

Synthesis of a New Ligand Containing 1, 7-Diaza-12-crown-4 and the Application in Asymmetric Cyclopropanation Reaction

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Abstract: A new chiral multidentate ligand (S, S)-1,7-bis(4-benzyloxazolin-2-yl-methyl)-1,7-diaza-12-crown-4 **1** has been synthesized and used as ligand in the copper catalyzed asymmetric cyclopropanation of 1,1-diphenylethylene.

Keywords: (S, S)-1, 7-Bis (4-benzyloxazolin-2-yl-methyl)-1,7-diaza-12-crown-4, asymmetric cyclopropanation.

Asymmetric cyclopropanation of simple olefins using transition metal catalysts is of great interest in organic chemistry. Recently, many chiral oxazoline ligands have been successfully employed in metal-catalyzed asymmetric cyclopropanation reactions with diazoacetates¹. As we know, the ligands in which chiral oxazolines were connected to aza crown ether, which used in asymmetric reactions, have not been reported. Because the aza crown ethers and their derivatives could form powerful complexes with many transition-metal ions, we introduced 1,7-diaza-12-crown-4 to the chiral ligands. In this paper, we report the synthesis of a new chiral multidentate ligand (S,S)-1,7-bis(4-benzyloxazolin-2-yl-methyl)-1,7-diaza-12-crown-4 (**1**) and its application in the asymmetric cyclopropanation of 1,1-diphenylethylene with various diazoacetates.

The procedure is shown in **Scheme 1**. The chiral side chain (4S)-2-chloromethyl-4-benzyloxazoline **2** was prepared according to literatures^{2,3}. The chiral multidentate ligand **1** was obtained by the reaction of compound **2** and 1,7-diaza-12-crown-4 **3** in CH₃CN in the presence of anhydrous K₂CO₃ at refluxing temperature for 16 hours. The structure of **1** was confirmed by elemental analysis, IR, MS, ¹H NMR spectra. The asymmetric cyclopropanation reaction was run in CH₂Cl₂ at room temperature and under nitrogen atmosphere, the ligand **1** (0.2 mmol) and anhydrous cupric acetate (0.2 mmol) were taken in 3 mL CH₂Cl₂ and stirred for 1 h. The blue-green coloured reaction mixture was filtered. The filtrate and a drop of phenylhydrazine were added to 1,1-diphenylethylene (5 mL) solution in CH₂Cl₂ (13 mL) in sequence. Then, diazoester (8 mmol) solution in 3 mL of CH₂Cl₂ was added over a period of 3 h. The mixture was stirred for 10 h. The product was purified by column chromatography (silica gel, first cyclohexane, then methylene chloride). The results were obtained after hydrolysis and

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collected in **Table 1**.

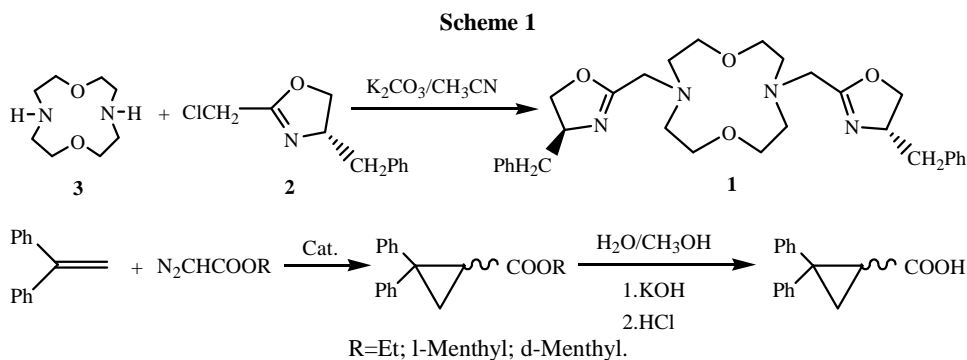


Table 1 Asymmetric cyclopropanation of 1,1-diphenylethylene using ligand **1**/copper(I) complex as a catalyst

R	Yield (%)	% e.e. ^a	Configuration ^a
Et	48.3	12.6	R
l-Menthyl	56.5	28.8	R
d-Menthyl	54.2	25.3	R

a. Obtained by comparison of the optical rotation value of the compounds with that in literature⁴.

References and Notes

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- 1**: colorless solid, mp: 114~116°C; $[\alpha]_D^{15}$ -45.7 (c 0.88, CH₂Cl₂); MS (*m/z*, %): 521 (M⁺, 2), 378 (8), 260 (15), 117 (11), 100 (25), 91 (57), 60 (52), 42 (100); C₃₀H₄₀N₄O₄ (Calcd: C, 69.21; H, 7.74; N, 10.76; Found: C, 69.06; H, 7.83; N, 10.92); IR (KBr) ν : 2944, 1667, 1496, 1454, 1363, 1122, 1072, 999, 704 cm⁻¹; ¹H NMR (CDCl₃, δ ppm): 2.59 (t, 8H, *J*=4.5 Hz, 4×O-C-CH₂-N), 2.88 (m, 2H, 2×C-CH_{2a}-Ph), 2.91 (m, 2H, 2×C-CH_{2b}-Ph), 3.18 (s, 4H, 2×C-CH₂-N), 3.47 (t, 8H, *J*=4.6 Hz, 4×O-CH₂-C-N), 3.53 (m, 2H, 2×C-CH_{2a}-O), 3.69 (m, 2H, 2×C-CH_{2b}-O), 4.22 (m, 2H, 2×C-CH-N), 7.18-7.29 (m, 10H, Ph).

Received 20 May, 2002