Supplementary Materials

Chiral Macrocycle-Catalyzed Highly Enantioselective Phenylacetylene Addition to Aliphatic and Vinyl Aldehydes

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General Data. All reactions were carried out under nitrogen. All reagents were purchased from Aldrich Chemical Co and used directly unless indicated otherwise. Dimethylzinc was purchased from Strem. Toluene was distilled over sodium under nitrogen. Methylene chloride, diethyl ether and THF were dried by passing through activated alumina columns under nitrogen. ^1H NMR spectra were obtained using the Varian-300 MHz spectrometer, and ^{13}C NMR spectra were obtained using the Varian-500 MHz spectrometer. Mass spectra were recorded on a LCQ Finnigan mass spectrometer by using APCI (Atmospheric Pressure Chemical Ionization). HPLC analyses were carried out on the Waters 600 instrument by using the Diacel Chiralcel OD column and eluting with 10% *i*-PrOH in hexane at 1.0 mL/min and were detected at 254 nm by the Waters 486.

The following products were obtained by using (S)-2.

1-Phenyl-undec-1-yn-3-ol.^{S-1a} 76% yield. 93% *ee* determined by HPLC analysis. Retention time: $t_{\text{major}} = 6.9$ min, and $t_{\text{minor}} = 14.3$ min. ^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.

1-Phenyl-dec-1-yn-3-ol.^{S-1a} 64% yield. 93% *ee* determined by HPLC analysis. Retention time: $t_{\text{major}} = 6.9$ min, and $t_{\text{minor}} = 13.7$ min. ^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, 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.

1-Phenyl-hept-1-yn-3-ol.^{S-1a} 67% yield. 93% *ee* determined by HPLC analysis. Retention time: $t_{\text{major}} = 7.4$ min and $t_{\text{minor}} = 15.3$. ^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-ol.^{S-2} 54% yield. 95% *ee* determined by HPLC analysis. Retention time: $t_{\text{major}} = 7.4$ min and $t_{\text{minor}} = 12.1$ min. ^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).

1-Cyclohexyl-3-phenyl-prop-2-yn-1-ol.^{S-3} 68% yield. 89% *ee* determined by HPLC analysis. Retention time: $t_{\text{major}} = 7.4$ min, and $t_{\text{minor}} = 13.4$ min. ^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).

5-Methyl-1-phenyl-1-hexyn-3-ol.^{S-4} 72% yield. 93% *ee* determined by HPLC analysis. Retention time: $t_{\text{major}} = 7.8$ min, and $t_{\text{minor}} = 15.8$ min. ^1H NMR (300 MHz, CDCl_3) δ 7.43-7.40 (m, 2H), 7.33-7.25 (m, 3H), 4.64 (t, $J = 7.2$ Hz, 1H), 1.97-1.87 (m, 1H), 1.79-1.61 (m, 2H), 1.01-0.97 (m, 6H).

1,5-Diphenyl-pent-1-yn-3-ol.^{S-1a} 76% yield. 91% *ee* determined by HPLC. Retention time: $t_{\text{major}} = 14$ min, and $t_{\text{minor}} = 25.4$ min. ¹H NMR (300 MHz, CDCl₃) 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). ¹³C NMR (125 MHz, 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.

4-Methyl-1-phenyl-hex-4-en-1-yn-3-ol.^{S-1a} 52% yield. 91% *ee* determined by HPLC analysis. Retention time: $t_{\text{major}} = 8.8$ min, and $t_{\text{minor}} = 27$ min. ¹H NMR (300 MHz, CDCl₃) 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). ¹³C 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.

1-Phenyl-hex-4-en-1-yn-3-ol.^{S-1a} 76% yield. 96% *ee* determined by HPLC analysis. Retention time: $t_{\text{major}} = 9.3$ min, and $t_{\text{minor}} = 24.1$ min. ¹H NMR (300 MHz, CDCl₃) 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). ¹³C NMR (125 MHz, acetone-*d*₆) δ 132.4, 132.2, 129.3, 129.1, 127.3, 124.1, 121.4, 91.0, 85.0, 68.2, 13.2, 12.1.

1,5-Diphenyl-pent-1-en-4-yn-3-ol.^{S-1a} 79% yield. 96% *ee* determined by HPLC. Retention time: $t_{\text{major}} = 17.0$ min, and $t_{\text{minor}} = 50.6$ min. ¹H NMR (300 MHz, CDCl₃) 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).

5-phenylpent-1-en-4-yn-3-ol.^{S-5} 67% yield. 87% *ee* determined by HPLC. Retention time: $t_{\text{major}} = 9.9$ min, and $t_{\text{minor}} = 19.8$ min. ¹H NMR (300 MHz, CDCl₃) δ 7.54-7.42 (m, 2H), 7.38-7.28 (m, 3H), 6.12-6.01 (m, 1H), 5.57 (dt, *J* = 1.2, 15.9 Hz, 1H), 5.30 (dt, *J* = 1.2,

11.4 Hz, 1H), 5.12 (d, J = 5.4 Hz, 1H), 2.05 (s, 1H).

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 tetrahydrofuran (3 mL) in a 25 mL flask was cooled to -78 °C with dry ice/acetone bath. n-BuLi in hexanes (1.6 M, 0.7 mmol) was added. The reaction mixture was then brought to room temperature and stirred for 3 h. An aldehyde (0.5 mmol) was 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 column to afford the product.

References

- S-1. (a) Gao, G.; Moore, D.; Xie, R.-G.; Pu, L. *Org. Lett.* **2002**, 4, 4143- 4146. (b) Moore, D.; Pu, L. *Org. Lett.* **2002**, 4, 1855-1857.
- S-2. Matsumura, K.; Hashiguchi, S.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1997**, 119, 8738.
- S-3. Corey, E. J.; Cimprich, K. A. *J. Am. Chem. Soc.* **1994**, 116, 3151.
- S-4. Ma, S-M; Wu B.; Zhao S-M. *Org. Lett.* **2003**, 5, 4429-4432.
- S-5. Deussen, H-J.; Jeppesen, L.; Schaerer, N.; Junager, F.; Bentzen, B.; Weber, B.; Weil, V.; Mozer, S. J.; Sauerberg, P. *Organic Process Research & Development.* **2004**, 8, 363-371.

(S)-2

1-Phenyl-undec-1-yn-3-ol

1-Phenyl-dec-1-yn-3-ol

1-Phenyl-hept-1-yn-3-ol

4-Methyl-1-phenyl-pent-1-yn-3-ol.

1-Cyclohexyl-3-phenyl-prop-2-yn-1-ol

1,5-Diphenyl-pent-1-yn-3-ol

4-Methyl-1-phenyl-hex-4-en-1-yn-3-ol

1,5-Diphenyl-pent-1-en-4-yn-3-ol

1-Phenyl-hex-4-en-1-yn-3-ol