Supporting Information

A convenient, one-step synthesis of optically active tertiary aminonaphthol and its applications in the highly enantioselective alkenylations of aldehydes

Jian-Xin Ji, Li-Qin Qiu, Chiu Wing Yip, Albert S. C. Chan^{*}

Open Laboratory of Chirotechnology of the Institute of Molecular Technology for Drug Discovery and Synthesis and Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hong Kong, China

1. (R)-1-cyclohexyl-5-phenyl-pent-2-en-1-ol

According to the general procedure, the reaction of 4-phenyl-1-butyne (140 μ L, 1 mmol), cyclohexanecarboxaldehyde (60 μ L, 0.5 mmol) and dimethylzinc afforded 113 mg (93% yield based on the aldehyde) of (R)-1-Cyclohexyl-5-phenyl-pent-2-en-1-ol as a colorless oil. $[\alpha]_D^{20} +1.47$ (c 2.0, CHCl_3). HPLC (Chiracel OD, hexane:EtOAc = 99:1): 95% ee. ^1H NMR (500 MHz, CDCl_3): δ 7.29-7.16 (m, 5H, H_{Ar}), 5.67 (dt, 1H, $J = 15.0, 7.0$ Hz, CHCHCH_2), 5.45 (ddt, 1H, $J = 15.5, 8.0, 1.5$ Hz, CH(OH)CHCH), 3.72 (dd, 1H, $J = 7$ Hz, ArCH(OH)CH), 2.70 (m, 2H, CHCH_2CH_2), 2.37 (m, 2H), 1.80-1.60 (m, 5H), 1.40-1.08 (m, 4H), 0.87 (m, 2H). ^{13}C NMR (125 MHz, CDCl_3): δ 141.78, 132.44, 132.41, 128.43, 128.36, 125.94, 77.74, 43.70, 35.69, 34.18, 28.80, 26.60, 26.21, 26.14. MS (EI) m/z (rel intensity) 244 (M^+ , 8), 226 (5), 161 (49), 143 (25), 105 (57), 91 (100), 55 (20), 41 (10).

2. (R)-2-methyl-7-phenyl-hept-4-en-3-ol

According to the general procedure, the reaction of 4-phenyl-1-butyne (140 μ L, 1 mmol), isobutyraldehyde (46 μ L, 0.5 mmol) and dimethylzinc afforded 96 mg (94% yield based on the aldehyde) of (R)-2-Methyl-7-phenyl-hept-4-en-3-ol as a colorless oil. $[\alpha]_D^{20} +4.53$ (c 0.6, CHCl_3). HPLC (Chiracel OD, hexane:EtOAc = 99:1): 94% ee. ^1H NMR

(500 MHz, CDCl₃): δ 7.40-7.26 (m, 5H, H_{Ar}), 5.76 (dt, 1H, J = 15.0, 7.5 Hz, CHCHCH₂), 5.58 (dd, 1H, J = 15.5, 7.0 Hz, CH(OH)CHCH), 3.87 (dd, 1H, J = 6.0 Hz, ArCH(OH)CH), 2.81 (t, J = 7.5, 2H), 2.48 (m, 2H), 1.77 (m, 1H), 0.99 (d, J = 6.5 Hz, 3H), 0.93 (d, J = 6.5 Hz, 3H)

3. (*R*)-1-phenyl-hept-2-en-1-ol¹

According to the general procedure, the reaction of 1-hexyne (114 μ l, 1 mmol), benzaldehyde (51 μ L, 0.5 mmol) and dimethylzinc afforded 85.5 mg (90% yield based on the aldehyde) of (*R*)-1-Phenyl-hept-2-en-1-ol as a colorless oil. $[\alpha]_D^{20}$ -37.1 (c 1.34, CHCl₃). HPLC (Chiracel OD, hexane:EtOAc = 90:10): 97% ee. ¹H NMR (500 MHz, CDCl₃): δ 7.40-7.27 (m, 5H, H_{Ar}), 5.78 (dt, 1H, J = 15.0, 6.8 Hz, CHCHCH₂), 5.60 (dd, 1H, J = 15.5, 6.5 Hz, CH(OH)CHCH), 5.17 (d, 1H, J = 6.5 Hz, ArCH(OH)CH), 2.08-2.04 (m, 2H, CHCH₂CH₂), 1.44-1.26 (m, 4H), 0.89 (t, 3H, J = 6.5 Hz, CH₃).

3.2 (*R*)-1-(4-bromo-phenyl)-hept-2-en-1-ol

According to the general procedure, the reaction of 1-hexyne (114 μ l, 1 mmol), 4-bromobenzaldehyde (92.8 mg, 0.5 mmol) and dimethylzinc afforded 119.3 mg (89% yield based on the aldehyde) of (*R*)-1-(4-Bromo-phenyl)-hept-2-en-1-ol as a colorless oil. $[\alpha]_D^{20}$ -40.5 (c 1.03, CHCl₃). HPLC (Chiracel AD, hexane:i-PrOH = 99:1): 94% ee. R_f = 0.36 (hexane:EtOAc = 4:1). ¹H NMR (500 MHz, CDCl₃): δ 7.46 (d, 2H, J = 9.0 Hz, H_{Ar}), 7.24 (d, 2H, J = 8.0 Hz, H_{Ar}), 5.74 (dt, 1H, J = 15.5, 6.5 Hz, CHCHCH₂), 5.59 (ddt, 1H, J = 15.0, 6.5, 1.5 Hz, CH(OH)CHCH), 5.47 (d, 1H, J = 6.5 Hz, ArCH(OH)CH), 2.07-2.02 (m, 2H, CHCH₂CH₂), 1.38-1.28 (m, 4H), 0.89 (t, 3H, J = 7.3 Hz, CH₃). ¹³C NMR (125 MHz, CDCl₃): δ 142.98, 133.60, 131.96, 131.62, 128.01, 121.37, 74.75, 31.96, 31.28, 22.36, 14.04. MS (EI) m/z (rel intensity) 270 (M⁺+2, 8), 268 (M⁺, 8), 213 (50), 211 (52), 198 (32), 196 (33), 132 (100), 115 (10), 91 (8), 77 (56), 55 (15). HRMS (EI) Calcd for C₁₃H₁₇OBr: 268.0463, found 268.0449.

4 (*R*)-1-(4-nitro-phenyl)-hept-2-en-1-ol

According to the general procedure, the reaction of 1-hexyne (114 μ l, 1 mmol), 4-nitrobenzaldehyde (75.1 mg, 0.5 mmol) and dimethylzinc afforded 92.8 mg (79% yield based on the aldehyde) of (*R*)-1-(4-Nitro-phenyl)-hept-2-en-1-ol as a colorless oil. $[\alpha]_D^{20}$ -32.76 (c 0.62, CHCl_3). HPLC (Chiracel AD, hexane:i-PrOH = 92:8): 95% ee. R_f = 0.31 (hexane:EtOAc = 4:1). ^1H NMR (500 MHz, CDCl_3): δ 8.20 (d, 2H, J = 8.5 Hz, H_{Ar}), 7.55 (d, 2H, J = 9.0 Hz, H_{Ar}), 5.82 (dt, 1H, J = 15.0, 7.0 Hz, CHCHCH_2), 5.59 (dd, 1H, J = 15.0, 7.5 Hz, CH(OH)CHCH), 5.26 (d, 1H, J = 7.5 Hz, ArCH(OH)CH), 2.09-2.04 (m, 2H, CHCH_2CH_2), 1.40-1.24 (m, 4H), 0.89(t, 3H, J = 7.0 Hz, CH_3). MS (EI) m/z (rel intensity) 235 (M^+ , 4), 218 (7), 178 (31), 165 (43), 150 (21), 132 (45), 77 (11), 55 (11), 28 (69), 18 (100). HRMS (EI) Calcd for $\text{C}_{13}\text{H}_{17}\text{NO}_3$: 235.1208, found 235.1364.

5 (*R*)-1-(2-chloro-phenyl)-hept-2-en-1-ol

According to the general procedure, the reaction of 1-hexyne (114 μ l, 1 mmol), 2-chlorobenzaldehyde (56.0 μ L, 0.5 mmol) and dimethylzinc afforded 100.8 mg (90% yield based on the aldehyde) of (*R*)-1-(2-Chloro-phenyl)-hept-2-en-1-ol as a colorless oil. $[\alpha]_D^{20}$ -39.06 (c 1.22, CHCl_3). HPLC (Chiracel OD, hexane:i-PrOH = 99:1): >99% ee. R_f = 0.38 (hexane:EtOAc = 4:1). ^1H NMR (500 MHz, CDCl_3): δ 7.56 (d, 1H, J = 8.0 Hz, H_{Ar}), 7.34-7.27 (m, 2H, H_{Ar}), 7.20 (t, 1H, J = 7.8 Hz, H_{Ar}), 5.79 (dt, 1H, J = 15.0, 7.0 Hz, CHCHCH_2), 5.65 (dd, 1H, J = 15.0, 6.5 Hz, CH(OH)CHCH), 5.56 (d, 1H, J = 7.0 Hz, ArCH(OH)CH), 2.07-2.03 (m, 2H, CHCH_2CH_2), 1.39-1.27 (m, 4H), 0.88 (t, 3H, J = 7.0 Hz, CH_3). ^{13}C NMR (125 MHz, CDCl_3): δ 140.81, 133.60, 132.43, 130.29, 129.61, 128.65, 127.56, 127.23, 71.62, 32.04, 31.29, 22.35, 14.06. MS (EI) m/z (rel intensity) 225 ($\text{M}^+ + 1$, 10), 224 (M^+ , 2), 223 ($\text{M}^+ - 1$, 15), 209 (34), 207 (100), 153 (11), 151 (31), 141 (6), 139 (18), 127 (29), 125 (16), 81 (29). HRMS (EI) Calcd for $\text{C}_{13}\text{H}_{17}\text{OCl}$: 224.0968, found 224.1048.

6 (*R*)-1-(2-bromo-phenyl)-hept-2-en-1-ol

According to the general procedure, the reaction of 1-hexyne (114 μ l, 1 mmol), 2-bromobenzaldehyde (59 μ L, 0.5 mmol) and dimethylzinc afforded 116.8 mg (87% yield based on the aldehyde) of (*R*)-1-(2-Bromo-phenyl)-hept-2-en-1-ol as a colorless oil.

$[\alpha]_D^{20}$ -53.34 (c 1.52, CHCl_3). HPLC (Chiracel OD, hexane:i-PrOH = 95:5): 98% ee. R_f = 0.35 (hexane:EtOAc = 4:1). ^1H NMR (500 MHz, CDCl_3): δ 7.56-7.52 (m, 2H, H_{Ar}), 7.34 (m, 1H, H_{Ar}), 7.13 (m, 1H, H_{Ar}), 5.80 (dt, 1H, J = 16.0, 7.0 Hz, CHCHCH_2), 5.60 (dd, 1H, J = 15.5, 6.5 Hz, CH(OH)CHCH), 5.53 (d, 1H, J = 6.5 Hz, ArCH(OH)CH), 2.07-2.03 (m, 2H, CHCH_2CH_2), 1.40-1.29 (m, 4H), 0.88(t, 3H, J = 7.0 Hz, CH_3). ^{13}C NMR (125 MHz, CDCl_3): δ 142.34, 133.72, 132.85, 130.27, 128.98, 127.87, 127.85, 122.57, 73.68, 32.05, 31.28, 22.35, 14.05. MS (EI) m/z (rel intensity) 270 (M^+ +2, 8), 268 (M^+ , 8), 213 (19), 211 (20), 132 (100), 115 (9), 91 (12), 77 (32), 55 (14). HRMS (EI) Calcd for $\text{C}_{13}\text{H}_{17}\text{OBr}$: 268.0463, found 268.0533.

7 (*R*)-1-(2-nitro-phenyl)-hept-2-en-1-ol

According to the general procedure, the reaction of 1-hexyne (114 μl , 1 mmol), 2-nitrobenzaldehyde (75.5 mg, 0.5 mmol) and dimethylzinc afforded 90.5 mg (77% yield based on the aldehyde) of (*R*)-1-(2-Nitro-phenyl)-hept-2-en-1-ol as a colorless oil. $[\alpha]_D^{20}$ -39.35 (c 0.89, CH_3Cl). HPLC (chiracel AD, hexane:i-PrOH = 98:2): 98% ee. R_f = 0.30 (hexane:EtOAc = 4:1). ^1H NMR (500 MHz, CDCl_3): δ 7.87 (d, 1H, J = 8.5 Hz, H_{Ar}), 7.77 (d, 1H, J = 8.0 Hz, H_{Ar}), 7.63 (t, 1H, J = 7.3 Hz, H_{Ar}), 7.42 (t, 1H, J = 7.0 Hz, H_{Ar}), 5.80 (dt, 1H, J = 15.5, 6.5 Hz, CHCHCH_2), 5.75 (d, 1H, J = 6.0 Hz, ArCH(OH)CH), 5.65 (dd, 1H, J = 16.0, 6.0 Hz, CH(OH)CHCH), 2.06-2.02 (m, 2H, CHCH_2CH_2), 1.36-1.25 (m, 4H), 0.88(t, 3H, J = 7.3 Hz, CH_3). MS (EI) m/z (rel intensity) 235 (M^+ , 1), 234 (M^+ -1, 6), 219 (12), 218 (90), 207 (14), 206 (100), 202 (49), 188 (45), 118 (9), 106 (10). HRMS (EI) Calcd for $\text{C}_{13}\text{H}_{17}\text{NO}_3$: 235.1208, found 235.0912.

8 (*R*)-1-(3-methoxy-phenyl)-hept-2-en-1-ol¹

According to the general procedure, the reaction of 1-hexyne (114 μl , 1 mmol), *m*-anisaldehyde (61 μL , 0.5 mmol) and dimethylzinc afforded 100.4 mg (91% yield based on the aldehyde) of (*R*)-1-(3-Methoxy phenyl)-hept-2-en-1-ol as a colorless oil. $[\alpha]_D^{20}$ -44.35 (c 1.78, CHCl_3). HPLC (Chiracel OD, hexane:i-PrOH = 95:5): 94% ee. ^1H NMR (500 MHz, CDCl_3): δ 7.26 (m, 1H, H_{Ar}), 6.96-6.94 (m, 2H), 6.83-6.80 (m, 1H), 5.77 (dt, 1H, J = 15.5, 6.5 Hz, CHCHCH_2), 5.66 (dd, 1H, J = 15.0, 7.0 Hz, CH(OH)CHCH), 5.14 (d, 1H,

$J = 7.0$ Hz, ArCH(OH)CH), 3.81 (s, 3H, OCH₃), 2.08-2.04 (m, 2H, CHCH₂CH₂), 1.44-1.28 (m, 4H), 0.89 (t, 3H, $J = 7.0$ Hz, CH₃).

9 (*R*)-1-(3-bromo-phenyl)-hept-2-en-1-ol

According to the general procedure, the reaction of 1-hexyne (114 μ l, 1 mmol), 3-bromobenzaldehyde (58 μ L, 0.5 mmol) and dimethylzinc afforded 123.4 mg (92% yield based on the aldehyde) of (*R*)-1-(3-Bromo-phenyl)-hept-2-en-1-ol as a colorless oil. $[\alpha]_D^{20}$ -39.51 (c 0.92, CHCl₃). HPLC (Chiracel AD, hexane:i-PrOH = 99:1): 94% ee. R_f = 0.38 (hexane:EtOAc = 4:1). ¹H NMR (500 MHz, CDCl₃): δ 7.50 (s, 1H, H_{Ar}), 7.39 (m, 1H, H_{Ar}), 7.28 (t, 1H, $J = 7.5$ Hz, H_{Ar}), 7.21 (t, 1H, $J = 7.7$ Hz, H_{Ar}), 5.77 (dt, 1H, $J = 15.5, 7.0$ Hz, CHCHCH₂), 5.60 (dd, 1H, $J = 15.0, 7.0$ Hz, CH(OH)CHCH), 5.12 (d, 1H, $J = 7.0$ Hz, ArCH(OH)CH), 2.08-2.01 (m, 2H, CHCH₂CH₂), 1.41-1.26 (m, 4H), 0.89 (t, 3H, $J = 7.0$ Hz, CH₃). ¹³C NMR (125 MHz, CDCl₃): δ 145.77, 133.93, 131.79, 130.57, 130.13, 129.37, 124.89, 122.69, 74.72, 31.97, 31.26, 22.38, 14.04. MS (EI) m/z (rel intensity) 270 ($M^+ + 2$, 3), 268 (M^+ , 3), 241 (96), 239 (100), 213 (32), 211 (34), 132 (68), 77 (20), 55 (16). HRMS (EI) Calcd for C₁₃H₁₇OBr: 268.0463, found 268.0585.

Reference

1 Wipf, P.; Ribe, S. *J. Org. Chem.* **1998**, *63*, 6454.