Ligand-catalyzed Asymmetric Alkynylboration of Enones: A New Paradigm for Asymmetric Synthesis using Organoboranes

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Supporting Information

General Experimental

All reactions were performed using flame-dried glassware under an argon atmosphere. Dichloromethane was freshly distilled from CaH_2 . Diethyl ether was freshly distilled from Na/benzophenone. Diisopropyl alkynylboronates were prepared as reported by Brown.¹ Chiral 3,3'-disubstituted binaphthols were synthesized using procedures described previously.² ^1H NMR and ^{13}C NMR spectra were recorded in CDCl_3 at 300 MHz and 75 MHz, respectively.

General procedure for stoichiometric alkynylation of enones:

Alkynylations of enones using stoichiometric amount of binaphthol-modified alkynylboronates were carried out according to a previous procedure:³ (S)-3,3'-Diiodo-2,2'-dihydroxy-1,1'-binaphthyl (127 mg, 0.236 mmol) and lithium triisopropyl *B*-1-alkynylborate (0.232 mmol) were placed in a 25 mL round-bottomed flask under argon. THF (5 mL) was added slowly to the mixture at 0 °C. The solution was stirred at 0 °C for 1 h then warmed up to room temperature for 5 h. Solvent was evaporated under high vacuum. The enone (0.154 mmol) and CH_2Cl_2 (15 mL) were added followed by $\text{BF}_3\cdot\text{OEt}_2$ (58 μL , 0.461 mmol). The

reaction was stirred at room temperature for 3 h. After the reaction was complete, saturated NH_4Cl (aq.) was added to quench the reaction. The organic layer was separated and the aqueous layer was washed with CH_2Cl_2 (2 x 5 mL). The combined organic phase was washed with water and dried over Na_2SO_4 . Most of the binaphthol was collected by crystallization from CH_2Cl_2 /hexanes and the mother liquid was purified by column chromatography (acetone/hexane 1:10) to give the 1,4-addition product. Enantiomeric excesses of all products were determined by HPLC with a Chiralcel OD column. Absolute configurations for phenylacetylene and 1-octyne adducts to 1,3-bis(4-bromophenyl)-2-propen-1-one were determined by X-ray crystallography.^{3,4} The absolute configurations of other adducts have been assigned based on these known absolute configurations and the assumption that the enones are sufficiently similar in structure (all with β -aryl substituents) that the sense of asymmetric induction should be invariant.

General procedure for catalytic alkynylation of enones (procedure A):

A mixture of diisopropyl *B*-1-octynylboronate (215 mg, 0.9 mmol), enone (0.3 mmol) and (S)-3,3'-diiodo-2,2'-dihydroxy-1,1'-binaphthyl (32 mg, 0.06 mmol) were stirred in CH_2Cl_2 (4 mL) under argon at room temperature for 6 h, then brought to reflux for 24 h. The reaction was quenched with saturated aqueous NH_4Cl . The organic phase was washed with brine and dried over Na_2SO_4 . Purification was done by column chromatography (acetone/hexane 1:10) on silica gel. The chiral ligand was recovered in quantitative yield.

One-pot procedure for catalytic alkynylation of enones from 1-alkyne (procedure B):

To a solution of 1-alkyne (1.0 mmol) in Et_2O (5 mL) was added 0.63 mL of *n*-BuLi (1.0 mmol, 1.6 M) dropwise at -78°C . The resulting solution was stirred at that temperature for 20 minutes then added dropwise to a mixture of $(i\text{-PrO})_3\text{B}$ in 5 mL Et_2O at -78°C . The suspension was stirred at

-78 °C for 2 h and warmed up to room temperature for 1 h. The reaction was again cooled to -78°C, and 0.5 mL anhydrous HCl in Et₂O (2 M, 1 mmol) was added slowly. After the reaction was allowed to warm to room temperature, volatiles were pumped off under high vacuum. To the yellowish oily residue was added CH₂Cl₂ (4 mL), enone (0.3 mmol) and catalyst (0.06 mmol) at room temperature. The mixture was stirred at ambient temperature for 6 h then brought to reflux for 24 h. Workup was the same as procedure A.

(S)-1,3-Diphenyl-4-undecyn-1-one (7a)

$[\alpha]_D = +31.4$ (c 2.04, CHCl₃, 85 %ee); IR (neat): C=O 1684 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 0.86 (3H, t, J = 6.7Hz), 1.15-1.48 (8H, m), 2.14 (2H, dt, J = 2.2Hz, 6.8Hz), 3.26 (1H, dd, J = 16.4Hz, 6Hz), 3.52 (1H, dd, J = 16.4Hz, 8.3Hz), 4.35-4.40 (1H, m), 7.18-7.94 (10H, m); ¹³C NMR (CDCl₃) δ 197.3, 141.9, 136.9, 132.9, 128.4, 128.0, 127.4, 126.6, 83.5, 80.9, 47.6, 33.3, 31.2, 28.7, 28.4, 22.4, 18.7, 13.9; MS (EI), m/e (relative intensity) 318 (1, M⁺), 247 (13), 233 (33), 128 (20), 105 (100), 91 (27), 77 (53). Anal. Calcd for C₂₃H₂₆O: C, 86.75; H, 8.23. Found C, 86.55; H, 8.20. %ee was determined by HPLC (hexane/iPrOH = 99.9/0.1, flow rate = 0.5 mL/min), t_R = 55 min (S), t_R = 61 min (R).

(R)-3-Naphthalen-1-yl -1-phenyl-4-undecyn-1-one (7b)

$[\alpha]_D = -13.1$ (c 1.39, CHCl_3 , 96 %ee); IR (neat): $\text{C}=\text{O}$ 1684 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 0.87 (3H, t, $J = 6.9\text{Hz}$), 1.12-1.47 (8H, m), 2.17 (2H, dt, $J = 2.2\text{Hz}$, 6.8 Hz), 3.32 (1H, dd, $J = 16.8\text{Hz}$, 3.9Hz), 3.65 (1H, dd, $J = 16.8\text{Hz}$, 9.6Hz), 5.18-5.22 (1H, m), 7.43-8.18 (12H, m); ^{13}C NMR (CDCl_3) δ 197.6, 137.4, 137.0, 134.0, 133.0, 129.0, 128.5, 128.2, 127.6, 126.2, 125.5, 125.4, 125.2, 123.0, 84.1, 80.8, 46.5, 31.2, 30.0, 28.7, 28.4, 22.4, 18.8, 14.0; MS (EI), m/e (relative intensity) 368 (3, M^+), 284 (23), 283 (83), 179 (48), 178 (32), 165 (30), 105 (100). Anal. Calcd for $\text{C}_{27}\text{H}_{28}\text{O}$: C, 88.00; H, 7.66. Found C, 88.10; H, 7.58. %ee was determined by HPLC (hexane/iPrOH = 99.5/0.5, flow rate = 1 mL/min), $t_R = 17$ min (*S*), $t_R = 24$ min (*R*). Note that the difference in absolute configuration between **7a** and **7b** is due to differences in CIP priorities: 1-naphthyl > 1-octynyl > phenyl.

(*R*)-3-(2-Furanyl)-1-phenyl-4-undecyn-1-one (7c)

$[\alpha]_D = -10.4$ (c 2.0, CHCl_3 , 88 %ee); IR (neat): $\text{C}=\text{O}$ 1689 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 0.84 (3H, t, $J = 6.9\text{Hz}$), 1.10-1.50 (8H, m), 2.09-2.15 (2H, dt, $J = 2.4\text{Hz}$, 6.9Hz), 3.43-3.46 (2H, m), 4.43-4.49 (1H, m), 6.22 (1H, dd, $J = 3.3\text{Hz}$, 0.9Hz), 6.27 (1H, dd, $J = 3.3\text{Hz}$, 1.9 Hz), 7.30 (1H, dd, $J = 0.9\text{Hz}$, 1.9Hz), 7.39-7.60 (5H, m), 7.90-8.02 (2H, m); ^{13}C NMR (CDCl_3) δ 196.9, 154.1, 136.9, 133.1, 128.5, 128.2, 110.3, 105.9, 82.9, 78.3, 43.8, 31.3, 28.7, 28.4, 27.2, 22.5, 18.7, 14.0; MS (EI), m/e (relative intensity) 308 (1, M^+), 105 (100), 77 (43). Anal. Calcd for $\text{C}_{21}\text{H}_{24}\text{O}_2$: C, 81.78; H, 7.84. Found C, 81.90; H, 7.76. %ee was determined by HPLC (hexane/iPrOH = 99.8/0.2, flow rate = 0.5 mL/min), $t_R = 34$ min (*R*), $t_R = 36$ min (*S*).

(S)-4-Phenyl-5-dodecyn-2-one (7d)

$[\alpha]_D = +2.4$ (c 1.4, CHCl_3 , 94 %ee); IR (neat): $\text{C}=\text{O}$ 1706 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 0.87 (3H, t, $J = 6.9\text{Hz}$), 1.26-1.49 (8H, m), 2.11 (3H, s), 2.15-2.19 (2H, dt, $J = 2.1\text{Hz}$, 6.9Hz), 2.69 (1H, dd, 16.1Hz , 6.1Hz), 2.86 (1H, dd, $J = 16.1\text{Hz}$, 8.5Hz), 4.10-4.15 (1H, m), δ 7.17-7.40 (5H, m); ^{13}C NMR (CDCl_3) δ 206.1, 141.6, 128.5, 127.3, 126.8, 83.6, 80.6, 52.3, 33.2, 31.3, 30.6, 28.9, 28.5, 22.5, 18.8, 14.0; MS (EI), m/e (relative intensity) 256 (1, M^+), 185 (52), 171 (49), 129 (39), 128 (41), 43 (100). Anal. Calcd for $\text{C}_{18}\text{H}_{24}\text{O}$: C, 84.32; H, 9.44. Found C, 84.26; H, 9.32. %ee was determined by HPLC (hexane/*i*PrOH = 99.9/0.1, flow rate = 0.5 mL/min), $t_R = 54$ min (*R*), $t_R = 60$ min (*S*).

(S)-1,3,5-Triphenyl-4-pentyn-1-one (7e)

$[\alpha]_D = +30.1$ (c 1.44, CHCl_3 , 82 %ee); IR (KBr): $\text{C}=\text{O}$ 1680 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 3.39 (1H, dd, $J = 16.5\text{Hz}$, 6.2 Hz), 3.65 (1H, dd, $J = 16.5\text{Hz}$, 7.8Hz), 4.63 (1H, dd, $J = 6.2\text{Hz}$, 7.8Hz), 7.31-8.05 (15H, m); ^{13}C NMR (CDCl_3) δ 197.0, 141.2, 136.8, 133.1, 131.6, 128.6, 128.5, 128.1, 127.8, 127.5, 127.0, 123.3, 90.7, 83.3, 47.2, 33.7; MS (EI), m/e (relative intensity) 310 (10, M^+), 205 (100), 191 (44), 105 (71), 77 (57). Anal. Calcd for $\text{C}_{23}\text{H}_{18}\text{O}$: C, 89.00; H, 5.84. Found C, 89.13; H, 5.83. %ee was determined by HPLC (hexane/*i*PrOH = 99.8/0.2, flow rate = 0.5 mL/min), $t_R = 100$ min (*R*), $t_R = 115$ min (*S*).

(R)-3-(1-Naphthalenyl)-1,5-diphenyl-4-pentyn-1-one (7f)

$[\alpha]_D = +37.3$ (c 1.01, CHCl_3 , 90 %ee); IR (KBr): $\text{C}=\text{O}$ 1686 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 3.45 (1H, dd, $J = 16.8\text{Hz}$, 4.2 Hz), 3.81 (1H, dd, $J = 16.8\text{Hz}$, 9.6Hz), 5.42 (1H, dd, $J = 9.6\text{Hz}$, 4.2Hz), 7.33-8.30 (17H, m); ^{13}C NMR (CDCl_3) δ 197.2, 136.8, 136.7, 134.0, 133.2, 130.3, 129.0, 128.6, 128.2, 128.1, 127.9, 127.8, 126.4, 125.7, 125.5, 125.4, 123.4, 122.9, 90.6, 83.8, 46.2, 30.4; MS (EI), m/e (relative intensity) 360 (11, M^+), 255 (35), 207 (100). Anal. Calcd for $\text{C}_{27}\text{H}_{20}\text{O}$: C, 89.97; H, 5.59. Found C, 90.05; H, 5.58. %ee was determined by HPLC (hexane/*i*PrOH = 99/1, flow rate = 1 mL/min), $t_R = 17$ min (*S*), $t_R = 22$ min (*R*). Note that the difference in absolute configuration between **7e** and **7f** is due to differences in CIP priorities: 1-naphthyl > phenylethynyl > phenyl.

(S)-6-Benzyloxy-1,3-diphenyl-4-hexyn-1-one (7g)

$[\alpha]_D = -1.5$ (c 1.6, CHCl_3 , 86 %ee); IR (neat): 3062, 3030, 2232, 1684, 1598, 1495, 1450, 1352, 1255, 1205, 1072, 1035 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 3.33(1H, dd, $J = 16.8\text{Hz}$, 6Hz), 3.58 (1H, dd, $J = 16.8\text{Hz}$, 7.8Hz), 4.16-4.17 (2H, m), 4.46-4.53 (3H, m), 7.26-7.99 (15H, m); ^{13}C NMR (CDCl_3) δ 196.8, 140.9, 137.5, 136.7, 133.2, 128.6, 128.5, 128.3, 128.1, 128.0, 127.7, 127.5, 127.0, 87.9, 78.7, 71.2, 57.5, 47.0, 33.0; MS (EI), m/e (relative intensity) 354 (1, M^+), 105 (100), 77 (31). Anal. Calcd for $\text{C}_{25}\text{H}_{22}\text{O}_2$: C, 84.72; H, 6.26. Found C, 84.98; H, 6.17. %ee was determined by

HPLC (hexane/iPrOH = 97/3, flow rate = 1 mL/min), t_R = 16 min (*R*), t_R = 26 min (*S*).

(*S*)-6-Benzyloxy-3-naphthyl-1-phenyl-4-hexyn-1-one (7h)

$[\alpha]_D = +10.5$ (c 0.84, CHCl_3 , 95 %ee); IR (neat): C=O 1683 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 3.41(1H, dd, J = 17.1Hz, 4.2Hz), 3.75 (1H, dd, J = 17.1Hz, 6.6Hz), 4.18-4.19 (2H, m), 4.52 (2H, s), 5.27-5.32 (1H, dd, J = 4.2Hz, 6.6Hz), 7.26-8.24 (17H, m); ^{13}C NMR (CDCl_3) δ 197.1, 137.5, 136.7, 136.4, 134.1, 133.3, 130.3, 129.1, 128.6, 128.3, 128.2, 128.1, 128.0, 127.7, 126.4, 125.7, 125.5, 125.3, 122.9, 87.9, 79.4, 71.2, 57.5, 46.0, 38.8, 29.8; MS (EI), m/e (relative intensity) 404 (1, M^+), 296 (17), 105 (100), 91 (33), 77 (33). Anal. Calcd for $\text{C}_{29}\text{H}_{24}\text{O}_2$: C, 86.11; H, 5.98. Found C, 85.99; H, 5.91. %ee was determined by HPLC (hexane/iPrOH = 99/1, flow rate = 1 mL/min), t_R = 58 min (*R*), t_R = 63 min (*S*).

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