**ORIGINAL PAPER** 



# Biomimetics of mononuclear and dinuclear Cu(II) and Fe(III) complexes of a newly synthesized piperazyl Mannich base with or without thiocyanate towards catechol

Ayowole Olaolu Ayeni<sup>1,2</sup> (b) · Gareth Mostyn Watkins<sup>1</sup>

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#### Abstract

This paper presents the synthesis and characterization of Cu(II) and Fe(III) complexes of a newly synthesized Mannich base N-[4-hydroxy-3-[[4-(pyridin-2-yl)piperazin-1-yl]methyl]phenyl]acetamide. The spectro-analytical techniques employed include <sup>1</sup>H, <sup>13</sup>C NMR, IR, UV spectroscopy, conductivity measurements, and elemental analysis. Both mononuclear and dinuclear metal complexes were encountered in the study. Utilizing 3,5-di-*tert*-butyl catechol (3,5-DTBC) as the substrate, catecholase activity of all four complexes was evaluated with the detailed kinetic studies reported. The nature of the bonding of the thiocyanate is discussed based on the observation of vCN (2150–2050 cm<sup>-1</sup>). All the metal complexes are catalytically active with turn over numbers ranging from 9.47 to 31.86 h<sup>-1</sup> in DMF.

#### **Graphical abstract**



Keywords p-Acetamidophenol · Aminomethylation · Catechol oxidase · Turnover · 3,5-DTBC

### Introduction

Research into Mannich bases and their metal complexes are expanding into new frontiers. This class of ligands are usually NO or NNO donor, bidentate and tridentate ligands, respectively, and possesses a variety of applications including biological and catalytic ones [1, 2]. One of such area of researchis that of model coordination compounds as metalloenzymes with oxidase (oxygenase) activity and is of particular interest for the development of bioinspired catalysts for oxidation reactions [3, 4]. In that context, the type-3 dicopper enzyme catechol oxidase and catechol dioxygenases use atmospheric dioxygen to achieve the selective oxidation of catechols to *ortho*-quinones and muconic acid, respectively. Metal complexes—Cu(II), Fe(III), and Mn(II) particularly dinuclear ones are more popular in this regard [5, 6].

Various sources of substrate have been employed in the synthetic process including amongst others substituted phenols and acetophenones as revealed in the literature [7]. Syntheses involving substituted acetamidophenols are very

Ayowole Olaolu Ayeni aayeni@oauife.edu.ng

<sup>&</sup>lt;sup>1</sup> Department of Chemistry, Rhodes University, Grahamstown 6139, South Africa

<sup>&</sup>lt;sup>2</sup> Department of Chemistry, Obafemi Awolowo University, Ile Ife 22005, Nigeria

rare to come by in the literature and those reported are listed herein [8–10]. We have reported on the synthesis and characterization of new Mannich bases of cresols and acetamidophenol as well as the catecholase activity of Cu(II) and Fe(III) complexes, while taking into consideration the role played by thiocyanate. The promising results obtained and previously reported are a motivation for this study [11–13] (Scheme 1).

To the best of our knowledge, the several desirable properties of Mannich bases and their metal complexes make acetamidophenol-Mannich bases an untapped mine field. We now, in this study report the synthesis and characterization of a new Mannich base N-[4-hydroxy-3-[[4-(pyridin-2-yl)piperazin-1-yl]methyl]phenyl]acetamide alongside its Cu(II) and Fe(III) complexes. In addition, the detailed kinetic study of the catecholase activity of all the metal complexes and the bonding modes of thiocyanate with its impact on catalytic activity are also reported.

### **Results and discussion**

In this work, a new Mannich base *N*-[4-hydroxy-3-[[4-(pyridin-2-yl)piperazin-1-yl]methyl]phenyl]acetamide has been synthesized alongside its Cu(II) and Fe(III) complexes. The synthesis of the thiocyanate analogs of the metal complexes is equally reported. All the synthesized compounds were characterized by a range of analytical and spectroscopic techniques including elemental analyses, FT-IR, UV–Vis, <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy. All the metal complexes are colored, air stable, and insoluble in most solvents except DMF and DMSO.

The molar conductivities ( $\Lambda_{\rm m}$ ) of 1 × 10<sup>-3</sup> M solutions of the complexes in DMSO were measured at 25 °C. The molar conductance values of the complexes are in the range 17.88–83.30  $\Omega^{-1}$  cm<sup>2</sup> mol<sup>-1</sup>. From these observed values of  $\Lambda_{\rm m}$ , complexes 2 and 4 are considered as 1:1 electrolyte solutions while 1 and 3 are non-electrolytes [14, 15]. Complexes 1 and 3 are mononuclear with metal–ligand ratio of 1:1, while the thiocyanate containing metal complexes 2 and 4 are dinuclear with metal–ligand ratio of 2:1.

The data on the characterization of the synthesized ligand and its transition metal complexes are reported in Table 1.

#### Scheme 1



#### Characterization of ligand and its complexes

#### NMR spectra

Data from the characterization of the novel ligand by <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy revealed the formation of a mono-aminomethylated Mannich base. Notable diagnostic peaks in the spectra of the ligand include the presence of the aminomethylated hydrogens and carbons (denoted by  $H_f$  and  $C_f$ ) at 3.73 (s, 2H) and 61.7 ppm, respectively. The presence of this signal has been used in distinguishing mono- from bis-Mannich products [16, 17]. In addition, two different environments are identified within the piperazine moiety of the ligand; 2.67 ppm (t, 4H) and 3.57 ppm (t, 4H) for protons and 45.0, 52.2 ppm for the carbons. Aromatic signals are within (6.63–8.20) ppm and (107.2–168.2) ppm for hydrogen and carbon atoms, respectively.

#### Infrared spectra

The Mannich base displayed a medium intense band at  $3354 \text{ cm}^{-1}$  attributed to the stretching mode of the hydroxyl group in the ligand. Shifts to lower frequencies were observed in all the metal complexes indicating the coordination through the hydroxyl group with the ligand not deprotonated [18]; however, the shifts were more pronounced in the thiocyanate complexes. The extent of the shifts ranged from  $165-197 \text{ cm}^{-1}$  in **1** and **3** to  $235-274 \text{ cm}^{-1}$  in **2** and **4**. Support for the coordination of the hydroxyl group can be obtained by considering the vC-O (sharp intense band) as well which shifted a little significantly from 1249 cm<sup>-1</sup> by 4 cm<sup>-1</sup> downward in **1** and upward in **3** by  $6 \text{ cm}^{-1}$  with all the bands appearing broader. Cases of upward shifts have been previously reported upon complexation without deprotonation for some lanthanide complexes of Schiff bases of aniline [19] and have to do with the impact of complexation on hydrogen bonding within the ligand. The vCN of the pyridine ring of the ligand shifts downwards from 1657 cm<sup>-1</sup> to within 1641–1652  $\text{cm}^{-1}$  in the metal complexes, which is an evidence to show the involvement of the pyridine ring of the ligand in complexation with the central metal ion as previously reported in the literature [20, 21].

Two bands assigned to the stretching modes of the two vCNC of the piperazine within the ligand are designated as  $v1 = 1213 \text{ cm}^{-1}$  and  $v2 = 1142 \text{ cm}^{-1}$ . Considerable lowering to within 1180–1162 cm<sup>-1</sup> and 1129–1062 cm<sup>-1</sup> is observed for v1 and v2, respectively, with the effect being most pronounced in complex **2**. This observation is evidence of both N-atoms of the piperazine moiety of the ligand being involved in the complexation [22].

 Table 1 Data on the characterization of the synthesized ligand and its transition metal complexes

Complex/ligand	<i>d</i> - <i>d</i> transition	Assignment	$\Omega^{-1}$ cm <sup>2</sup> mol <sup>-1</sup>	Geometry	M/g mol <sup>-1</sup>	Yield/ %	Color
$1 [Cu(HL)Cl_2] \bullet 4H_2O$	741 <sup>a</sup> , 733 <sup>b</sup>	${}^{2}E_{g} \rightarrow {}^{2}T_{2g}$	17.88	Octahedral	532.94	53	Brown
$2 [Cu_2(HL)(NCS)_2(H_2O)_2]Cl_2 \bullet 2H_2O$	687 <sup>a</sup> , 775 <sup>b</sup>	${}^{2}E_{g} \rightarrow {}^{2}T_{2g}$	78.56	Square Planar	711.54	56	Light brown
<b>3</b> [Fe(HL)Cl <sub>3</sub> ]•6H <sub>2</sub> O	496 <sup>a</sup>	CT from UV to Vis region	44.16	Octahedral	576.80	63	Dark brown
4 Fe <sub>2</sub> (HL)(NCS) <sub>2</sub> (H <sub>2</sub> O) <sub>2</sub> Cl <sub>2</sub> ]Cl <sub>2</sub> •6H <sub>2</sub> O	472 <sup>b</sup>	CT from UV to Vis region	83.30	Octahedral	875.28	45	Brown
HL	-				326.38	52	White

*CT* charge transfer <sup>a</sup>DMF <sup>b</sup>DMSO

Bonding of the thiocyanate to the central metal ion was confirmed by the observation of strongly intense bands at  $2140 \text{ cm}^{-1}$  (split) in the copper(II) complex and  $2051 \text{ cm}^{-1}$  (broad) in the iron(III) complex. These bands support the following bonding modes: S-bonding and N-bonding in the copper and iron complexes, respectively [23, 24]. The bonding modes are supported by the vCS at 868 cm<sup>-1</sup> and 737 cm<sup>-1</sup> for **2** and **4**, respectively, as reported in the literature [25, 26].

#### **Electronic spectra**

The ligand has a maximum absorption ( $\lambda_{max}$ ) at 299 and 289 nm in DMF and DMSO, respectively, attributed to the  $n-\pi^*$  transition [27]. Complex 1 only displays a single d–d transition at 741 nm in DMF typical of an octahedral geometry; a similar transition is observed and equally assigned in DMSO at 733 nm alongside a ligand–metal charge transfer transition at 454 nm. Complex 2 showed a single transition at 687 nm attributed to a 4-coordinate geometry in the coordination sphere with a ligand–metal charge transfer transition typical of thiocyanates being observed at 427 nm. In DMSO, the d–d transition observed for 34 at 775 nm is attributed to  ${}^2\text{Eg} \rightarrow {}^2\text{T}_{2g}$  which may suggest an octahedral configuration upon coordination with the solvent [1].

Complexes **3** and **4** display medium–intense bands at 496, 472 nm in DMF, respectively, assigned to the *d*–*d* transitions and the transitions at 370 and 350 nm for **3** and **4**, respectively, in DMSO is assigned to the charge transfer transition peculiar to a Fe<sup>3+</sup> ion in an octahedral configuration [28]. Viswanathan et al. reported that the electronic spectra of all the iron(III) phenolate complexes they studied exhibit an intense band in the visible region (490–550 nm) [5]. This band is assigned to the phenolate  $(\pi_1)$ –Fe(III)( $d\pi$ ) charge transfer transition. Similar observations are well documented in the literature [29–31]. In general, the charge transfer bands are known to

overshadow the d–d transitions in Fe(III) complexes, thus making conclusions on geometry quite difficult. The proposed structures of the metal complexes are given in Fig. 1.

#### **Catecholase activity**

All the metal complexes showed significant catalytic oxidation activity towards 3,5-di-*tert*-butylcatechol (3,5-DTBC). This substrate with bulky substituents on the ring has low quinone–catechol reduction potential, makes it widely used and is easily oxidized to the corresponding *o*quinone 3,5-DTBQ [32–34], which is highly stable and showed maximum absorption at 399 nm in DMF.

The product 3,5-DTBQ was isolated in moderate yield (averagely 55.3%) by the slow evaporation of the eluent and was identified by <sup>1</sup>H NMR spectroscopy: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta = 1.22$  (s, 9H), 1.27 (s, 9H), 6.22 (d, J = 3.0 Hz, 1H), 6.92 (d, J = 3.0 Hz, 1H) ppm. These values of chemical shifts are similar to those earlier reported by Mitra et al. [35]. Figure 2 shows the spectral change for **2** upon addition of 100-fold 3,5-DTBC ( $1 \times 10^{-2}$  M) observed at an interval of 5 min in DMF. All the complexes showed saturation kinetics and a treatment based on the Michaelis–Menten model seemed appropriate. The binding constant ( $K_{\rm M}$ ), maximum velocity ( $V_{\rm max}$ ), and rate constant for dissociation of substrates (i.e., turnover number,  $k_{\rm cat}$ ) were calculated for all the complexes using the Lineweaver–Burk graph.

The plot of  $\log A_{\infty}/(A_{\infty} - A_t)$  vs time for all the metal complex in the presence of 100 equiv. of 3,5-DTBC is displayed in Fig. 3 above, while Fig. 4 is a plot of the initial rates versus substrate concentration for the oxidation of 3,5-DTBC catalyzed by the metal complexes.

The kinetic parameters obtained from the Lineweaver– Burk plots (Fig. 5) are listed in Table 2. All the metal complexes show moderately high turnover rates ranging from 9.47  $\pm$  0.52 to 31.86  $\pm$  1.20 h<sup>-1</sup> with the order of activity as 3 > 1 > 4 > 2. These values are comparable to





Fig. 1 Proposed structures of metal complexes 1-4



Fig. 2 Changes observed in UV–Vis spectra of complex 2 (1  $\times$  10<sup>-4</sup> M) in DMF medium upon the addition of 100-fold 3,5-DTBC (1  $\times$  10<sup>-2</sup> M)



Fig. 3 A plot of the difference in absorbance vs. time to evaluate the initial rate of the catalytic oxidation of 3,5-DTBC by 1-4 in DMF

those previously reported in the literature [36, 37] and considering the fact that rates are lower in coordinating solvents like DMF owing to the retarded formation of complex–substrate adduct [38], higher turnover rates are likely with less coordinating solvent like methanol. However, complexes **1** and **3** showed higher turnover rates than those of similar complexes of phenolic Mannich bases ( $< 23 h^{-1}$ ) [39, 40] though lower than the dinuclear ones (about 78 h<sup>-1</sup>) possessing better leaving groups like chlorides [41, 42].

Complex **3** exhibited the highest turnover rate amongst all the Cu(II) and Fe(III) complexes. As the iron(III) complexes appear to be better catalysts compared to their copper(II) counterparts, we suggest that the Fe(III)/Fe(II) reduction process appear more favorable than the Cu(II)/ Cu(I) process particularly in the presence of a more positively inductive acetamido group.

As previously reported, the non-thiocyanate metal complexes outshine their counterparts in catecholase activity. The lowering of catecholase activity of metal complexes by the inclusion of thiocyanate within their coordination sphere as previously reported by Ramadan et al. [43] and Pajan [44] is attributed to the poor dissociation (weak leaving group) of the thiocyanate to create a dissociation results in the negative impact on catecholase activity. Reports that the nature of the exogenous bridging ligand in the dimeric complexes also shows a remarkable influence on the activity, owing to the fact that a weakly coordinating ligand may easily be displaced by the incoming catechol, thus enhancing the activity may be applicable here [45].

Insight into the mechanism of the catalytic reaction involving the Cu(II) and Fe(III) complexes was gained by the identification of the presence of  $H_2O_2$ . Iodimetric titration as performed led to the observation of the iodide ion as a product of oxidation by hydrogen peroxide. The



Fig. 4 Plots of the initial rates versus substrate concentration for the oxidation of 3,5-DTBC catalyzed by complexes 1-4



Fig. 5 Lineweaver-Burk plots for complexes 1-4

reaction pathway that involves the formation of semiquinolate intermediate can, therefore, be proposed.

### Conclusion

The newly synthesized and characterized Mannich monobase N-[4-hydroxy-3-[[4-(pyridin-2-yl)piperazin-1yl]methyl]phenyl]acetamide acts as a tetradentate ligand with Cu(II) and Fe(III) ions to afford mono- and binuclear complexes. The coordination and geometry around the metal center were elucidated by spectroscopic studies and molar conductivity measurements of all the complexes. Mono- and binuclear complexes exhibit tetrahedral or octahedral geometries. Both SCN- and NCS-bonding modes were identified through IR spectroscopy in the study. The synthesized metal complexes were evaluated for their catecholase activity and the results showed that they were all catalytically active towards the oxidation of catechol to the corresponding o-quinone. Finally, it was observed that the presence of thiocyanate hinders the ease

Table 2 Kinetics parameters forthe oxidation of 3,5-DTBCcatalyzed by metal complexes1-4	Complex	$V_{\rm max}/{ m M~s}^{-1}$	K <sub>m</sub> /M	$k_{\rm cat}/{\rm h}^{-1}$
	1	$(7.84 \pm 0.44) \times 10^{-7}$	$(4.03 \pm 0.22) \times 10^{-4}$	$28.22 \pm 1.11$
	2	$(2.63 \pm 0.11) \times 10^{-7}$	$(8.96 \pm 0.28) \times 10^{-4}$	$9.47 \pm 0.52$
	3	$(8.85 \pm 0.62) \times 10^{-7}$	$(8.25 \pm 0.49) \times 10^{-3}$	$31.86 \pm 1.20$
	4	$(5.48 \pm 0.12) \times 10^{-7}$	$(6.82 \pm 0.31) \times 10^{-4}$	$19.73\pm0.89$

of complex–substrate adduct formation and, thus, leads to a reduced turnover rate in the thiocyanate containing binuclear complexes.

### Experimental

Formaldehyde solution, *p*-acetamidophenol, 1 - (2 pyridyl)piperazine, potassium thiocyanate, and 3,5-di-tertbutylcatechol were purchased from Sigma Aldrich and used as such. Methanol, isopropanol, and chloroform were purchased from Sigma Aldrich, are of analytical grade and used as received without purification. The metal salts were in the hydrated form, i.e., CuCl<sub>2</sub>•2H<sub>2</sub>O (copper(II) chloride dihydrate) and FeCl<sub>3</sub>•6H<sub>2</sub>O (iron(III) chloride hexahydrate). Elemental analysis (C, H and N) was obtained using Elementar Analysensysteme VarioMICRO V1.62 GmbH analysis System. NMR spectra (<sup>1</sup>H and <sup>13</sup>C NMR) were acquired in CDCl<sub>3</sub> using Bruker AMX 300 MHz spectrometer with tetramethylsilane (TMS) as an internal standard for <sup>1</sup>H. Attenuated total reflection Fourier transform infrared (ATR-FTIR) spectra for all the samples were recorded on a PerkinElmer Spectrum400 spectrophotometer in the range 4000–650 cm<sup>-1</sup>. Electronic spectra were recorded for the solutions of the synthesized compounds in DMF and DMSO on a Perkin Elmer UV-Vis spectrophotometer model Lamba 25. Molar conductivities were measured in DMSO using a  $10^{-3}$  M solution on AZ 86555 conductivity meter. The melting points were determined on a Gallenkamp melting point apparatus.

### *N*-[4-Hydroxy-3-[[4-(pyridin-2-yl)piperazin-1-

yl]methyl]phenyl]acetamide (HL, C<sub>18</sub>H<sub>22</sub>N<sub>4</sub>O<sub>2</sub>) 10 mmol each of 1-(2-pyridyl)piperazine and paraformaldehyde were stirred in 10 cm<sup>3</sup> of isopropyl alcohol for about 30 min over a steam bath followed by the addition of equimolar quantity of *p*-acetamidophenol dissolved in the same solvent. Reflux was continued for another 4 h with the reaction being monitored by TLC. Standing the reaction mixture for few days at completion led to the formation of white precipitates which were collected and washed with ethanol. Recrystallization was carried out in chloroform/ethanol mixture to give 1.70 g (52%) white crystalline solid of the title substance (Scheme 2). M.p.: 179 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 8.19 (d, 1H, m), 7.49 (dd, 1H, c), 7.35 (t, 1H, k), 7.18 (s, 1H, b), 7.09 (dd, 1H, e), 6.79 (d, 1H, j), 6.67 (t, 1H, l), 6.63 (d, 1H, d); 3.73 (s, 2H, f), 3.57 (t, 4H, i, i'), 2.67 (t, 4H, h, h'), 2.17 (s, 3H, a) ppm; <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 168.2$  (s), 159.3 (s), 154.5 (s), 147.9 (s), 137.60 (s), 129.7 (s), 121.5 (s), 121.2 (s), 116.3 (s), 113.8 (s), 107.8 (s), 61.4 (s), 52.3 (s), 45.0 (s), 24.6 (s) ppm; IR (ATR-FTIR):  $\bar{v} = 3534$  (OH), 1657 (C=N<sub>pvridine</sub>), 1249 (C-O), 1213 and 1142 (C-N-C) cm<sup>-1</sup>; UV–Vis (DMF,  $c = 10^{-3}$  mol dm<sup>-3</sup>):  $\lambda = 270$ ,

299 nm; UV–Vis (DMSO,  $c = 10^{-3} \text{ mol dm}^{-3}$ ):  $\lambda = 289$  nm.

### Synthesis of transition metal complexes

The Cu(II) and Fe(III) complexes were prepared by the following general procedure: 5 mmol of the ligand dissolved in 5 cm<sup>3</sup> of chloroform was added to an equivalent amount of the metal salt dissolved in methanol and stirred at room temperature for 6 h. The synthesis of the thiocyanate complexes involved dissolving an equivalent amount of KSCN in methanol and added to the chloroform solution of the ligand followed by the addition of the solution of the metal salt. The desired products were usually obtained as precipitates after allowing the reaction mixture to stand, once the reaction is completed. This was collected and washed with methanol–chloroform mixture and dried in a desiccator.

### (N,N,N,O)-[N-[4-Hydroxy-3-[[4-(pyridin-2-yl)piperazin-1-

yl]methyl]phenyl]acetamido]copper(II) chloride tetrahydrate ([Cu(HL)Cl<sub>2</sub>]•4H<sub>2</sub>O, 1, C<sub>18</sub>H<sub>30</sub>Cl<sub>2</sub>CuN<sub>4</sub>O<sub>6</sub>) A solution of CuCl<sub>2</sub>•2H<sub>2</sub>O (5.00 mmol) in 5 cm<sup>3</sup> methanol was added gradually to a solution of the ligand (5.00 mmol) in  $5 \text{ cm}^3$ 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, once the reaction is completed. This was collected and washed with methanol-chloroform mixture and dried in a desiccator. Yield 1.42 g (53%) of a brown powder. M.p.: 169 °C; IR (ATR-FTIR):  $\overline{v} = 3337$ (OH), 1641 (C=N<sub>pyridine</sub>), 1248 (C–O), 1162 and 1120 (C–N–C) cm<sup>-1</sup>; UV–Vis (DMF,  $c = 10^{-3} \text{ mol dm}^{-3}$ ):  $\lambda = 278$ , 307, 741 nm; UV–Vis (DMSO,  $c = 10^{-3} \text{ mol dm}^{-3}$ ):  $\lambda = 313$ , 454, 733 nm;  $\Lambda_{\rm M} = 17.88 \ \Omega^{-1} \ {\rm cm}^2 \ {\rm mol}^{-1}$ .

### (*N*,*N*,*N*,*O*)-[*N*-[4-Hydroxy-3-[[4-(pyridin-2-yl)piperazin-1-

yl]methyl]phenyl]acetamido](diaqua)(dithiocyanato)dicopper(II) dichloride dihydrate ([Cu<sub>2</sub>(HL)(NCS)<sub>2</sub>(H<sub>2</sub>O)<sub>2</sub>]Cl<sub>2</sub>•2H<sub>2</sub>O, 2, C<sub>20</sub>H<sub>22</sub>Cl<sub>4</sub>Cu<sub>2</sub>N<sub>6</sub>O<sub>2</sub>S<sub>2</sub>) Compound 2 was prepared in the same way as 1 with the addition of KSCN (5.00 mmol) in 1 cm<sup>3</sup> methanol. Yield 2.01 g (56%) of a light brown powder. M.p.: > 250 °C; IR (ATR-FTIR):  $\bar{\nu} = 3299$  (OH), 2173, 2156 (CN<sub>thiocyanate</sub>), 1642 (C=N<sub>pyridine</sub>), 1244 (C–O), 1180 and 1062 (C–N–C), 868 (CS) cm<sup>-1</sup>; UV–Vis (DMF,  $c = 10^{-3}$  mol dm<sup>-3</sup>):  $\lambda = 260$ , 319, 427, 687 nm; UV–Vis (DMSO,  $c = 10^{-3}$  mol dm<sup>-3</sup>):  $\lambda = 269$ , 324, 775 nm;  $\Lambda_{\rm M} = 78.56 \ \Omega^{-1} \ {\rm cm}^2 \ {\rm mol}^{-1}$ .

### (N,N,N,O)-[N-[4-Hydroxy-3-[[4-(pyridin-2-yl)piperazin-1-

yl]methyl]phenyl]acetamido]iron(III) chloride hexahydrate [Fe(HL)Cl<sub>3</sub>] $\bullet$ 6H<sub>2</sub>O, 3, C<sub>18</sub>H<sub>34</sub>Cl<sub>3</sub>FeN<sub>4</sub>O<sub>8</sub>) Compound 3 was prepared in the same way as 1 using FeCl<sub>3</sub> $\bullet$ 6H<sub>2</sub>O (5.00 mmol) as starting material. Yield 1.81 g (63%) of a

#### Scheme 2



dark brown powder. M.p.: 123 °C; IR (ATR-FTIR): (OH), 1638 (C=N<sub>pyridine</sub>), 1265 (C–O), 1162 and 1112 (C– N–C) cm<sup>-1</sup>; UV–Vis (DMF,  $c = 10^{-3}$  mol dm<sup>-3</sup>):  $\lambda = 269$ , 304, 496 nm; UV–Vis (DMSO,  $c = 10^{-3}$ mol dm<sup>-3</sup>):  $\lambda = 287$ , 370 nm;  $\Lambda_{\rm M} = 44.16 \ \Omega^{-1} \ {\rm cm}^2 \ {\rm mol}^{-1}$ .

## (*N*,*N*,*N*,*O*)-[*N*-[4-Hydroxy-3-[[4-(pyridin-2-yl)piperazin-1yl]methyl]phenyl]acetamido](aqua)dichlorodithiocyana-

todiiron(III) chloride hexahydrate) [Fe<sub>2</sub>(HL)(NCS)<sub>2</sub>(H<sub>2</sub>O)<sub>2</sub>. Cl<sub>2</sub>]Cl<sub>2</sub>•6H<sub>2</sub>O, 4, C<sub>20</sub>H<sub>34</sub>Cl<sub>6</sub>Fe<sub>2</sub>N<sub>6</sub>O<sub>8</sub>S<sub>2</sub>) Compound 4 was prepared in the same way as 3 with the addition of KSCN (5.00 mmol) in 1 cm<sup>3</sup> methanol. Yield 1.98 g (45%) of a brown powder. M.p.: 182 °C; IR (ATR-FTIR):  $\overline{v} = 3260$ (OH), 2051 (CN<sub>thiocyanate</sub>), 1652 (C=N<sub>pyridine</sub>), 1251 (C–O), 1161 and 1129 (C–N–C), 737 (CS) cm<sup>-1</sup>; UV–Vis (DMF,  $c = 10^{-3} \mod dm^{-3}$ ):  $\lambda = 272$ , 302, 472 nm; UV–Vis (DMSO,  $c = 10^{-3} \mod dm^{-3}$ ):  $\lambda = 291$ , 350 nm;  $\Lambda_{\rm M} = 83.30 \ \Omega^{-1} \ cm^2 \ mol^{-1}$ .

#### **Kinetic assays**

Before proceeding into the detailed kinetic study, the ability of the Cu(II) and Fe(III) complexes to oxidize 3,5-DTBC was evaluated. For this purpose,  $1 \times 10^{-4}$  mol dm<sup>-3</sup> solutions of complexes **1–4** were treated with  $1 \times 10^{-2}$  mol dm<sup>-3</sup> (100 equivalents) of 3,5-DTBC under aerobic condition. The course of the reaction was followed by UV–Vis spectroscopy. Time-dependent UV–Vis spectral scan was performed in pure DMF. All the complexes behaved similarly, showing a smooth conversion of 3,5-DTBC into 3,5-DTBQ which was purified by column chromatography. The kinetics of the oxidation of 3,5-DTBC oxidation was determined at room temperature by

monitoring the increase in the absorbance of the product 3,5-DTBQ using 20–100 equivalents of 3,5-DTBC with  $10^{-4}$  M solutions of the metal complexes.

Kinetic experiments were conducted in duplicates with 20–100 equiv. of 3,5-DTBC. To determine if hydrogen peroxide was formed as the reduced oxygen species during the 3,5-DTBC oxidation, reaction mixtures were prepared as described above in the kinetic experiments. After 1 h of reaction, an equal volume of water was added and the quinone formed was extracted three times with dichloromethane. The aqueous layer was acidified with H<sub>2</sub>SO<sub>4</sub> to pH = 2 to stop further oxidation, followed by the addition of 1 cm<sup>3</sup> of a 10% solution of KI and three drops of 3% solution of ammonium molybdate. In the presence of hydrogen peroxide, the following reaction occurs:

$$H_2O_2 + 2I^- + 2H^+ \rightarrow 2H_2O + I_2$$

and with an excess of iodide ions, the triiodide ion is formed according to the reaction

$$I_2(aq) + I^- \rightarrow I^{3-}$$
.

The increase in the  $I^{3-}$  absorption band at 353 nm ( $\varepsilon = 26,000 \text{ M}^{-1} \text{ cm}^{-1}$ ) was monitored by UV–Vis spectroscopy [46, 47]. The isolation of the product 3,5-di-*tert*-butylquinone (3,5-DTBQ) was achieved and identified by <sup>1</sup>H NMR spectroscopy.

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