Supplementary Materials for

Highly Enantioselective Phenylacetylene Additions to both Aliphatic and Aromatic Aldehydes

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Experimental

General Data. All reactions were carried out either in drybox or under vacuum line. Unless otherwise specified, all reagents were purchased from Aldrich Chemical Co and used directly. Diethylzinc (95%) was purchased from Strem. Deuterated chloroform was stored over 4 Å molecular sieves before use.

Toluene was distilled with sodium under nitrogen. Methylene chloride, diethyl ether and tetrahydrofuran were dried by passing through activated alumina columns under nitrogen. All the solvents were stored over 4 Å molecular sieves under nitrogen before use.

¹H NMR spectra were obtained using the Varian-300 MHz spectrometer, and ¹³C NMR spectra were obtained using the Varian-500 MHz spectrometer. High Resolution Mass Spectra were obtained using the UC Riverside Mass Spectroscopy facility. HPLC analyses were carried out with the Waters 600 by using the Diacel Chiralcel OD column and eluting with 10% *i*-PrOH in hexane at 1.0 mL/min unless otherwise indicated, and were detected at 254 nm by the Waters 486. The optical rotations were measured on the JASCO DIP-1000 Polarimeter.

General Procedure for the Asymmetric Addition. In 25 mL flask, 1 mL toluene solution of phenylacetylene (2.0 mmol, 226 µL) and diethylzinc (2.0 mmol, 210 µL) was refluxed for 1 h under nitrogen. After the solution was cooled to room temperature, (*S*)-BINOL (>99% *ee*, 0.2 mmol, 57.2 mg), diethyl ether (8 mL) and Ti(O^{*i*}Pr)₄ (0.5 mmol, 150 µL) were added sequentially. The solution was stirred for another hour, and aldehyde (0.5 mmol) was added. After additional 4 h, the reaction was quenched with saturated ammonium chloride. The resulting mixture was

extracted with methylene chloride and concentrated under vacuum. Purification of the residue by passing through a short silica gel column afforded the pure propargylic alcohol product.

1-Phenyl-undec-1-yn-3-ol. 66% yield. 91% *ee* determined by HPLC analysis. Retention time: $t_{\text{major}} = 6.9$ min, and $t_{\text{minor}} = 14.3$ min. $[\alpha]_{\text{D}}^{27} = -6.2$ ($c = 1.02$, CHCl_3). ^1H NMR (300 MHz, CDCl_3) δ 7.38-7.33 (m, 2H), 7.26-7.22 (m, 3H), 4.55-4.50 (t, $J = 5.4$ Hz, 1H), 1.82 (s, 1H), 1.7 (m, 2H), 1.45-1.1.2 (m, 12H), 0.82-0.78 (m, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 131.6, 128.3, 128.2, 122.7, 90.2, 84.8, 63.0, 37.9, 31.8, 29.5, 29.3, 29.2, 25.2, 22.6, 14.1; HRMS: calcd. for $[\text{C}_{17}\text{H}_{24}\text{O}]^+$: 244.1827, found: 244.1823.

1-Phenyl-dec-1-yn-3-ol. 70% yield. 93% *ee* determined by HPLC analysis. Retention time: $t_{\text{major}} = 6.9$ min, and $t_{\text{minor}} = 13.7$ min. $[\alpha]_{\text{D}}^{27} = -6.5$ ($c = 0.62$, CHCl_3). ^1H NMR (300 MHz, CDCl_3) δ 7.38-7.34 (m, 2H), 7.24-7.22 (m, 3H), 4.55-4.50 (m, 1H), 1.83 (s, 1H), 1.77-1.68 (m, 2H), 1.44-1.21 (m, 10H), 0.82-0.78 (m, 3H); ^{13}C NMR (125 MHz, $\text{acetone-}d_6$) δ 132.2, 129.3, 129.0, 124.2, 92.7, 84.0, 62.6, 39.0, 32.5, 30.02, 29.98, 26.1, 23.3, 14.3; HRMS: calcd. for $[\text{C}_{16}\text{H}_{22}\text{O}]^+$: 230.1671, found: 230.1667.

1-Phenyl-hept-1-yn-3-ol. 91% yield. 93% *ee* determined by HPLC analysis; Retention time: $t_{\text{major}} = 7.4$ min and $t_{\text{minor}} = 15.3$. $[\alpha]_{\text{D}}^{26} = -1.4$ ($c = 1.50$, CHCl_3). ^1H NMR (300 MHz, CDCl_3) δ 7.38-7.34 (m, 2H), 7.25-7.21 (m, 3H), 4.5 (t, $J = 6.6$ Hz, 1H), 1.9 (s, 1H), 1.77-1.69 (m, 2H), 1.48-1.27 (m, 4H), 0.89-0.84 (t, $J = 7.2$ Hz, 3H).

4-Methyl-1-phenyl-pent-1-yn-3-ol¹. 84% yield. 97% *ee* determined by HPLC analysis; Retention time: $t_{\text{major}} = 7.4$ min and $t_{\text{minor}} = 12.1$. $[\alpha]_{\text{D}}^{26} = -3.6$ ($c = 1.01$, CHCl_3). ^1H NMR (300 MHz, CDCl_3) δ 7.37-7.33 (m, 2H), 7.25-7.20 (m, 3H), 4.32 (t, $J = 5.7$ Hz, 1H), 1.90 (m, $J = 6.6$ Hz, 1H), 1.80-1.78 (d, $J = 5.7$ Hz, 1H), 1.01-0.97 (t, $J = 6.6$ Hz, 3H).

(R)-1-Phenyl-pent-1-yn-3-ol². 60% yield. 94% *ee* determined by HPLC analysis. Retention time: $t_{\text{major}} = 7.8$ min, and $t_{\text{minor}} = 14.3$ min. $[\alpha]_{\text{D}}^{26} = +19.2$ ($c = 1.24$, Et_2O). ^1H NMR (300 MHz, CDCl_3) δ 7.38-7.34 (m, 2H), 7.25-7.22 (m, 3H), 4.47 (t, $J = 6.3$ Hz, 1H), 1.85 (s, 1H), 1.80-1.70 (m, $J = 7.5$ Hz, 2H), 1.03-0.98 (t, $J = 7.5$ Hz, 3H).

(R)-1-Cyclohexyl-3-phenyl-prop-2-yn-1-ol³. 58% yield. 95% *ee* determined by HPLC analysis. Retention time: $t_{\text{major}} = 7.4$ min, and $t_{\text{minor}} = 13.4$ min. $[\alpha]_{\text{D}}^{27} = -10.8$ ($c = 0.64$, CHCl_3). ^1H NMR (300 MHz, CDCl_3) δ 7.38-7.34 (m, 2H), 7.24-7.22 (m, 3H), 4.3 (d, $J = 5.7$ Hz, 1H), 1.87-1.04 (m, 12H).

1,5-Diphenyl-pent-1-yn-3-ol. 99% yield. 93% *ee* determined by HPLC. Retention time: $t_{\text{major}} = 14$ min, and $t_{\text{minor}} = 25.4$ min. $[\alpha]_{\text{D}}^{27} = -62.2$ ($c = 1.03$, CHCl_3). ^1H NMR (300 MHz, CDCl_3) δ 7.39-7.35 (m, 4H), 7.26-7.15 (m, 6H), 4.54-4.50 (m, 1H), 2.83-2.76 (m, 2H), 2.1-2.02 (m, 2H), 1.86 (s, 1H); ^{13}C NMR (125 MHz, $\text{acetone-}d_6$) δ 142.7, 132.2, 129.28, 129.26, 129.17, 129.05, 126.6, 124.0, 92.2, 84.4, 61.9, 40.7, 32.2; HRMS: calcd. for $[\text{C}_{17}\text{H}_{16}\text{O}]^+$: 236.1201, found: 236.1192.

1,4-Diphenyl-but-3-yn-2-ol. 93% yield. 91% *ee* determined by HPLC. Retention time: $t_{\text{major}} = 9.7$ min, and $t_{\text{minor}} = 19.3$. $[\alpha]_{\text{D}}^{27} = -76.3$ ($c = 0.58$, acetone). ^1H NMR (300 MHz, CDCl_3) δ

7.33-7.15 (m, 10H), 4.73-4.69 (t, $J = 6.0$ Hz, 1H), 3.0 (m, 1H), 1.9 (s, 1H); ^{13}C NMR (125 MHz, acetone- d_6) δ 138.6, 132.1, 130.6, 129.2, 129.0, 128.8, 124.0, 92.0, 85.0, 64.0, 45.3; HRMS: calcd. for $[\text{C}_{16}\text{H}_{14}\text{O}]^+$: 22.1045, found: 22.1040.

1-Phenyl-hex-4-en-1-yn-3-ol. 92% yield. 96% *ee* determined by HPLC analysis. Retention time: $t_{\text{major}} = 9.3$ min, and $t_{\text{minor}} = 24.1$ min. $[\alpha]_{\text{D}}^{27} = -67.0$ ($c = 1.08$, acetone). ^1H NMR (300 MHz, CDCl_3) δ 7.47-7.44 (m, 2H), 7.34-7.31 (m, 3H), 6.0 (m, 1H), 5.75 (m, 1H), 5.05 (m, 1H), 1.89 (m, 1H), 1.80 (m, 3H); ^{13}C NMR (125 MHz, acetone- d_6) δ 132.4, 132.2, 129.3, 129.1, 127.3, 124.1, 91.0, 85.0, 63.2, 17.5; HRMS: calcd. for $[\text{C}_{12}\text{H}_{12}\text{O}]^+$: 172.0888, found: 172.0883.

4-Methyl-1-phenyl-hex-4-en-1-yn-3-ol. 90% yield. 96% *ee* determined by HPLC analysis. Retention time: $t_{\text{major}} = 8.8$ min, and $t_{\text{minor}} = 27$ min. $[\alpha]_{\text{D}}^{27} = -61.9$ ($c = 1.03$, acetone). ^1H NMR (300 MHz, CDCl_3) δ 7.40-7.35 (m, 2H), 7.26-7.22 (m, 3H), 5.70 (m, 1H), 4.91 (m, 1H), 1.81 (m, 1H), 1.75 (m, 3H), 1.61 (m, 3H); ^{13}C NMR (125 MHz, acetone- d_6) δ 136.8, 132.2, 129.3, 129.1, 124.1, 121.4, 91.0, 85.0, 68.2, 13.2, 12.1; HRMS: calcd. for $[\text{C}_{13}\text{H}_{14}\text{O}]^+$: 186.1045, found: 186.1041.

1,5-Diphenyl-pent-1-en-4-yn-3-ol. 89% yield. 97% *ee* determined by HPLC. Retention time: $t_{\text{major}} = 17$ min, and $t_{\text{minor}} = 50.6$ min. $[\alpha]_{\text{D}}^{27} = +1.8$ ($c = 1.02$, CHCl_3). ^1H NMR (300 MHz, CDCl_3) δ 7.4-7.2 (m, 10H), 6.77-6.72 (dd, $J = 3.9, 15.6$ Hz, 1H), 6.33-6.26 (m, 1H), 5.2 (s, 1H), 1.98 (s, 1H).

2-Methyl-1,5-diphenyl-pent-1-en-4-yn-3-ol. 96% yield. 99% *ee* determined by HPLC analysis. Retention time: $t_{\text{major}} = 11.3$ min and $t_{\text{minor}} = 41.4$ min. $[\alpha]_{\text{D}}^{27} = -23.2$ ($c = 1.02$, acetone). ^1H NMR (300 MHz, CDCl_3) δ 7.4-7.16 (m, 10H), 6.68 (s, 1H), 5.07 (t, $J = 5.1$ Hz, 1H), 2.0 (m, 4H); ^{13}C NMR (125 MHz, acetone- d_6) δ 138.8, 138.4, 132.3, 129.7, 129.3, 129.2, 129.0, 127.4, 126.7, 123.9, 90.5, 85.4, 68.5, 14.4; HRMS: calcd. for $[\text{C}_{18}\text{H}_{16}\text{O}]^+$: 248.1201, found: 248.1198.

General Procedure for the Preparation of Racemic Propargylic Alcohols. All the racemic propargylic alcohols were prepared for the HPLC analysis according to the following procedure. Under nitrogen, a solution of an alkyne (0.75 mmol) in 3 mL tetrahydrofuran in a 25 mL flask was cooled to -78°C with dryice/acetone bath, and *n*-BuLi in hexanes (1.6 M, 0.7 mmol) was added. The reaction was brought to room temperature and stirred for 3 h. An aldehyde (0.5 mmol) was then added and the mixture was stirred for additional 8 h. The reaction was quenched with ice, and the resulting mixture was extracted with methylene chloride. After dried over magnesium sulfate, the volatile solvent was removed by roto-evaporation and the residue was passed through a short silica gel to afford the product.

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