

Synthesis of New Chiral C₂-Symmetrical Bis(oxazoline) Compounds

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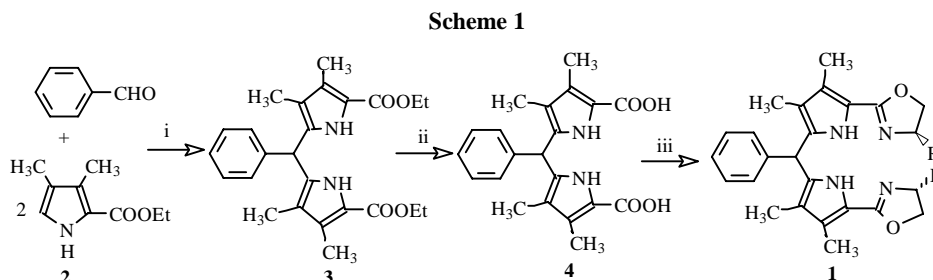
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Abstract: New chiral C₂-symmetrical bis(oxazoline) compounds bearing one *isobutyl*-, *secbutyl*-, *benzyl*- or *isopropyl*-substituent at the 4-position have been prepared and characterized.

Keywords: Synthesis, chiral, C₂-symmetrical, bis(oxazoline).

Chiral C₂-symmetrical bis(oxazoline)-metal complexes have played an important role in the catalytic enantioselective reactions¹. Recent interest has been focused on structural modification of chiral C₂-symmetrical bis(oxazoline), for example, introducing the substituents at the 4- and 5-positions of oxazoline units², to modify the bridges which link the two oxazoline units³, and the number of the coordinate atoms⁴.

Those methods mentioned above are intent to change the steric and electronic nature of the ligands. In this report, we designed and synthesized new chiral C₂-symmetrical bis(oxazoline) compounds **1a-d**, which contain two pyrrole units (**Scheme 1**). These new compounds can be used as ligands to prepare tetradentate bis(oxazoline)-metal complexes. Up to now, there have not been reported on the synthesis and application of the corresponding compounds.



Reagents and conditions: i) HCl/EtOH, reflux, 86%; ii) NaOH/H₂O/EtOH, reflux, then AcOH/H₂O, 95%; iii) CCl₄/Et₃N / CH₃CN /Py/Ph₃P/L-H₂N HC^{*}(R)CH₂OH, rt., 24h.

In our synthetic process, **2** was prepared by following the literature method⁵. Then **2** and benzaldehyde (mol/mol 2/1) were reacted in the presence of a catalytic amount of

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hydrochloric acid to give **3** with yield of 86%. **4** was obtained by hydrolysis of **3** with NaOH, then the reaction mixture was treated with acid.

Compounds **1** were prepared partially following the reference method⁶. The solution of Ph₃P (1.85 g, 7.0 mmol) in 8 mL of CH₃CN-Py (1:1) was added dropwise into the mixture of **4** (0.37 g, 1.0 mmol), L-H₂NHC*(R)CH₂OH (2.0 mmol), CCl₄ (2 mL), Et₃N (1.4 mL), and CH₃CN-Py (8 mL, 1:1). The reaction was conducted at rt. for 24 h and monitored by TLC. The products **1** were purified by flash column chromatography (petroleum ether/ethyl acetate 8/1), followed by preparative thin layer chromatography (petroleum ether/THF 4/1). Thus, four novel C₂-symmetrical bis(oxazoline) compounds **1a-d** were synthesized and characterized by elemental and spectral analyses⁷.

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References and Notes

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7. **1a**: yield 48%; mp: 177-178°C; $[\alpha]_D^{20} = -51.8$ (c 0.41, CHCl₃); ¹HNMR (DMSO-d₆, δ ppm): 0.91 (d, 12H, J=6.6Hz, CH₃), 1.31 (m, 2H, CH), 1.47 (m, 2H, CH₂), 1.75 (m, 2H, CH₂), 1.95 (s, 6H, CH₃), 2.16 (s, 6H, CH₃), 3.79 (m, 2H, O-CH₂), 4.14 (m, 2H, O-CH₂), 4.37 (m, 2H, N-CH), 5.65 (s, 1H, CH), 6.94 (d, 2H, J=7.2Hz, ArH), 7.25 (m, 3H, ArH), 10.80 (d, 2H, J=5.1Hz, NH); MS (APCI)[M⁺+1]: *m/z* 529, 309; Anal. Calcd. for C₃₃H₄₄N₄O₂ (528.74): C, 74.96; H, 8.39; N, 10.59. Found: C, 75.204; H, 8.335; N, 10.218. **1b**: yield 46.2%; mp: 155-156°C; $[\alpha]_D^{20} = -17.72$ (c 0.47, CHCl₃); ¹HNMR (DMSO-d₆, δ ppm): 0.79 (m, 6H, CH₃), 0.88 (m, 6H, CH₃), 1.16 (m, 2H, CH), 1.52 (m, 4H, CH₂), 1.95 (s, 6H, CH₃), 2.17 (s, 6H, CH₃), 3.97 (m, 4H, O-CH₂), 4.27 (m, 2H, N-CH), 5.66 (s, 1H, CH), 6.95 (d, 2H, J=7.8Hz, ArH), 7.25 (m, 3H, ArH), 10.80 (d, 2H, J=6.9Hz, NH); MS (APCI)[M⁺+1]: *m/z* 529, 309; Anal. Calcd for C₃₃H₄₄N₄O₂ (528.74): C, 74.96; H, 8.39; N, 10.59. Found: C, 75.204; H, 8.336; N, 10.218. **1c**: yield 41.6%; mp: 164-165°C; $[\alpha]_D^{20} = -41.4$ (c 0.495, CHCl₃); ¹HNMR (DMSO-d₆, δ ppm): 0.88 (m, 12H, CH₃), 1.67 (m, 2H, CH), 1.95 (s, 6H, CH₃), 2.18 (s, 6H, CH₃), 3.93 (m, 4H, O-CH₂), 4.27 (m, 2H, N-CH), 5.66 (s, 1H, CH), 6.95 (d, 2H, J=7.2Hz, ArH), 7.25 (m, 2H, ArH), 10.80 (d, 2H, J=6.9Hz, NH); MS (APCI)[M⁺+1]: *m/z* 501, 295; Anal. Calcd. for C₃₁H₄₀N₄O₂ (500.68): C, 74.38; H, 8.05; N, 11.19. Found: C, 74.507; H, 7.884; N, 11.003. **1d**: yield 52.8%; mp: 137-138°C; $[\alpha]_D^{20} = +32.7$ (c 0.49, CHCl₃); ¹HNMR (DMSO-d₆, δ ppm): 1.96 (s, 6H, CH₃), 2.18 (s, 6H, CH₃), 2.70 (m, 2H, CH₂), 2.96 (m, 2H, CH₂), 3.91 (m, 2H, O-CH₂), 4.24 (m, 2H, O-CH₂), 4.43 (m, 2H, N-CH), 5.66 (s, 1H, CH), 6.94 (d, 2H, J=7.8Hz, ArH), 7.26 (m, 13H, ArH), 10.87 (d, 2H, J=5.4Hz, NH); MS (APCI)[M⁺+1]: *m/z* 597, 343. Anal. Calcd. for C₃₉H₄₀N₄O₂ (596.77): C, 78.49; H, 6.75; N, 9.39. Found: C, 79.079; H, 6.616; N, 9.357.

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