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ORIGINAL ARTICLE

Synthesis of new derivatized pyrazole based ligands and their catecholase activity studies

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KEYWORDS

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Abstract A synthesis of three new tripodal ligands: 3-[bis-(3,5-dimethyl-pyrazol-1-ylmethyl)-amino]-propan-1-ol **L1**, 3-[bis-(5-methyl-3-carbomethoxy-pyrazol-1-ylmethyl)-amino]-propan-1-ol, **L2** and 3-[bis-(5-methyl-3-carboethoxy-pyrazol-1-ylmethyl)-amino]-propan-1-ol **L3** is reported. The *in situ*-generated copper(II) complexes of three new compounds (**L1**–**L3**) were examined for their catalytic activities and were found to catalyse the oxidation reaction of catechol to *o*-quinone with the atmospheric dioxygen. These activities depend on the nature of the ligand and the copper salts.

1. Introduction

It is now well-documented that copper containing metalloproteins play a very important role in transport, activation, and metabolism of dioxygen in living organisms (Albada et al., 2007; Chen and Solomon, 2004; Decker and Tuczek, 2000; Holm et al., 1996). A notable advance in the understanding of the properties of these proteins has been achieved through the comparison of synthetic models to the naturally occurring molecules (Decker et al., 2000; Kitajima and Moro-oka, 1994; Van Gelder et al., 1997). Several catechol derivative substrates were used in the literature to understand the mechanisms of oxidase enzyme research (Gerdemann et al., 2002; Rompel et al., 1999). It was observed that the catalytic activities of the complexes are not only dependent on the organic ligand but also on the type of inorganic anion coordinated to the copper center (Koval et al., 2006). In this paper, we report the synthesis of three new pyrazolyl ligands. The copper(II) *in situ*-generated complexes of these new products, were examined as catalysts to-

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ward atmospheric dioxygen oxidation reaction of catechol to *o*-quinone.

2. Results and discussion

2.1. Synthesis

Pyrazolyl and triazolyl derivatives **N**–C–**N** junction ligands **L1**–**L3** (Scheme 1) were prepared using two different methods. The first one consists of condensation of 1-(hydroxymethyl)-3,5-dimethylpyrazole (Dvoretzky and Richter, 1950), 1-hydroxymethyl-5-methyl-1H-pyrazole-3-carboxylic acid methyl ester (Touzani et al., 2000), 1-hydroxymethyl-5-methyl-1H-pyrazole-3-carboxylic acid ethyl ester (Touzani et al., 1999) with a series of alcohol amines such as aminopropanol in 2:1 ratio at room temperature during four days in acetonitrile (Touzani et al., 2001). In the second method, the similar reactions were carried out with some drops of solvent at 60 °C for 4 h. The target products were isolated with good yields in the two methods from 75% to 89% (Table 1).

All the new compounds were characterized by ^{1}H NMR, ^{13}C NMR and mass spectrometry. The proton NMR spectra of **L1** product, show two signals at 4.90 and 4.36 ppm corresponding to methylene protons (N–CH_2–N). When the pyrazolic rings are linked to the ester (–CO_2R) moieties (**L2**, **L3**), these proton signals appears between 5.06 and 5.29 ppm.

2.2. Catecholase studies

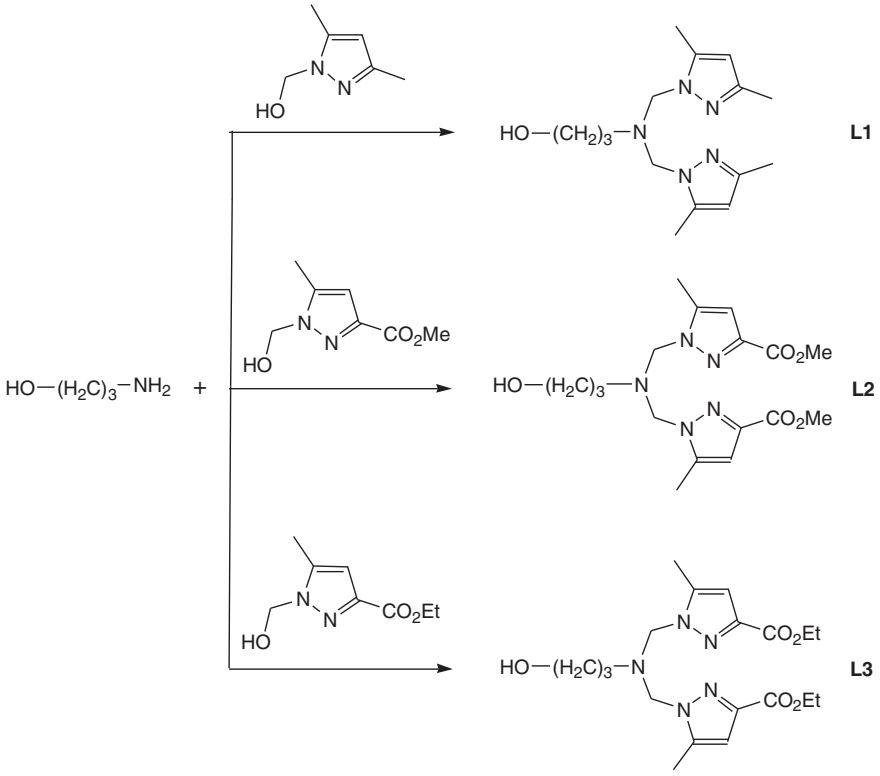
The progress of the catechol oxidation reaction is conveniently followed monitoring the strong absorbance peak of quinone in the UV/Vis spectrophotometer (Scheme 2).

The metal complex solution and catechol reductant were added together in the spectrophotometric cell at 25 °C (El Kodadi et al., 2008; Bouabdallah et al., 2007; Boussalah et al., 2009a,b). Formation of *o*-quinone was monitored by the increase in absorbance at 390 nm as a function of time. Figs. 1–6 show the absorbance versus time spectrum for the first 60 min of the oxidation reaction, while the rates are shown in Table 2. In all cases, catecholase activity was noted.

As can be seen from Table 2, all of the complexes with pyrazolyl ligands catalyze the oxidation reaction of catechol to *o*-quinone with the rate varying from a high of 0.0289 μmol substrate per mg catalyst per min for the **L1[CuSO$_4$]** complex to a low of 0.0018 μmol substrate per mg catalyst per min for **L1[CuCl$_2$]**. These rates are comparable to the values reported by (Malachowski et al., 1996) from 0.018 to 0.186 μmol substrate per mg catalyst per minute, for the similar tripodal ligands. The catalytic activity depends strongly on both the R substituent and the type of inorganic anion. The copper complexes of ligand **L1** were observed to be the lowest active, except in the case when we have used SO_4^{--} anion. The order of reactivity for the oxidation of catechol by $CuCl_2$ and $Cu(NO_3)_2$ complexes is **L2** > **L3** > **L1**. The order of reactivity for the oxidation of catechol by $Cu(CH_3COO)_2$ complexes is **L1** with the other ligands the rate of activity decreases strongly. The order of reactivity for the oxidation of catechol by $CuSO_4$ complexes is **L1** > **L2** > **L3**.

3. Conclusion

We report the synthesis of amino acid functional tridentate ligands with good and excellent yields. The oxidation of catechol is very efficient to give quinone by complexes of



Scheme 1