Highly Enantioselective Addition of Phenylacetylene to Aldehydes Catalyzed by a Camphorsulfonamide Ligand

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Supporting Information

Camphorsulfonylamino **7** were synthesized according to literature procedures: a) Chittenden, R. A.; Cooper, G. H. *J. Chem. Soc. C*, **1970**, 49; b) You, J. S.; Shao, M. Y.; Gau, H. M. *Tetrahedron: Asymmetry* **2001**, 12, 2971. c) Shinichi Itsuno, Katsuhiko Watanabe, Takeshi Matsunomo, Shizue Kuroda, Ayako Yokoi and Ashraf El-Shehawy. *J. Chem. Soc., Perkin Trans. 1*, 2011-2016. It was purified by flash column chromatography (silica gel, 30% EtOAc in hexane) and recrystallized in hexane- EtOAc.

Characterization of **7**: White needles (42% overall yield). m.p. 142-143°C. $[\alpha]_D^{19} = -36$ (c=1.61, EtOH), $[\alpha]_D^{21} = +7$ (c=1.8, CH₂Cl₂). ¹H NMR(200MHz, CDCl₃): δ0.75(s, 3H), δ0.89(s, 3H), δ0.91-0.95(m, 2H), δ1.05(s, 3H), δ1.38-1.49(m, 1H), δ1.57-1.67(m, 2H), δ2.44(s, 3H), δ2.02(Br, 1H), δ3.21-3.28(t, J=7Hz, 1H), δ3.55-3.58(d, J=7.6Hz, 1H), δ5.26-5.29(d, J=6.2Hz, 1H), δ7.29-7.33(d, J=8.2Hz, 2H), δ7.74-7.78(d, J=8.2Hz, 2H). ¹³C NMR(DEPT) (75MHz, CDCl₃): δ143.3, 136.9, 48.9, 46.9(C); 129.7, 127.2, 79.0, 60.1, 50.6(CH); 32.8, 26.1(CH₂); 21.5, 21.4, 20.8, 11.2(CH₃). IR (KBr) 3517, 3333, 3301, 3040, 2956, 2890, 1912, 1647, 1597, 1480, 1453, 1400, 1346, 1156, 1092, 1057, 941, 815, 740, 710, 664, 563 cm⁻¹. MS (ESI) m/z: 322(M-H)⁻. Anal. Calcd. for C₁₇H₂₅NO₃S: C, 63.16; H, 7.74. Found: C, 63.19; H, 7.76.

General procedures for addition of phenylacetylene to aldehydes: All manipulations were carried out under argon atmosphere using dried and degassed solvent. The ligand **7** (8.1mg, 0.025mmol) and Ti(OⁱPr)₄ (27.4μL, 0.1mmol) were mixed in dry CH₂Cl₂ at room temperature. Then, a solution of Et₂Zn (1.0 M in CH₂Cl₂,

0.75mL) was added. After the mixture was stirred at the room temperature for 2h, phenylacetylene(82.4 μ L, 0.75mmol) was added and the stirring continued for 1h. The yellow solution was cooled to 0°C and treated with aldehyde(0.25mmol), then the resultant mixture was allowed to warm up to room temperature and stirred for 12-14h. After the reaction was completed, checked by TLC, it was cooled to 0°C and quenched by 5% aqueous HCl. The mixture was extracted with ether. The organic layer was washed with brine, dried over Na₂SO₄, and concentrated under vacuum. The residue was purified by flash column chromatography (silica gel, 12.5% EtOAc in hexane) to give the product.

1,3-Diphenyl-prop-2-yn-1-ol: 93% yield. 97% ee determined by HPLC analysis (Chiralcel OD column, IPA:hexane=1:10). Retention time: t_{major} =18.14 min, t_{minor} =35.49 min. $[\alpha]_{\text{D}}^{15}$ = +5 (c =0.89, CHCl₃). ¹H NMR(200MHz, CDCl₃): δ 7.60-7.32(m, 10H), 5.66(s, 1H), 2.39(br, 1H). Anal. Calcd. for C₁₅H₁₂O: C, 86.54; H, 5.77. Found: C, 86.31; H, 5.93. (E.J.Corey, K.A.Cimprich. *J. Am. Chem. Soc.* **1994**, *116*, 3151.)

1-(4-Fluorophenyl)-3-phenyl-prop-2-yn-1-ol: 87% yield. 93% ee determined by HPLC analysis (Chiralcel OD column, IPA:hexane=1:10). Retention time: t_{major} =7.72 min, t_{minor} =29.46 min. $[\alpha]_{\text{D}}^{15}$ = +3 (c =0.94, CHCl₃). ¹H NMR(200MHz, CDCl₃): δ 7.58-7.45(m, 4H), 7.35-7.26(m, 3H), 7.12-6.97(m, 2H). 5.65(s, 1H), 2.41(br, 1H). Anal. Calcd. for C₁₅H₁₁OF: C, 79.65; H, 4.87. Found: C, 79.77; H, 5.01. (David Moore, Lin Pu, *Org. Lett.* **2002**, *4*, 1855)

1-(2-Naphthyl)-3-phenyl-prop-2-yn-1-ol: 75% yield. 98% ee determined by HPLC analysis (Chiralcel OD column, IPA:hexane=1:10). Retention time: t_{major} =16.51 min, t_{minor} =59.38 min. $[\alpha]_{\text{D}}^{19}$ = -12 (c =2.42, CHCl₃). ¹H NMR(200MHz, CDCl₃): δ 7.92(s, 1H), 7.73-7.68(m, 3H), 7.58(s, 1H). 7.45-7.32(m, 4H), 7.26(s, 3H), 5.66(s, 1H), 2.41(br, 1H). Anal. Calcd. for C₁₉H₁₄O: C, 88.37; H, 5.43. Found: C, 88.17; H, 5.41. (Li, Zhen; Upadhyay, Veena; DeCamp, Ann E.; DiMichele, Lisa; Reider, Paul J. *Synthesis.* **1999**, 1453)

1-(1-Naphthyl)-3-phenyl-prop-2-yn-1-ol: 67% yield. 91% ee determined by HPLC analysis (Chiralcel OD column, IPA:hexane=1:10). Retention time: t_{major} =16.92 min, t_{minor} =39.61 min. $[\alpha]_{\text{D}}^{19}$ = -26 (c =1.84, CHCl₃). ¹H NMR(200MHz, CDCl₃): δ 8.28(d, J =7.6, 1H), 7.78-7.66(m, 3H), 7.54-7.38(m, 5H). 7.23-7.16(m, 3H), 6.23(s, 1H), 2.24(br, 1H). Anal. Calcd. for C₁₉H₁₄O: C, 88.37; H, 5.43. Found: C, 88.24; H, 5.62. (David Moore, Lin Pu, *Org. Lett.* **2002**, *4*, 1855)

1-(2-Methoxyphenyl)-3-phenyl-prop-2-yn-1-ol: 89% yield. 97% ee determined by HPLC analysis (Chiralcel OD column, IPA:hexane=1:10). Retention time: t_{major} =16.28 min, t_{minor} =22.23 min. $[\alpha]_{\text{D}}^{18}$ = -8 (c =0.42, CHCl₃). ¹H NMR(200MHz, CDCl₃): δ 7.67-7.63(d, J =7.4Hz, 1H), 7.47-7.45(m, 2H), 7.32-7.25(m, 4H), 7.00-6.91(m, 2H), 5.93(m, 1H). 3.93(s, 3H), 3.13(s, 1H). Anal. Calcd. for C₁₆H₁₄O₂: C,

80.67; H, 5.88. Found: C, 80.38; H, 5.31. (Li, Zhen; Upadhyay, Veena; DeCamp, Ann E.; DiMichele, Lisa; Reider, Paul J. *Synthesis*. **1999**, 1453)

1-(3-Methoxyphenyl)-3-phenyl-prop-2-yl-1-ol: 85% yield. 95% ee determined by HPLC analysis (Chiralcel OD column, IPA:hexane=1:10). Retention time: $t_{\text{major}}=18.03$ min, $t_{\text{minor}}=31.52$ min. $[\alpha]_{\text{D}}^{15}=+7$ ($c=0.77$, CHCl_3). ^1H NMR(200MHz, CDCl_3): δ 7.47-7.45(m, 2H), 7.33-7.17(m, 6H), 6.9(m, 1H), 5.63(s, 1H), 3.79(s, 3H), 2.40(brs, 1H). Anal. Calcd. for $\text{C}_{16}\text{H}_{14}\text{O}_2$: C, 80.67; H, 5.88. Found: C, 80.80; H, 5.71. (David Moore, Lin Pu, *Org. Lett.* **2002**, 4, 1855)

1-(4-Methoxyphenyl)-3-phenyl-prop-2-yl-1-ol: 90% yield. 92% ee determined by HPLC analysis (Chiralcel OD column, IPA:hexane=1:10). Retention time: $t_{\text{major}}=49.79$ min, $t_{\text{minor}}=71.37$ min. $[\alpha]_{\text{D}}^{15}=+3$ ($c=0.93$, CHCl_3). ^1H NMR(200MHz, CDCl_3): δ 7.55-7.45(m, 2H), 7.32-7.23(m, 5H), 6.93-6.84(m, 2H), 5.62(s, 1H), 3.86(s, 3H), 2.31(brs, 1H). ^{13}C NMR (50MHz, CDCl_3): δ 159.7, 136.8, 133.1, 131.8, 128.6, 128.3, 127.2, 113.9, 89.2, 86.6, 65.9, 55.3. IR(KBr): 3369, 3062, 2875, 2836, 2188, 1248, 1034, 832, 758, 691 cm^{-1} . HRMS(FAB), m/z : $[\text{M}+1-\text{H}_2\text{O}]^+$, Calac: 221.0961. Found: 221.0959. Anal. Calcd. for $\text{C}_{16}\text{H}_{14}\text{O}_2$: C, 80.67; H, 5.88. Found: C, 80.80; H, 5.71.

1-(3-Bromophenyl)-3-phenyl-prop-2-yl-1-ol: 91% yield. 94% ee determined by HPLC analysis (Chiralcel OD column, IPA:hexane=1:10). Retention time: $t_{\text{major}}=11.26$ min, $t_{\text{minor}}=48.63$ min. $[\alpha]_{\text{D}}^{15}=+6$ ($c=0.92$, CHCl_3). ^1H NMR(200MHz, CDCl_3): δ 7.76(m, 1H), 7.48-7.21(m, 8H), 5.62(s, 1H), 2.57(brs, 1H). ^{13}C NMR (50MHz, CDCl_3): δ 146.9, 143.0, 131.5, 130.2, 129.8, 129.0, 128.5, 125.3, 122.5, 88.3, 86.7, 65.7. IR(KBr): 3348, 3060, 2875, 2230, 1592, 1487, 1070, 1010, 903, 822, 756, 691 cm^{-1} . HRMS(FAB), m/z : $[\text{M}+1-\text{H}_2\text{O}]^+$, Calac: 268.9960. Found: 268.9959. Anal. Calcd. for $\text{C}_{15}\text{H}_{11}\text{OBr}$: C, 62.74; H, 3.83. Found: C, 62.97; H, 3.71.

1-(4-Bromophenyl)-3-phenyl-prop-2-yl-1-ol: 85% yield. 92% ee determined by HPLC analysis (Chiralcel OD column, IPA:hexane=1:10). Retention time: $t_{\text{major}}=10.64$ min, $t_{\text{minor}}=39.58$ min. $[\alpha]_{\text{D}}^{15}=+4$ ($c=0.76$, CHCl_3). ^1H NMR(200MHz, CDCl_3): δ 7.51-7.41(m, 4H), 7.35-7.29(m, 3H), 7.22-7.15(m, 2H), 5.61(s, 1H), 2.94(brs, 1H). ^{13}C NMR (50MHz, CDCl_3): δ 143.5, 139.7, 131.5, 128.7, 128.3, 127.7, 122.2, 121.1, 88.3, 86.8, 65.8. IR(KBr): 3344, 3060, 2960, 2232, 1570, 1471, 1426, 1071, 1041, 785, 695 cm^{-1} . HRMS(FAB), m/z : $[\text{M}+1-\text{H}_2\text{O}]^+$, Calac: 268.9960. Found: 268.9960. Anal. Calcd. for $\text{C}_{15}\text{H}_{11}\text{OBr}$: C, 62.74; H, 3.83. Found: C, 62.71; H, 4.03.

4-Methyl-1-phenyl-pent-1-yl-3-ol: 88% yield. 75% ee determined by HPLC analysis (Chiralcel OD column, IPA:hexane=1:10). Retention time: $t_{\text{major}}=6.13$ min, $t_{\text{minor}}=10.68$ min. $[\alpha]_{\text{D}}^{15}=-2$ ($c=0.69$, CHCl_3). ^1H NMR(200MHz, CDCl_3): δ 7.46-7.41(m, 2H), 7.32-7.29(m, 3H), 4.39(d, $J=5.6\text{Hz}$, 1H), 2.26(brs, 1H), 1.99-1.93(m, 1H), 1.07(d, $J=6.4\text{Hz}$, 6H). Anal. Calcd. for $\text{C}_{12}\text{H}_{14}\text{O}$: C, 82.76; H, 8.05.

Found: C, 82.71; H, 8.03. (Matsumura, K.; Hashiguchi, S.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1997**, *119*, 8738.)

1-phenyl-hex-1-yn-3-ol: 82% yield. 85% ee determined by HPLC analysis (Chiralcel OD column, IPA:hexane=1:10). Retention time: $t_{\text{major}}=6.28$ min, $t_{\text{minor}}=15.93$ min. $[\alpha]_{\text{D}}^{15}=+3$ ($c=0.75$, CHCl_3). ^1H NMR(200MHz, CDCl_3): δ 7.45-7.42(m, 2H), 7.33-7.28(m, 3H), 4.61(t, $J=6.2\text{Hz}$, 1H), 2.26(brs, 1H), 1.85-1.74(m, 2H), 1.61-1.50(m, 2H), 0.98(t, $J=7.4\text{Hz}$, 3H). ^{13}C NMR (50MHz, CDCl_3): δ 131.6, 128.3, 128.2, 122.7, 90.3, 84.7, 62.7, 39.9, 29.7, 13.7. IR(KBr): 3331, 3059, 2959, 2933, 2871, 2227, 1598, 1489, 1066, 1026, 756, 691 cm^{-1} . HRMS(FAB), m/z : $[\text{M}+1-\text{H}_2\text{O}]^+$, Calcd: 157.1012. Found: 157.1012. Anal. Calcd. for $\text{C}_{12}\text{H}_{14}\text{O}$: C, 82.76; H, 8.05. Found: C, 82.84; H, 7.71.

1-(4-Chlorophenyl)-3-phenyl-prop-2-yl-1-ol: 81% yield. 92% ee determined by HPLC analysis (Chiralcel OD column, IPA:hexane=1:10). Retention time: $t_{\text{major}}=10.15$ min, $t_{\text{minor}}=36.96$ min. $[\alpha]_{\text{D}}^{15}=+6$ ($c=0.72$, CHCl_3). ^1H NMR(200MHz, CDCl_3): δ 7.54-7.45(m, 4H), 7.33-7.25(m, 5H), 5.63(s, 1H), 2.30(brs, 1H). Anal. Calcd. for $\text{C}_{15}\text{H}_{11}\text{OCl}$: C, 74.24; H, 4.54. Found: C, 74.51; H, 4.33. (David Moore, Lin Pu, *Org. Lett.* **2002**, *4*, 1855).

1,5-Diphenyl-pent-1-en-4-yl-3-ol: 71% yield. 93% ee determined by HPLC analysis (Chiralcel OD column, IPA:hexane=1:10). Retention time: $t_{\text{major}}=22.58$ min, $t_{\text{minor}}=71.62$ min. $[\alpha]_{\text{D}}^{18}=+1$ ($c=2.58$, CHCl_3). ^1H NMR(200MHz, CDCl_3): δ 7.47-7.23(m, 10H), 6.88-6.80(d, $J=15.8\text{Hz}$, 1H), 6.33-6.26(m, 1H), 5.28(d, $J=5.6\text{Hz}$, 1H), 2.04(s, 1H). (Gao, G.; Moore, D.; Xie, R. G.; Pu, L. *Org. Lett.* **2002**, *4*, 4143)