Supporting Information Kirsch

IBX-Mediated α -Hydroxylation of α -Alkynyl Carbonyl Systems. A Convenient Method for the Synthesis of Tertiary Alcohols

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Supporting Information

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General experimental details: Alkynyl alcohols **4** were prepared according to published procedures by alkynylation of oxiranes [$\text{Li}-\text{C}\equiv\text{C}-\text{R}$ (1 equiv.), $\text{BF}_3\cdot\text{OEt}_2$ (1 equiv.), $-78\text{ }^\circ\text{C}$, THF].¹ All α -alkynyl carbonyl compounds **1** were synthesized by the oxidation of the corresponding alkynylalcohols **4** with PCC.² DMSO contained less than 0.005% of water. IBX was prepared according to a procedure developed by Santagostino and co-workers.³

¹ Yamaguchi, M.; Hirao, I. *Tetrahedron Lett.* **1983**, 24, 391–394.

² Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 16, 2647–2650.

³ Frigerio, M.; Santagostino, M.; Sputore, S. *J. Org.Chem.* **1999**, 64, 4537–4538.

¹H NMR spectra were obtained on 500 MHz and 360 MHz FT-NMR spectrometers. ¹³C NMR spectra were recorded at 90.6 MHz. Chemical shifts are reported in ppm relative to solvent signal. Multiplicity is indicated as follows: s (singlet); d (doublet); t (triplet); m (multiplet); dd (doublet of doublets); etc.; app (apparent). Flash chromatography was performed with E. Merck silica gel (43–60 μm). The eluent used is reported in parentheses. Thin-layer chromatography (TLC) was performed on precoated glass-backed plates (Merck Kieselgel 60 F₂₅₄), and components were visualized by observation under UV light or by treating the plates with KMnO₄/H₂SO₄ followed by heating.

General procedure for the IBX-mediated α-hydroxylation starting from 2-alkynyl alcohols **4 (Method B).**

2-Hydroxy-2-(2-phenylethynyl)cyclopentanone (2a). IBX (0.42 mmol, 118 mg) was added to a solution of alcohol **4a** (78 mg, 0.42 mmol) in DMSO (0.9 mL) and the reaction vial was sealed, protected from light and stirred at room temperature. After 4 h, additional IBX (0.84 mmol, 235 mg) was added. The reaction mixture was then stirred at room temperature for 8 h (until TLC analysis indicated complete consumption of starting material), diluted with CH₂Cl₂ (10 mL), and stirring was continued for 30 min to precipitate the insoluble byproduct, which was removed by filtration. The precipitate was washed with CH₂Cl₂ (2 × 5 mL), and the combined filtrate was subsequently diluted with aqueous saturated NaHCO₃ (20 mL). The phases were separated and the aqueous phase was extracted with CH₂Cl₂ (2 × 5 mL). The combined organic phases were washed with water (30 mL) and brine (30 mL), dried (Na₂SO₄), and concentrated under reduced pressure. The residue was purified by flash chromatography on silica (10% EtOAc/pentane) to afford **2a** as a pale yellow oil (46 mg, 0.23 mmol, 55%): R_f 0.27 (10% Et₂O/hexanes). ¹H NMR (360 MHz, CDCl₃): δ = 2.04–2.17 (m, 3 H), 2.27–2.42 (m, 1 H), 2.51–2.67 (m, 2 H), 3.09 (s, 1 H), 7.29–7.34 (m, 3 H), 7.40–7.44 (m, 2 H); ¹³C NMR (90.6 MHz, CDCl₃): δ = 17.1, 33.7, 37.8, 74.0, 86.1, 87.7, 121.8, 128.3, 128.9, 131.9, 212.4; LRMS (EI) 200 (34%) [M⁺], 199 (100%), 144 (90%). HRMS 200.0832 [200.0837 calcd for C₁₃H₁₂O₂ (M⁺)].

General procedure for the IBX-mediated α -hydroxylation of α -alkynyl carbonyl compounds **1 (Method A).**

2-Hydroxy-2-(2-phenylethynyl)cyclohexanone (2b). IBX (0.48 mmol, 134 mg) was added to a solution of ketone **1a** (82 mg, 0.64 mmol) in DMSO (1.3 mL) and the reaction vial was sealed, protected from light and stirred at room temperature. After 3 h, additional IBX (0.48 mmol, 134 mg) was added. The reaction mixture was then stirred at room temperature for 17 h (until TLC analysis indicated complete consumption of starting material), diluted with CH₂Cl₂ (10 mL), and stirring was continued for 30 min to precipitate the insoluble byproduct, which was removed by filtration. The precipitate was washed with CH₂Cl₂ (2 $\times$ 5 mL), and the combined filtrate was subsequently diluted with aqueous saturated NaHCO₃ (20 mL). The phases were separated and the aqueous phase was extracted with CH₂Cl₂ (2 $\times$ 5 mL). The combined organic phases were washed with water (30 mL) and brine (30 mL), dried (Na₂SO₄), and concentrated under reduced pressure. The residue was purified by flash chromatography on silica (10% Et₂O/pentane) to afford **2b** as a pale yellow oil (115 mg, 0.54 mmol, 84%): R_f 0.39 (20% EtOAc/pentane). ¹H NMR (500 MHz, CDCl₃): δ = 1.69 (dt, J = 13.6, 3.9 Hz, 1 H), 1.76 (dt, J = 3.5, 13.1 Hz, 1 H), 1.91–1.93 (m, 1 H), 2.12 (tt, J = 13.6, 3.6 Hz, 1 H), 2.11–2.20 (m, 1 H), 2.57–2.61 (m, 2 H), 3.04 (dt, J = 6.2, 13.7 Hz, 1 H), 4.32 (s, 1 H), 7.33–7.38 (m, 3 H), 7.46 (dd, J = 7.3, 1.4 Hz, 2 H); ¹³C NMR (90.6 MHz, CDCl₃): δ = 22.9, 27.7, 37.3, 42.5, 74.1, 87.5, 87.8, 122.0, 128.3, 128.8, 131.8, 207.5; LRMS (EI) 214 (82%) [M⁺], 185 (70%), 129 (100%). HRMS 214.0993 [214.0994 calcd for C₁₄H₁₄O₂ (M⁺)].

2-Hydroxy-2-[2-(thiophen-3-yl)ethynyl]cyclohexanone (2c). Method A: 78% yield after flash chromatography on silica (5% Et₂O/pentane): R_f 0.41 (20% EtOAc/pentane). ¹H NMR (360 MHz, CDCl₃): δ = 1.68 (dt, J = 13.9, 4.1 Hz, 1 H), 1.72 (dt, J = 3.6, 13.4 Hz, 1 H), 1.85–1.91 (m, 1 H), 2.04 (tt, J = 13.7, 3.6 Hz, 1 H), 2.09–2.18 (m, 1 H), 2.52–2.58 (m, 2 H), 2.99 (dt, J = 6.1, 13.7 Hz, 1 H), 4.28 (s, 1 H), 7.10 (dd, J = 5.0, 0.9 Hz, 1 H), 7.27 (dd, J = 5.0, 2.9 Hz, 1 H), 7.47 (dd, J = 2.9, 0.9 Hz, 1 H); ¹³C NMR (90.6 MHz, CDCl₃): δ = 22.9, 27.7, 37.3, 42.4, 74.2, 82.6, 87.5, 121.0, 125.5, 129.6, 129.8, 207.4; LRMS (EI) 220 (100%) [M⁺], 192 (44%), 163 (50%), 135 (84%). HRMS 220.0555 [220.0558 calcd for C₁₂H₁₂O₂S (M⁺)].

2-Hydroxy-2-[4-(tert-butyldimethylsilyloxy)but-1-ynyl]cyclohexanone (2d). Method A: 70% yield after flash chromatography on silica (10% Et₂O/pentane): R_f 0.50 (20%

EtOAc/pentane). ^1H NMR (360 MHz, CDCl_3): δ = 0.06 (s, 6 H), 0.89 (s, 9 H), 1.56–1.66 (m, 2 H), 1.78–1.84 (m, 1 H), 1.98 (tt, J = 13.6, 3.4 Hz, 1 H), 2.06–2.13 (m, 1 H), 2.39–2.48 (m, 2 H), 2.45 (t, J = 7.0 Hz, 2 H), 2.95 (dt, J = 6.1, 13.6 Hz, 1 H), 3.72 (t, J = 7.0 Hz, 2 H), 4.15 (s, 1 H); ^{13}C NMR (90.6 MHz, CDCl_3): δ = –5.3, 18.2, 22.8, 23.2, 25.8, 27.7, 37.1, 42.5, 61.6, 73.8, 80.2, 85.6, 208.1; LRMS (EI) 296 (4%) [M^+], 239 (35%), 84 (62%), 75 (100%). HRMS 296.1806 [296.1808 calcd for $\text{C}_{16}\text{H}_{28}\text{O}_3\text{Si}$ (M^+)].

2-Hydroxy-2-[5-(tetrahydro-2H-pyran-2-yloxy)pent-1-ynyl]cyclohexanone (2e). Method A: 81% yield after flash chromatography on silica (20% Et_2O /pentane): R_f 0.38 (20% EtOAc/pentane). ^1H NMR (360 MHz, CDCl_3): δ = 1.51–1.75 (m, 7 H), 1.79–1.86 (m, 4 H), 1.99 (tt, J = 13.4, 3.4 Hz, 1 H), 2.07–2.14 (m, 1 H), 2.38 (t, J = 7.3 Hz, 2 H), 2.41–2.51 (m, 2 H), 2.93 (dt, J = 6.1, 13.8 Hz, 1 H), 3.44–3.52 (m, 2 H), 3.79–3.88 (m, 2 H), 4.17 (s, 1 H), 4.58–4.59 (m, 1 H); ^{13}C NMR (90.6 MHz, CDCl_3): δ = 15.7, 19.5, 22.8, 25.4, 27.6, 28.7, 30.6, 37.1, 42.5, 62.2, 65.8, 73.7, 79.5, 87.8, 98.8, 208.0; LRMS (EI) 280 (0.5%) [M^+], 196 (18%), 85 (100%). HRMS 280.1686 [280.1675 calcd for $\text{C}_{16}\text{H}_{24}\text{O}_4$ (M^+)].

2-Hydroxy-2-[2-(pyridin-2-yl)ethynyl]cyclohexanone (2f). Method B: 73% yield after flash chromatography on silica (40% EtOAc/pentane): R_f 0.48 (50% EtOAc/pentane). ^1H NMR (360 MHz, CDCl_3): δ = 1.68 (dt, J = 13.9, 4.1 Hz, 1 H), 1.75 (dt, J = 3.9, 13.2 Hz, 1 H), 1.87–1.94 (m, 1 H), 2.10–2.22 (m, 2 H), 2.55–2.65 (m, 2 H), 3.06 (dt, J = 6.4, 13.9 Hz, 1 H), 4.36 (s, 1 H), 7.25 (ddd, J = 7.7, 4.8, 1.0 Hz, 1 H), 7.44 (dt, J = 7.7, 1.0 Hz, 1 H), 7.66 (dt, J = 1.8, 7.7 Hz, 1 H), 8.59 (app. d, J = 4.8 Hz, 1 H); ^{13}C NMR (90.6 MHz, CDCl_3): δ = 22.82, 27.7, 37.5, 42.3, 74.1, 86.4, 87.6, 123.3, 127.4, 136.2, 142.3, 150.1, 207.0; LRMS (EI) 215 (10%) [M^+], 159 (72%), 130 (100%). HRMS 215.0950 [215.0946 calcd for $\text{C}_{13}\text{H}_{13}\text{NO}_2$ (M^+)].

2-Hydroxy-2-[2-(trimethylsilyl)ethynyl]cyclohexanone (2g). Method B: 91% yield after flash chromatography on silica (10% Et_2O /pentane): R_f 0.44 (20% EtOAc/pentane). ^1H NMR (360 MHz, CDCl_3): δ = 0.18 (s, 9 H), 1.56–1.69 (m, 2 H), 1.79–1.99 (m, 3 H), 2.40–2.52 (m, 2 H), 2.92 (dt, J = 6.1, 13.8 Hz, 1 H), 4.19 (s, 1 H); ^{13}C NMR (90.6 MHz, CDCl_3): δ = –0.3, 22.9, 27.7, 37.1, 42.4, 74.2, 92.7, 104.0, 207.5; LRMS (EI) 210 (32%) [M^+], 167 (55%), 75 (100%). HRMS 210.1077 [210.1076 calcd for $\text{C}_{11}\text{H}_{18}\text{O}_2\text{Si}$ (M^+)].

6-Benzyloxy-2-hydroxy-2-(2-phenylethynyl)cyclohexanone (2h). Method B: d.r. = 74:26 according to ^1H NMR of crude mixture; 68% yield of major (*trans*) diastereoisomer after flash chromatography on silica (10% Et₂O/pentane): R_f 0.40 (20% EtOAc/pentane). ^1H NMR (360 MHz, CDCl₃): δ = 1.78–1.95 (m, 3 H), 2.19–2.39 (m, 2 H), 2.48–2.55 (m, 1 H), 3.87 (s, 1 H), 4.23 (t, J = 4.3 Hz, 1 H), 4.43 (d, J = 11.8 Hz, 1 H), 4.72 (d, J = 11.8 Hz, 1 H), 7.22–7.34 (m, 10 H); ^{13}C NMR (90.6 MHz, CDCl₃): δ = 18.1, 34.2, 42.8, 71.8, 73.8, 80.1, 86.2, 87.2, 122.2, 127.7, 127.8, 128.1, 128.3, 128.5, 131.8, 137.3, 206.0. Minor Diastereoisomer: R_f 0.38 (20% EtOAc/pentane). ^1H NMR (360 MHz, CDCl₃): δ = 1.67–1.79 (m, 2 H), 1.85–2.06 (m, 2 H), 2.35–2.42 (m, 1 H), 2.51–2.58 (m, 1 H), 4.29 (s, 1 H), 4.56 (d, J = 11.6 Hz, 1 H), 4.73 (dd, J = 12.3, 6.8 Hz, 1 H), 4.87 (d, J = 11.6 Hz, 1 H), 7.23–7.41 (m, 10 H); ^{13}C NMR (90.6 MHz, CDCl₃): δ = 19.7, 34.8, 42.5, 72.1, 74.3, 78.2, 87.2, 87.9, 121.6, 128.0, 128.2, 128.3, 128.5, 129.0, 131.8, 137.4, 206.0. LRMS (EI) 320 (4%) [M^+], 229 (78%), 91 (100%). HRMS 320.1424 [320.1412 calcd for C₂₁H₂₀O₃ (M^+)].

5-Hydroxy-5-(2-phenylethynyl)octan-4-one (2i). Method B: 77% yield after flash chromatography on silica (5% Et₂O/pentane): R_f 0.65 (20% EtOAc/pentane). ^1H NMR (500 MHz, CDCl₃): δ = 0.99 (t, J = 7.5 Hz, 3 H), 1.00 (t, J = 7.5 Hz, 3 H), 1.33–1.45 (m, 1 H), 1.62–1.84 (m, 4 H), 2.05 (dt, J = 4.5, 13.2 Hz, 1 H), 2.61 (dt, J = 17.3, 6.6 Hz, 1 H), 3.00 (dt, J = 17.3, 7.3 Hz, 1 H), 4.20 (s, 1 H), 7.33–7.35 (m, 3 H), 7.44–7.46 (dd, J = 6.8, 1.6 Hz, 2 H); ^{13}C NMR (90.6 MHz, CDCl₃): δ = 13.7, 14.0, 17.0, 17.5, 37.8, 41.9, 76.1, 85.8, 87.8, 122.1, 128.3, 128.7, 131.8, 208.1; LRMS (EI) 244 (3%) [M^+], 173 (100%), 129 (18%). HRMS 244.1462 [244.1463 calcd for C₁₆H₂₀O₂ (M^+)].

5-Hydroxy-5-[2-(trimethylsilyl)ethynyl]octan-4-one (2j). Method B: 74% yield after flash chromatography on silica (5% Et₂O/pentane): R_f 0.58 (10% EtOAc/pentane). ^1H NMR (360 MHz, CDCl₃): δ = 0.16 (s, 9 H), 0.94 (t, J = 7.0 Hz, 3 H), 0.96 (t, J = 7.3 Hz, 3 H), 1.23–1.33 (m, 1 H), 1.54–1.78 (m, 4 H), 1.94 (dt, J = 4.3, 13.4 Hz, 1 H), 2.51 (dt, J = 17.3, 6.8 Hz, 1 H), 2.93 (dt, J = 17.3, 7.3 Hz, 1 H), 4.08 (s, 1 H); ^{13}C NMR (90.6 MHz, CDCl₃): δ = –0.3, 13.6, 14.0, 16.8, 17.6, 37.6, 41.8, 76.1, 90.9, 104.0, 208.1; LRMS (EI) 240 (28%) [M^+], 169 (100%), 75 (72%). HRMS 240.1544 [240.1546 calcd for C₁₃H₂₄O₂Si (M^+)].