Supporting Information for
***trans*-Selective Conversions of γ -Hydroxy- α,β -Alkynoic Esters**
to γ -Hydroxy- α,β -Alkenoic Esters

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Experimental Section

General Techniques All reactions were carried out with dry, freshly distilled solvents under anhydrous conditions, unless otherwise noted. Tetrahydrofuran (THF) was distilled from sodium-benzophenone, and methylene chloride (CH_2Cl_2) was distilled from calcium hydride. Acetonitrile was dried over 3 Å molecular sieves. Yields refer to chromatographically and spectroscopically (^1H NMR) homogenous materials, unless otherwise stated.

All reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25-mm E. Merck silica gel plates (60F-254) using UV-light (254 nm) with anisaldehyde in ethanol and heat as developing agents. TSI silica gel (230-400 mesh) was used for flash column chromatography.

NMR spectra were recorded on AM300 or AM500 (Bruker) instruments and calibrated using a solvent peak or tetramethylsilane as an internal reference. The following abbreviations are used to indicate the multiplicities; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. High-resolution mass spectra were obtained by using EBE geometry.

Abbreviations Ac, acetyl; EI, electron impact; Et, ethyl; Et_2O , diethyl ether; EtOAc, ethyl acetate; EtOH, ethanol; Hex, hexanes; HRMS, high resolution mass spectrum; *i*- Pr_2NH , diisopropyl amine; Me, methyl; MeOH, methanol; NaHCO_3 , sodium bicarbonate; Na_2SO_4 , sodium sulfate; NH_4Cl , ammonium chloride; NH_4OH , ammonium hydroxide; Ph, phenyl; THF, tetrahydrofuran.

General procedure for reduction of propargylic alcohol **C with NaBH_4 .** Sodium borohydride (1.2 – 4.0 mmol) was added to a solution of alcohol **C** (1.0 mmol) in MeOH (4.0 mL) in one portion at -34°C . The reaction mixture was allowed to warm to 0°C , upon quenching with saturated aqueous NH_4Cl (60 mL). The mixture was separated, and the aqueous layer was extracted with EtOAc (20 mL x 1). The combined organic layers were washed with saturated aqueous NaHCO_3 (30 mL x 1) and brine (30 mL x 1), dried over Na_2SO_4 , and concentrated under reduced pressure. The resulting residue was purified by silica gel chromatography (EtOAc in Hex) to afford an inseparable mixture of alcohol **D** and lactone **E**.

General procedure for reduction of propargylic alcohol **C with Red-Al.** Alcohol **C** (1.0 mmol) in THF (5.0 mL) was added to a solution of Red-Al (2.0 mmol) in THF (4.0 mL) dropwise at -72°C under nitrogen atmosphere. After stirring at the same temperature for 20 min, the solution was quenched with 0.1 M HCl^* (53 mL). The solution was concentrated under reduced pressure and was then diluted with EtOAc (20 mL). The mixture was separated, and the aqueous layer was extracted with EtOAc (20 mL x 1). The combined organic layers were then washed with saturated aqueous NaHCO_3 (15 mL x 1) and brine (15 mL x 1), dried over Na_2SO_4 , and concentrated under reduced pressure. The resulting residue was purified through a plug of silica gel to afford an inseparable mixture of alcohol **D** and lactone **E**.

*In the case of acid-sensitive compounds, 1 M Na⁺K⁺-tartrate can be used in lieu of HCl.

Alcohol **3** data was consistent with literature (*Tetrahedron Lett.* **2003**, 44, 443-445).

Data for alcohol **4D**: yellow oil; R_f 0.26 (30% EtOAc in Hex); ^1H NMR (300 MHz, 293K, CDCl_3) δ 7.47-7.28 (m, 5H), 7.05 (dd, 1H, J = 15.6, 4.8 Hz), 6.18 (dd, 1H, J = 15.6, 1.7 Hz), 5.36 (dd, 1H, J = 4.7, 1.6 Hz), 3.73 (s, 3H). Consistent with literature (*J. Org. Chem.* **1991**, 56, 2050-2058).

Data for alcohol **12D**: white powder; mp 139.8-141.5 °C; R_f 0.32 (50% EtOAc in Hex); IR (film) 3354 (broad, O-H), 2924, 1718 (C=O), 1532, 1450, 1260, 741 cm^{-1} ; ^1H NMR (300 MHz, 293K, CDCl_3) δ 7.76 (d, 2H, J = 7.4 Hz), 7.59-7.53 (m, 2H), 7.40 (apparent t, 2H, J = 7.4 Hz), 7.31 (td, 2H, J = 7.4, 1.1 Hz), 6.90 (br dd, 1H, J = 15.6, 4.1 Hz), 6.16 (br d, 1H, J = 15.6 Hz), 5.25-5.17 (m, 1H), 4.45-4.39 (m, 2H), 4.20 (broad t, 1H, J = 6.6 Hz), 3.73 (s, 3H), 3.22-3.11 (m, 2H); ^{13}C NMR (75 MHz, 293K, CDCl_3) δ 166.6, 157.5, 146.7, 143.7, 141.3, 127.7, 127.1, 125.0, 121.7, 120.0, 70.8, 67.0, 51.7, 47.1, 46.1; HRMS (EI⁺) calcd for $\text{C}_{21}\text{H}_{21}\text{NO}_5$ (M^+) 367.1420; found 367.1424 m/z .

Data for alcohol **13D**: yellow oil; R_f 0.31 (30% EtOAc in Hex); ^1H NMR (300 MHz, 293 K, CDCl_3) δ = 6.98 (dd, 1H, J = 15.7, 5.2 Hz), 6.04 (dd, 1H, J = 15.7, 1.7 Hz), 4.10 (td, 1H, J = 5.3, 1.5 Hz), 3.75 (s, 3H), 1.85-1.67 (m, 5H), 1.60-1.49 (m, 2H), 1.28-1.02 (m, 4H). Consistent with literature (*Tetrahedron Lett.* **2003**, 44, 443-445).

Data for alcohol **14D**: yellow oil; R_f 0.44 (30% EtOAc in Hex); ^1H NMR (300 MHz, 293K, CDCl_3) δ 7.04 (d, 1H, J = 15.7 Hz), 6.07 (d, 1H, 15.7 Hz), 3.74 (s, 3H), 1.70-1.52 (m, 7H), 1.35-1.25 (m, 3H). Consistent with literature (*Synthesis* **1983**, 134-135).

Data for alcohol **15D**: The unambiguous stereochemistry has yet to be determined; clear oil; R_f 0.24 (30% EtOAc in Hex); IR (film) 3458 (broad, O-H), 2921, 1724 (C=O), 1652, 1437, 1270, 1171 cm^{-1} ; ^1H NMR (300 MHz, 293K, CDCl_3) δ 6.95 (dd, 1H, J = 15.7, 5.1 Hz), 6.14 (dd, 1H, J = 15.7, 1.7 Hz), 4.89-4.86 (m, 1H), 4.80-4.78 (m, 1H), 4.35-4.29 (m, 1H), 3.75 (s, 3H), 2.89 (d, 1H, J = 4.6 Hz), 2.71 (d, 1H, J = 4.7 Hz), 2.47 (br d, 1H, J = 14.7 Hz), 2.34 (br d, 1H, J = 14.6 Hz), 1.76 (s, 3H); ^{13}C NMR (75 MHz, 293K, CDCl_3) δ 166.4, 145.0, 140.6, 122.4, 114.8, 72.0, 59.8, 51.7, 49.5, 39.1, 23.3; HRMS (EI⁺) calcd for $\text{C}_{11}\text{H}_{13}\text{O}_3$ ($\text{M}^+ - \text{H}_3\text{O}$) 193.0865; found 193.0861 m/z .

Preparation of vinyl iodide 16. Alcohol **4** (477 mg, 2.51 mmol) in THF (12.5 mL) was added to a solution of Red-Al (1.17 g of a 65+wt % solution in toluene, 3.76 mmol) in THF (7.5 mL) dropwise at -72 °C under nitrogen atmosphere. The reaction was stirred for 40 min at the same temperature upon which iodine (3.18 g, 12.54 mmol) dissolved in THF (25 mL) was added dropwise to the reaction at -72 °C. The solution was allowed to warm to -10 °C over 50 min, upon which it was quenched with a 10% aqueous solution of $\text{Na}_2\text{S}_2\text{O}_3$ (15 mL). The solution was concentrated under reduced pressure and was then diluted with EtOAc (30 mL). The mixture was separated, and the aqueous layer was extracted with EtOAc (30 mL x 1). The

combined organic layers were then washed with saturated aqueous NaHCO₃ (30 mL x 1) and brine (30 mL x 1), dried over Na₂SO₄, and concentrated under reduced pressure. The resulting residue was purified through a plug of silica gel to afford vinyl iodide **16** (622 mg, 78% yield) as a clear oil.

Data for vinyl iodide **16**: *R*_f 0.32 (30% EtOAc in Hex); IR (film) 3427 (broad, O-H), 2951, 1720 (C=O), 1257, 699 cm⁻¹; ¹H NMR (300 MHz, 293K, CDCl₃) δ 7.52-7.47 (m, 2H), 7.42-7.33 (m, 4H, vinyl proton in aromatic region), 5.57 (d, 1H, *J* = 8.0 Hz), 3.81 (s, 3H), 2.27 (br s, 1H); ¹³C NMR (75 MHz, 293K, CDCl₃) δ 163.2, 152.2, 140.2, 128.9, 128.6, 126.4, 93.9, 77.8, 53.8; HRMS (EI+) calcd for C₁₁H₁₁IO₃ (M⁺) 317.9753, found 317.9767 *m/z*.

To unambiguously determine the stereochemistry of vinyl iodide **16**, we prepared diol **19**. NOE experiments proved unsuccessful with diol **19**, presumably due to the molecule's rapid tumbling in solution. Diol **21** was prepared from propargyl alcohol **20** in the same manner. NOE enhancement between the vinyl proton and methylene protons confirms the *cis* geometry.

Stille coupling of vinyl iodide 16. Cl₂Pd(PPh₃)₂ (2.6 mg, 3.7 μmol) was dissolved in THF (0.4 mL) under nitrogen atmosphere. Vinyl iodide **16** (58.8 mg, 0.185 mmol) in THF (0.5 mL) was added dropwise to the flask, followed by dropwise addition of tributyl(vinyl)tin (64.9 μL, 0.222 mmol). After 48 h, the reaction was quenched with 10% NH₄OH (2 mL). The reaction was concentrated under reduced pressure, followed by dilution with Et₂O (10 mL) and water (10 mL). The aqueous layer was extracted with Et₂O (10 mL x 1). The organic layers were washed with brine (10 mL), dried over Na₂SO₄, and concentrated under reduced pressure. The resulting residue was purified by silica gel (8 mL) column chromatography (10 → 40% EtOAc in Hex) to afford diene **18** (18.0 mg, 45% yield) as a yellow oil.

Data for diene **18**: *R*_f 0.32 (30% EtOAc in Hex); IR (film) 3427 (broad, O-H), 2952, 1721 (C=O), 1436, 1234, 699 cm⁻¹; ¹H NMR (300 MHz, 293K, CDCl₃) δ 7.47-7.28 (m, 5H), 6.86 (br d, 1H, *J* = 9.0 Hz), 6.56 (dd, 1H, *J* = 17.6, 11.4 Hz), 5.66 (dd, 1H, *J* = 9.0, 4.0 Hz), 5.58 (dd, 1H, *J* = 17.6, 1.6 Hz), 5.46 (ddd, 1H, *J* = 11.4, 1.4, 1.0 Hz), 3.78 (s, 3H), 2.22 (d, 1H, *J* = 4.0 Hz); ¹³C NMR (75 MHz, 293K, CDCl₃) δ 167.1, 142.2, 141.8, 131.0, 128.8, 128.2, 126.5, 126.3, 121.5, 70.2, 52.1; HRMS (EI+) calcd for C₁₃H₁₄O₃ (M⁺) 218.0943, found 218.0942 *m/z*.

Sonogashira coupling of vinyl iodide 16. Pd(PPh₃)₄ (12.1 mg, 10.5 μmol) was dissolved in *i*-Pr₂NH (0.21 mL) under nitrogen atmosphere. Vinyl iodide **16** (33.4 mg, 0.105 mmol) in *i*-Pr₂NH (0.40 mL) was added dropwise to the flask, followed by dropwise addition of 1-hexyne

(24.1 μ L, 0.210 mmol) and addition of CuI (0.9 mg, 5.3 μ mol). After 25 min, the reaction was concentrated under reduced pressure. The mixture was then diluted with Et₂O (10 mL) and water (10 mL). The aqueous layer was extracted with Et₂O (10 mL x 1). The organic layers were washed with brine (10 mL x 1), dried over Na₂SO₄, and concentrated under reduced pressure. The resulting residue was purified by silica gel (5 mL) column chromatography (5 $\rightarrow$ 30% EtOAc in Hex) to afford enyne **17** (18.3 mg, 64% yield) as a yellow oil.

Data for enyne **17**: *R_f* 0.33 (30% EtOAc in Hex); IR (film) 3432 (broad, O-H), 3030, 2956, 2929, 2872, 2228 (C $\equiv$ C), 1727 (C=O), 1436, 1238, 1145, 1012, 756, 699 cm⁻¹; ¹H NMR (300 MHz, 293K, CDCl₃) δ 7.46-7.42 (m, 2H), 7.39-7.27 (m, 3H), 7.17 (d, 1H, *J* = 8.6 Hz), 5.80 (d, 1H, *J* = 8.6 Hz), 3.77 (s, 3H), 2.46 (t, 2H, *J* = 6.9 Hz), 1.65-1.53 (m, 2H), 1.52-1.41 (m, 2H), 0.94 (t, 3H, *J* = 7.3 Hz); ¹³C NMR (75 MHz, 293K, CDCl₃) δ 165.1, 150.2, 141.2, 128.7, 128.1, 126.0, 116.9, 99.4, 73.7, 72.2, 52.6, 30.5, 22.0, 19.3, 13.6; HRMS (EI⁺) calcd for C₁₇H₂₀O₃ (M⁺) 272.1412, found 272.1409 *m/z*.

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