Synthesis and Characterization of Multifunctional Chiral Schiff Base Derivatives

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Abstract

Multifunctional chiral Schiff base ligands were synthesized by the condensation of 4-(3-chloro-2-hydroxypropoxy)-2-hydroxybenzaldehyde **1** with primary amines (2-aminophenol and 2-amino-2-methyl-1-propanol) and were characterized by elemental analysis, IR, ^{1}H and ^{13}C NMR spectroscopies. These ligands have a stereocenter in addition to the alkyl halide and alcohol functional groups.

Key words: Schiff base, mutifunctional ligand, ring-opening of epoxides

Introduction

The enantioselective ring-opening of epoxides with different nucleophiles is an important strategy for the formation of 1,2-bifunctionalized building blocks. Oxygen nucleophiles are among the most important ones. Enantiopure α-alkoxy and α-aryloxy alcohols are valuable target molecules for asymmetric synthesis because of their role as key synthetic intermediates in a variety of pharmaceutically important compounds [1-3]. Recently, we reported the first ring-opening of epichlorohydrin with salicylaldehyde derivatives in the presence of Jacobsen's Co(III) salen catalyst [4]. The final ring-opened product is a multifunctional aldehyde **1** containing a stereocenter in addition to the alkyl halide and alcohol functional groups.

In this study, the ring-opening of epichlorohydrin was performed using 2,4-dihydroxybenzaldehyde in the presence of Jacobsen's Co(III) salen catalyst to obtain multifunctional aldehydes and using this aldehyde two novel salen type Schiff base ligands were synthesized and characterized by elemental analysis and spectroscopic techniques. Schiff base ligands which have similar functional groups are of great importance owing to their biological, antifungal and antibacterial, properties [5-8].

Experimental

All chemicals were purchased from Merck and Sigma-Aldrich and used without any purification. Solvents were used as received from commercial suppliers. IR spectra were recorded using a Perkin Elmer 100 FTIR spectrometer. ^{1}H NMR and ^{13}C NMR spectra were carried out using a 400 MHz Varian NMR spectrometer at ambient temperature. Melting points were recorded with an Electrothermal digital melting point apparatus. The Co(III) salen catalyst [9] and compound **1** were prepared according to the literature method [4].

*Preparation of 5-(3-chloro-2-hydroxypropoxy)-2-{(E)-[(2-hydroxyphenyl)imino]methyl}phenol (**2**)*

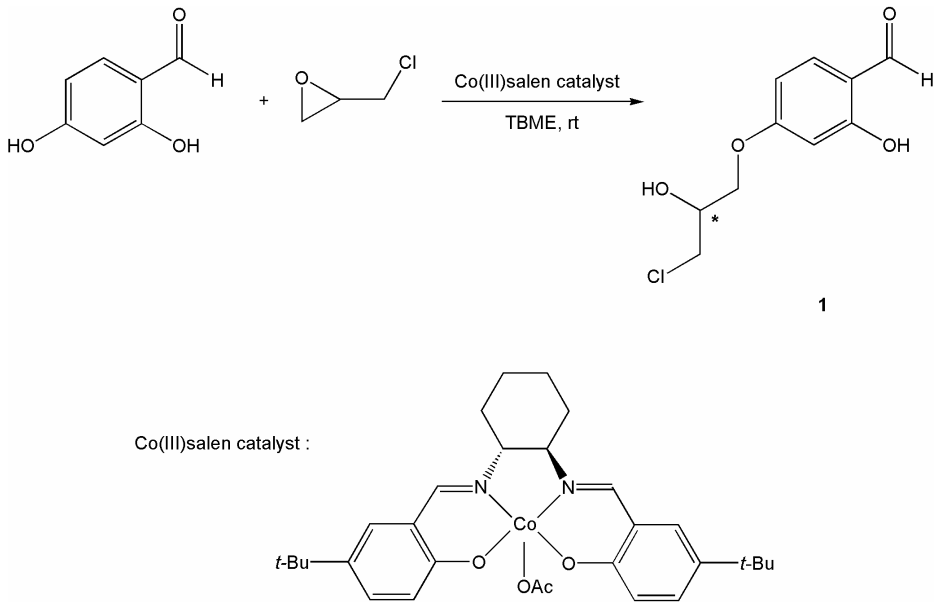
A solution of aldehyde **1** (46 mg, 0.19 mmol) and 2-aminophenol (22 mg, 0.19 mmol) in 10 mL ethanol was stirred at rt for 2 hours. The product was crystallized from ethanol to give the title compound as yellow crystals (82% yield). mp. 164-165.7 °C. ^{1}H NMR (400 MHz, DMSO) δ (ppm) 14.33 (s, 1H), 9.69 (s, 1H), 8.83 (s, 1H), 7.45 (d, J= 8.4 Hz, 1H), 7.33 (dd, J= 8.0, 1.6 Hz, 1H), 7.07 (t, J= 7.2, 1.6 Hz, 1H), 6.93 (dd, J= 8.0, 1.2 Hz, 1H), 6.85 (t, J= 7.4, 1.2 Hz, 1H), 6.48 (dd, J= 8.8, 2.4 Hz, 1H), 6.39 (d, J= 2.4 Hz, 1H), 5.55 (s, 1H), 4.04 – 3.99 (m, 3H), 3.75 – 3.63 (m, 2H). ^{13}C NMR (400 MHz, DMSO) δ (ppm) 166.03, 163.52, 160.63, 151.16, 134.71, 134.58, 128.03, 120.30, 119.74, 117.08, 113.93, 107.45, 102.38, 69.87, 69.25, 47.24. Anal. Calcd. for: $C_{16}H_{16}ClNO_4$: C, 59.73; H, 5.01; N, 4.39. Found: C, 59.73; H, 5.01; N, 4.35%. IR (KBr): 3319, 1615, 1598, 1524, 1465 cm^{-1}.

*Preparation of 5-(3-chloro-2-hydroxypropoxy)-2-{(E)-[(2-hydroxy-1,1-dimethylethyl)imino]methyl}phenol (**3**)*

The product was synthesized with the same method used in the preparation of **2**, using aldehyde **1** (46 mg, 0.19 mmol) and 2-amino-2-methyl-1-propanol (16.5 mg, 0.19 mmol). The product was crystallized from ethanol to give the title compound as yellow crystals (80% yield). mp. 140-142 °C. ^{1}H NMR (400 MHz, DMSO) δ (ppm) 14.55 (s, 1H), 8.32 (s, 1H), 7.23 (d, J= 8.8 Hz, 1H), 6.23 (dd, J= 8.4, 2.4 Hz, 1H), 6.13 (d, J= 2.4 Hz, 1H), 5.51 (d, J= 4.8 Hz, 1H), 5.01 (s, 1H), 4.00 – 3.92 (m, 2H), 3.67 (ddd, J= 10.8, 4.8, 4.4 Hz, 2H), 3.41 (d, J= 4 Hz, 2H), 1.22 (s, 6H). ^{13}C NMR (400 MHz, DMSO) δ (ppm) 171.31, 163.95, 161.44, 134.67, 112.20, 106.01, 102.85, 69.54, 69.21, 59.69, 47.24, 24.47, 22.93. Anal. Calcd. for: $C_{14}H_{20}ClNO_4$: C, 55.72; H, 6.68; N, 4.64. Found: C, 55.45; H, 6.61; N, 4.72%. IR (KBr): 3281, 1633, 1613, 1529 cm^{-1}.

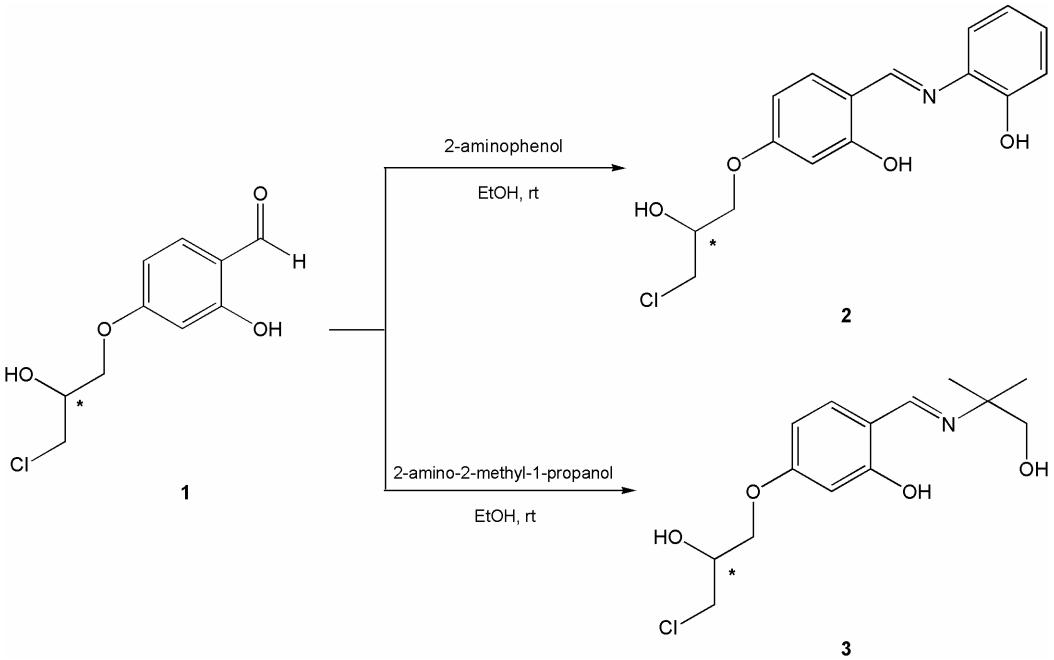
Results and Discussion

The ring opening reaction of epichlorohydrin was carried out with 2,4-dihydroxybenzaldehyde in the presence of Jacobsen's Co(III) salen catalyst [4, 9]. We obtained a single product arising from selective reaction at the 4-OH group (Scheme 1).



Scheme 1. The ring opening of epichlorohydrin with 2,4-dihydroxybenzaldehyde

Schiff base derivatives of 4-(3-chloro-2-hydroxypropoxy)-2-hydroxybenzaldehyde **1** were prepared using primary amines such as 2-aminophenol and 2-amino-2-methyl-1-propanol (Scheme 2) and were fully characterized.



Scheme 2. Synthesis of the multifunctional chiral Schiff base derivatives of **1**

The resulting products have the ability to act as tridentate ONO ligands and they contain a stereogenic center on a side-chain. Thus, they have a high potential for demonstrating biological activity [8].

Conclusions

Potentially biological active two novel multifunctional chiral Schiff bases were synthesized in very good yields. All compounds were characterized by spectroscopic methods.

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