Multiple Dendritic Catalysts for Asymmetric Transfer Hydrogenation

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1. General procedure for asymmetric transfer hydrogenation of ketones¹

[RuCl₂(cymene)]₂ (1.3mg, 0.002mmol), Dendritic ligand (1.1eq. of Ru) and NEt₃ (1.3 L, 0.008mmol) were heated in methanol at 65 °C for 2h, and methanol was removed under vacuum. Then ketone **8** (0.4mmol) and formic acid/triethylamine azeotrope (0.2mL) were added in turn. The solution was stirred at 28 °C and monitored by TLC. After completion, the solution was diluted with 3mL diethyl ether, washed with brine and dried (Na₂SO₄). The ether solution was passed through silica gel and concentrated under pressure to give (*R*)-alcohol. (*Ru*: ligand: substrate = 1:1.1: 100)

(*R*)-1-Phenylethanol, [α]_D²⁸ +48.2 (c 1.20, DCM), GC: CP-Cyclodex-236M, 110 °C, t_R=6.9min, t_S=7.5min, 96.4%ee.

(*R*)-1-(*o*-Fluorophenyl)ethanol, [α]_D²⁸ +43.2 (c 0.66, CHCl₃), GC: CP-Cyclodex-236M, 114 °C, t_R=7.2min, t_S=7.7min, 93.2%ee.

(*R*)-1-(*p*-Fluorophenyl)ethanol, [α]_D²⁸ +44.0 (c 0.72, CHCl₃), GC: CP-Cyclodex-236M, 114 °C, t_R=7.8min, t_S=8.5min, 89.4%ee.

(*R*)-1-(*o*-Chlorophenyl)ethanol, [α]_D²⁸ +61.0 (c 0.84, CHCl₃), GC: CP-Cyclodex-236M, 144 °C, t_R=4.9min, t_S=5.4min, 95.5%ee.

(*R*)-1-(*o*-Bromophenyl)ethanol, [α]_D²⁸ +51.7 (c 1.36, CHCl₃), GC: CP-Cyclodex-236M, 154 °C, t_R=5.1min, t_S=5.7min, 94.6%ee.

(*R*)-1-(*p*-^tButylphenyl)ethanol, [α]_D²⁸ +44.1 (c 0.68, CHCl₃), GC: CP-Cyclodex-236M, 120 °C, t_R=12.1min, t_S=12.4min, 97.2%ee.

2. General procedure for asymmetric transfer hydrogenation of diones

[RuCl₂(cymene)]₂ (1.3mg, 0.002mmol), Dendritic ligand (1.1eq. of Ru) and NEt₃ (1.3 L, 0.008mmol) were heated in methanol at 65 °C for 2h, and methanol was removed under

vacuum. Then dione **9** (0.4mmol), DMF (0.2mL) and formic acid/triethylamine azeotrope (0.4mL) were added in turn. The solution was stirred at 40 C and monitored by TLC. After completion, the solution was dilute with 10mL ethyl acetate, washed with brine and dried. Flash chromatography through silica gel (petroleum ether/EtOAc=1:3) and concentrated under vacuum to give (*R,R*)-diol. (*Ru: ligand: substrate* = 1:1.1: 100)

(*R,R*)-1,3-Diphenyl-1,3-propanediol,² [α _D²⁸ +68.6 (c 1.0, C₂H₅OH), **HPLC**: Chiralcel OD column, 2-propanol:hexane=9:91, 1.0mL/min, *t*_{S,S}=12.1min, *t*_{R,R}=14.2min, *t*_{meso}=17.5min, >99%*ee*, 98.7%*de*.

(*R,R*)-1,6-Diphenyl-1,6-hexanediol,³ [α _D²⁸ +20.3 (c 0.92, CH₃OH), **HPLC**: ChiralPak AD column, 2-propanol:hexane=20:80, 1.0mL/min, *t*_{S,S}=9.0min, *t*_{R,R+meso}=10.6min; Chiralcel OB column, 2-propanol:hexane=20:80, 1.0mL/min, *t*_{S,S+meso}=8.4min, *t*_{R,R}=114.1min, >99%*ee*, 84.2%*de*.

3. General procedure for asymmetric transfer hydrogenation of imines⁴

[RuCl₂(cymene)]₂ (1.3mg, 0.002mmol), Dendritic ligand (1.1eq. of Ru) and NEt₃ (1.3 L, 0.008mmol) were heated in methanol at 65 C for 2h, and methanol was removed under vacuum. Then imine **10** (0.4mmol), DCM (0.8mL) and formic acid/triethylamine azeotrope (0.2mL) were added in turn. The solution was stirred at 28 C and monitored by TLC. After completion, the solution was dilute with 5mL ethyl acetate, washed with brine and dried. Flash chromatography through silica gel (petroleum ether/EtOAc=1:4) and concentrated under vacuum to give (*R*)-amine. (*Ru: ligand: substrate* = 1:1.1: 100)

3-Benzyl-2,3-dihydrobenzo[*d*]isothiazoline 1,1-dioxide, [α _D²⁸ +61.5 (c 1.10, CHCl₃), **HPLC**: Chiralcel OD column, 2-propanol:hexane= 20:80, 1.0mL/min, *t*_S=13.2min, *t*_R=17.0 min, 95.9%*ee*.

3-*t*-Butyl-2,3-dihydrobenzo[*d*]isothiazoline 1,1-dioxide, [α _D²⁸ +51.6 (c 0.68, CHCl₃), **HPLC**: Chiralcel OD column, 2-propanol:hexane= 20:80, 1.0mL/min, *t*_S=7.4min, *t*_R=17.8min,

98.3%ee.

N-*t*-Butylsulfonyl-1-phenylethylamine, $[\alpha]_D^{28} +19.0$ (c 0.85, CHCl₃), HPLC: Chiralcel AD column, 2-propanol:hexane=10:90, 1.0mL/min, $t_R=5.71$ min, $t_S=6.39$ min, 51.8%ee.

4. References

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5. Spectra of dendritic ligands

Compound 9

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Compound 10

Compound 10

Compound 10

Compound 16

Compound 17

Compound 17

Compound 17