Supporting Information for "Catalyst-based Control of [2,3] and [3,3] Rearrangement in α-Diazoketone-derived Propargyloxy Enols"

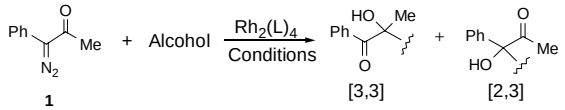
George A. Moniz and John L. Wood*

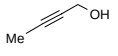
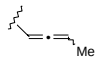
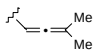
Sterling Chemistry Laboratory, Department of Chemistry, Yale University, New Haven, Connecticut 06520-8107.

Materials and Methods

Unless otherwise stated, reactions were performed in flame-dried glassware under a nitrogen atmosphere using freshly distilled solvents. All commercially obtained reagents were used as received. Analytical thin-layer chromatography (TLC) was performed using silica gel 60 F254 pre-coated plates (0.25 mm). Silica gel (particle size 0.032-0.063 mm) was used for flash chromatography. High-performance liquid chromatography (HPLC) was performed with either a Rainin Microsorb 80-199-C5 or 80-120-C5 column. ^{1}H and ^{13}C NMR chemical shifts are reported as δ values relative to internal chloroform (^{1}H δ 7.27 ppm, ^{13}C δ 77.0 ppm) or benzene-d_6 (^{1}H δ 7.15 ppm). Where inseparable mixtures of diastereomers are isolated, ^{1}H NMR spectral integration reflects a 1:1 mixture. Melting points are uncorrected. High resolution mass spectra were acquired at the University of Illinois Mass Spectrometry Center.

Table 1



Entry	Alcohol	Conditions	Yield [3,3]	Yield [2,3]
1a 1b		A[a] B[b]	22%[c] -	- 87% 
2a 2b		A[d] B	- -	- 68% 
3a 3b		A B	81% -	- 82% 
4a 4b		A B	52% -	- 50% 

[a] Conditions A: 0.5 mol% $Rh_2(cap)_4$, PhH, reflux, 10 min. [b] Conditions B: 0.25 mol% $Rh_2(tfa)_4$, PhH, rt, 10 min. [c] A 44% yield of tautomerized product was also isolated. [d] An 83% yield of tautomerized product was isolated exclusively.

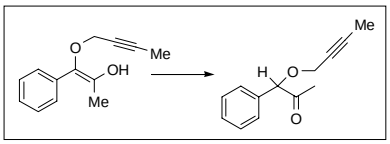
General Procedure for Effecting [3,3]-Rearrangement with α-Diazoketone 7 (Table 1, Entry 3a, 3-butyn-2-ol): To a stirred solution of 1 (95 mg, 0.593 mmol, 1.0 equiv) and 3-butyn-2-ol (56 μL, 0.714 mmol, 1.2 equiv) in benzene (6 mL) was added $Rh_2(cap)_4$ (1.9 mg, 0.003 mmol, 0.005 equiv). The mixture was immersed in a preheated oil bath and heated at reflux for 10 min, then cooled to room temperature and concentrated under reduced pressure. The residue was purified by flash chromatography (8:1 hexane:EtOAc eluent) to furnish allenyl α-hydroxyketone (97 mg, 81% yield) as a pale yellow oil.[1]

General Procedure for Effecting [2,3]-Rearrangement with α-Diazoketone 7 (Table 1, Entry 2b, 2-butyn-1-ol): To a stirred solution of **1** (113 mg, 0.705 mmol, 1.0 equiv) and 2-butyn-1-ol (63 μL, 0.842 mmol, 1.2 equiv) in benzene (7 mL) was added $Rh_2(tfa)_4$ (1.2 mg, 0.0018 mmol, 0.0025 equiv) resulting in rapid loss of N_2(g). The resulting pale green solution was stirred for 10 min at room temperature, then concentrated under reduced pressure. Flash chromatography of the residue (15:1 hexane:acetone eluent) afforded allenyl α-hydroxyketone (97 mg, 68% yield) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (m, 2H), 7.37 (m, 3H), 4.87 (dq, *J*=3.0, 10.8 Hz, 1H), 4.80 (dq, *J*=3.0, 10.3 Hz, 1H), 4.72 (s, 1H), 2.10 (s, 3H), 1.76 (t, *J*=3.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.5, 205.9, 138.7, 128.5, 128.2, 127.5, 100.0, 85.5, 77.1, 26.0, 14.8; IR (thin film/NaCl) 3448 (br. m), 3060 (w), 2984 (w), 2926 (w), 1957 (m), 1710 (s), 1448 (m), 1356 (m), 1062 (m), 756 (m), 703 (s) cm^{-1}; HRMS (EI) *m/z* found: 201.0915 [calc'd for $C_{13}H_{14}O_2$ (M-H): 201.0916].

Table 1, Entry 4b ([2,3]-Rearrangement, 2-methyl-3-butyn-2-ol): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (m, 2H), 7.36 (m, 3H), 5.59 (septet, *J*=3.5 Hz, 1H), 4.53 (s, 1H), 2.08 (s, 3H), 1.79 (d, *J*=3.5 Hz, 3H), 1.73 (d, *J*=3.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.6, 201.2, 140.7, 128.5, 128.2, 126.8, 100.3, 92.8, 82.2, 24.7, 20.2, 20.1; IR

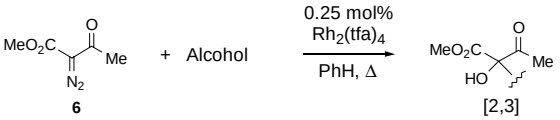
(thin film/NaCl) 3460 (br. m), 2979 (w), 2920 (w), 1713 (s), 1447 (m), 1353 (m), 1118 (m), 764 (m), 700 (s) cm^{-1}; HRMS (EI) *m/z* found: 217.1220 [calc'd for $C_{14}H_{17}O_2$ (M+H): 217.1229].

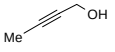
Tautomerized (OH-Insertion) Product, 3-butyn-2-ol:



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.31 (comp. m, 5H), 5.04 (s, 1H), 4.26 (dq, *J*=2.4, 15.6 Hz, 1H), 4.04 (dq, *J*=2.4, 16.0 Hz, 1H), 2.16 (s, 3H), 1.86 (t, *J*=2.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.2, 135.4, 128.8, 128.7, 127.3, 85.6, 83.6, 74.2, 56.9, 25.6, 3.6; IR (thin film/NaCl) 3062 (w), 3030 (w), 2920 (w), 2858 (w), 2226 (w), 2225 (w), 1721 (s), 1452 (m), 1354 (m), 1094 (m), 1071 (m), 745 (m), 701 (s) cm^{-1}; HRMS (EI) *m/z* found: 201.0911 [calc'd for $C_{13}H_{14}O_2$ (M-H): 201.0916].

Table 2



Entry	Alcohol	Yield [2,3]	
1		62%	
2		61%	
3		60%	
4		43%	

General Procedure for Effecting [2,3]-Rearrangement with α-Diazoketone 6 (Table 2, Entry 1, propargyl alcohol): To a stirred solution of **6** (129 mg, 0.905 mmol, 1.0 equiv) and propargyl alcohol (63 μL, 1.08 mmol, 1.2 equiv) in benzene (9 mL) was added $Rh_2(tfa)_4$ (1.5 mg, 0.0023 mmol, 0.0025 equiv). The mixture was immersed in a preheated oil bath and heated under reflux for 10 min, after which it was cooled and concentrated under reduced pressure. Flash chromatography of the residue (6:1 hexane:EtOAc eluent) afforded allenyl α-hydroxyketone (95 mg, 62% yield) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.70 (t, *J*=6.5 Hz, 1H), 5.05 (dd, *J*=6.5, 11.8 Hz, 1H), 5.02 (dd, *J*=6.5, 12.0 Hz, 1H), 4.31 (s, 1H), 3.83 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.6, 202.2, 169.8, 90.8, 81.4, 80.0, 58.5, 24.7; IR (thin film/NaCl) 3457 (br. m), 3069 (w), 3009 (w), 2957 (w), 1958 (m), 1725 (s), 1436 (m), 1357 (m),

1260 (s), 1193 (m), 1154 (m) cm^{-1}; HRMS (EI) *m/z* found: 171.0660 [calc'd for $C_8H_{11}O_4$ (M+H): 171.0657].

Table 2, Entry 2, 2-butyn-1-ol

^1H NMR (500 MHz, $CDCl_3$) δ 4.91 (dq, *J*=3.0, 10.8 Hz, 1H), 4.88 (dq, *J*=3.0, 10.8 Hz, 1H), 4.34 (s, 1H), 3.82 (s, 3H), 2.40 (s, 3H), 1.70 (t, *J*=3.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.7, 203.9, 169.7, 98.1, 85.2, 78.0, 53.2, 25.5, 13.9; IR (thin film/NaCl) 3456 (br. m), 2988 (w), 2956 (w), 2928 (w), 1960 (m), 1725 (s), 1436 (m), 1356 (m), 1253 (s), 1106 (s) cm^{-1}; HRMS (EI) *m/z* found: 184.0735[calc'd for $C_9H_{12}O_4$ (M+): 184.0736].

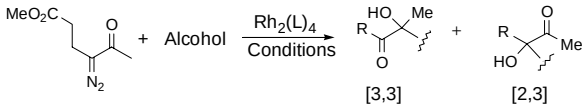
Table 2, Entry 3, 3-butyn-2-ol (2.4:1 mixture of diastereomers)

^1H NMR (500 MHz, $CDCl_3$) δ 5.59 (m, 2H), 5.45 (m, 2H), 4.25 (s, 2H), 3.82 (s, 6H), 2.34 (s, 3H), 2.33 (s, 3H), 1.71 (dd, *J*=3.0, 7.0 Hz, 3H), 1.70 (dd, *J*=3.0, 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.3, 204.3, 202.7, 202.6, 170.0, 170.0, 91.5, 90.8, 81.9, 81.8, 53.4, 24.7, 24.6, 13.6, 13.6; IR (thin film/NaCl) (3459, br. m), 2956 (w), 2928 (w), 1968 (w), 1725 (s), 1437 (m), 1356 (m), 1254 (s), 1191 (m), 1158 (m), 1114 (m) cm^{-1}; HRMS (EI) *m/z* found: 185.0808 [calc'd for $C_9H_{13}O_4$ (M+H): 185.0814].

Table 2, Entry 4, 2-methyl-3-butyn-2-ol

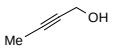
^1H NMR (500 MHz, $CDCl_3$) δ 5.45 (septet, *J*=2.8 Hz, 1H), 4.19 (s, 1H), 3.82 (s, 3H), 2.34 (s, 3H), 1.74 (t, *J*=2.5 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.1, 201.7, 170.1, 101.7, 89.5, 82.1, 53.3, 24.7, 19.9, 19.9; IR (thin film/NaCl) 3462 (br. m), 2984 (w), 2954 (w), 2911 (w), 1972 (w), 1726 (s), 1437 (m), 1356 (m), 1265 (s), 1143 (m) cm^{-1}; HRMS (EI) *m/z* found: 197.0816 [calc'd for $C_{10}H_{13}O_4$ (M-H): 197.0814].

Table 3



7 [3,3] [2,3]

R = $CH_2CH_2CO_2Et$

Entry	Alcohol	Conditions	Yield [3,3]	Yield [2,3]
1a		A[a]	64%	-
1b		B[b]	-	60% 
2a		A	66%	-
2b		B	-	68% 
3a		A	60%	-
3b		B	-	65% 
4a		A	41%	-
4b		B[c,d]	-	40% 

[a] Conditions A: 0.25 mol% $Rh_2(cap)_4$, PhH, reflux, 10 min. [b] Conditions B: 5 mol% $Rh_2(oct)_4$, PhH, reflux, 10 min. [c] 20 mol % $Rh_2(oct)_4$ was employed. [d] An 11% yield of the corresponding enone was also isolated.

General Procedure for Effecting [3,3]-Rearrangement with α-Diazoketone 7 (Table 3, Entry 1a, propargyl alcohol): To a stirred solution of **7** (100 mg, 0.543 mmol, 1.0 equiv) and propargyl alcohol (38 μL, 0.652 mmol, 1.2 equiv) in benzene (3 mL) was added $Rh_2(cap)_4$ (1.0 mg, 0.0015 mmol, 0.0027 equiv). This mixture was heated at reflux for 10 min, then cooled and concentrated under reduced pressure. Purification of the residue by flash chromatography (4:1 hexane:EtOAc eluent) afforded allenyl α-hydroxyketone (74 mg, 64% yield) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.27 (t, *J*=6.5 Hz, 1H), 5.03 (dd, *J*=6.5, 11.3 Hz, 1H), 5.00 (dd, *J*=6.5, 11.5 Hz, 1H), 4.14 (q, *J*=7.0 Hz, 2H), 3.87 (s, 1H), 2.97 (dt, *J*=6.5, 19.0 Hz, 1H), 2.87 (dt, *J*=6.5, 18.5 Hz, 1H), 2.67 (dt, *J*=6.5, 17.0 Hz, 1H), 2.61 (dt, *J*=6.5, 17.5 Hz, 1H), 1.52 (s, 3H), 1.26 (t, *J*=7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.3, 207.4, 172.4, 95.6, 79.2, 76.9, 60.7, 30.9, 28.2, 24.4, 14.2; IR (thin film/NaCl) 3466 (br. m), 2983 (m), 2934 (w), 1955 (m), 1716 (s), 1374 (m), 1349 (m), 1208 (m), 1100 (m), 1077 (m) cm^{-1}; HRMS (EI) *m/z* found: 213.1128 [calc'd for $C_{11}H_{17}O_4$ (M+H): 213.1127].

Table 3, Entry 2a, 2-butyn-1-ol
^{1}H NMR (500 MHz, $CDCl_3$) δ 4.90 (q, *J*=3.0 Hz, 1H), 4.14 (q, *J*=7.0 Hz, 2H), 4.01 (br. s, 1H), 2.92 (ddd, *J*=6.5, 7.2, 18.9 Hz, 1H), 2.86 (ddd, *J*=6.5, 7.0, 18.5 Hz, 1H), 2.65 (dt, *J*=6.5, 17.5 Hz, 1H), 2.59 (ddd, *J*=6.5, 7.0, 17.0 Hz, 1H), 1.59 (t, *J*=3.0 Hz, 3H), 1.51 (s, 3H), 1.26 (t, *J*=7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 211.1, 206.5, 172.3, 101.8, 78.6, 77.5, 60.7, 30.4, 28.0, 24.0, 14.2, 13.8; IR (thin film/NaCl) 3476 (br. m), 2983 (m), 2932 (m), 1957 (m), 1735 (s), 1715 (s), 1374 (m), 1349 (m), 1193 (s), 1104 (s) cm^{-1}; HRMS (EI) *m/z* found: 227.1276 [calc'd for $C_{12}H_{18}O_4$ (M+H): 227.1283].

Table 3, Entry 3a, 3-butyn-2-ol (2.2:1 mixture of diastereomers)
^{1}H NMR (500 MHz, $CDCl_3$) δ 5.41 (m, 2H), 5.19 (m, 2H), 4.14 (q, *J*=7.5 Hz, 4H), 3.86 (s, 1H), 3.83 (s, 1H), 2.99 (dt, *J*=6.5, 18.5 Hz, 1H), 2.96 (dt, *J*=6.5, 18.5 Hz, 1H), 2.86 (dt, *J*=6.5, 18.5 Hz, 2H), 2.66 (dt, *J*=6.5, 17.0 Hz, 2H), 2.60 (dt, *J*=6.5, 17.0 Hz, 2H), 1.74 (dd, *J*=3.0, 7.0 Hz, 3H), 1.73 (dd, *J*=3.0, 7.3 Hz, 3H), 1.49 (s, 6H), 1.26 (t, *J*=7.5 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 211.1, 204.2, 204.1, 172.7, 96.3, 96.3, 90.9, 90.9, 77.7, 61.1, 31.2, 28.6, 28.6, 24.8, 14.5, 14.3, 14.2; IR (thin film/NaCl) 3479 (br. m), 2984 (m), 2931 (m), 1963 (w), 1733 (s), 1715 (s), 1447 (m), 1374 (m), 1349 (m), 1208 (s) cm^{-1}; HRMS (EI) *m/z* found: 225.1133 [calc'd for $C_{12}H_{17}O_4$ (M-H): 225.1127].

Table 3, Entry 4a, 2-methyl-3-butyn-2-ol
^{1}H NMR (500 MHz, $CDCl_3$) δ 5.08 (septet, *J*=3.0 Hz, 1H), 4.15 (q, *J*=7.0 Hz, 2H), 2.00 (dt, *J*=6.5, 19.0 Hz, 1H), 2.86 (dt, *J*=6.5, 18.5 Hz, 1H), 2.66 (dt, *J*=6.5, 16.5 Hz, 1H), 2.58 (dt, *J*=6.5, 17.0 Hz, 1H), 1.77 (d, *J*=3.0 Hz, 6H), 1.48 (s, 3H), 1.27 (t, *J*=7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 211.0, 200.9, 172.4, 100.7, 94.6, 77.7, 60.7, 30.7, 28.2, 24.3, 20.3, 20.1, 14.2; IR (thin film/NaCl) 3479 (br. m), 2982 (m), 2934 (m), 2911 (m), 1968 (w), 1736 (s), 1716 (s), 1374 (m), 1348 (m), 1189 (s) cm^{-1}; HRMS (EI) *m/z* found: 239.1286 [calc'd for $C_{13}H_{19}O_4$ (M-H): 239.1283].

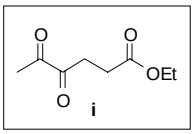
General Procedure for Effecting [2,3]-Rearrangement with α-Diazoketone 7 (Table 3, Entry 1b, propargyl alcohol): To a stirred solution of **7** (50.5 mg, 0.274 mmol, 1.0 equiv) and propargyl alcohol (19 μL, 0.326 mmol, 1.2 equiv) in benzene (3 mL) was added $Rh_2(oct)_4$ (11.4 mg, 0.015 mmol, 0.054 equiv) resulting in rapid loss of N_2(g). Once complete, the reaction mixture was immersed in a preheated oil bath and heated at reflux for 10 min, after which it was cooled and concentrated under reduced pressure. Flash chromatography of the residue (3:2 pentane:Et_2O eluent) afforded allenyl α-hydroxyketone (34.9 mg, 60% yield) as a clear yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.20 (t, *J*=6.8 Hz, 1H), 5.04 (dd, *J*=6.9, 11.4 Hz, 1H), 5.00 (dd, *J*=6.4, 11.6 Hz, 1H), 4.13 (q, *J*=7.2 Hz, 2H), 4.09 (s, 1H), 2.48 (ddd, *J*=5.3, 9.6, 16.0 Hz, 1H), 2.28 (s, 3H), 2.33-2.08 (comp. m, 3H), 1.26 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.9, 207.4, 173.4, 94.2, 79.3, 78.8, 60.6, 31.8, 28.5, 23.9, 14.2; IR (thin film/NaCl) 3465 (br. m), 2982 (m), 2932 (m), 1954 (m), 1731 (s), 1713 (s), 1374 (m), 1356 (m), 1184 (s), 1100 (s) cm^{-1}; HRMS (EI) *m/z* found: 213.1119 [calc'd for $C_{11}H_{17}O_4$ (M+H): 213.1127].

Table 3, Entry 2b, 2-butyn-1-ol
^{1}H NMR (500 MHz, $CDCl_3$) δ 4.92 (m, 2H), 4.11 (q, *J*=7.2 Hz, 2H), 4.05 (s, 1H), 2.42 (m, 1H), 2.23 (s, 3H), 2.30-2.10 (comp. m, 3H), 1.56 (t, *J*=3.0 Hz, 3H), 1.24 (t, *J*=7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.7, 206.3, 173.3, 100.6, 80.6, 77.8, 60.5, 31.0, 28.6, 23.2, 14.2, 13.9; IR (thin film/NaCl) 3459 (br. m), 2983 (m), 2932 (w), 1956 (m), 1734 (s), 1712 (s), 1443 (m), 1374 (m), 1186 (m), 1114 (m) cm^{-1}; HRMS (EI) *m/z* found: 227.1286 [calc'd for $C_{12}H_{18}O_4$ (M+H): 227.1283].

Table 3, Entry 3b, 3-butyn-2-ol (2.3:1 mixture of diastereomers)
^{1}H NMR (500 MHz, $CDCl_3$) δ 5.42 (m, 2H), 5.11 (m, 2H), 4.13 (q, *J*=7.5 Hz, 4H), 4.00 (s, 1H), 3.98 (s, 1H), 2.46 (ddd, *J*=5.5, 10.0, 16.4 Hz, 1H), 2.46 (ddd, *J*=5.5, 9.5, 16.3 Hz, 1H), 2.27 (s, 3H), 2.26 (s, 3H), 2.22-2.07 (comp. m, 4H), 1.73 (dd, *J*=3.5, 7.0 Hz, 6H), 1.25 (t, *J*=7.5 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.1, 204.0, 204.0, 173.4, 94.6, 94.5, 90.7, 90.5, 79.3, 79.2, 60.5, 31.9, 28.6, 28.6, 23.7, 23.7, 14.1, 13.8, 13.7; IR (thin film/NaCl) 3464 (br m), 2982 (m), 2930 (m), 1964 (w), 1733 (s), 1714 (s), 1444 (m), 1373 (m), 1356 (m), 1185 (s), 1106 (s) cm^{-1}; HRMS (EI) *m/z* found: 225.1137 [calc'd for $C_{12}H_{17}O_4$ (M-H): 225.1127].

Table 3, Entry 4b, 2-methyl-3-butyn-1-ol
^{1}H NMR (500 MHz, $CDCl_3$) δ 4.99 (septet, *J*=3.0 Hz, 1H), 4.13 (q, *J*=7.2 Hz, 2H), 3.93 (s, 1H), 2.46 (ddd, *J*=6.0, 9.9, 16.0 Hz, 1H), 2.29 (m, 1H), 2.26 (s, 3H), 2.16 (ddd, *J*=6.0, 9.8, 14.5 Hz, 1H), 2.09 (ddd, *J*=6.5, 9.8, 14.5 Hz, 1H), 1.76 (d, *J*=3.0 Hz, 6H), 1.26 (t, *J*=7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.5, 201.2, 173.5, 100.8, 93.2, 79.6, 60.5, 31.9, 28.7, 23.6, 20.2, 20.0, 14.2; IR (thin film/NaCl) 3466 (br. m), 2980 (m), 2933 (m), 2858 (w), 1374 (s), 1713 (s), 1588 (w), 1354 (m), 1188 (s), 1098 (m) cm^{-1}; HRMS (EI) *m/z* found: 241.1437 [calc'd for $C_{13}H_{21}O_4$ (M+H): 241.1440].

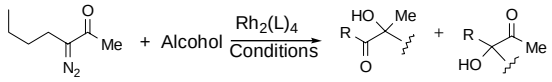
Ethyl 4,5-dioxohexanoate (i):



i

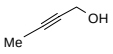
Inefficient carbenoid capture (e.g., by 2-methyl-3-butyn-2-ol) in the presence of significant moisture and oxygen can give rise to this species in varying amounts. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.14 (q, *J*=7.0 Hz, 2H), 3.03 (t, *J*=6.5 Hz, 2H), 2.66 (t, *J*=6.5 Hz, 2H), 2.36 (s, 3H), 1.26 (t, *J*=7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.6, 197.0, 172.3, 60.9, 30.8, 28.0, 23.6, 14.1; IR (thin film/NaCl) 2984 (w), 2936 (w), 1733 (s), 1717 (s), 1395 (m), 1376 (m), 1351 (m), 1202 (s), 1076 (m) cm^{-1}; HRMS (EI) *m/z* found: 173.0810 [calc'd for $C_8H_{13}O_4$ (M+H): 173.0814].

Table 4



8 [3,3] [2,3]

R = $CH_2CH_2CH_2CH_3$

Entry	Alcohol	Conditions	Yield [3,3]	Yield [2,3]
1a 1b		A[a] B[b]	68% -	- 62% 
2a 2b		A B	67% -	- 66% 
3a 3b		A B	69% -	- 60% 
4a 4b		A[c] B[d]	38% -	- - 

[a] Conditions A: 0.25 mol% $Rh_2(cap)_4$, PhH, reflux, 10 min. [b] Conditions B: 5 mol% $Rh_2(oct)_4$, PhH, reflux, 10 min. [c] A 5% yield of enone **ii** was also isolated [d] Only enone **ii** was isolated in 25% yield

General Procedure for Effecting [3,3]-Rearrangement with α-Diazoketone 8 (Table 4, Entry 1a, propargyl alcohol): To a stirred solution of **8** (139 mg, 0.992 mmol, 1.0 equiv) and propargyl alcohol (69 μL, 1.19 mmol, 1.2 equiv) in benzene (10 mL) was added $Rh_2(cap)_4$ (1.6 mg, 0.0024 mmol, 0.0025 equiv). The resulting mixture was heated at reflux for 10 min, then cooled to room temperature. Concentration under reduced pressure provided a residue that was purified by flash chromatography (6:1 hexane:EtOAc eluent), affording allenyl α-hydroxyketone (113 mg, 68% yield) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.20 (t, *J*=7.0 Hz, 1H), 5.00 (dd, *J*=7.0, 15.0 Hz, 1H), 4.98 (dd, *J*=6.5, 15.0 Hz, 1H), 4.10 (br. s, 1H), 2.64 (dt, *J*=7.5, 17.5 Hz, 1H), 2.51 (dt, *J*=7.5, 17.5 Hz, 1H), 1.61 (m, 2H), 1.48 (s, 3H), 1.33 (sextet, *J*=7.5 Hz, 2H), 0.92 (t, *J*=7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 211.9, 207.6, 95.5, 78.9, 35.4,

25.9, 24.0, 22.3, 13.8; IR (thin film/NaCl) 3467 (br. s), 2958 (s), 2934 (s), 2873 (s), 1955 (m), 1710 (s), 1455 (m), 1360 (m), 1125 (m), 853 (m) cm^{-1}; HRMS (EI) *m/z* found: 168.1153 [calc'd for $C_{10}H_{16}O_2$ (M+): 168.1150].

Table 4, Entry 2a, 2-butyn-1-ol
^1H NMR (500 MHz, $CDCl_3$) δ 4.88 (m, 1H), 4.20 (s, 1H), 2.58 (ddd, *J*=6.5, 8.3, 17.5 Hz, 1H), 2.50 (ddd, *J*=6.5, 8.5, 17.4 Hz, 1H), 1.59 (m, 2H), 1.56 (t, *J*=3.5 Hz, 3H), 1.47 (s, 3H), 1.32 (m, 2H), 0.92 (t, *J*=7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.9, 206.7, 101.6, 78.6, 77.2, 34.8, 26.0, 23.7, 22.3, 13.8, 13.8; IR (thin film/NaCl) 3466 (br. m), 2959 (s), 2933 (s), 2873 (m), 1957 (m), 1708 (s), 1456 (m), 1354 (m), 1125 (m), 1092 (m), 851 (m) cm^{-1}; HRMS (EI) *m/z* found: 182.1303 [calc'd for $C_{11}H_{18}O_2$ (M+): 182.1307].

Table 4, Entry 3a, 3-butyn-2-ol (2.2:1 mixture of diastereomers)
^1H NMR (500 MHz, $CDCl_3$) δ 5.40 (m, 2H), 5.15 (dq, *J*=3.0, 6.0 Hz, 2H), 4.09 (s, 1H), 4.08 (s, 1H), 2.68 (dt, *J*=7.5, 17.0 Hz, 1H), 2.65 (dt, *J*=7.5, 16.5 Hz, 1H), 2.51 (ddd, *J*=7.0, 8.0, 17.2 Hz, 1H), 2.51 (ddd, *J*=7.0, 8.0, 16.0 Hz, 1H), 1.75 (dd, *J*=3.5, 7.0 Hz, 3H), 1.74 (dd, *J*=3.5, 7.0 Hz, 3H), 1.62 (m, 4H), 1.47 (s, 6H), 1.34 (sextet, *J*=7.5 Hz, 2H), 1.34 (sextet, *J*=7.5 Hz, 2H), 0.94 (t, *J*=7.5 Hz, 3H), 0.93 (t, *J*=7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.2, 204.0, 95.8, 95.8, 90.1, 90.1, 35.3, 35.3, 26.0, 26.0, 24.1, 24.0, 22.3, 22.3, 14.0, 13.9, 13.8; IR (thin film/NaCl) 3466 (br. m), 2959 (s), 2933 (s), 2873 (m), 1964 (w), 1711 (s), 1456 (m), 1370 (m), 1125 (m), 1037 (m) cm^{-1}; HRMS (EI) *m/z* found: 181.1227 [calc'd for $C_{11}H_{17}O_2$ (M-H): 181.1229].

Table 4, Entry 4a, 2-methyl-3-butyn-1-ol
^1H NMR (500 MHz, $CDCl_3$) δ 5.01 (m, 1H), 4.05 (s, 1H), 2.65 (ddd, *J*=6.5, 8.5, 17.5 Hz, 1H), 2.48 (ddd, *J*=6.5, 8.5, 17.2 Hz, 1H), 1.77 (d, *J*=2.0 Hz, 3H), 1.76 (d, *J*=2.0 Hz, 3H), 1.60 (m, 1H), 1.43 (s, 3H), 1.33 (sextet, *J*=7.5 Hz, 2H), 0.92 (t, *J*=7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.5, 201.2, 100.0, 94.5, 77.7, 35.3, 26.0, 24.0, 22.3, 20.3, 20.1, 13.8; IR (thin film/NaCl) 3469 (br. m), 2959 (s), 2934 (s), 2872 (m), 1968 (w), 1708 (s), 1449 (m), 1364 (m), 1348 (m), 1123 (m) cm^{-1}; HRMS (EI) *m/z* found: 195.1376 [calc'd for $C_{12}H_{19}O_2$ (M-H): 195.1385].

General Procedure for Effecting [2,3]-Rearrangement with α-Diazoketone 8 (Table 4, Entry 1b, propargyl alcohol): To a stirred solution of **8** (106 mg, 0.752 mmol, 1.0 equiv) and propargyl alcohol (53 μL, 0.910 mmol, 1.2 equiv) in benzene (8 mL) was added $Rh_2(oct)_4$ (29.3 mg, 0.038 mmol, 0.05 equiv) resulting in rapid N_2(g) loss. Once complete, the reaction mixture was immersed in a preheated oil bath and heated at reflux. After 10 min, the mixture was cooled to room temperature and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (6:1 hexane:EtOAc eluent), affording allenyl α-hydroxyketone (77.2 mg, 62% yield). ^1H NMR (500 MHz, $CDCl_3$) δ 5.23 (t, *J*=6.5 Hz, 1H), 5.01 (dd, *J*=6.5, 11.0 Hz, 1H), 4.97 (dd, *J*=6.5, 11.5 Hz, 1H), 4.02 (s, 1H), 2.25 (s, 3H), 1.83 (m, 2H), 1.46 (m, 1H), 1.34 (sextet, *J*=7.5 Hz, 2H), 1.07 (m, 1H), 0.91 (t, *J*=7.0 Hz, 3H); ^{13}C NMR (125 MHz,

$CDCl_3$) δ 209.4, 207.4, 94.9, 79.6, 78.8, 37.0, 25.3, 23.8, 22.8, 13.9; IR (thin film/NaCl) 3467 (br. s), 2957 (s), 2872 (s), 1954 (s), 1711 (s), 1588 (m), 1357 (s), 1193 (s), 1136 (s), 852 (s) cm^{-1}; HRMS (EI) *m/z* found: 169.1225 [calc'd for $C_{10}H_{17}O_2$ (M+H): 169.1229].

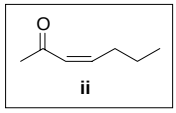
Table 4, Entry 2b, 2-butyn-1-ol

^1H NMR (500 MHz, $CDCl_3$) δ 4.87 (m, 2H), 4.05 (s, 1H), 2.19 (s, 3H), 1.86 (dd, *J*=7.3, 9.8 Hz, 2H), 1.56 (t, *J*=3.0 Hz, 3H), 1.42 (m, 1H), 1.31 (sextet, *J*=7.4 Hz, 2H), 0.96 (m, 1H), 0.89 (t, *J*=7.3 Hz, 3H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 210.4, 206.5, 101.1, 81.4, 77.2, 35.9, 25.4, 23.3, 22.9, 14.0, 13.9; IR (thin film/NaCl) 3467 (br. m), 2957 (s), 2929 (m), 2862 (m), 1956 (m), 1709 (s), 1429 (m), 1356 (m), 1135 (m), 852 (m) cm^{-1}; HRMS (EI) *m/z* found: 182.1307 [calc'd for $C_{11}H_{18}O_2$ (M+): 182.1307].

Table 4, Entry 3b, [2,3]-3-butyn-2-ol (2.3:1 mixture of diastereomers)

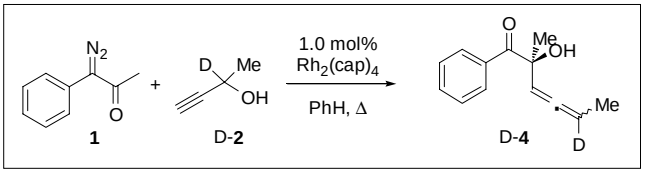
^1H NMR (500 MHz, $CDCl_3$) δ 5.38 (m, 1H), 5.15 (m, 1H), 5.13 (m, 1H), 2.25 (s, 3H), 2.23 (s, 3H), 1.81 (dd, *J*=7.5, 9.5 Hz, 2H), 1.80 (dd, *J*=7.5, 9.5 Hz, 2H), 1.74 (dd, *J*=3.5, 7.3 Hz, 3H), 1.73 (dd, *J*=3.5, 7.3 Hz, 3H), 1.50-1.42 (comp. m, 2H), 1.33 (sextet, *J*=7.0 Hz, 4H), 1.13-1.03 (comp. m, 2H), 0.91 (t, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.8, 209.8, 204.0, 204.0, 95.2, 95.1, 90.1, 89.9, 80.2, 80.1, 36.9, 36.9, 25.4, 23.7, 23.7, 22.9, 22.9, 13.9, 13.8, 13.7; IR (thin film/NaCl) 3468 (br. m), 2957 (s), 2930 (s), 2863 (m), 1964 (m), 1711 (s), 1461 (m), 1355 (s), 1135 (m), 868 (m) cm^{-1}; HRMS (EI) *m/z* found: 183.1381 [calc'd for $C_{11}H_{19}O_2$ (M+H): 183.1385].

(*Z*)-3-hepten-2-one (ii)



This compound is isolated as a by-product under both [3,3] and [2,3] rearrangement conditions with 2-methyl-3-butyn-2-ol due to inefficient carbenoid capture· ^1H NMR (500 MHz, $CDCl_3$) δ 6.15 (d, *J*=11.5 Hz, 1H), 6.07 (dt, *J*=7.0, 11.5 Hz, 1H), 2.59 (qd, *J*=1.5, 7.5 Hz, 2H), 2.21 (s, 3H), 1.46 (sextet, *J*=7.5 Hz, 2H), 0.94 (t, *J*=7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.3, 148.4, 127.2, 31.6, 31.3, 22.4, 13.7; IR (thin film/NaCl) 2961 (s), 2933 (s), 2873 (s), 1694 (s), 1614 (s), 1458 (m), 1415 (s), 1355 (s), 1178 (s), 969 (m), 738 (m) cm^{-1}; HRMS (EI) *m/z* found: 112.0889 [calc'd for $C_7H_{12}O$ (M+): 112.0888].

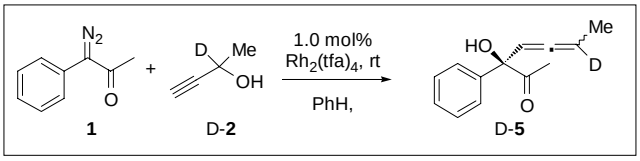
Preparation of Deuterium-Labeled Allenyl α-Hydroxyketone (D-4)



To a stirred solution of **1** (73 mg, 0.456 mmol, 1.2 equiv) and D-**2** (30 μL, 0.377 mmol, 1.0 equiv) in benzene (5 mL) was added $Rh_2(cap)_4$ (3.1 mg, 0.005 mmol, 0.01 equiv). The mixture was immersed in a preheated oil bath and heated at reflux for 10 min, after

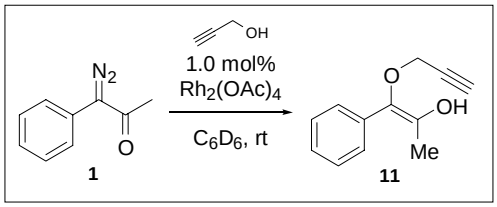
which it was cooled and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (CH_2Cl_2 eluent) to afford D-**4** (2.5:1 mixture of diastereomers, 35 mg, 38% yield) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (m, 2H), 8.09 (m, 2H), 7.58 (m, 2H), 7.46 (m, 4H), 5.45 (m, 2H), 4.54 (s, 1H), 4.52 (s, 1H), 1.67 (s, 3H), 1.67 (s, 3H), 1.74 (d, *J*=3.0 Hz, 3H), 1.64 (s, *J*=3.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.3, 204.2, 202.2, 202.1, 133.4, 133.2, 130.2, 130.1, 128.3, 128.2, 97.0, 96.9, 90.4 (t, *J* = 25.3 Hz), 26.3, 26.1, 13.3, 13.2; IR (thin film/NaCl) 3448 (br. m), 2980 (w), 2924 (w), 1955 (m), 1675 (s), 1597 (m), 1449 (m), 1371 (m), 1351 (w), 1254 (s), 1128 (s), 1096 (s) cm^{-1}; HRMS (EI) *m/z* found: 204.1130 [calc'd for $C_{13}H_{14}O_2D$ (M+H): 204.1135].

Preparation of Deuterium-Labeled Allenyl α-Hydroxyketone (D-5)



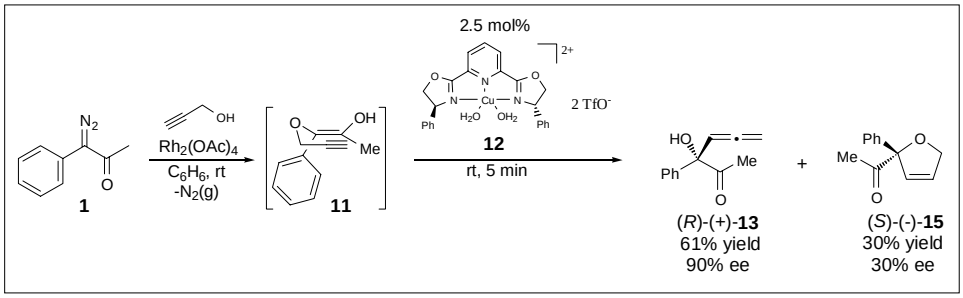
A mixture of **1** (84 mg, 0.524 mmol, 1.0 equiv) and D-**2** (68 μL, .899 mmol, 1.6 equiv) in benzene (5 mL) was treated with $Rh_2(tfa)_4$ (3.4 mg, 0.005 mmol, 0.01 equiv). After 10 min at room temperature, the mixture was concentrated under reduced pressure and the residue purified by flash chromatography (CH_2Cl_2 eluent) to afford D-**5** (2.4:1 mixture of diastereomers, 27 mg, 25% yield) as a clear yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55-7.51 (comp. m, 4H), 7.42-7.31 (comp. m, 6H), 5.72 (m, 2H), 4.58 (s, 1H), 4.53 (s, 1H), 2.11 (s, 3H), 2.10 (s, 3H), 1.75 (d, *J*=3.2 Hz, 3H), 1.71 (d, *J*=3.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.2, 207.1, 140.3, 128.6, 128.5, 128.3, 128.2, 126.7, 94.0, 94.0, 90.3 (t, *J*=28.0 Hz), 82.0, 24.8, 24.7, 13.8, 13.7; IR (thin film/NaCl) 3452 (br. m), 3028 (w), 2979 (w), 2922 (w), 1955 (w), 1713 (s), 1448 (m), 1354 (m), 1171 (m), 763 (m), 700 (s) cm^{-1}; HRMS (EI) *m/z* found: 204.1130 [calc'd for $C_{13}H_{14}O_2D$ (M+H): 204.1135].

Generation and Observation of Enol 11



To a stirred solution of **1** (53 mg, 0.311 mmol, 1.0 equiv) and propargyl alcohol (18 μL, 0.309 mmol, 0.99 equiv) in C_6D_6 (3 mL) was added $Rh_2(OAc)_4$ (1.4 mg, 0.003 mmol, 0.01 equiv) resulting in N_2(g) loss with concomitant conversion to enol **11**. ^{1}H NMR (400 MHz, C_6D_6) δ 7.22 (m, 2H), 7.10-7.00 (comp. m, 3H), 5.97 (s, 1H), 3.85 (d, *J*=2.8 Hz, 2H), 1.93 (t, *J*=2.4 Hz, 1H), 1.83 (s, 3H).

Asymmetric [2,3]-Rearrangement using [Cu(*S,S*)-Ph-pybox(H_2O)$_2$](OTf)$_2$ Additive.

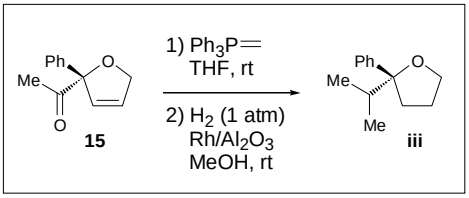


A stirred solution of **1** (353 mg, 2.20 mmol, 1.0 equiv) and propargyl alcohol (0.15 mL, 2.6 mmol, 1.2 equiv) in benzene (22 mL) was treated with $Rh_2(OAc)_4$ (9 mg, 0.02 mmol, 0.01 equiv) at room temperature resulting in vigorous N_2(g) loss. Once gas evolution had ceased (ca. 3 min), [Cu(*S,S,*)-Ph-pybox(H_2O)$_2$](OTf)$_2$ (**12**, 42 mg, 0.055 mmol, 0.025 equiv) in CH_2Cl_2 (1 mL) was added. The mixture was allowed to stir for 5 min, after which triethylamine (0.5 mL) was added as a quench. The mixture was concentrated under reduced pressure and the residue purified by flash chromatography (8:1 hexanes:EtOAc eluent) to furnish (*R*)-(+)-**13** (251 mg, 61% yield, 90% ee)[2] as a colorless oil and (*S*)-(-)-**15** (125 mg, 30% yield, 30% ee)[3] as a clear yellow oil.

(*R*)-(+)-**13**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (m, 2H), 7.32-7.53 (m, 3H), 5.81 (t, *J*=6.7 Hz, 1H), 5.03 (dd, *J*=6.7, 11.5 Hz, 1H), 5.00 (dd, *J*=6.6, 11.5 Hz, 1H), 4.61 (s, 1H), 2.12 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.4, 206.6, 140.2, 128.6, 128.4, 126.6, 93.7, 81.7, 79.3, 24.8; IR (thin film/NaCl) 3453 (br m), 3061 (w), 3028 (w), 1956 (m), 1714 (s), 1492 (m), 1356 (s), 1173 (m), 1063 (m), 855 (m), 765 (m), 701 (s) cm^{-1}; HRMS (EI) *m/z* found: 188.0842 [calc'd for $C_{12}H_{12}O_2$ (M+): 188.0837]; $[\alpha]_D^{20}$ +179.5° (*c* 1.3, $CHCl_3$).

(*S*)-(-)-**15**: : ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48-7.27 (comp. m, 5H), 6.23 (m, 1H), 6.04 (m, 1H), 4.88 (m, 1H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.0, 140.2, 129.3, 128.6, 127.9, 127.6, 125.1, 98.7, 75.8, 25.6; IR (thin film/NaCl) 3059 (w), 2856 (m), 1715 (s), 1490 (w), 1447 (w), 1416 (w), 1351 (m), 1229 (w), 1200 (w), 1068 (s) cm^{-1}; HRMS (EI) *m/z* found: 186.0677 [calc'd for $C_{12}H_{10}O_2$ (M-2H): 186.0681]; $[\alpha]_D^{20}$ -13.4° (c 1.3, $CHCl_3$).

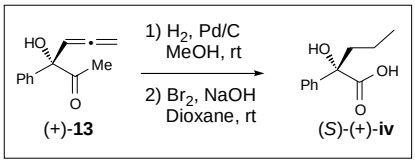
Confirmation of Structure of Dihydrofuran 15



To a solution of methyl triphenylphosphonium iodide (278 mg, 0.687 mmol, 2.0 equiv) in THF (4 mL) was added dropwise, *sec*-butyllithium (1.3 M solution in THF, 0.58 mL, 0.754 mmol, 2.2 equiv) at room temperature. The orange mixture was stirred for 2 h,

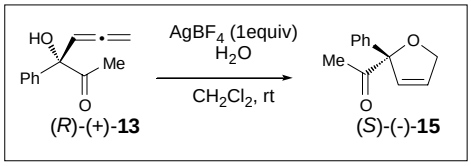
after which a solution of **15** (64 mg, 0.340 mmol, 0.5 equiv) in THF (1 mL) was added dropwise, the resulting mixture allowed to stir overnight at room temperature. The mixture was concentrated under reduced pressure with concomitant adsorption onto silica gel. Flash chromatography (12:1 hexane:EtOAc eluent) furnished a pale yellow oil (35 mg), a fraction (27 mg) of which was dissolved in methanol (1 mL) and added to a suspension of Rh/Al_2O_3 in MeOH under H_2(g) (1 atm). This mixture was allowed to stir for 18 h after which the Rh/Al_2O_3 was removed by filtration and the filtrate concentrated under reduced pressure. Flash chromatography of the residue (12:1 hexane: EtOAc eluent) afforded tetrahydrofuran **iii** (14 mg, 38% yield) as a yellow oil. ^{1}H NMR spectral data for this material corresponded very well with reported values.[4] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.21 (comp. m, 5H), 3.95 (td, *J*=6.5, 7.7 Hz, 1H), 3.79 (td, *J*=6.0, 8.2 Hz, 1H), 2.25 (ddd, *J*=4.5, 8.1, 12.5 Hz, 1H), 2.09 (m, 1H), 2.01 (m, 1H), 1.91 (m, 1H), 1.71 (m, 1H), 0.87 (d, *J*=6.5 Hz, 3H), 0.82 (d, *J*=6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.0, 127.5, 126.3, 126.2, 89.5, 67.1, 37.9, 35.5, 25.7, 18.5, 17.5; IR (thin film/NaCl) 2965 (s), 2873 (m), 1489 (w), 1469 (w), 1445 (w), 1382 (w), 1364 (w), 1055 (s), 760 (s), 703 (s) cm^{-1}; HRMS (EI) *m/z* found: 189.1276 [calc'd for $C_{13}H_{17}O$ (M-H): 189.1279].

Determination of Absolute Stereochemistry of (+)-13



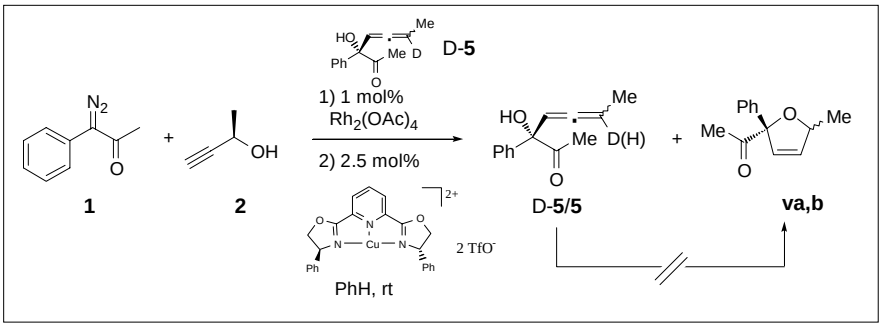
A solution of α-hydroxyketone (+)-**13** (144 mg, 0.762 mmol, 1.0 equiv) in methanol (2 mL) was added to a suspension of Pd/C (17.1 mg) in methanol (6 mL) under H_2(g) (1 atm). The mixture was stirred at room temperature for 1h, then filtered to remove Pd/C. Concentration of the filtrate under reduced pressure afforded a pale yellow oil (143 mg) that was used without further purification. To a solution of the oil (133 mg, 0.690 mmol, 1.0 equiv) in dioxane (3 mL) was added 4N NaOH (20 mL). The resulting suspension was stirred rapidly at room temperature as bromine (106 μL, 2.07 mmol, 3.0 equiv) was added slowly dropwise, allowing the faint yellow color that developed during each addition to dissipate before the next addition (ca. 3 min delay). Once addition was complete, the mixture was washed with Et_2O (2 x 10 mL). The organic washes were discarded and the aqueous layer was acidified with 1N HCl and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic phases were dried ($MgSO_4$), filtered and concentrated under reduced pressure. Purification of the residue by flash chromatography (6:1 EtOAc:hexane/1% HOAc eluent) to afford α-hydroxyacid (*S*)-(-)-**iv** (72 mg, 54%) as a white solid whose spectral and physical data matched those reported in the literature.[5] The optical rotation of material derived from (+)-**13** was measured at $[\alpha]_D^{20}$ + 23.2° (*c* 1.5, EtOH).

Determination of Absolute Stereochemistry of (-)-15



To a solution of (*R*)-(+)-**13** (65 mg, 0.347 mmol, 1.0 equiv) in CH_2Cl_2 (4 mL) at room temperature was added H_2O (50 μL) and $AgBF_4$ (72 mg, 0.370 mmol, 1.1 equiv). The mixture was allowed to stir for 5 h, after which it was concentrated under reduced pressure with concomitant adsorption onto silica gel. Flash chromatography (6:1 hexane:EtOAc eluent) afforded (*S*)-(-)-**15** (30 mg, 46% yield) as a pale yellow oil. $[\alpha]_D^{20}$ -14.4° (*c* 1.4, $CHCl_3$).

Investigation of Interconversion Between α-Hydroxyketone 5 and Dihydrofuran v.



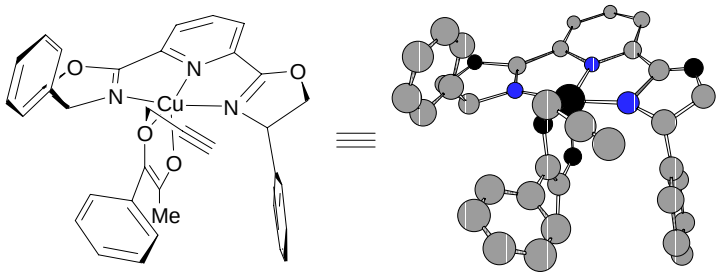
Cu(II)(pybox)-catalyzed [2,3]-rearrangement of propargyloxy enol **3** in the presence of D-**5** gives rise to a mixture of protonated and deuterated α-hydroxyketone (**5** and D-**5**, respectively) but exclusively protic dihydrofuran **v** indicating that **v** does not derive from **5**. It is suspected that both products arise from the same Cu-enol complex. Further investigations are in progress.

To a stirred solution of **1** (19 mg, 0.119 mmol, 1.0 equiv), **2** (11 μL, 0.140 mmol, 1.2 equiv), and D-**5** (13 mg, 0.063 mmol, 0.5 equiv) in benzene (1 mL) was added $Rh_2(OAc)_4$ (0.5 mg, 0.001 mmol, 0.01 equiv) resulting in N_2(g) loss. Once gas evolution had ceased, [Cu(*S,S,*)-Ph-pybox](OTf)$_2$ (0.03M, 97 uL, 0.003 mmol, 0.025 equiv) was added. The mixture was allowed to stir for 25 min, after which, Et_3N (0.5 mL) was added. The red solution was concentrated under reduced pressure and the residue purified by flash chromatography (8:1 hexane:EtOAc eluent) to afford a mixture of **5** and D-**5** (0.0284 g, 100% recovery D-**5** + 64% yield **5**) and exclusively protic **v** (1:1 mixture of diastereomers, 4 mg, 16% yield). The two diastereomers could be separated by flash chromatography using pentane:Et_2O as eluent. First to elute was **va**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (m, 2H), 7.32 (m, 3H), 6.22 (dd, *J*=2.0, 6.5 Hz, 1H), 5.89 (d, *J*=6.5 Hz, 1H), 5.14 (m, 1H), 2.22 (s, 3H), 1.41 (d, *J*=6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ

209.3, 140.5, 132.0, 129.3, 128.5, 127.8, 125.0, 98.5, 82.9, 25.1, 21.8; IR (thin film/NaCl) 3061 (w), 2972 (w), 2926 (w), 2866 (w), 1715 (s), 1447 (w), 1350 (m), 1102 (m), 754 (m), 699 (m) cm^{-1}; HRMS (EI) *m/z* found: 203.0709 [calc'd for $C_{13}H_{15}O_2$ (M+H): 203.0708].

This was followed by diastereomer **vb**: : ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (m, 2H), 7.38-7.28 (comp. m, 3H), 6.17 (dd, *J*=2.5, 6.0 Hz, 1H), 5.92 (dd, *J*=1.5, 6.0 Hz, 1H), 5.19 (m, 1H), 2.20 (s, 3H), 1.37 (d, *J*=6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.4, 140.8, 132.3, 129.1, 128.5, 127.7, 125.1, 98.8, 83.1, 25.6, 22.0; IR (thin film/NaCl) 2974 (w), 1714 (s), 1489 (w), 1447 (w), 1350 (m), 1102 (m), 1085 (m), 1052 (w), 753 (m), 699 (m) cm^{-1}; HRMS (EI) *m/z* found: 203.0700 [calc'd for $C_{13}H_{15}O_2$ (M+H): 203.0782].

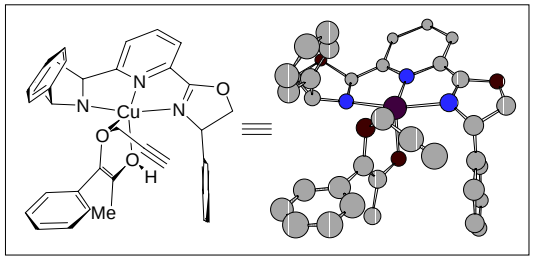
Computation of (pybox)Cu-enol complex 14[6]



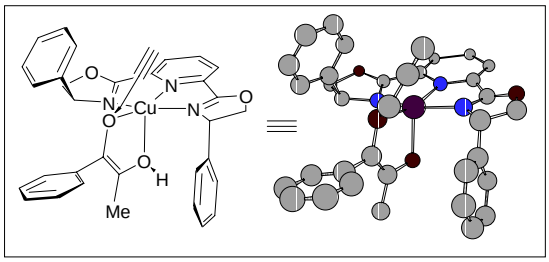
14

Initial Monte Carlo Screening:

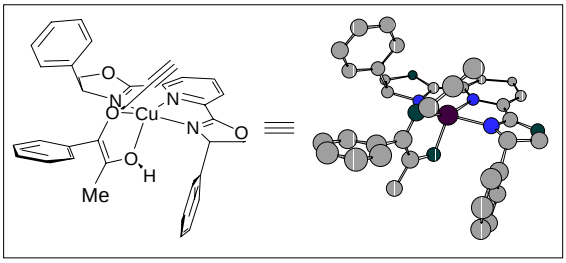
Monte Carlo calculations were performed using the parameters contained in the Merck Molecular Force Field (MMFF). To simulate the square-pyramidal geometry of known $[Cu(pybox)(substrate)]^{2+}$ complexes,[7] the $N_{pyridine}$-Cu-$O_{propargyloxy}$ bond angle was constrained to 160° during the calculations.[8] In addition, to prevent flexing of the alkyne, the angle of the propargyl moiety was constrained to 180°. These calculations resulted in three low-energy structures **A-C** (see below). In the global minimum structure (**A**), the propargyl side-chain is situated in close proximity to the enol olefin and appears poised to participate in an S_NI' process. This structure is separated by 9.4 kcal/mol from the next lowest-energy structure (**B)**, in which the alkyne is oriented away from the copper-bound enol. The propargyl side-chain is equally inaccessible in **C**.



A
35.2 kcal/mol



B
44.6 kcal/mol



C
44.8 kcal/mol

PM3 (tm) Minimization of Complex A:

Further optimization of complex **A** was carried out using semi-empirical parameters contained in the PM3 (tm) force field. The identical angle constraints were imposed as in the Monte Carlo calculations. Minimization afforded complex **14**, in which the distance between the reacting alkyne and enol termini is reduced to 3.57 Å.

Notes and References:

(1) Spectral data for this compound and others in Table 1 may be found in: Wood, J. L.; Moniz, G. A. *Org. Lett.* 1999, *1*, 371 and the accompanying supporting information.

(2) Enantiomeric excess determined by Mosher ester analysis of the derived diol.

(3) Enantiomeric excess determined by Mosher ester analysis of the derived alcohol.

(4) Dana, G.; Touboul, E.; Convert, O.; Pascal, Y. V. *Tetrahedron* **1988**, *44*, 429. This reference reports only ^{1}H NMR data for **iii**. For completeness, we have reported ^{13}C NMR and FT-IR data as well.

(5) For spectral and optical rotation data, see: (a) Meyers, A. I.; Slade, J. *J. Org. Chem.* **1980**, *45*, 2785. (b) Frater, G.; Muller, U.; Gunther, W. *Tetrahedron Lett.* **1981**, *22*, 4221. (c) Boireau, G.; Deberly, A.; Abenhaim, D. *Tetrahedron* **1989**, *45*, 5837. (d) Moorlag, H.; Kellogg, R. M.; Kloosterman, M.; Kamphius, J.; Schoemaker, H. E. *J. Org. Chem.* **1990**, *55*, 5878.

(6) All calculations were performed using: Spartan version 5.0, Wavefunction, Inc.

18401 Von Karman Avenue, Suite 370, Irvine, CA 92612 U.S.A.

(7) For X-Ray structures of related complexes, see: Evans, D. A.; Kozlowski, M. C.; Murry, J. A.; Burgey, C. S.; Campos, K. R.; Connell, B. T.; Staples, R. J. *J. Am. Chem. Soc.* **1999** *121*, 669.

(8) (a) Use of this angle constraint is precedented, see: Evans, D. A.; Burgey, C. S.; Kozlowski, M. C.; Tregay, S. W. *J. Am. Chem. Soc.* **1999**, *121*, 686.

(b) The orientation of the enol in complex **14**, wherein the *propargyloxy* oxygen is bound in the ligand plane, was selected based on two criteria:

i. The equivalent model with pyruvate esters (i.e., ketone bound in ligand plane) successfully predicts the stereochemical outcome of Mukaiyama aldol reactions (See ref. 8a).

ii. The equatorial site (ligand plane) is more strongly coordinating than the axial site, making this orientation consistent with the notion that electron conduction must proceed from the enol hydroxyl to the propargyloxy arm to effect an S_NI' displacement.