

Material and Methods

Chloroperoxidase was provided by Chirazyme Laboratories, 2004 S. Wright st., Urbana, IL 61801. 3-Heptyne, 3-octyne and 3-hexyn-2-one were obtained from Lancaster Synthesis Inc. 2-Pentyne, 3-hexyne, 2-pentyn-1-ol, 2-hexyn-1-ol, 3-hexyn-1-ol were purchased from Aldrich Chemical Co. All acetates of acetylenic alcohols were prepared from the corresponding alcohols and Ac_2O , the substrates containing a bromide group were prepared from the corresponding alcohols and PBr_3 in ether and pyridine.¹ S-(+)-Methoxy- α -(trifluoromethyl)phenylacetyl chloride (MTPA) is available from Aldrich. NMR spectra were recorded on a 400 MHz or a 500 MHz spectrometer. High resolution mass spectra were obtained on a VSE-A spectrometer. Optical rotations were measured on a DIP-360 digital polarimeter. Enantiomeric excesses were determined by gas chromatography on a chiral G-TA column or a β -CDX column, or by NMR analysis of the MTPA esters. Silica gel 60 for flash chromatography was purchased from Merck Co.

General procedure. Alkyne (1.0 mmol) and CPO (1.1×10^{-3} mmol) was stirred vigorously with *t*-BuOOH (2.0 mmol) in 10.0 ml of 10 mM Na citrate buffer adjusted to pH 5.5. When using H_2O_2 as terminal oxidant it was provided to the system via a syringe pump in a continuous and slow addition protocol (1.7 M, 10 $\mu\text{l}/\text{min}$.). The reaction vial was capped, and the reaction was stirred for 2 h at room temperature, after which $\text{Na}_2\text{S}_2\text{O}_3$ was added and the mixture was extracted twice with CH_2Cl_2 . The combined organic extracts were dried over MgSO_4 , and the products were purified by flash chromatography using pentane/ether as eluent. Quantitative gas chromatography was carried out with decane or dodecane as an internal standard.

(R)-3-pentyn-2-ol (1). 7% yield determined by GC analysis; e.e. 59% determined by capillary GLC on a β -CDX column chromatography (60°C, t_R = 9.5 min, R isomer, 10.2 min, S isomer). The structure was confirmed by comparison with the racemic alcohol, prepared from 1-propynmagnesium bromide and acetaldehyde according to the literature

procedure. The absolute configuration was determined by hydrogenation (Pd/C, MeOH) to afford the commercially available (R)-2-pentanol (Aldrich).

(R)-3-hexyn-2-ol (2). 26% yield; 91% e.e. determined by capillary GLC using a β -CDX column chromatography (60°C, t_R = 15.1 min, R isomer, 16.6 min, S isomer) and by GC analysis of the corresponding trifluoroacetate using a chiral G-TA column (70°C). ^1H NMR (400 MHz, CD_3COCD_3) δ 4.40 (m, 1H), 4.08 (d, J = 5.2 Hz, 1H), 2.15 (dq, J = 7.6 and 2.0 Hz, 2H), 1.30 (d, J = 6.8 Hz, 3H), 1.05 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, CD_3COCD_3) δ 83.58, 82.52, 57.03, 24.38, 13.39, 11.58. ^1H and ^{13}C NMR spectra are consistent with the commercially available sample (Lancaster Synthesis Inc.). The absolute configuration was determined by hydrogenation (Pd/C, MeOH) to afford (R)-2-hexanol (commercially available, Aldrich).

(R)-3-heptyn-2-ol (3a). 30% yield; 87% e.e. determined by gas chromatography analysis of the corresponding trifluoroacetate on a chiral G-TA column (40°C, 20 min, 1°C/min; t_R = 33.5 min, R isomer; 35.7 min, S isomer). ^1H NMR (400 MHz, CD_3COCD_3) δ 4.41 (m, 1H), 4.07 (d, J = 5.6 Hz, 1H), 2.12 (dt, J = 7.2 and 2.0 Hz, 2H), 1.46 (m, 2H), 1.31 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, CD_3COCD_3) δ 83.43, 82.07, 57.07, 24.43, 21.85, 19.92, 12.57. MS (CI) m/e 130 ($[\text{M}+\text{NH}_4]^+$, 38), 113 ($[\text{M}+\text{H}]^+$, 24), 112 (M^+ , 17), 58 (100). The absolute configuration was determined by hydrogenation (Pd/C, MeOH) to afford the commercially available (R)-2-heptanol (Aldrich).

4-heptyn-3-ol (3b). 3% yield by GC analysis; 36% e.e. determined by GC analysis of the corresponding trifluoroacetate on a chiral G-TA column (40°C, 20 min, 1°C/min; t_R = 36.6 min, major isomer; 36.9 min, minor isomer). ^1H NMR (400 MHz, CD_3COCD_3) δ 4.18 (m, 1H), 4.04 (d, J = 5.6 Hz, 1H), 2.17 (m, 2H), 1.59 (m, 2H), 1.07 (t, J = 7.6 Hz, 3H), 0.94 (t, J = 7.2 Hz, 3H). ^1H NMR spectra is identical with the commercial available sample (Lancaster).

(R)-3-Octyn-2-ol (4a). 8% yield; 78% e.e. determined by GLC analysis of the corresponding trifluoroacetate using a chiral G-TA column (80°C, t_R = 11.7 min, R isomer; 11.9 min, S isomer). ^1H NMR (400 MHz, CD_3Cl) δ 4.51 (tq, J = 6.4 and 2.0 Hz, 1H), 2.20 (m, 2H), 1.43 (m, 4H), 1.42 (d, J = 6.4 Hz, 3H), 0.91 (t, J = 7.2 Hz, 3H). ^1H

NMR spectra is the same as reported previously. MS (CI) m/e 144 ($[M+NH_4]^+$, 100), 126 (M^+ , 85),

(R)-4-phenyl-3-butyn-2-ol (5a). 10% yield (TBHP as the terminal oxidant); 50% e.e. determined by 1H NMR analysis of MTPA ester and by gas chromatography analysis of the corresponding trifluoroacetate on a chiral G-TA column (80°C, 20 min, 1°C/min; t_R = 49.3 min, major isomer; 49.6 min, minor isomer). $[\alpha]^{25}_D +24.6^\circ$ (c 0.21, ether). 1H NMR (400 MHz, CD_3Cl) δ 7.42 (m, 2H), 7.30 (m, 3H), 4.75 (m, 1H), 1.85 (d, J = 5.5 Hz, 1H), 1.54 (d, J = 5.5 Hz, 3H); 1H NMR spectra is the same as the literature; MS (CI) m/e 146 (M^+ , 100).

4-phenyl-3-butyn-2-one (5b). 14% yield (TBHP as the terminal oxidant); 1H NMR (500 MHz, CD_3Cl) δ 7.57 (m, 2H), 7.45 (m, 1H), 7.38 (m, 2H), 2.46 (br.t, J = 2.5 Hz, 1H), 1.88 (d, J = 5.0 Hz, 1H), 1.55 (d, J = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, CD_3COCD_3) δ 184.73, 133.09, 133.09, 130.77, 128.66, 128.66, 119.92, 90.36, 88.28, 32.77; MS (CI) m/e 144 (M^+ , 100).

(R)-5-(acetoxy)-3-pentyn-2-ol (6). 52% yield; 95% e.e. determined by 1H NMR analysis of MTPA ester and by GLC analysis of the corresponding trifluoroacetate using a chiral G-TA column (80°C, t_R = 20.7 min, R isomer; 21.1 min, S isomer). $[\alpha]^{25}_D +14.1^\circ$ (c 2.11, $CHCl_3$). 1H NMR (400 MHz, CD_3COCD_3) δ 4.69 (d, J = 1.7 Hz, 1H), 4.51 (m, 1H), 4.39 (br.d, J = 5.6 Hz, 1H), 1.36 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CD_3COCD_3) δ 169.44, 89.23, 76.82, 57.01, 51.59, 23.83, 19.65. MS (CI) m/e 160 ($[M+NH_4]^+$, 100), 125 (8). HRMS (CI) calcd for $C_7H_9O_2$ ($[M-17]^+$) 125.0603, found 125.0601. The absolute configuration was determined by hydrogenation (Pd/C, MeOH) to afford (R)-(-)-1,4-pentanediol.

(R)-6-(acetoxy)-3-hexyn-2-ol (7a). 24% yield (TBHP as the terminal oxidant); 76% e.e. determined by GLC analysis of the corresponding trifluoroacetate using a chiral G-TA column (100°C, 1°C/min; t_R = 17.4 min, R isomer; 17.7 min, S isomer) and by 1H NMR analysis of MTPA ester. $[\alpha]^{25}_D +11.0^\circ$ (c 0.69, $CHCl_3$). 1H NMR (400 MHz, CD_3Cl) δ 4.51 (m, 1H), 4.15 (t, J = 6.8 Hz, 2H), 2.54 (dt, J = 6.8 and 2.0 Hz, 2H), 2.07 (s, 3H), 1.77 (d, J = 5.2 Hz, 3H); ^{13}C NMR (100 MHz, CD_3Cl) δ 170.74, 83.62, 79.93, 62.11, 58.35,

24.39, 20.76, 19.04. MS (CI) m/e 174 ($[M+NH_4]^+$, 100), 139 (53). HRMS (CI) calcd for $C_8H_{11}O_2$ ($[M-17]^+$) 139.0759, found 139.0762. The absolute configuration was determined by hydrogenation (Pd/C, MeOH) to afford (R)-(-)-1,5-hexanediol.

6-(acetoxy)-3-hexyn-2-one (7b). 20% yield (TBHP as the terminal oxidant); 1H NMR (500 MHz, CD_3Cl) 4.21 (t, $J = 6.5$ Hz, 2H), 2.71 (t, $J = 5.2$ Hz, 2H), 2.33 (s, 3H), 2.09 (s, 3H); ^{13}C NMR (125 MHz, CD_3Cl) δ 184.50, 170.74, 88.74, 82.12, 61.09, 32.70, 20.79, 19.44; MS (CI) m/e 155 ($[M+H]^+$, 21), 95 (100).

(-)-6-(acetoxy)-4-hexyn-3-ol (8). 8% yield; 87% e.e. determined by GLC analysis of the corresponding trifluoroacetate using a chiral G-TA column (70°C, 20min, 1°C/min, $t_R = 49.6$ min, major isomer; 50.0 min, minor isomer). $[\alpha]^{25}_D -2.8^\circ$ (c 0.45, $CHCl_3$). 1H NMR (500 MHz, CD_3COCD_3) δ 4.68 (d, $J = 2.0$ Hz, 2H), 4.31 (br.d, $J = 5.5$ Hz, 1H), 4.28 (m, 1H), 2.02 (s, 3H), 1.64 (9m, 2H), 0.95 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR (125 MHz, CD_3COCD_3) δ 169.44 (?), 88.21, 77.74, 62.49, 51.62, 30.76, 19.64, 8.91. MS (CI) m/e 174 ($[M+NH_4]^+$, 100), 139 (10). HRMS (CI) calcd for $C_8H_{11}O_2$ ($[M-17]^+$) 139.0759, found 139.0763.

(R)-5-bromo-3-pentyn-2-ol (9). 60% yield (TBHP as the terminal oxidant); 88% e.e. determined by GLC using a chiral G-TA column (100°C, 10min, 1°C/min; $t_R = 23.1$ min, S isomer; 23.5 min, R isomer). $[\alpha]^{25}_D +13.9^\circ$ (c 0.35, $CHCl_3$). 1H NMR (400 MHz, CD_3COCD_3) δ 4.51 (m, 1H), 4.40 (d, $J = 5.6$ Hz, 1H), 4.13 (d, $J = 2.0$ Hz, 1H), 1.34 (d, $J = 6.4$ Hz, 3H). ^{13}C NMR (100 MHz, CD_3COCD_3) δ 89.75, 77.93, 57.12, 54.06, 23.73. MS (CI) m/e 180 ($[M-1+NH_4]^+$, 100), 164 ($[M+H]^+$, 40). The absolute configuration was determined by hydrogenation (Pd/C, MeOH) to (R)-2-pentanol (commercially available, Aldrich).

(R)-6-bromo-3-hexyn-2-ol (10). 25% yield; 94% e.e. determined by GLC using a chiral G-TA column (100°C, 10min, 1°C/min; $t_R = 27.7$ min, S isomer; 28.2 min, R isomer), and by 1H NMR analysis of MTPA ester. $[\alpha]^{25}_D +14.7^\circ$ (c 1.12, $CHCl_3$). 1H NMR (400 MHz, CD_3Cl) δ 4.51 (m, 1H), 3.42 (t, $J = 7.2$ Hz, 2H), 2.77 (dt, $J = 7.2$ and 2.0 Hz, 2H), 1.43 (d, $J = 6.4$ Hz, 3H). ^{13}C NMR (100 MHz, CD_3Cl) δ 84.09, 81.04, 58.32, 53.31, 24.32, 22.99. MS (CI) m/e 196 ($[M+1+NH_4]^+$, 96), 194 ($[M-1+NH_4]^+$, 100), 178 ($[MH]^+$,

3). HRMS (CI) calcd for C_6H_8BrO ($[M-2]^+$) 174.9759, found 174.9763. The absolute configuration was determined by hydrogenation (Pd/C, MeOH) to (R)-2-hexanol (commercially available, Aldrich).