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Design and Fine-Tuning Redox Potentials of Manganese(II) Complexes with Isoindoline-Based Ligands: H₂O₂ Oxidation and Oxidative Bleaching Performance in Aqueous Solution

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Abstract: A series of divalent manganese complexes [M^{II}(HL^{1–6})Cl₂] with the 1,3-bis(2'-Ar-imino)isoindolines (HLⁿ, n = 1–6, Ar = pyridyl, 4-methylpyridyl, imidazolyl, thiazolyl, benzimidazolyl and N-methylbenzimidazolyl, respectively) including the previously reported ligands (HL^{1–2, 4–6}) and complexes ([M^{II}(HL^{1,5})Cl₂]) have been prepared and characterized by electrochemical and spectroscopic methods. In these complexes, it was possible to control the redox potential of the metal center by varying the aryl substituent on the bis-iminoisoindoline moiety, and investigate its effect in a catalase-like reaction, and oxidative bleaching process in buffered aqueous solution. The kinetics of the dismutation of H₂O₂ into H₂O and O₂, and the oxidative degradation of morin by H₂O₂ were investigated in buffered water, where the reactivity of the catalysts in both systems was markedly influenced by the redox and Lewis acidic properties of the metal centers and the concentration of the bicarbonate ions. Both the catalase-like and bleaching activity of the catalysts showed a linear correlation with the Mn^{III}/Mn^{II} redox potentials. The E_{1/2} spans a 561 mV range from 388 mV (Ar = benzimidazolyl) to 948 mV (Ar = 4-methylpyridyl) vs. the SCE. The amount of bicarbonate is a critical issue for the in situ formation of peroxycarbonate as a versatile oxidant, and its participation in the formation of high valent Mn^{IV} = O species.

Keywords: manganese complexes; isoindolines; catalase activity; bleach catalyst; oxidation

1. Introduction

1,3-bis(2'-Ar-imino)isoindolines are pincer type ligands with a tridentate coordination mode and aromatic planarity around the metal centers [1]. They can behave either as monoanionic or protonated ligands during the complexation reaction (Scheme 1). Manganese ion as redox center plays an important role in many oxidoreductases such as manganese-containing ribonucleotide reductase (RNS) from *Corynebacterium* [2], heme-type peroxidase (MnP) from the *Aspergillus* species [3–5] and non-heme-type binuclear catalases (MnCat) from *Lactobacillus plantarum* [6,7], *Thermus thermophilus* [8,9] and *Thermoleophilum album* [10]. These enzymes are responsible for many types of oxidative processes in biological systems. For example, MnCat enzymes, as important alternatives to heme-type catalases, catalyze the redox disproportionation of hydrogen peroxide into dioxygen and water, protecting the living organisms from the reactive oxygen species (ROS) induced “oxidative stress” reactions [11,12], while the ribonucleotide reductases provide the DNA precursors, deoxyribonucleotides required for DNA replication and repair in all living organisms [2]. Finally, the MnP can oxidize Mn(II) to Mn(III) and in turn oxidizes the phenolic moieties of lignin and some organic pollutants. MnP has also been shown to promote the peroxidation of unsaturated lipids in the absence of H₂O₂. After the discovery

of lignolytic enzymes such as MnP, the pulp industry had great expectations with regard to developing cell-free enzymatic delignification and/or a bleaching system in its industrial processes [13,14].

Scheme 1. Structure of the 1,3-bis(2'-Ar-imino)isoindoline ligands involved in this study.

Many synthetic biomimetics of catalase and peroxidase are being developed as potential therapeutic agents against cancer, Alzheimer's aging and inflammatory and heart diseases [15–18], and as efficient catalytic systems for the degradation of various pollutants and bleaching which can be applied for example in food, dairy and textile industries [19–24]. Recently, we synthesized and characterized a series of mononuclear transition metal complexes with $[M^{II}(L^n)_2]$ ($M = \text{Fe(II)}$ [25], Mn(II) [26,27], Ni(II) [27], Co(II) [28] and Cu(II) [29], $n = 1, 2$ and $4-6$), $[\text{Fe}^{III}(L^n)\text{Cl}_2]$ [30], $[\text{Cu}^{II}(\text{HL}^n)\text{X}_2]$ ($\text{X} = \text{ClO}_4, \text{Cl}$, $n = 1, 2$ and $4-6$) [29] and $[\text{Mn}^{II}(\text{HL}^{1 \text{ and } 5})\text{Cl}_2]$ [31,32] compositions, and used as biomimetics of superoxide dismutase (SOD) [27], catalase [26,31,32], phenoxazinone synthase, catechol oxidase [33] and dioxygenase [30] enzymes. As a continuity of our research, we synthesized the analogs of $[\text{Mn}^{II}(\text{HL}^{2-4, \text{ and } 6})\text{Cl}_2]$ complexes as catalysts against H_2O_2 , and morin by the use of H_2O_2 as an oxidant in context with the ligand modification by varying the aryl substituent on the bis-iminoisoindoline moiety and redox chemistry. These systems may serve as functional models for the MnCat enzyme, and furthermore, the title complexes could serve as potential candidates for oxidative delignification and/or bleaching performance.

2. Results and Discussion

2.1. Synthesis and Characterization of $[\text{Mn}^{II}(\text{HL}^n)\text{Cl}_2]$ Complexes

The synthesis of the new 1,3-bis(2'-imidazolyl)isoindoline ligand was carried out according to the literature by the reaction of 1,3-diiminoisoindoline with two equivalents of 2-amino-imidazole sulfate in 1-butanol in the presence of sodium carbonate [1]. It was characterized by electronic, ^1H -NMR, ^{13}C -NMR, IR and UV-vis measurements. Reaction of equimolar amounts of 1,3-bis(2'-Ar-imino)isoindoline and $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$ in methanol resulted in the formation of mononuclear pentacoordinate complexes with $[\text{Mn}^{II}(\text{HL}^n)\text{Cl}_2]$ composition ($\text{Ar} = \text{pyridyl}$ ($n = 1$), 4-methylpyridyl ($n = 2$), imidazolyl ($n = 3$), thiazolyl ($n = 4$), benzimidazolyl ($n = 5$) and *N*-methylbenzimidazolyl ($n = 6$)). In the infrared region, the free and the nondeprotonated isoindoline ligands exhibit intense bands in the $1600\text{--}1660\text{ cm}^{-1}$ region that can be assigned as coupled nonspecific $\nu_{\text{C=N}}$ vibrations which can be explained by the two different endocyclic and exocyclic position of the amino groups, and one additional weak absorption around 3300 cm^{-1} , characteristic of a nondeprotonated (ν_{NH}) isoindoline ligand [1]. Absorption maxima in the UV-vis spectra of $[\text{Mn}^{II}(\text{HL}^{1-6})\text{Cl}_2]$ that are found between 350 and 500 nm can be assigned to the $\pi\text{--}\pi^*$ transitions of the coordinated neutral ligands, except for the lowest energy bands in the range of 450–600 nm, which can be attributed to charge transfer transitions from the manganese(II) ion to a ligand π^* orbital (LUMO, MLCT; Figure 1). Deprotonation of the

NH group of the isoindoline moiety could be reduced the difference in energy between occupied and unoccupied π -molecular orbitals of the ligand resulting in a red shift of π - π^* transitions. In the absence of the significant (>40 nm) bathochromic shift in the three lowest energy bands, the anionic binding of the ligands can be excluded in all cases [1].

Figure 1. Electronic spectra of $[\text{Mn}^{\text{II}}(\text{HL}^n)\text{Cl}_2]$ ($\text{HL} = 1,3\text{-bis}(2'\text{-Ar-imino})\text{isoindoline}$) complexes in DMF solution with nonannulated ($\text{Ar} = \text{pyridyl}$ ($n = 1$), 4-methylpyridyl ($n = 2$), imidazolyl ($n = 3$), thiazolyl ($n = 4$)), aromatic side chains (A) and annulated $\text{Ar} = \text{benzimidazolyl}$ ($n = 5$) and N -methylbenzimidazolyl ($n = 6$) aromatic side chains (B).

Redox properties of the model complexes $[\text{Mn}^{\text{II}}(\text{HL}^{1-6})\text{Cl}_2]$ were also examined in cyclic voltammetry (CV) experiments in DMF (Figure 2). Electrochemical data for the complexes are listed in Table 1 in mV at 100 mV/s scan rate. The $E_{1/2}$ spans a 561 mV range from 388 mV ($\text{Ar} = \text{benzimidazolyl}$) to 948 mV ($\text{Ar} = 4\text{-methylpyridyl}$) vs. the SCE. A narrower range (400 to 600 mV versus SCE) with lower potentials was observed for the recently studied $\text{Mn}^{\text{II}}(\text{L})_2$ complexes. Compound $[\text{Mn}^{\text{II}}(\text{HL}^3)\text{Cl}_2]$ (3) undergoes an irreversible transition in the observed potential range in contrast to the quasi-reversible transition of 1–2 and 4–6. It can be concluded that the annulation of the imidazolyl group results in a shift (~ 400 mV) in the $\text{Mn}^{\text{III}}/\text{Mn}^{\text{II}}$ potentials and stabilizes both the reduced and oxidized forms of the transition (see 5 and 6 in Figure 2). Surprisingly, the applied ligand affects not only the formal potential, but the peak separations ($\Delta E_p = E_{pa} - E_{pc}$), too. Significantly larger values (120–140 mV) were observed for the $[\text{Mn}^{\text{II}}(\text{HL}^{1-2})\text{Cl}_2]$ complexes with 6-membered pyridyl side chains than those found for $[\text{Mn}^{\text{II}}(\text{HL}^{4-6})\text{Cl}_2]$ with five-membered N -donor thiazolyl and benzimidazolyl containing side chains.

Table 1. Electrochemical and spectroscopic data for $[\text{Mn}^{\text{II}}(\text{HL}^{1-6})\text{Cl}_2]$ complexes.

Catalyst	E_{pa} (mV)	E_{pc} (mV)	$E_{1/2}^0$ (mV vs SCE)	$\Delta E_p = E_{pa} - E_{pc}$ (mV)	$\lambda_{\text{max}}(\pi-\pi^*)^1$ (nm)	ν_1 ($\lambda_{\text{max}}^{-1}$) ¹ (10^4cm^{-1})	ν_2 ($\lambda_{\text{max}}^{-1}$) ² (10^4cm^{-1})
$[\text{Mn}(\text{HL}^1)\text{Cl}_2]$ (1)	987	865	926	122	386	2.591	2.174
$[\text{Mn}(\text{HL}^2)\text{Cl}_2]$ (2)	1016	880	948	136	366	2.73	2.188
$[\text{Mn}(\text{HL}^3)\text{Cl}_2]$ (3)	816	-	-	131	391	2.56	2.128
$[\text{Mn}(\text{HL}^4)\text{Cl}_2]$ (4)	625	573	600	52	419	2.39	2.028
$[\text{Mn}(\text{HL}^5)\text{Cl}_2]$ (5)	421	354	388	67	455	2.20	1.859
$[\text{Mn}(\text{HL}^6)\text{Cl}_2]$ (6)	455	395	425	60	448	2.23	1.894

¹ Charge transfer (CT), ² ligand-to-metal charge transfer (LMCT) bands.

Figure 2. Cyclic voltammetry of the $[\text{Mn}^{\text{II}}(\text{HL}^n)\text{Cl}_2]$ ($\text{HL} = 1,3\text{-bis}(2'\text{-Ar-imino})\text{isoindoline}$; $\text{Ar} = \text{pyridyl}$ ($n = 1$), 4-methylpyridyl ($n = 2$), imidazolyl ($n = 3$), thiazolyl ($n = 4$), benzimidazolyl ($n = 5$) and $N\text{-methylbenzimidazolyl}$ ($n = 6$)) complexes in DMF at 25 °C.

More importantly, a linear correlation was found between the energy of the $\pi\text{-}\pi^*$ (charge transfer (CT)) absorption (and ligand-to-metal charge transfer (LMCT)) band (ν_1 and $\nu_2 = \lambda_{\text{max}}^{-1}$, respectively) and the oxidation potential, E_{pa} of the manganese center of the $[\text{Mn}^{\text{II}}(\text{HL}^{1-6})\text{Cl}_2]$ complexes (Figure 3A,B), indicating that the observed shift in the p-p* and LMCT absorption bands can be assigned indirectly to the electronic effect of the ligands (Figure 3). This feature can be attributed to the oxidation of the metal center ($\text{Mn}^{\text{II}}/\text{Mn}^{\text{III}}$) being sensitive to the isoindoline ligand used in this study.

Figure 3. Correlation between the oxidation potential of the $[\text{Mn}^{\text{II}}(\text{HL}^{1-6})\text{Cl}_2]$ complexes and the energy of the $\pi\text{-}\pi^*$ absorption band (A). Correlation of the oxidation potential of the $[\text{Mn}^{\text{II}}(\text{HL}^{1-6})\text{Cl}_2]$ complexes and the energy of the LMCT absorption band (B) in DMF.

2.2. Catalase-Like Reactivity of $[\text{Mn}^{\text{II}}(\text{HL}^{1-7})\text{Cl}_2]$ Complexes in Aqueous Solution

It was found earlier that the manganese-catalyzed disproportionation of H_2O_2 at physiological pH occurs only in the bicarbonate (HCO_3^-) containing buffer solution [34]. Recent work in our group has found that complex $[\text{Mn}^{\text{II}}(\text{HL}^1)\text{Cl}_2]$ in bicarbonate buffer solution catalyzes the disproportionation of H_2O_2 into water and O_2 , and its reactivity increases with the increasing pH and goes through a

maximum (pH ~9.6). Under this condition, the reaction rate is directly proportional to the concentration of Mn(II) and shows Michaelis–Menten-type saturation kinetics on $[\text{H}_2\text{O}_2]_0$ ($V_{\text{max}} = 8.1 \times 10^{-3} \text{ Ms}^{-1}$, $K_M = 489 \text{ mM}$, $k_{\text{cat}} = 38 \pm 2 \text{ s}^{-1}$ and $k_2(k_{\text{cat}}/K_M) = 79 \pm 4 \text{ M}^{-1}\text{s}^{-1}$) at pH 9.5 by the use of carbonate buffer [32]. Thus, we attempted to investigate the effect of the HCO_3^- and prepare new isoindoline-based manganese catalysts by introducing different side chains at the imine functions in order to elucidate the role of electronic factors, and obtain a new catalyst with an increase of its stability and reactivity in the catalase-like reaction.

Catalase activity was carried out volumetrically via the measurements of dioxygen evolution at 20 °C in bicarbonate buffers at pH 9.6. Experiments by Stadtman [34] show that the bicarbonate concentration increases with increasing pH and the effect of pH on the manganese-dependent disproportionation of H_2O_2 can be assigned to the bicarbonate content alone. Similarly to the previously published results, the initial rate of the reaction (V_0) is a linear function of the bicarbonate concentration, suggesting that one equivalent of HCO_3^- is coordinated to the manganese center during the formation of the catalytically active complex. The first-order dependence with respect to the concentration of bicarbonate is shown in Figure 4. It can be seen that a 10-fold increase in bicarbonate concentration results in a two-fold increase in the rate of H_2O_2 disproportionation. The increase in the reaction rate may be explained by the formation of the versatile oxidizing agent, HCO_4^- , from the reaction of H_2O_2 with HCO_3^- . Earlier studies led to the proposition that the dismutation of hydrogen peroxide undergoes redox cycling between Mn(II), Mn(III) and Mn(IV) species [19,35]. The results of previous kinetic studies, as well as the results described here, may suggest both the formation of high valent $\text{Mn}^{\text{IV}}\text{O}$ species in Route 1 (Scheme 2) and carbonate radical in Fenton-type chemistry in Route 2 (Scheme 2, [34]) as key catalytic intermediates which may lead to the dismutation of H_2O_2 . We believe that bicarbonate ions act upon the redox potential of an Mn(II) complex.

Scheme 2. Proposed mechanisms for dismutation of H_2O_2 by $[\text{Mn}^{\text{II}}(\text{HL}^{1-6})\text{Cl}_2]$ complexes.

In the next step, we investigated the effect of the ligand modification by varying the aryl substituent on the bis-iminoisoindoline moiety with emphasis on the redox potential and Lewis acidity of the catalyst that may serve as guidelines for the synthesis of more active and more selective catalysts. The six manganese complexes, $[\text{Mn}^{\text{II}}(\text{HL}^{1-6})\text{Cl}_2]$ and the MnCl_2 salt have been compared to investigate the effect of the various aryl substituents (Figures 5 and 6). Figure 5 shows the results of the catalase activity for the $[\text{Mn}^{\text{II}}(\text{HL}^{1-6})\text{Cl}_2]$ complexes and demonstrates significant differences based on the number of H_2O_2 molecules (TON = turnover number) disproportionate by one molecule of the complex after four minutes (240 s). The turnover frequency (TOF = $\text{mol H}_2\text{O}_2/\text{mol catalyst/h}$) values, which present the ratios of initial rates ($-\text{d}[\text{H}_2\text{O}_2]/\text{dt}$) and concentrations of catalysts, are given in Table 2. It was found that complex $[\text{Mn}^{\text{II}}(\text{HL}^2)\text{Cl}_2]$ with nonannulated 4-methylpyridyl side chains is the most efficient catalyst with the fastest rate observed at $0.682 \times 10^{-3} \text{ Ms}^{-1}$ and approximately 6.5

(TOF) molecules of H_2O_2 broken down per second at the fastest rate of activity (V_0), while complex $[\text{Mn}^{\text{II}}(\text{HL}^5)\text{Cl}_2]$ with annulated benzimidazolyl side chains is a less efficient catalase mimic when compared to complex **2** with the fastest rate of $0.187 \times 10^{-3} \text{ Ms}^{-1}$ and a TOF of 1.77 s^{-1} for H_2O_2 . Based on these results the lower activity may be due to the annulated aromatic side chains within the ligand system which may prevent access of H_2O_2 to the manganese center (steric effect) and/or the unfavorable redox and Lewis acidic properties of the catalyst.

Figure 4. Kinetic analysis for the hydrogen peroxide degradation catalyzed by MnCl_2 and $[\text{Mn}^{\text{II}}(\text{HL}^1)\text{Cl}_2]$ (**1**) in bicarbonate buffer (pH = 9.6). (A) Time traces for the reaction of MnCl_2 and **1** with H_2O_2 in the presence of bicarbonate. (B) Dependence of the reaction rate on the bicarbonate concentration for the $[\text{Mn}^{\text{II}}(\text{HL}^1)\text{Cl}_2]$ -catalyzed disproportionation of H_2O_2 . Conditions: $[\text{1 or MnCl}_2]_0 = 2.11 \times 10^{-4} \text{ M}$, $[\text{H}_2\text{O}_2]_0 = 4.47 \times 10^{-1} \text{ M}$ at 20°C .

Figure 5. Comparison of the catalase-like activity of $[\text{Mn}^{\text{II}}(\text{HL}^n)\text{Cl}_2]$ (**1**–**6**, $\text{HL}^n = 1,3\text{-bis}(2'\text{-Ar-imino})\text{isoindoline}$, Ar = pyridyl ($n = 1$), 4-methylpyridyl ($n = 2$), imidazolyl ($n = 3$), thiazolyl ($n = 4$), benzimidazolyl ($n = 5$) and $N\text{-methylbenzimidazolyl}$ ($n = 6$) complexes in bicarbonate buffer (pH = 9.6). Conditions: $[\text{Mn}]_0 = 2.11 \times 10^{-4} \text{ M}$, $[\text{H}_2\text{O}_2]_0 = 4.47 \times 10^{-1} \text{ M}$ at 20°C .

Table 2. Comparison of the catalase-like activity of $[\text{Mn}^{\text{II}}(\text{HL}^n)\text{Cl}_2]$ (**1**–**6**) complexes in bicarbonate buffer (pH = 9.6; $\text{HL}^n = 1,3\text{-bis}(2'\text{-Ar-imino})\text{isoindoline}$, Ar = pyridyl ($n = 1$), 4-methylpyridyl ($n = 2$), imidazolyl ($n = 3$), thiazolyl ($n = 4$), benzimidazolyl ($n = 5$) and $N\text{-methylbenzimidazolyl}$ ($n = 6$)).

Catalyst ¹	E^0_{pa} (mV)	E^0_{pc} (mV)	$E^0_{1/2 \text{ vs SCE}}$ (mV)	Yield (%)	TON	V_0 (10^{-3} Ms^{-1})	TOF (h^{-1})
$[\text{Mn}(\text{HL}^1)\text{Cl}_2]$ (1)	987	865	926	32.6	692	0.569	19416
$[\text{Mn}(\text{HL}^2)\text{Cl}_2]$ (2)	1016	880	948	36.6	775	0.682	23272
$[\text{Mn}(\text{HL}^3)\text{Cl}_2]$ (3)	816	685	750	27.1	574	0.422	13820
$[\text{Mn}(\text{HL}^4)\text{Cl}_2]$ (4)	625	573	600	21.8	463	0.328	12012
$[\text{Mn}(\text{HL}^5)\text{Cl}_2]$ (5)	421	354	388	16.9	320	0.187	6382
$[\text{Mn}(\text{HL}^6)\text{Cl}_2]$ (6)	455	395	425	15.13	357	0.204	6962
$\text{MnCl}_2/\text{HCO}_3^-$	-	-	-	8.88	188	0.081	1382

¹ Conditions: $[\text{Mn}]_0 = 2.11 \times 10^{-4} \text{ M}$, $[\text{H}_2\text{O}_2]_0 = 4.47 \times 10^{-1} \text{ M}$ at 20°C .

Since the redox potential of the catalysts can be measured under the same conditions, it can be used as an excellent reactivity descriptor. By the use of these data, we have clear evidence that the activity (V_0) increases almost linearly with the redox potential (E_{pa} for Mn^{III}/Mn^{II}) of the catalyst (Figure 6). This finding also suggests that the redox potential of the catalysts acts as the driving force of the reaction, and the dismutation would most likely involve the $Mn(II)/Mn(IV)O$ redox couple (Scheme 2), similarly to what was proposed for the peroxynitrite reductase activity of the manganese porphyrin system [36–40]. The redox potential values of the Mn^{III}/Mn^{II} redox couple describe the propensity of the manganese(II) complexes to react with the nucleophilic HO_2^- and/or HCO_4^- ; where the more electron-deficient metal center has a much higher affinity for HO_2^- and/or HCO_4^- binding. In summary, the higher the redox potentials of the Mn^{III}/Mn^{II} redox couple, the higher is the catalase-like activity, $\log V_0$. $[Mn^{II}(HL^{1-2})Cl_2]$ (1–2) complexes with pyridyl side chains, whose metal sites are electron-deficient and faster in catalyzing H_2O_2 disproportionation than electron-rich derivatives $[Mn^{II}(HL^{5-6})Cl_2]$ (5–6) with more Lewis basic benzimidazolyl side chains.

Figure 6. Kinetic analysis for the hydrogen peroxide degradation catalyzed by $[Mn^{II}(HL^{1-6})Cl_2]$ (1–6) complexes in bicarbonate buffer (pH = 9.6). (A) Time traces for the reaction of $[Mn^{II}(HL^{1-6})Cl_2]$ (1–6) complexes with H_2O_2 in the presence of bicarbonate. (B) Dependence of the reaction rate on the oxidation potential (E_{pa}) of the $[Mn^{II}(HL^{1-6})Cl_2]$ complexes for the $[Mn^{II}(HL^1)Cl_2]$ -catalyzed disproportionation of H_2O_2 . Conditions: $[1-6]_0 = 2.11 \times 10^{-4}$ M, $[H_2O_2]_0 = 4.47 \times 10^{-1}$ M at 20 °C.

2.3. Oxidative Degradation of Morin: $[Mn^{II}(HL^{1-6})Cl_2]$ Complexes as Bleaching Catalysts

Several manganese complexes with terpyridine, Schiff base, 1,4,7-triazacyclononane and *N*-methylpropanoate (*N*-propanoate)-*N,N*-bis-(2-pyridylmethyl)amine [41] ligands have been tested earlier as bleaching catalysts, where generally high-valent oxo species, $LMn^{IV}(O)$ or $LMn^V(O)$, have been proposed as key oxidants [42]. In order to evaluate the bleaching potential of $[Mn^{II}(HL^{1-6})Cl_2]$ complexes, we investigated the oxidation of morin (2',3,4',5,7-pentahydroflavone), which can be considered as a good model compound for bleaching stain. Experiments were carried out at 25 °C with 1.6 μ M catalyst, and the oxidation of morin was followed as the decrease in absorbance at 410 nm (Scheme 3, Figure 7A).

Scheme 3. Catalytic oxidation of morin by $[\text{Mn}^{\text{II}}(\text{HL}^{1-6})\text{Cl}_2]$ complexes.

Under this condition as described previously for terpyridine manganese complexes [22], the best activity was observed for $[\text{Mn}^{\text{II}}(\text{HL}^2)\text{Cl}_2]$ (**2**) where the bleaching of morin was completed within five minutes with approximately 20 catalytic cycles per minute (Figure 7B). From our detailed kinetic measurements, the rate of morin decomposition is described by the relationship $-d[\text{morin}]/dt = V = k_{\text{ox}}[1-6][\text{H}_2\text{O}_2][\text{HCO}_3^-][\text{morin}]$, where $k_{\text{ox}} = 7.79 \times 10^6 \text{ M}^{-3}\text{s}^{-1}$ for **1** and $0.675 \times 10^6 \text{ M}^{-3}\text{s}^{-1}$ for **5** (Figure 8, Tables 3 and 4). The catalytic activity of the 4-methylpyridyl containing manganese complex (**2**) was at least 10–12 times higher than that of $[\text{Mn}^{\text{II}}(\text{HL}^5)\text{Cl}_2]$ (**5**) with benzimidazolyl side chains. At low substrate concentration, the reaction is first-order on all reactants; H_2O_2 (Figure 8A), HCO_3^- (Figure 8B), $[\text{Mn}^{\text{II}}(\text{HL}^1)\text{Cl}_2]$ (Figure 8C) and morin (Figure 8D). It is worth noting that the bicarbonate concentration similarly to our previous results plays an important role in the bleaching process, probably during the formation of the catalytically active $\text{Mn}^{\text{IV}}(\text{O})$ species (Scheme 2), which can easily oxidize the morin in an intermolecular or intramolecular manner. In separate experiments under air without H_2O_2 , we found clear evidence for the complexation ($\sim 4\text{--}500 \text{ nm}$) and for the slow base-catalyzed oxidation of morin (Figure 9) [43–46]. Based on these results, the intramolecular oxidation of the coordinated morin cannot be excluded.

Figure 7. (A) Time-dependent UV-vis spectra of a 0.16 mM solution of morin at pH 10 in the presence of 10 mM H_2O_2 and 1.6 μM $[\text{Mn}^{\text{II}}(\text{HL}^1)\text{Cl}_2]$ (**1**) at 25 °C. (B) Typical kinetic traces of morin oxidation catalyzed by $[\text{Mn}^{\text{II}}(\text{HL}^{1-6})\text{Cl}_2]$ (**1–6**) complexes. Conditions: $[\text{morin}]_0 = 0.16 \text{ mM}$, $[\text{H}_2\text{O}_2]_0 = 10 \text{ mM}$, $[1-6]_0 = 1.6 \mu\text{M}$, pH = 10, at 25 °C.

Table 3. Summary of kinetic data for the catalytic oxidation of morin with $[\text{Mn}(\text{HL}^1)\text{Cl}_2]$ (1) in bicarbonate buffer at pH 10 and 25 °C.

Catalyst (1) (10^{-6}M)	$[\text{H}_2\text{O}_2]$ (10^{-3}M)	$[\text{HCO}_3^-]$ (10^{-3}M)	$[\text{Morin}]$ (10^{-3}M)	k_{obs} (10^{-3}s^{-1})	k_{ox} ($10^6\text{M}^{-3}\text{s}^{-1}$)
0.62	10	50	0.16	1.63 ± 0.06	5.26 ± 0.2
1.6	10	50	0.16	4.19 ± 0.16	5.24 ± 0.2
2.5	10	50	0.16	6.73 ± 0.37	5.38 ± 0.3
0.62	10	50	0.16	1.63 ± 0.06	5.33 ± 0.2
0.62	7.5	50	0.16	1.22 ± 0.05	5.25 ± 0.2
0.62	5.0	50	0.16	0.78 ± 0.02	5.12 ± 0.1
0.62	2.5	50	0.16	0.41 ± 0.01	5.29 ± 0.2
0.62	10	50	0.16	1.63 ± 0.06	5.26 ± 0.2
0.62	10	100	0.16	3.02 ± 0.06	5.24 ± 0.1
0.62	10	200	0.16	7.01 ± 0.13	5.24 ± 0.1
0.62	10	300	0.16	10.5 ± 0.6	5.37 ± 0.3
0.62	10	50	0.16	1.63 ± 0.06	5.26 ± 0.2
0.62	10	50	0.12	1.65 ± 0.03	5.32 ± 0.1
0.62	10	50	0.08	1.70 ± 0.06	5.48 ± 0.2
0.62	10	50	0.04	1.73 ± 0.06	5.5 ± 0.2

Figure 8. Catalytic oxidation of morin with $[\text{Mn}(\text{HL}^1)\text{Cl}_2]$ (1) in bicarbonate buffer at pH 10 and 25 °C. (A) Dependence of the first-order rate constant (k_{obs}) for morin oxidation on the H_2O_2 concentration (Table 3). (B) Dependence of the first-order rate constant (k_{obs}) for morin oxidation on the HCO_3^- concentration (Table 3). (C) Dependence of the first-order rate constant (k_{obs}) for morin oxidation on the $[\text{Mn}(\text{HL}^1)\text{Cl}_2]$ (1) concentration (Table 3). (D) Dependence of the reaction rate (V_0) for morin oxidation on the morin concentration (Table 3).

Table 4. Summary of kinetic data for the catalytic oxidation of morin with $[\text{Mn}(\text{HL}^{1-6})\text{Cl}_2]$ (1–6) in bicarbonate buffer at pH 10 and 25 °C.

Catalyst ¹	E_{pa}^0 (mV)	E_{pc}^0 (mV)	$E_{1/2}^0$ vs SCE (mV)	k_{obs} (10^{-3} s^{-1})	k_{ox} ($106 \text{ M}^{-3} \text{ s}^{-1}$)
$[\text{Mn}(\text{HL}^1)\text{Cl}_2]$ (1)	987	865	926	4.194 ± 0.126	5.241 ± 0.161
$[\text{Mn}(\text{HL}^2)\text{Cl}_2]$ (2)	1016	880	948	6.230 ± 0.156	7.790 ± 0.192
$[\text{Mn}(\text{HL}^3)\text{Cl}_2]$ (3)	816	685	750	2.171 ± 0.086	2.713 ± 0.108
$[\text{Mn}(\text{HL}^4)\text{Cl}_2]$ (4)	625	573	600	1.101 ± 0.022	1.376 ± 0.028
$[\text{Mn}(\text{HL}^5)\text{Cl}_2]$ (5)	421	354	388	0.541 ± 0.015	0.676 ± 0.018
$[\text{Mn}(\text{HL}^6)\text{Cl}_2]$ (6)	455	395	425	0.780 ± 0.021	0.975 ± 0.026
-	-	-	-	0.0076 ± 0.0002	-

¹ Conditions: $[\text{morin}]_0 = 0.16 \text{ mM}$, $[\text{H}_2\text{O}_2]_0 = 10 \text{ mM}$, $[1-6]_0 = 1.6 \text{ }\mu\text{M}$, pH = 10, at 25 °C.

The activity of the isoindolin complexes increases significantly in the order of $[\text{Mn}(\text{HL}^5)\text{Cl}_2]$ (5) < $[\text{Mn}(\text{HL}^6)\text{Cl}_2]$ (6) < $[\text{Mn}(\text{HL}^4)\text{Cl}_2]$ (4) < $[\text{Mn}(\text{HL}^3)\text{Cl}_2]$ (3) < $[\text{Mn}(\text{HL}^1)\text{Cl}_2]$ (1) < $[\text{Mn}(\text{HL}^2)\text{Cl}_2]$ (2). Hence, by changing the more Lewis basic five-membered benzimidazolyl rings to six-membered pyridyl pendant arms, the catalytic activity can be remarkably enhanced. Furthermore, the calculated k_{ox} for 1–6 correlate with the observed oxidation potentials, E_{pa} ($\text{Mn}^{\text{III}}/\text{Mn}^{\text{II}}$), giving further evidence that the activity of the catalyst can be controlled by the modification of electron donor properties of the ligand (Figure 10). A similar correlation has been described previously for our catalase-like system (Figure 6B), suggesting that the same oxidant ($\text{Mn}^{\text{IV}}(\text{O})$) is responsible for the decomposition of H_2O_2 and morin.

Figure 9. Time-dependent UV-vis spectra of a 0.16 mM solution of morin at pH 10 in the presence of 1.6 μM $[\text{Mn}^{\text{II}}(\text{HL}^1)\text{Cl}_2]$ (1) under air at 25 °C without H_2O_2 . (B) Kinetic traces of complexation and oxidation of morin. **Figure 10.** Dependence of the first-order rate constant (k_{obs}) for morin oxidation on the oxidation potential (E_{pa}) of the $[\text{Mn}^{\text{II}}(\text{HL}^{1-6})\text{Cl}_2]$ complexes in bicarbonate buffer (pH 10). Conditions: $[1-6]_0 = 1.6 \times 10^{-6} \text{ M}$, $[\text{morin}]_0 = 0.16 \times 10^{-3} \text{ M}$, $[\text{H}_2\text{O}_2]_0 = 0.010 \text{ M}$ at 25 °C.

3. Materials and Methods

3.1. Materials and Methods

The ligands 1,3-bis(2'-pyridylimino)isoindoline (HL¹), 1,3-bis(4'-methyl-2'-pyridylimino)isoindoline (HL²), 1,3-bis(2'-thiazolylimino)isoindoline (HL⁴), 1,3-bis(2'-benzimidazolylimino)isoindoline (HL⁵) and 1,3-bis(2'-N-methyl-benzimidazolylimino)isoindoline (HL⁶), and the complexes [Mn^{II}(HL^{1 and 6})Cl₂] were synthesized according to published procedures [1]. All manipulations were performed under a pure argon atmosphere using standard Schlenk-type inert-gas techniques. Solvents used for the reactions were purified by literature methods and stored under argon. The starting materials for the ligand are commercially available and they were purchased from Sigma-Aldrich Kft. (Budapest, Hungary).

The UV–visible spectra were recorded on an Agilent 8453 diode-array spectrophotometer (Agilent Technologies, Hewlett-Packard-Strasse 8, Waldbronn, Germany) using quartz cells. IR spectra were recorded using a Thermo Nicolet Avatar 330 FT-IR instrument (Thermo Nicolet Corporation, Madison, WI, USA). Samples were prepared in the form of KBr pellets. The NMR spectrum was recorded on a Bruker Avance 400 spectrometer (Bruker Biospin AG, Fällanden, Switzerland). Elemental analysis was done by the Microanalytical Service of the University of Pannonia. Cyclic voltammograms (CV) were taken on a Volta Lab 10 potentiostat with Volta Master 4 software for data processing. The electrodes were as follows: glassy carbon (working), Pt wire (auxiliary) and Ag/AgCl with 3M KCl (reference). The potentials were referenced vs. the ferrocenium/ferrocene (Fc⁺/Fc) redox couple.

3.2. Syntheses and Characterization

3.2.1. 1,3-Bis(2'-imidazoly)isoindoline (HL³)

A mixture of 10.81 mmol (1.57 g) of 1,3-diiminoisoindoline and 22.70 mmol (3.00 g) of 2-amino-imidazole sulfate in 25 mL of 1-butanol with sodium carbonate. The solution was heated with stirring at reflux for 20 h. The reaction mixture was cooled, filtered and the solid part obtained was washed with distilled water and cold methanol. The crude product was recrystallized from methanol to yield 0.919 g (30%) of brownish-red crystals. UV–vis [dmf], [$\lambda_{\max}$, nm log ϵ /dm³ mol^{−1} cm^{−1}], 356 (3.84), 391 (3.83), 415 (3.84), 443 (3.67), FT-IR bands (KBr pellet cm^{−1}): 3289 w, 3215 w, 3156 w, 3107 w, 2872 w, 1657 s, 1613 s, 1567 s, 1499 m, 1452 m, 1382 w, 1324 w, 1274 s, 1160 m, 1033 m, 753 m, 689 m, 641 m, 574 w, 517 w. Anal Calcd for C₄₀H₃₇F₆FeN₆O₁₀S₂: C, 48.25; H, 3.75; N, 8.45. Found: C, 48.22; H, 3.72; N, 8.47. ¹H-NMR (DMSO-d₆), δ (ppm): 5.75 (s, 1 H); 7.10 (m, 4H); 7.70 (m, 2H); 7.90 (m, 2H); 12.50 (s, 2H). ¹³C-NMR (DMSO-d₆), δ (ppm): 121.9 (2C); 123.5; 130.3; 131.9; 132.3; 134; 134.5; 136.3; 149.2 (2C); 150.2 (2C); 167.5.

3.2.2. [Mn^{II}(HL³)Cl₂] (3)

A solution of 0.14 g (0.72 mmol) of MnCl₂ 4H₂O in 2.5 cm³ CH₃OH was added to a suspension of 0.20 g (0.72 mmol) LH³ in 2.5 cm³ CH₃CN and the brown suspension was refluxed for 6 h. The solvent was removed by evaporation and the crude product was washed with cold CH₃OH and diethyl ether, and then dried under vacuum (0.16 g, 53%). UV–vis [dmf], [$\lambda_{\max}$, nm log ϵ /dm³ mol^{−1} cm^{−1}], 382 (4.04), 403sh (3.85), 430sh (3.49), 460 (3.25), FT-IR bands (KBr pellet cm^{−1}): 3382 w, 3253 w, 3100 w, 2920 w, 2847 w, 1657 s, 1614 s, 1469 m, 1361 w, 1311 w, 1254 w, 1092 m, 1048 m, 780 m, 709 m, 694 m, 530 w. Anal Calcd for C₁₄H₁₁Cl₂MnN₇: C, 41.71; H, 2.75; N, 24.32. Found: C, 41.66; H, 2.72; N, 24.35.

3.2.3. [Mn^{II}(HL²)Cl₂] (2)

Yield: 75%. UV–vis [dmf] [$\lambda_{\max}$, nm log ϵ /dm³ mol^{−1} cm^{−1}]: 227 (4.26), 296 (4.22), 330 (4.19), 347 (4.21), 367 (4.28), 386 (4.37), 409 (4.14), 453 (3.32), FT-IR bands (KBr pellet cm^{−1}): 3444 w, 3239 w, 3039 w, 2953 w, 2847 w, 1654 s, 1634 s, 1597 m, 1517 m, 1491 s, 1356 w, 1209 m, 1066 m, 939 m, 829 w, 719 m, 453 m. Anal Calcd for C₂₀H₁₇Cl₂MnN₅: C, 53.00; H, 3.78; N, 15.45. Found: C, 53.02; H, 3.80; N, 15.48.

3.2.4. $[\text{Mn}^{\text{II}}(\text{HL}^4)\text{Cl}_2]$ (4)

Yield: 70%. UV-vis [dmf] [λ_{max} , nm log $\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$]: 287 (4.22), 373 (4.29), 396 (4.39), 419 (4.44), 448 (4.22), FT-IR bands (KBr pellet cm^{-1}): 3423 w, 3199 w, 3105 w, 3084 w, 1656 s, 1622 s, 1504 s, 1364 m, 1291 m, 1213 m, 1123 m, 1099 m, 1052 m, 874 m, 772 m, 702 m, 624 w, 526 w. Anal Calcd for $\text{C}_{14}\text{H}_9\text{Cl}_2\text{MnN}_5\text{S}_2$: C, 38.46; H, 2.07; N, 16.02. Found: C, 38.45; H, 2.05; N, 16.03.

3.2.5. $[\text{Mn}^{\text{II}}(\text{HL}^6)\text{Cl}_2]$ (6)

Yield: 75%. UV-vis [dmf] [λ_{max} , nm log $\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$]: 371 (4.02), 382 (4.00), 420 (3.91), 448 (3.96), 482sh (3.75), 535 (2.93), FT-IR bands (KBr pellet cm^{-1}): 3427 w, 3043 w, 2925 w, 1629 s, 1613 s, 1552 s, 1499 m, 1475 m, 1290 m, 1180 m, 1090 m, 1066 m, 735 s, 706 m, 543 w. Anal Calcd for $\text{C}_{24}\text{H}_{19}\text{Cl}_2\text{MnN}_7$: C, 54.26; H, 3.60; N, 18.45. Found: C, 54.24; H, 3.57; N, 18.43.

3.3. Test Reactions of the Catalase-Like Activity

All reactions were carried out at 20 °C in a 30 cm^3 reactor containing a stirring bar under air. The stoichiometry of the reaction was measured by the simultaneous determination of the amount of O_2 and H_2O_2 concentrations. The evolved dioxygen was measured volumetrically. In a typical experiment, the appropriate aqueous solutions (19 cm^3 0.025 M $\text{Na}_2\text{B}_4\text{O}_7 \cdot 10\text{H}_2\text{O}$ /0.1 M HCl pH 9.5; or 0.05 M NaHCO_3 /0.1 M KOH pH 9.5 buffer and $I = 0.15$ M KNO_3) was added to the complex (final concentration is 0.211 mM) dissolved in 1 cm^3 DMF, and the flask was closed with a rubber septum. Hydrogen peroxide (final concentration is 0.447 M) was injected through the septum with a syringe. The reactor was connected to a graduated burette filled with oil and dioxygen evolution was measured volumetrically at time intervals of 15 s. Observed initial rates were expressed as $\text{mol}/\text{dm}^3 \text{ s}^{-1}$ by taking the volume of the solution (20 cm^3) into account and calculated from the maximum slope of the curve describing the evolution of O_2 versus time.

3.4. Bleaching of Morin

Oxidative degradation of morin in the presence of $[\text{Mn}^{\text{II}}(\text{HL}^{1-6})\text{Cl}_2]$ complexes was measured in 3 mL optical quartz cells. In a typical experiment, the cuvette was filled with a 1.5 mL buffer solution containing 0.16 mM morin, 10 mM H_2O_2 and 1.6 μM catalyst, and the bleaching reaction was followed by measuring the decrease in the absorption maximum of morin at 410 nm with 10 s intervals at 25 °C.

4. Conclusions

Efforts have been made to work out a highly efficient and highly selective manganese-based catalytic system for the disproportionation reaction of H_2O_2 as synthetic catalase mimics and for the oxidation of morin as oxidative bleaching performances. We synthesized six manganese $[\text{M}^{\text{II}}(\text{HL}^{1-6})\text{Cl}_2]$ complexes with 1,3-bis(2'-Ar-imino)isoindolines (HL^n , $n = 1-6$, Ar = pyridyl, 4-methylpyridyl, imidazolyl, thiazolyl, benzimidazolyl and *N*-methylbenzimidazolyl) ligands, and characterized by various electrochemical and spectroscopic methods. In the next step, we investigated the effect of the ligand modification by varying the aryl substituent on the bis-iminoisoindoline moiety with emphasis on the redox potential and Lewis acidity of the catalyst that may serve as guidelines for the synthesis of more active and more selective catalysts toward H_2O_2 , and morin by the use of H_2O_2 as oxidant. In conclusion, we observed that the higher the redox potentials of the $\text{Mn}^{\text{III}}/\text{Mn}^{\text{II}}$ redox couple the higher is the catalase-like and bleaching activity. In summary, whose metal sites are electron-deficient are faster in catalyzing H_2O_2 disproportionation and morin oxidation than electron-rich derivatives with more Lewis basic side chains. It is also worth noting that the bicarbonate concentration plays an important role in both the catalase-like reaction and bleaching process, probably during the formation of the proposed catalytically active $\text{Mn}^{\text{IV}}(\text{O})$ species. These studies may lead to the development of more active oxidation catalysts.

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