Direct Asymmetric Aldol Reactions of Acetone Using Bimetallic Zinc Catalysts

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Supporting Information

Typical experimental procedure is as follows: Catalyst generation: Under an argon atmosphere, a solution of diethylzinc (1M in hexanes, 0.4 ml, 0.4 mmol) was added to the solution of ligand **1a** (128 mg, 0.2 mmol) or **1b** (130 mg, 0.2 mmol) in THF (2 ml) at r.t. After stirring for 30 min with the evolution of ethane gas, the resulting solution was used as catalyst for the aldol reaction (ca. 0.1 M solution). Aldol reaction: To a suspension of aldehyde (0.5 mmol), powdered molecular sieves (100 mg, dried at ca. 150 °C under vacuum overnight) and acetone (0.5 ml, 6.8 mmol) in THF (0.8 ml) was added the solution of catalyst (0.025 mmol for 5% catalyst, 0.05 mmol for 10% catalyst) at 0 °C and the mixture was stirred at 5 °C for 2 d. The resulting mixture was poured onto 1N HCl and extracted with ether. After normal workup, the crude product was purified by silica gel chromatography using a mixture of petroleum ether and ethyl acetate as eluent.

Characterization of Products.

(*S*)-4-Cyclohexyl-4-hydroxybutan-2-one (**4a**)
$[\alpha]_D^{25}$ +50.1 (c 1.5, $CHCl_3$) *ee*= 87% (lit.[1] $[\alpha]_D^{25}$ +52 (c 1.1, CCl_4)).

(*S*)-4-hydroxy-5-methylhexan-2-one (**4b**)
$[\alpha]_D^{25}$ +53.7 (c 1.5, $CHCl_3$) *ee*= 91% (lit.[2] $[\alpha]_D^{25}$ +61.7 (c 0.6, $CHCl_3$)).

(*S*)-5,5-dimethyl-4-hydroxyhexan-2-one (**4c**)
$[\alpha]_D^{25}$ +49.0 (c 0.8, $CHCl_3$) *ee*= 86% (lit.[3] $[\alpha]_D^{25}$ +43.9 (c 0.8, $CHCl_3$) *ee*= 86%, lit.[4] $[\alpha]_D^{25}$ +82.2 (c 0.6, $CHCl_3$) *ee*= 83%).

5,5-diphenyl-4-hydroxypentan-2-one (**4d**)
ee=87%. $[\alpha]_D^{21.5}$ +11.43 (c 0.9, $CHCl_3$). IR (neat) ν cm^{-1}; 3520 (OH), 1704 (C=O). ^{1}H-NMR (300 MHz, $CDCl_3$) δ; 7.41-7.19 (m, 10H), 4.86 (m, 1H), 3.92 (d, *J*=9.0 Hz, 1H), 3.66 (m, 1H), 2.50 (m, 2H), 2.02 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ; 209.3, 141.9, 141.2, 128.8, 128.7, 128.3, 127.2, 127.0, 126.8, 69.8, 57.6, 48.4, 30.9. MS (SIMS) M^+=254.3 Anal. calcd for $C_{17}H_{18}O_2$: C, 80.28; H, 7.13. Found C, 80.12; H, 7.14.

4-hydroxy-6-methylheptan-2-one (**4e**)
ee=84%. $[\alpha]_D^{21.5}$ +47.04 (c 0.7, $CHCl_3$). IR (neat) ν cm^{-1}; 3410 (OH), 1712 (C=O). ^{1}H-NMR (300 MHz, C_6D_6) δ; 3.75 (m, 1H), 2.22 (m, 2H), 2.17 (s, 3H), 2.11 (M, 1H),

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1.21 (m, 2H), 0.99 (d, *J*=6.3 Hz, 6H). ^{13}C-NMR (75 MHz, C_6D_6) δ; 195.9, 71.7, 48.5, 38.2, 30.4, 20.7, 17.5. MS (SIMS) M^+=144.2. Anal. calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found C, 66.33; H, 11.08.

(*S*)-4-hydroxy-6-phenylhexan -2-one (**4f**)
$[\alpha]_D^{25}$ +19.9 (c 0.7, $CHCl_3$) *ee*= 84% (lit.[5] $[\alpha]_D^{25}$ +20.6 (c 1.0, $CHCl_3$)).

(*S*)-4-hydroxyheptan-2-one (**4g**)
$[\alpha]_D^{25}$ +42.3 (c 5.0, $CHCl_3$) *ee*= 84% (lit.[6] $[\alpha]_D^{25}$ +35.1 (c 2.1, $CHCl_3$) *ee*=58%, lit.[7] $[\alpha]_D^{25}$ +39.1 (c 6.3, $CHCl_3$) *ee*=78%.).

(*S*)-4-hydroxy-4-phenylbutan-2-one (**4h**)
$[\alpha]_D^{25}$ +40.8 (c 1.0, $CHCl_3$) *ee*= 79% (lit.[7] $[\alpha]_D^{20}$ +40.9 (c 10.3, $CHCl_3$) *ee*=78%).

4-hydroxy-4-(4-nitrophenyl)butan-2-one (**4i**)
Mp 62 °C (lit.[8] 60-62 °C). *ee*=79%. $[\alpha]_D^{20}$ +36.8 (c 1.7, $CHCl_3$). IR (neat) ν cm^{-1}; 3493 (OH), 1710 (C=O). ^{1}H-NMR (300 MHz, $CDCl_3$) δ; 8.20 (d, *J*=8.5 Hz, 2H), 7.52 (d, *J*=8.5 Hz, 2H), 5.20 (dd, *J*=7.3 , 4.7 Hz, 1H), 4.77 (bs, 1H), 2.80 (m, 2H), 2.16 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ; 208.6, 149.85, 140.2, 128.8, 124.2, 68.9, 51.5, 30.8. MS (SIMS) M^+=209.2. Anal. calcd for $C_{10}H_{11}NO_4$: C, 57.41; H, 5.30, N, 6.70. Found C, 57.29; H, 5.34; N, 6.72.

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