

SYNTHESIS AND CATECHOLASE ACTIVITY OF Cu(II) AND Fe(III) COMPLEXES OF 4-METHYL-2- ((PIPERIDIN-1-YL)METHYL)PHENOL

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Received: April, 27, 2019
Accepted: October, 09, 2020

Abstract: This study is aimed at evaluating the impact of *N*- and *S*- bonding modes of thiocyanate substituent on catecholase activity as its presence in the coordination sphere of the metal complex can either reduce catecholase activity or otherwise. 4-Methyl-2-((piperidin-1-yl)methyl) phenol - the Mannich base and its synthesized metal complexes were characterized by various spectroscopic techniques including NMR, IR, and UV-Vis spectroscopy. Turnover rates obtained from the Cu(II) and Fe(III) complexes ranged between 6.02 - 22.72 h⁻¹ with the thiocyanate mode in the Fe(III) complex leading to increased catecholase activity.

Keywords: aminomethylation, monobase, oxidation, piperidine, quinone

INTRODUCTION

Mannich bases and their metal complexes have been extensively studied due to their medicinal properties. Also, biomimetic studies of the metal complexes with regards to various enzymes including catecholase oxidase, phenoxazinone synthase, and ascorbic acid oxidase that involve the catalytic oxidation of oxygen are been given great attention [1 – 3]. Some of our previous work [4, 5] has been directed towards the design of novel Mannich bases and synthesizing their Cu(II) and Fe(III) complexes especially as candidates to mimic *catecholase oxidase* with type-3 copper centers that catalyze exclusively the oxidation of *o*-diphenols to the corresponding *o*-quinones. The highly reactive quinones auto-polymerizes to brown polyphenolic catechol melanins, a process that is essential in the protection of damaged plants from pathogens or insects [6, 7]. Even though the oxidation process requires two Cu(II) centers in close proximity, some mononuclear metal complexes have yielded enviable results [8, 9], thus necessitating further investigation into an array of newly synthesized metal complexes.

Detailed spectroscopic studies of bioactive Mn(II) and Cu(II) complexes of similar Mannich bases obtained from catechol is also reported in addition to the ability of Zn(II) complexes of a Mannich base 2-((diethylamino)methyl)-4-methyl phenol to hydrolyze b-lactam antibiotics and toxic organophosphotriesters [10, 11]. To the best of our knowledge, neither the synthesis nor the applicability of this Mannich base and its metal complexes has been reported in the literature.

In this paper, the synthesis and characterization of Mannich base [4-methyl-2-((piperidin-1-yl)methyl)phenol] and its Cu(II) and Fe(III) complexes with or without thiocyanate is reported while also pointing out some of their different spectroscopic properties in the metal complexes. Also, the impact of thiocyanate within the coordination sphere of the metal ion on catecholase activity was further evaluated kinetically. All the synthesized compounds were obtained in very good quantity, the ligand was isolated purely by using purification techniques and was structurally characterized with the help of ^1H - and ^{13}C -NMR spectroscopy amongst other spectroscopic techniques.

MATERIALS AND METHODS

All reagents as purchased from Sigma Aldrich were of analytical grade and used as received without further purification. C, H, and N analyses were obtained on an Elementar Analysensysteme VarioMICRO V1.62 GmbH analysis System. ^1H and ^{13}C NMR spectra were recorded in CDCl_3 on a Bruker AMX 300 MHz spectrometer with tetramethylsilane (TMS) as an internal standard for ^1H . Infrared spectra ($4000 - 650 \text{ cm}^{-1}$) were measured with a PerkinElmer Spectrum 400 spectrophotometer at room temperature using the ATR technique. Electronic spectra (250 – 900 nm) were recorded for the solutions of the synthesized compounds in DMF on a Perkin Elmer UV-Vis spectrophotometer model Lambda 25. The melting points were determined on a Gallenhamp melting point apparatus by using open capillary tubes. The molar conductance (10^{-3} M solution in DMSO) of complexes was measured at $20 \pm 1^\circ\text{C}$ using 86555 AZ Multiparameter Benchtop pH/ ORP/ Conductivity/ TDS/ Salinity meter (cell constant $K = 0.9477$).

Synthesis of 4-methyl-2-((piperidin-1-yl)methyl)phenol (HL)

Following the literature procedure with some modifications, a mixture of piperidine (1.448 g, 17.0 mmol), paraformaldehyde (0.510 g, 17.0 mmol), and *p*-cresol (1.784 mL, 17.0 mmol) was refluxed in 5 mL of isopropanol for 4 hrs. After the reaction, the mixture was poured into water and refrigerated overnight. White solid precipitates obtained were collected and recrystallized from water: ethanol mixture to give a white crystalline solid (1.850 g, yield = 53 %).

Synthesis of the metal complexes

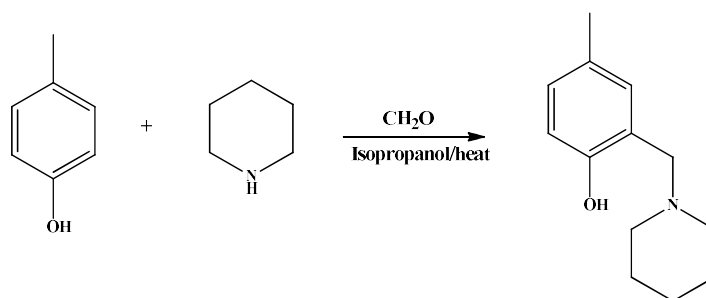
Metal complex **I** was prepared by a solution of CuCl₂·2H₂O (0.852 g, 5.00 mmol) in 5 mL methanol added gradually to a solution of the ligand (1.026 g, 5.00 mmol) in 5 mL chloroform. The reaction mixture was stirred at room temperature for 6 h. The desired product was obtained as precipitate after allowing the reaction mixture to stand for a few minutes after completion. This was collected, washed with the methanol-chloroform mixture, and dried in a desiccator. Similar techniques were used for the preparation of the other metal complexes. Metal complex **II** was prepared by adding an equimolar quantity of potassium thiocyanate in methanol to a similar solution used to prepare complex **I**. While FeCl₃·6H₂O was used to prepare complex **III** with an equimolar quantity of potassium thiocyanate in methanol added to a similar solution of complex **III** to obtain complex **IV**.

Catecholase activity

Kinetic experiments were performed for complexes **I** - **IV** on the substrate 3,5-di-*tert*-butylcatechol (3,5-DTBC) in DMF, a constant concentration of 1×10^{-4} M of the metal complex was added to varying concentration of 3,5-DTBC (1×10^{-3} M - 1×10^{-2} M). The conversion of 3,5-DTBC to the oxidation product 3,5-di-*tert*-butylquinone (3,5-DTBQ) was monitored with time at a wavelength of 400 nm. The rate for each concentration of the substrate was determined by the method of initial rate from a plot of $\log[A_{\infty}/(A_{\infty}-A_t)]$ vs time.

RESULTS AND DISCUSSION

The synthesis of the ligand is depicted in Scheme 1.



Scheme 1. Synthesis of the Mannich base (HL)

The analytical and physical data of the synthesized compounds are reported in Table 1 and Table 2. All the compounds except the ligand have high melting points and are highly soluble in DMF and DMSO. The metal complexes conformed to a 1:1 metal to ligand ratio as confirmed from elemental analysis. Molar conductivities of the metal complexes in DMSO ranged from $4.38 - 33.74 \Omega^{-1} \cdot \text{cm}^2 \cdot \text{mol}^{-1}$ thus indicating that the metal complexes are non-electrolytic in solution [12].

Table 1. Analytical data for 4-methyl-2-((piperidin-1-yl)methyl)phenol (HL) and its metal complexes

| Compound | Molecular formula | % Found (Calculated) | | | Λ_M [$\Omega^{-1} \cdot \text{cm}^2 \cdot \text{mol}^{-1}$] |
|------------|---|----------------------|-------------|-------------|--|
| | | C | H | N | |
| HL | $\text{C}_{13}\text{H}_{19}\text{NO}$ | 75.64 (76.05) | 9.44 (9.32) | 6.80 (6.82) | --- |
| I | $[\text{Cu}(\text{L})\text{ClH}_2\text{O}]$ | 48.58 (48.58) | 6.96 (6.59) | 4.00 (4.35) | 4.38 |
| II | $[\text{Cu}(\text{HL})(\text{NCS})\text{Cl}]$ | 46.44 (46.41) | 5.65 (5.88) | 7.26 (7.73) | 33.74 |
| III | $[\text{Fe}(\text{HL})\text{Cl}_3] \cdot \text{CHCl}_3$ | 25.17 (25.23) | 5.30 (5.65) | 2.60 (2.45) | 5.33 |
| IV | $[\text{Fe}(\text{HL})(\text{NCS})\text{Cl}_2] \cdot 4\text{H}_2\text{O}$ | 30.53 (36.37) | 5.58 (5.88) | 5.83 (6.05) | 27.96 |

Table 2. Physical data for 4-methyl-2-((piperidin-1-yl)methyl)phenol (HL) and its metal complexes

| Compounds | M.P [°C] | Molar mass | Colour |
|------------|-----------|------------|-------------|
| HL | 47 - 48 | 205.29 | White |
| I | 136 - 138 | 321.35 | Green |
| II | 182 - 184 | 362.29 | Dark green |
| III | 161 - 163 | 571.20 | Brown |
| IV | 220 - 222 | 462.28 | Light brown |

The proposed structures for the metal complexes are given in Figure 1.

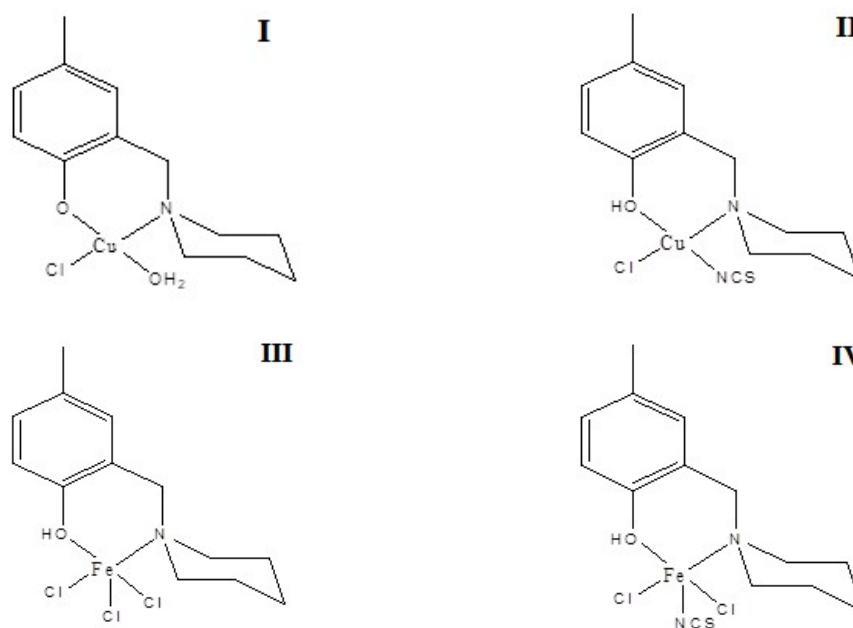


Figure 1. Proposed structures of metal complexes

The NMR data of the ligand with the characteristic peaks are reported in Table 3. The most important peak discussed herein is that of the aminomethylated group with the proton signals appearing upfield at 3.62 ppm while the carbon atom signal appears at 62.27 ppm. The integration supports the formation of a Mannich monobase as previously noted in the literature [13].

Table 3. NMR data of the Mannich base (HL): δ (ppm)

| | |
|--|---|
| ¹ H-NMR (300 MHz, CDCl ₃) | 1.49 – 1.66 (m, 6H, (CH ₂) ₃), 2.24 (s, 3H, CH ₃ -Ar), 2.50 (t, 4H, (CH ₂) ₂ N), 3.62 (s, 2H, Ar-CH ₂), 6.71 – 6.97 (m, 3H, Aromatic) |
| ¹³ C-NMR (75 MHz, CDCl ₃) | 20.57, 24.28, 25.98, 54.02, 62.27, 115.9, 121.5, 128.0, 129.0, 129.1, 155.7 |

The infrared data of the ligand with its metal complexes (Table 4) supports the formation of these metal complexes.

Table 4. Mid-infrared data for 4-methyl-2-((piperidin-1-yl)methyl)phenol (HL) and its metal complexes (cm⁻¹)

| Compounds | ν OH | ν CN | ν C-O | ν CNC | ν CS |
|------------|----------|-----------|-----------|-----------|----------|
| HL | 3014 | --- | 1252 | 1115 | --- |
| I | 3398 | --- | 1260 | 1136 | --- |
| II | --- | 2076s, sh | 1256 | 1135 | 783 |
| III | 3272 | --- | 1266 | 1154 | --- |
| IV | 3349 | 2042s, br | 1258 | 1153 | 824 |

sh = sharp, s = strong, br = broad

The Cu(II) ion in **I** is bonded to the deprotonated form of the ligand. The ν OH of the ligand is centered at 3014 cm⁻¹ a moderate-intense, broad band, a feature in support of strong intramolecular hydrogen bonding but shifts upward to 3298 – 3372 cm⁻¹ in the metal complexes. The band is not observed in the thiocyanate copper(II) complex **II** of the ligand indicating deprotonation of the hydroxyl group of the ligand before complexation and the absence of coordinated water molecules. In the Fe(III) complexes, the broad nature of the absorption band of the hydroxyl group ν OH may be indicative of the presence of coordinated water molecules [14, 15].

The stretching mode of ν CNC showed a positive shift $\sim 20 - 40$ cm⁻¹ in the metal complexes compared to the free ligand with the intensities also reduced. This is indicative of the involvement of the N-atom of the Mannich base in complexation [16]. The stretching vibration ν CN in the thiocyanato complexes is observed at 2076 cm⁻¹ (strong, sharp) in the copper complex and 2049 cm⁻¹ (broad) in the iron complex. In both metal complexes, N-bonding can be inferred because of the nature of the ν CN absorption band. The assertion is supported by the observation of the ν CS in the range of 783 cm⁻¹ and 824 cm⁻¹ for the copper and iron complexes respectively [17, 18].

UV/Visible spectra data of the ligand and its metal complexes are reported in Table 5. The transitions around 285 nm were assigned to $\pi \rightarrow \pi^*$ transition within the aromatic ring and the band shifted complexation. Complex I showed only one transition in DMF at 692 nm and may reflect a distorted square planar. In DMSO, the (phenolato-Cu) charge transfer band is observed at 454 nm in addition to a d-d transition at 733 nm leading to the conclusion on an octahedral geometry by the metal ion in DMSO.

Table 5. UV/Visible data for HL and its metal complexes (nm)

| Compounds | Solvent | Observed transitions | | | |
|------------|---------|----------------------|-----------|-----|-----|
| | | $\pi-\pi^*$ | $n-\pi^*$ | CT | d-d |
| HL | DMF | 285 | --- | --- | --- |
| | DMSO | 289 | --- | --- | --- |
| I | DMF | 288 | --- | --- | 692 |
| | DMSO | 270 | 313 | 454 | 733 |
| II | DMF | 288 | --- | 434 | 722 |
| | DMSO | 265 | 290 | 345 | 457 |
| III | DMF | 292 | --- | 369 | 513 |
| | DMSO | 287 | --- | 370 | --- |
| IV | DMF | --- | 290 | 413 | --- |
| | DMSO | 262 | 291 | 350 | 456 |

In complex **II** across the two solvents, two transitions assigned to CT and d-d transitions are observed. Thiocyanate complexes are well noted for their charge transfer transitions and that is observed at 434 and 345 nm in DMF and DMSO respectively [19]. The wavelengths at which the transitions occur in solution lead to the suggestion that the complex is square planar in shape. The d-d transitions are assigned to ${}^2B_{1g} \rightarrow {}^2E_g$ observed for Cu(II) complexes of Mannich bases. Madhu *et al.* [20] have previously reported values in the range of 463 – 515 nm corresponding to the ${}^6A_{1g} \rightarrow {}^4T_{1g}$ transition consistent with octahedral Fe(III) complexes [21, 22]. Furthermore, a strong band at 310 nm in complexes corresponds to charge-transfer transition.

Results of catecholase activity

The choice of 3,5-DTBC as a substrate is due to its two bulky *tert*-butyl substituents on the ring and low quinone-catechol reduction potential [23]. It was easily oxidized to the corresponding *o*-quinone, 3,5-DTBQ, which is highly stable and showed maximum absorption at 400 nm in DMF. The solution of the complexes was treated with 100 equivalents of 3,5-DTBC under aerobic conditions. After the addition of 3,5-DTBC, the time-dependent spectral scan showed a very smooth increase of the quinone band at 400 nm, which indicated the formation of 3,5-DTBQ as depicted in Figure 2.

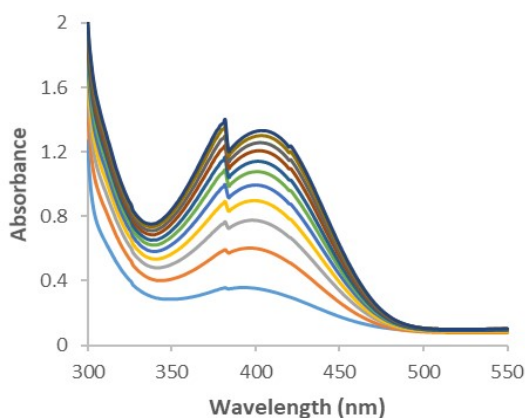


Figure 2. Changes observed in the absorption profile of a mixture of complex **II** (conc. 1×10^{-4} M) with 100-fold 3,5-DTBC conducted at 5 mins interval for 1 hr

The plot of $\log(A_{\infty}/A_{\infty}-A_t)$ versus time for catecholase activity of complexes **I** – **IV** is shown in Figure 3.

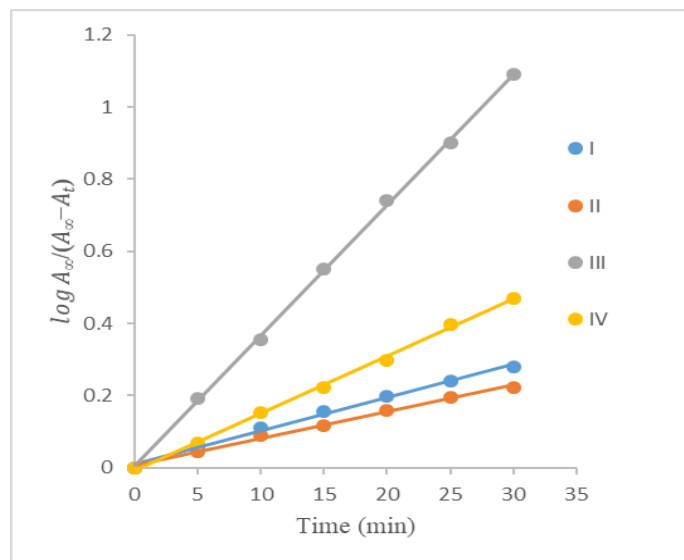


Figure 3. Catecholase activity of copper (II) and iron (III) complexes

The rate versus concentration of substrate data were analysed with Michaelis–Menten equation to get the Lineweaver–Burk (double reciprocal) plot as well as the various kinetic parameters V_{\max} , K_M and k_{cat} . The Lineweaver–Burk plot is given in Figure 4 while the observed rate vs. [substrate] plot in DMF solution is depicted in Figure 5.

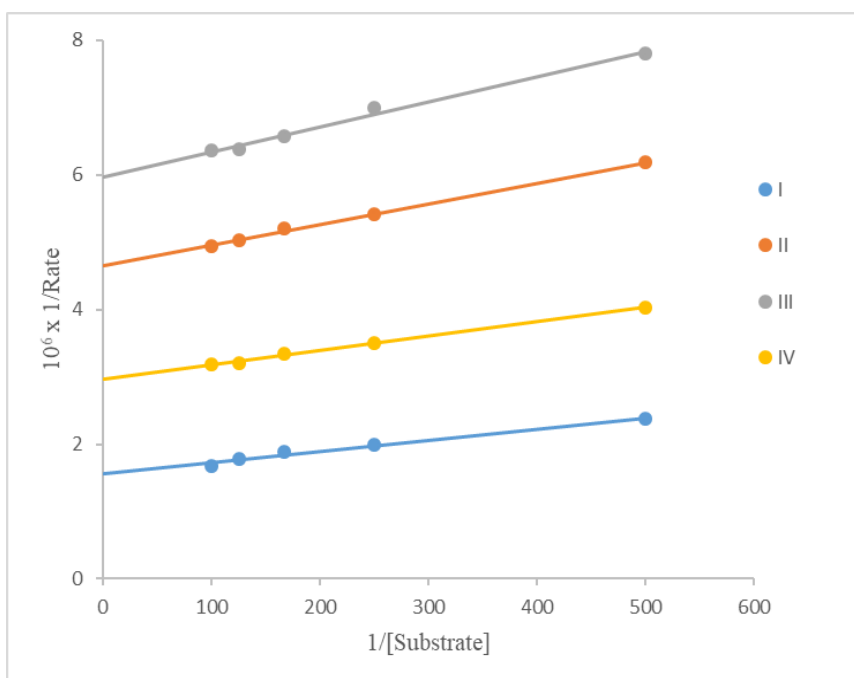


Figure 4. Lineweaver–Burk plots for complex **I** – **IV** in DMF medium for the oxidation of 3,5-DTBC

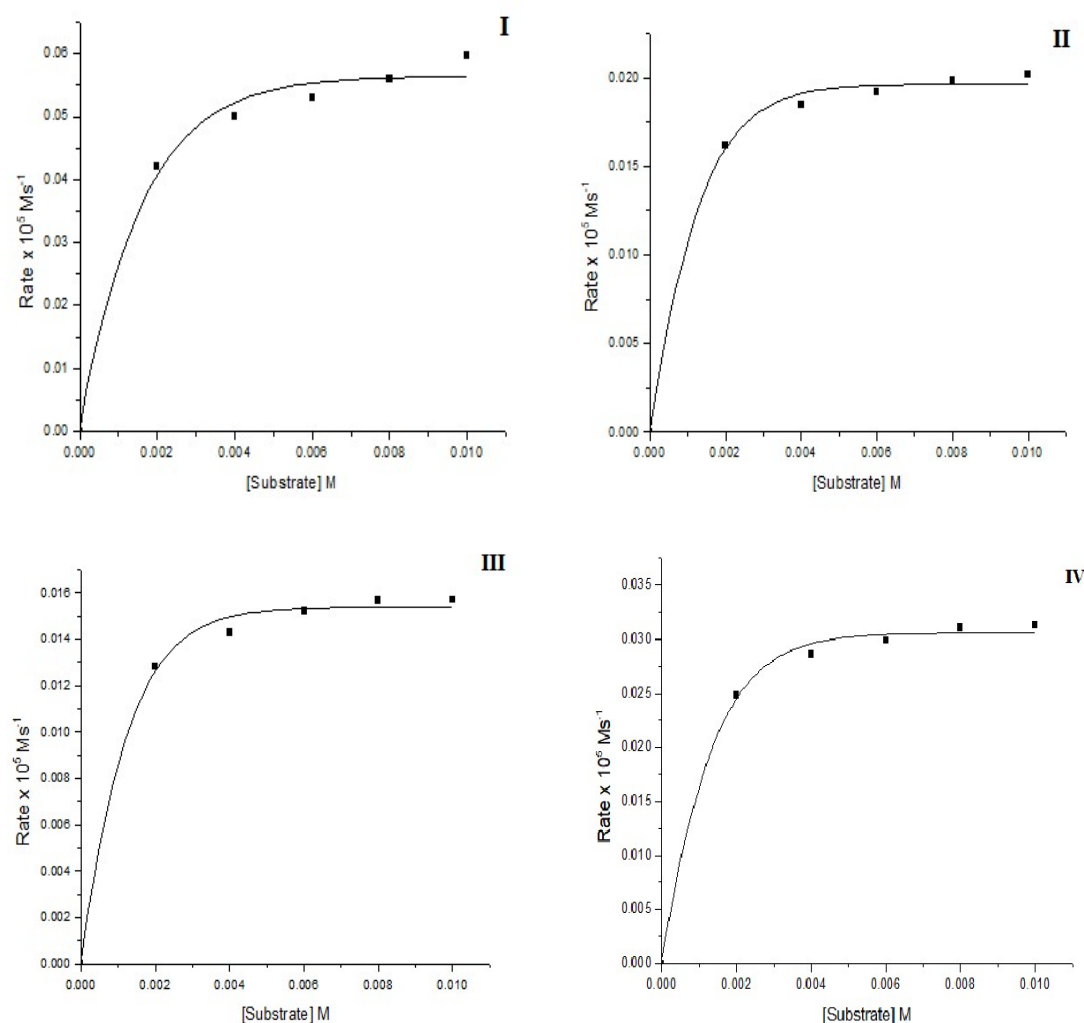


Figure 5. Dependence of the rate of reaction on substrate concentration for complexes **I** - **IV** (100 mM) at 25 °C in DMF for the oxidation of 3,5-DTBC

The kinetic parameters of the metal complexes are listed in Table 6. All the metal complexes demonstrated catecholase activity.

Table 6. Kinetic parameters for the oxidation of the model substrate 3,5-DTBC

| Complex | K_M [M] | V_{max} [M·s ⁻¹] | k_{cat} [h ⁻¹] |
|------------|----------------------------------|----------------------------------|------------------------------|
| I | $(1.04 \pm 0.06) \times 10^{-3}$ | $(6.31 \pm 0.33) \times 10^{-7}$ | 22.72 ± 1.01 |
| II | $(6.32 \pm 0.41) \times 10^{-4}$ | $(2.06 \pm 0.04) \times 10^{-7}$ | 7.42 ± 0.50 |
| III | $(6.22 \pm 0.41) \times 10^{-4}$ | $(1.67 \pm 0.09) \times 10^{-7}$ | 6.02 ± 0.41 |
| IV | $(7.08 \pm 0.43) \times 10^{-4}$ | $(3.33 \pm 0.17) \times 10^{-7}$ | 12.00 ± 0.78 |

Turnover rates ranging from 6.02 to 22.72 h⁻¹ are found to be comparable to those reported by Reim *et al.* [24] and Neves *et al.* [25] but are significantly lower than those reported by Yang *et al.* [26] and Wang *et al.* [27]. The comparative order of catecholase activity is in the order **I** > **IV** > **II** > **III**. Summarily, the nature of the bonding of the thiocyanate or isothiocyanate appears to disfavor or favor the biomimetic abilities of the metal complexes involved. The negative impact of thiocyanate on catecholase activity

or similar biomimetic studies has previously been highlighted in the literature [28, 29]. We also propose that the highest catecholase activity demonstrated by **I** may be attributed to the deprotonated nature of the ligand which may enhance a stronger Cu-O bond.

CONCLUSIONS

Four metal complexes which are potential catalysts for the oxidation of catechol to quinone by measuring the rate of aerial oxidation of 3,5-DTBC to 3,5-DTBQ in their presence have been synthesized and characterized as well as the Mannich base-ligand on which they are based. The presence of thiocyanate or isothiocyanate within the coordination sphere has been shown to either reduce or increase the efficiency depending on the ease of oxidation of the metal complex as well as the availability of the coordination site for the substrate.

ACKNOWLEDGMENTS

The authors thank Rhodes University, South Africa for funding this research.

REFERENCES

1. Wang, B.-L., Shi, Y.-X., Ma, Y., Liu, X.-H., Li, Y.-H., Song, H.-B., Li, B.-J., Li, Z.-M.: Synthesis and biological activity of some novel trifluoromethyl-substituted 1,2,4-triazole and bis(1,2,4-triazole) Mannich bases containing piperazine rings, *Journal of Agricultural and Food Science*, **2010**, **58** (9), 5515-5522;
2. Bugg, T.D.H.: Dioxygenase enzymes: catalytic mechanisms and chemical models, *Tetrahedron*, **2003**, **59** (36), 7075-7101;
3. Güell, A., Siegbahn, P.E.M.: Theoretical study of the catalytic mechanism of catechol oxidase, *JBIC Journal of Biological Inorganic Chemistry*, **2007**, **12** (8), 1251-1264;
4. Ayeni, A.O., Watkins, G.M.: Biomimetics of mononuclear and dinuclear Cu(II) and Fe(III) complexes of a newly synthesized piperazyl Mannich base with or without thiocyanate towards catechol, *Monatshefte für Chemie - Chemical Monthly*, **2018**, **149** (12), 2175-2182;
5. Ayeni, A.O., Watkins, G.M.: Synthesis and evaluation of catecholase activities of metal complexes of 1,4-substituted piperazine Mannich base of 4-acetamidophenol, *Turkish Journal of Chemistry*, **2018**, **42** (5), 1275-1284;
6. Deverall, B.J.: Phenolase and pectic enzyme activity in the chocolate spot disease of beans, *Nature*, **1961**, **189**, 311-315;
7. Cary, J.W., Lax, A.R., Flurkey, W.H.: Cloning and characterisation of cDNAs coding for *Vicia faba* polyphenol oxidase, *Plant Molecular Biology*, **1992**, **20** (2), 245-253;
8. Sanyal, R., Dash, S.K., Das, S., Chattopadhyay, S., Roy, S., Das, D.: Catecholase activity, DNA cleavage and cytotoxicity of six Zn(II) complexes synthesized from designed Mannich ligands: higher reactivity of mononuclear over dinuclear, *JBIC Journal of Biological Inorganic Chemistry*, **2014**, **19** (7), 1099-1111;
9. Mitra, M., Raghavaiah, P., Ghosh, R.: A mononuclear cobalt(III) complex and its catecholase activity, *New Journal of Chemistry*, **2015**, **39** (1), 200-205;
10. Harbatsevich, H.I., Loginova, N.V., Koval'chuk, T.V., Osipovich, N.P., Gres, A.T., Azarko, I.I., Polozov, G.I.: Spectroscopy of bioactive manganese(II) and copper(II) complexes with Mannich bases, *Journal of Applied Spectroscopy*, **2015**, **82** (5), 713-717;

11. Umayal, M., Mugesh, G.: Metallo- β -lactamase and phosphotriesterase activities of some zinc(II) complexes, *Inorganica Chimica Acta*, **2011**, 372 (1), 353-361;
12. Ali, I., Wani, W.A., Saleem, K.: Empirical formulae to molecular structures of metal complexes by molar conductance, *Synthesis and Reactivity in Inorganic, Metal-Organic, and Nano-Metal Chemistry*, **2013**, 43 (9), 1162-1170;
13. Ayeni, A.O., Watkins, G.M.: Impact of thiocyanate on the catecholase activity of Cu(II) and Fe(III) complexes of 2-((4-(2-hydroxy-4-methylbenzyl)piperazin-1-yl)methyl)-5-methylphenol (a Mannich base), *Acta Chemica Iasi*, **2018**, 26 (1), 59-73;
14. Prashanthi, Y., Kiranmai, K., Subhashini, N.J.P.: Synthesis, potentiometric and antimicrobial studies on metal complexes of isoxazole Schiff bases, *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, **2008**, 70 (1), 30-35;
15. Koll, A., Melikova, S.M., Karpfen, A., Wolschann, P.: Spectroscopic and structural consequences of intramolecular hydrogen bond formation in *ortho*-dimethylaminomethylphenol, *Journal of Molecular Structure*, **2001**, 559 (1-3), 127-145;
16. Bhat, I.U.H., Tabassum, S.: Synthesis of new piperazine derived Cu(II)/Zn(II) metal complexes, their DNA binding studies, electrochemistry and anti-microbial activity: Validation for specific recognition of Zn(II) complex to DNA helix by interaction with thymine base, *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, **2009**, 72 (5), 1026-1033;
17. Clark, R.J.H., Williams, C.S.: Infra-red spectra ($3000\text{-}200\text{ cm}^{-1}$) of metal-isothiocyanate complexes, *Spectrochimica Acta*, **1966**, 22 (6), 1081-1090;
18. You, Z.-L., Zhang, L., Shi, D.-H., Wang, X.-L., Li, X.-F., Ma, Y.-P.: Synthesis, crystal structures and urease inhibitory activity of copper(II) complexes with Schiff bases, *Inorganic Chemistry Communications*, **2010**, 13 (8), 996-998;
19. Al-Jeboori, M.J., Abdul-Ghani, A.J., Al-Karawi, A.J.: Synthesis and structural studies of new Mannich base ligands and their metal complexes, *Transition Metal Chemistry*, **2008**, 33 (7), 925-930;
20. Madhu, N.T., Radhakrishnan, P.K., Grunert, M., Weinberger, P., Linert, W.: Synthesis and thermal studies on iron(III) complexes of 4-*N*-(4'-antipyrilmethylidene)aminoantipyrine with varying counter ions, *Thermochimica Acta*, **2003**, 407 (1-2), 73-84;
21. Emir, N., Bilge, M., Tursun, M., Keşan, G., Parlak, C.: A joint theoretical and experimental study of 1-acetylpiperazine: Conformational stability, infrared and Raman spectra, *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, **2014**, 127, 388-395;
22. Cretu, C., Tudose, R., Cseh, L., Linert, W., Halevas, E., Hatzidimitriou, A., Costisor, O., Salifoglou, A.: Schiff base coordination flexibility toward binary cobalt and ternary zinc complex assemblies. The case of the hexadentate ligand *N*, *N'*-bis[(2-hydroxybenzylideneamino)-propyl]-piperazine, *Polyhedron*, **2015**, 85, 48-59;
23. Mukherjee, J., Mukherjee, R.: Catecholase activity of dinuclear copper(II) complexes with variable endogenous and exogenous bridge, *Inorganica Chimica Acta*, **2002**, 337, 429-438;
24. Reim, J., Werner, R., Haase, W., Krebs, B.: From tetranuclear μ_4 -oxo to μ_4 -peroxocopper(II) complexes, *Chemistry – A European Journal*, **1998**, 4 (2), 289-298;
25. Neves, A., Rossi, L.M., Bortoluzzi, A.J., Mangrich, A.S., Haase, W., Werner, R.: Synthesis, structure, physicochemical properties and catecholase-like activity of a new dicopper(II) complex, *Journal of the Brazilian Chemical Society*, **2001**, 12 (6), 747-754;
26. Yang, C.T., Vetrivelan, M., Yang, X., Moubaraki, B., Murray, K.S., Vittal, J.J.: Syntheses, structural properties and catecholase activity of copper(II) complexes with reduced Schiff base *N*-(2-hydroxybenzyl)-amino acids, *Dalton Transactions*, **2004**, 1, 113-121;
27. Wang, X., Ding, J., Vittal, J.J.: Syntheses, structures and properties of copper(II) complexes containing *N*-(2-hydroxybenzyl)-amino amide ligands, *Inorganica Chimica Acta*, **2006**, 359 (11), 3481-3490;
28. Panja, A.: Syntheses and structural characterizations of cobalt(II) complexes with N_4 -donor Schiff base ligands: Influence of methyl substitution on structural parameters and on phenoxazinone synthase activity, *Polyhedron*, **2014**, 80, 81-89;
29. Ramadan, A.E.M., Shaban, S.Y., Ibrahim, M.M.: Synthesis, characterization, and ascorbic acid oxidase biomimetic catalytic activity of cobalt(III) oxime complexes, *Journal of Coordination Chemistry*, **2011**, 64 (19), 3376-3392.