$] 317.2475, found 317.2468.

Phenyl (*Z*)-3-methyl-6-phenylhex-4-enoate (Table 1, entry 5). A run was carried out according to Procedure 1, using 16 mg of $[Rh(dppe)]_2(BF_4)_2$, 250 mg of PhOH, and 100 mg of 3-methyl-6-phenylhex-4-ynal. Reaction time: 48 h. Phenyl (*Z*)-3-methyl-6-phenylhex-4-enoate was obtained in 82% yield.

A run was carried out according to Procedure 2, using 7.9 mg of $[Rh(dppe)]_2(BF_4)_2$, 126 mg of PhOH, and 50.0 mg of 3-methyl-6-phenylhex-4-ynal. Reaction time: 40 h. Phenyl (*Z*)-3-methyl-6-phenylhex-4-enoate was obtained in 88% yield.

Colorless oil; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.06-7.41 (m, 10H), 5.64 (dt, J = 10.5 and 7.5 Hz, 1H), 5.45 (t, J = 10.5 Hz, 1H), 3.56 (dd, J = 16.0 and 7.5 Hz, 1H), 3.46 (dd, J = 16.0 and 7.5 Hz, 1H), 3.27-3.36 (m, 1H), 2.62 (dd, J = 15.0 and 6.5 Hz, 1H), 2.56 (dd, J = 15.0 and 8.5 Hz, 1H), 1.19 (d, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.7, 151.4, 141.5, 135.0, 130.1, 129.2, 129.11, 129.08, 126.7, 126.5, 122.3, 42.7, 34.4, 30.0, 21.8. FTIR (neat) 3028, 2963, 2928, 1756, 1594, 1494, 1454, 1197, 1141, 742, 698 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{21}O_2$ [$(M+H)^+$] 281.1536, found 281.1534.

Phenyl (*Z*)-3-phenyl-5-trimethylsilylpent-4-enoate (Table 1, entry 6). A run was carried out according to Procedure 1, using 12.8 mg of $[Rh(dppe)]_2(BF_4)_2$, 204 mg of PhOH, and 100 mg of 3-phenyl-5-trimethylsilylpent-4-ynal. Reaction time: 20 h. Phenyl (*Z*)-3-phenyl-5-trimethylsilylpent-4-enoate was obtained in 97% yield.

A run was carried out according to Procedure 2, using 6.4 mg of $[Rh(dppe)]_2(BF_4)_2$, 102 mg of PhOH, and 50.0 mg of 3-phenyl-5-trimethylsilylpent-4-ynal. Reaction time: 16 h. Phenyl (*Z*)-3-phenyl-5-trimethylsilylpent-4-enoate was obtained in 94% yield.

Colorless oil; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.20-7.40 (m, 8H), 6.91-6.93 (m, 2H), 6.56 (dd, J = 14.0 and 10.5 Hz, 1H), 5.69 (d, J = 13.5 Hz, 1H), 4.18-4.23 (m, 1H), 3.02 (dd, J = 15.0 and 8.5 Hz, 1H), 2.91 (dd, J = 15.0 and 7.5 Hz, 1H), 3.27-3.36 (m, 1H), 0.22 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.8, 151.3, 149.6, 143.3, 131.3, 130.1, 129.5, 127.9, 127.5, 126.5, 122.3, 46.4, 42.6, 1.0. FTIR (neat) 2955, 1760, 1598, 1493, 1249, 1196, 1127, 839, 757, 697 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{25}O_2Si$ [$(M+H)^+$] 325.1618, found 325.1611.

IV. Equations 4-6

Methyl (*Z*)-3-methylundec-4-enoate (Eq 4). In a N_2-filled glove box, $[Rh(dppe)]_2(BF_4)_2$ (8.2 mg, 0.0070 mmol), MeOH (112 μL, 2.77 mmol), and 3-methylundec-4-ynal (50.0 mg, 0.277 mmol) were added to a vessel with CH_2Cl_2 (2.5 mL). The mixture was stirred at r.t. for 38 h. The resulting solution was concentrated and purified by column chromatography (pentane:Et_2O = 20:1), which furnished methyl (*Z*)-3-methylundec-4-enoate (43.5 mg, 0.207 mmol, 75%).

Colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.32 (dt, *J* = 10.5 and 7.5 Hz, 1H), 5.14 (t, *J* = 10.5 Hz, 1H), 3.64 (s, 3H), 2.93-3.02 (m, 1H), 2.27 (dd, *J* = 14.5 and 7.0 Hz, 1H), 2.23 (dd, *J* = 14.5 and 7.5 Hz, 1H), 2.00-2.09 (m, 2H), 1.24-1.34 (m, 8H), 0.99 (d, *J* = 6.5 Hz, 3H), 0.88 (t, *J* = 6.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.3, 134.3, 130.5, 52.1, 42.6, 32.5, 30.4, 29.75, 29.68, 28.1, 23.3, 21.7, 14.8. FTIR (neat) 2957, 2928, 2857, 1743, 1436, 1357, 1283, 1166, 1009, 744 cm^{-1}; HRMS (EI) calcd for $C_{13}H_{24}O_2$ (M^+) 212.1771, found 212.1769.

Eq 5. Procedure 2 (Section III) was followed, using 3.3 mg (0.0028 mmol) of $[Rh(dppe)]_2(BF_4)_2$, 52 mg (0.55 mmol) of PhOH, and 20 mg (0.11 mmol) of 1-deuterio-3-methylundec-4-ynal.[2] Reaction time: 24 h. Phenyl (*Z*)-5-deuterio-3-methylundec-4-enoate was isolated by column chromatography as a colorless oil (pentane:Et_2O = 20:1).

^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.34-7.41 (m, 2H), 7.19-7.25 (m, 1H), 7.03-7.09 (m, 2H), 5.26 (d, *J* = 9.9 Hz, 1H), 3.06-3.21 (m, 1H), 2.54 (dd, *J* = 14.7 and 6.9 Hz, 1H), 2.47 (dd, *J* = 14.7 and 7.8 Hz, 1H), 1.98-2.18 (m, 2H), 1.22-1.40 (m, 8H), 1.10 (d, *J* = 6.6 Hz, 3H) , 0.87 (t, *J* = 6.9 Hz, 3H); ^{2}H NMR ($CHCl_3$) δ 5.45 (s, 1D).

Eq 6. Procedure 1 (Section III) was followed, using 3.3 mg (0.0028 mmol) of $[Rh(dppe)]_2(BF_4)_2$, 55 mg (0.55 mmol) of phenol-d_6, and 20 mg (0.11 mmol) of 3-methylundec-4-ynal. Reaction time: 24 h. The 4-deuteriated phenyl ester was isolated by column chromatography as a colorless oil (pentane:Et_2O = 20:1).

^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.41 (t, *J* = 7.5 Hz, 1H), 3.13 (tq, *J* = 7.0 and 7.0 Hz, 1H),

2.54 (dd, J = 15.0 and 7.0 Hz, 1H), 2.48 (dd, J = 14.0 and 8.0 Hz, 1H), 2.03-2.18 (m, 2H), 1.22-1.39 (m, 8H), 1.11 (d, J = 6.5 Hz, 3H), 0.88 (t, J = 7.0 Hz, 3H); ^{2}H NMR ($CHCl_3$) δ 7.40 (s, 2D), 7.25 (s, 1D), 7.09 (s, 2D), 5.30 (s, 1D).

V. References

(1) Halpern, J.; Riley, D. P.; Chan, A. S. C.; Pluth, J. J. *J. Am. Chem. Soc.* **1977**, *99*, 8055-8057.

(2) Tanaka, K.; Fu, G. C. *J. Am. Chem. Soc.*, in press.