

Synthesis of a New Chiral Ligand Containing 1, 5-Diazacyclooctane and the Application in Diethyl Zinc Addition to Benzaldehyde

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Abstract: A new chiral tetradentate ligand (S, S)-1, 5-bis (4-benzyloxazolin-2-yl-methyl)-1, 5-diazacyclo-octane **1** has been synthesized and the application of **1** as catalyst in the enantioselective addition of diethyl zinc to benzaldehyde is also described.

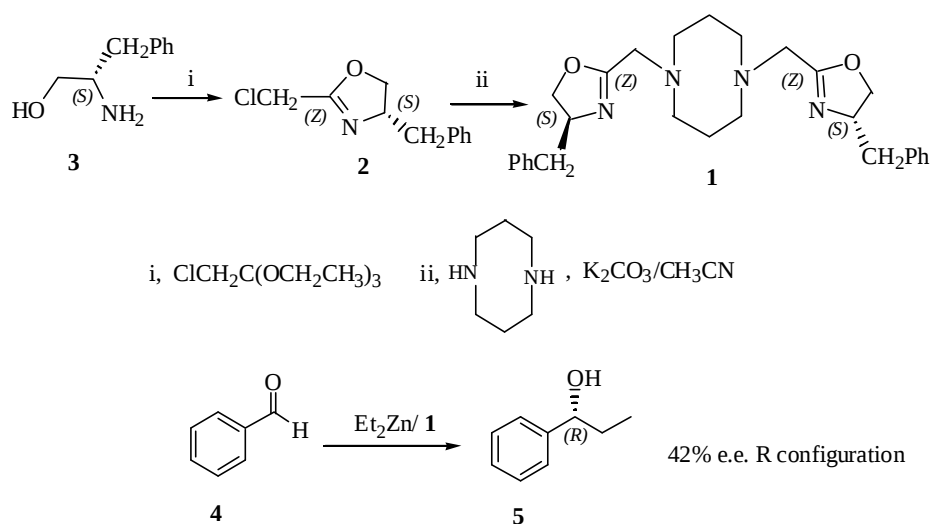
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In the field of transition-metal-catalyzed asymmetric reactions, design, synthesis of the suitable chiral ligand around a metal center is an important task. Recent interest has been focused on metal complexes incorporating oxazoline moieties as N-coordinating ligands¹. For example, rhodium complexes of pyridinyl oxazoline have been found to catalyze the hydrosilylation of ketones in high yields with up to 95% ee². Bis [4-(R)-phenyloxazolin-2-yl-methyl] amine is highly effective for the Ru-catalyzed asymmetric transfer hydrogenation of simple aryl-alkyl ketones³. As we known, the ligands in which chiral oxazolines were connected to polyazacyclics have not been reported. Because the aza crown ethers and their polycyclic derivatives could form strongly bond and well defined complexes with many metal ions, we introduced 1,5-diazacyclooctane to the chiral ligands. In this paper, we synthesized a new chiral tetradentate ligand (S, S)-1, 5-bis (4-benzyloxazolin-2-yl-methyl)-1, 5-diazacyclo-octane **1** and used it in the enantioselective reduction of benzaldehyde by diethyl zinc.

The procedure is shown in **Scheme 1**. The chiral side chain (4S)-2-chloromethyl-4-benzyloxazoline **2** was prepared from triethyl orthochloroacetate and (S)-phenylglycinol **3**⁴. Then the chiral tetradentate ligand **1** was obtained by the reaction of compound **2** and 1, 5-diazacyclooctane in CH₃CN in the present of anhydrous K₂CO₃ at refluxing temperature for 15 hours. The structure of **2** and **1** were confirmed by elemental analysis, IR, MS, ¹H and ¹³C NMR spectra⁵. The enantioselective addition reaction was run in toluene at 0°C, using a 2: 1: 0.05 molar ratio of diethylzinc and benzaldehyde **4** to ligand **1**. The mixture was stirred in argon for 40 hours and 1-phenylpropanol **5** (85% yield) was obtained by column chromatography. The enantiomeric excess (42% e.e., R configuration) was determined by chiral HPLC (chiracel OD column) and optical rotation.

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Scheme 1



References and Notes

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5. **2**: colorless oil, yield 71%; $[\alpha]_D^{20}$ -73.1 (c 4.31, CH_2Cl_2); MS (m/z , %): 209 (M^+ , 4), 179 (23), 143 (5), 130 (5), 118 (100), 103 (8), 91 (75), 77 (13); IR (neat) ν : 3028, 1667, 1497, 1454, 1363, 1244, 1156, 980, 755, 702 cm^{-1} ; ^1H NMR (CDCl_3 , δ ppm): 2.71 (m, 1H, $\text{CH}_2\text{-Ph}$), 3.12 (m, 1H, $\text{CH}_2\text{-Ph}$), 4.08 (m, 1H, $\text{C-CH}_2\text{-O}$), 4.10 (m, 2H, $\text{CH}_2\text{-Cl}$), 4.31 (m, 1H, $\text{C-CH}_2\text{-O}$), 4.47 (m, 1H, CH-N), 7.20-7.32 (m, 5H, Ph); ^{13}C NMR (CDCl_3 , δ ppm): 36.6, 41.4, 67.7, 73.0, 126.8, 128.8, 129.4, 137.5, 163.1. **1**: colorless oil, yield 84%; $[\alpha]_D^{20}$ -41.5 (c 0.96, CH_2Cl_2); MS (m/z , %): 461 (M^+ +1, 19), 441 (6), 304 (8), 286 (78), 258 (5), 243 (18), 217 (34), 175 (11), 162 (12), 125 (68), 91 (81), 84 (100); $\text{C}_{28}\text{H}_{36}\text{N}_4\text{O}_2$ (Calcd: C, 73.01; H, 7.88; N, 12.16; Found: C, 72.86; H, 7.97; N, 12.36); IR (neat) ν : 2922, 1664, 1496, 1454, 1357, 1157, 1078, 977, 702 cm^{-1} ; ^1H NMR (CDCl_3 , δ ppm): 1.69 (m, 4H, $2\times\text{C-CH}_2\text{-C}$), 2.68 (m, 2H, $2\times\text{CH}_2\text{-a-Ph}$), 2.84 (m, 8H, $4\times\text{C-CH}_2\text{-N}$), 3.06 (m, 2H, $2\times\text{CH}_2\text{-b-Ph}$), 3.39 (m, 4H, $2\times\text{C-CH}_2\text{-N}$), 4.00 (m, 2H, $2\times\text{C-CH}_2\text{-O}$), 4.21 (m, 2H, $2\times\text{C-CH}_2\text{-O}$), 4.38 (m, 2H, $2\times\text{C-CH-N}$), 7.06-7.31 (m, 10H, Ph); ^{13}C NMR (CDCl_3 , δ ppm): 26.6, 41.9, 52.6, 53.5, 67.3, 71.9, 126.8, 128.8, 129.5, 138.0, 172.8.

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