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A Brief Overview of the General Characteristics and Reactivity Towards Dioxygen of the Ferrous Tris (2-Pyridylmethyl Amine) Series Complexes is Presented

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Abstract: *This paper examines the coordination chemistry of iron to TPA-like nitrogenous tripod ligands, focusing on how the spin state of the metal is affected by the presence of steric constraints and the coordination of acetonitrile ligands, which can be displaced easily. Additionally, the reactivity of the derivatives with molecular oxygen, the conservation of geometry between the solid state and the solution and the various coordination geometries, electronic properties, and redox properties of ferrous tris(2-pyridylmethyl amine) series complexes are discussed. Furthermore, the molecular mechanisms of reactivity of these complexes are evaluated, providing an outlook for future research.*

Keywords: Ferrous tris (2-pyridylmethyl amine) series, Coordination chemistry, Ligand field theory, Redox properties, Electron transfer, O2 reactivity, Oxidation-reduction reaction, Catalytic activity, Kinetic studies, Dioxygen binding

I. INTRODUCTION

In this paper, we look at the coordination chemistry of iron to TPA-like nitrogenous tripod ligands to better understand the spin state of the metal. Firstly, we review the majority of published work in the field, looking at the ligands used and the geometry around the metal typically observed. We then examine different types of ligands that can be used to replace the acetonitrile ligands commonly employed, as well as the reaction of these derivatives with molecular oxygen. Finally, we examine the conservation of geometry between the solid state and the solution.

The coordination chemistry of iron to TPA-like nitrogenous tripod ligands is pretty standard. Considering the vast majority of published work in iron chemistry, the ligands used are essentially the parent tripod TPA (Figure 1), or derivatives substituted by simple alkyl or aromatic groups [1-3]. Some examples are given in the figure below:

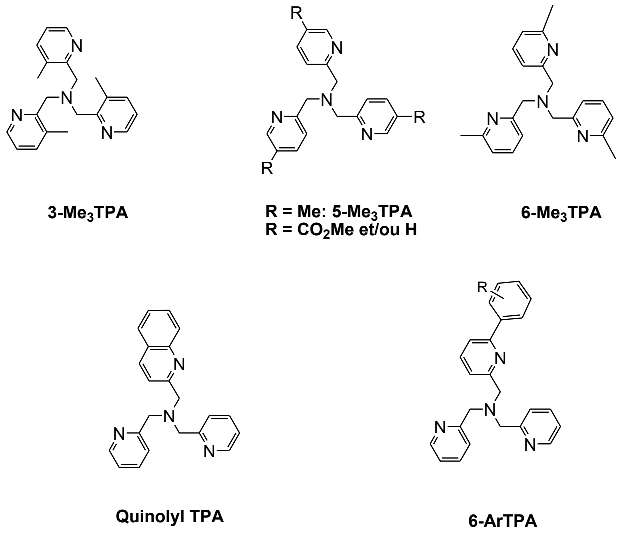

Figure 1: Some examples of ligands derived from the most used TPAs (in methylated series, mono and disubstituted ligands are also used).

Most of the time, and with a few exceptions, the ligands coordinate tetradentally. In the vast majority of cases, the geometry around the metal is of the distorted octahedral type (Figure 2). There are, however, some examples of bipyramidal geometry with a trigonal base in which the ligand is tridentally coordinated according to the (κ3-N) mode, and an example of cubic geometry around the metal [2,4,5].

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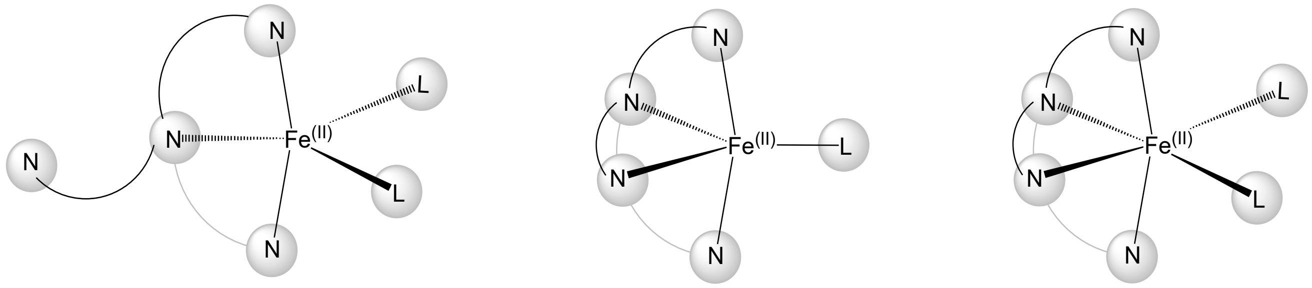


Figure 2: Main modes of coordination of TPA ligands to iron. TBP geometries are generally associated with critical steric genes around the metal. The tripod ligand can adopt a coordination mode called "hypodentate" ([κ3-N] on the left) or normal ([κ4-N]in the middle). The distorted Oh geometry (right) is the most common.

In general, the metal source is a salt with a weakly coordinating anion, such as perchlorate, hexafluorophosphate, tetrafluoroborate, or triflate. These tripods are neutral ligands, and the presence of weakly coordinating anions balances the charge of the metal ion. The complexes of TPA ligands or derivatives are generally poorly soluble in non-coordinating solvents, and the necessary recourse to acetone or acetonitrile has the effect of obtaining bications, the coordination sphere of the metal being completed by solvent molecules (acetonitrile). In a practical way, Figure 3 taken from reference [2] illustrates quite well the type of simple coordination chemistry that can be achieved.

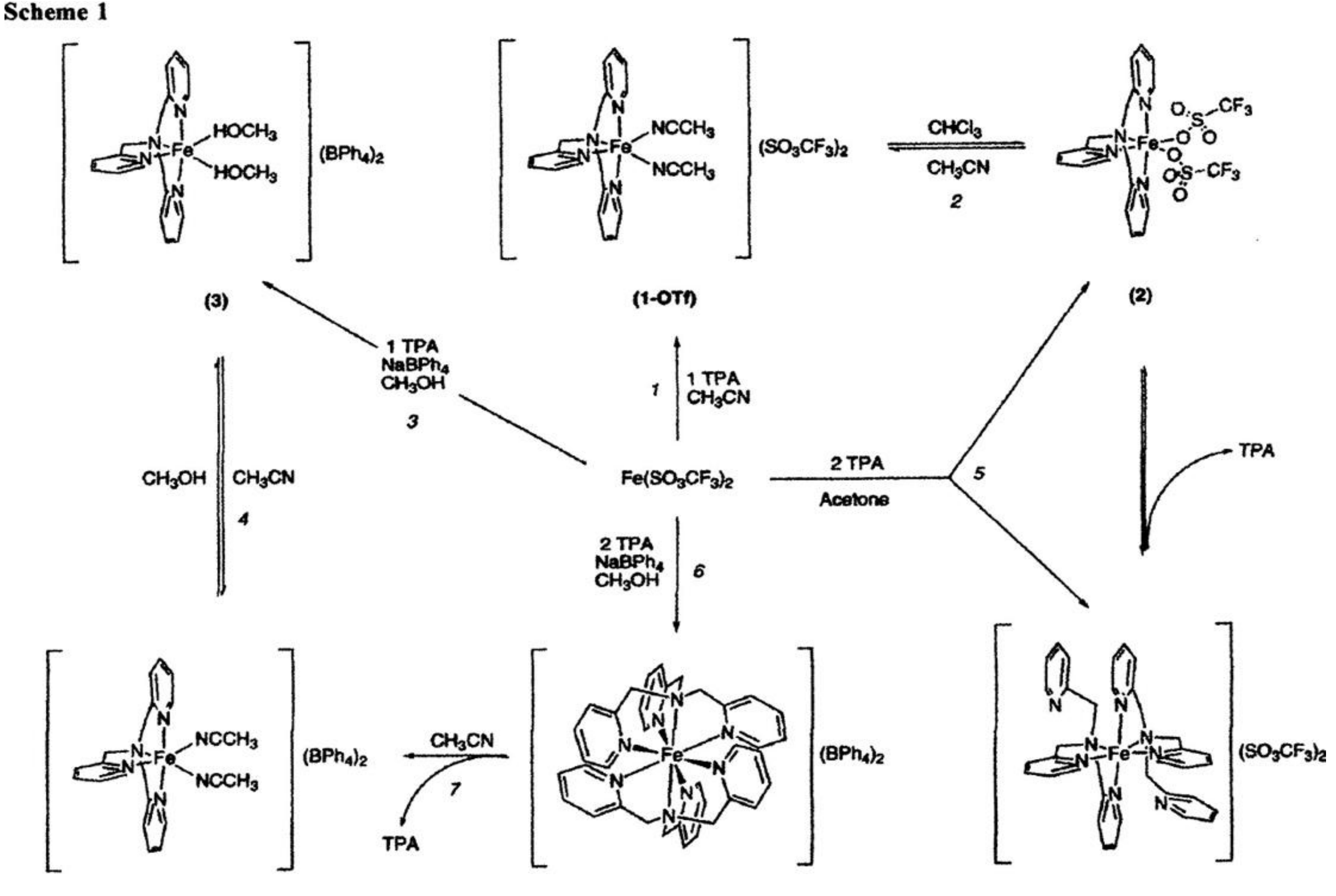


Figure 3: An example of simple coordination chemistry in the TPA series. According to reference [2].

The spin state of the metal in these complexes essentially depends on the ligand. In principle, an increase in the basicity of the latter should increase the ligand field, and therefore, a diamagnetic state for a ferrous complex. But this can be counterbalanced by steric constraints inherent in the presence of substituents in α-position of the nitrogen atom of the pyridine: in this case, the metal-pyridine distances are higher inducing a weak ligand field, and therefore a strong spin state. The structures of the ferrous derivatives of the ligands 6-Me3TPA and TPA are quite informative in this respect [5]: It is understood that the 6-Me3TPA derivative generates more steric hindrance around the metal than the parent derivative TPA. This is how [LFe $(CH_3CN)_2]^{2+}$ cations with a deformed octahedral structure (Figure 4) exhibit a weak spin state with L = TPA, but this becomes strong spin with L = 6-Me3TPA.

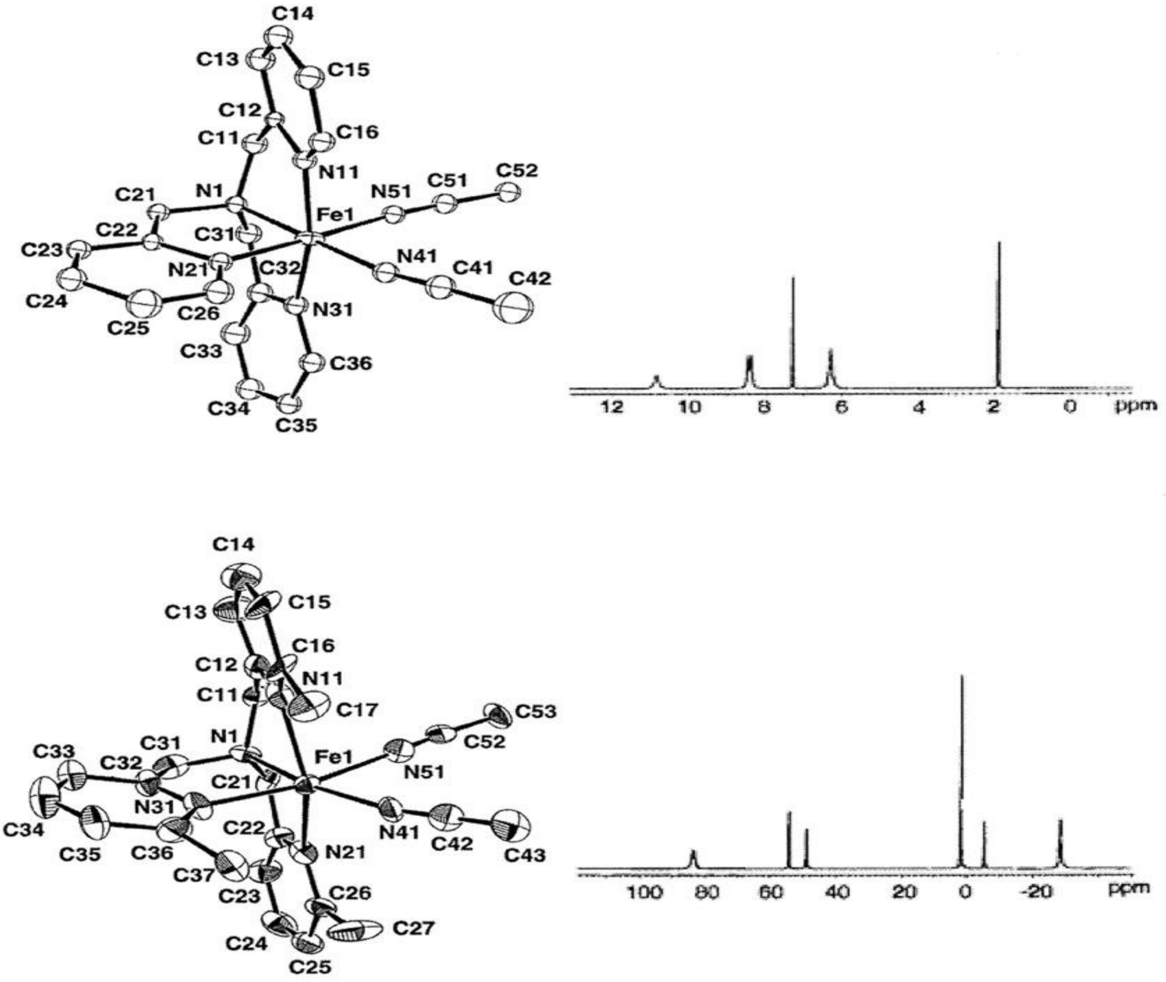
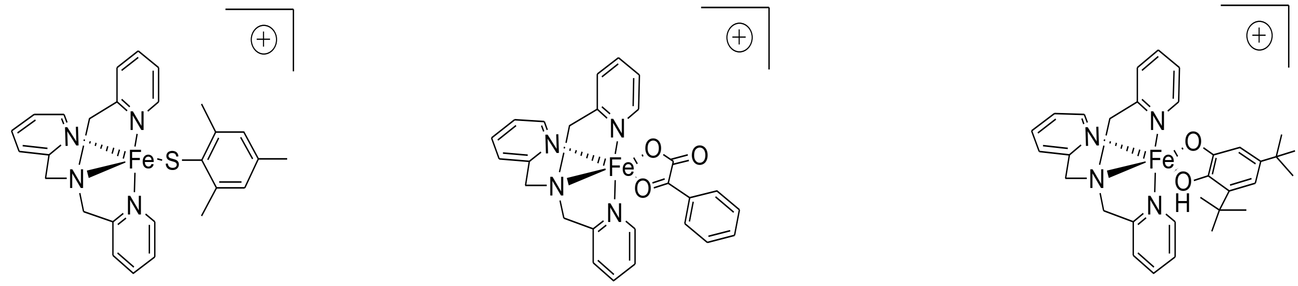


Figure 4: Representation of [TPAFe (CH3CN)2]2+ and [6-Me3TPAFe (CH3CN)2]2+ complexes and their corresponding 1H NMR spectra illustrating spin state differences.

The acetonitrile ligands present around the iron can be easily displaced: it is therefore tempting to replace them with simple models of substrates encountered in enzymes: thiolates, α-keto carboxylates or catecholates, to name but a few. This has been achieved, and three examples characterized by X-ray diffraction are shown below [4,6,7]. The derivatives shown in Figure 5 have been shown to react with molecular oxygen. We can certainly speak in these cases of a synergistic activation between the metal and the exogenous ligand, since the latter (tertiobutyl thiolate, ditertiobutyl catecholate, benzoyl formate) are already intrinsically quite reactive when they are not complexed.



[TPAFe(Sar)]$^+$ [TPAFe(BF)]$^+$ [TPAFe(DBCH)]$^+$

Figure 5: Biomimetic models of the active sites of iso-penicillin N-synthase, α-ketoglutarate type oxygenases, and extradiol catechol dioxygenases. According to references [4,6,7].

A priori, apart from the examples presented above, there is no mention in the literature of a particular reactivity vis-à-vis the dioxygen of ferrous complexes in the chemistry of TPAs. Everything happens as if the metal needed to be activated to react.

$FeCl_2$ as Iron Source: Dichloroferrous Complexes.

Our laboratory has been interested in the preparation of well-defined and very stable complexes, starting with the dichloroferrous complex of the single ligand TPA[8-11].

$$L + FeCl_2 \xrightarrow[\text{Ar, minimum 4 heures}]{\text{THF ou } CH_3CN} LFeCl_2$$

X-ray diffraction shows that the resulting complexes are either of distorted Oh geometry or of trigonal bipyramid (TBP) geometry. A priori, the determining factor would seem to be steric hindrance: the unhindered ligands, TPA, BrTPA, allowing a distorted Oh geometry, whereas Ph2TPA, Br2TPA and F3TPA lead to a TBP geometry, Figure 6, with a coordinating ligand tridentately [7-12]. The distances between the metal and the nitrogen atoms are generally greater than 2.1 Å, which characterizes a strong spin state for the metal ion.

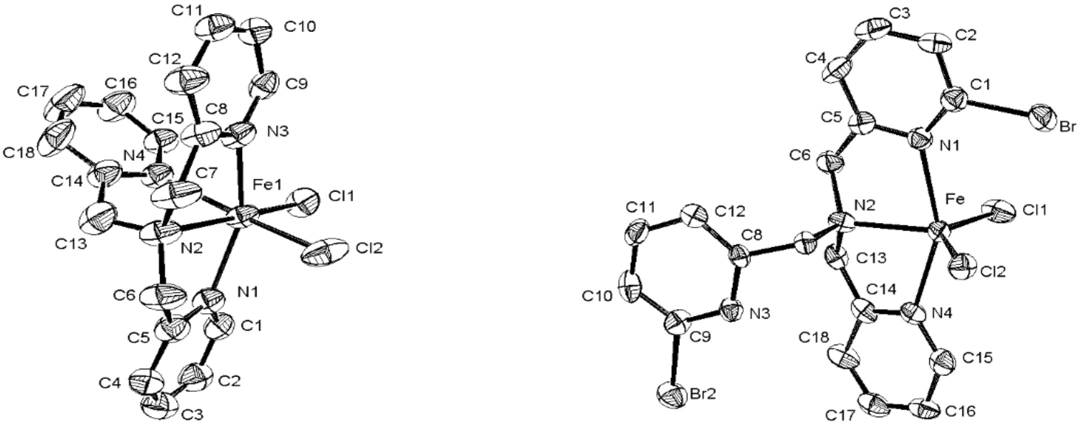
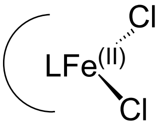


Figure 6: Three-Dimensional Structures of the TPAFeCl2 and Br2TPAFeCl2 Complexes, According to Reference [9].

The 1H NMR carried out on these complexes highlights the strong paramagnetic character, and especially a significant qualitative difference of the spectra according to the geometry of the complex in the solid state, fine lines characterizing a deformed Oh geometry, whereas the TBP geometry gives gives rise to a spectrum in solution characterized by broadened lines [9].The question of the conservation of the geometry between the solid state and the solution could be approached [9-11]. Firstly, UV-visible spectroscopy provides essential information: the complexes all exhibit an absorption of the MLCT type (Fe(II) • Pyridine) between 390 and 400 nm. The intensity of this absorption depends among other things on the number of coordinated ر pyridines. Typically, tetradental coordination leads to molecular extinction coefficients □ between 1 and 2103 mmol.cm^2. For a trident coordination involving only two pyridines, these values never exceed 0.7 to 0.8 103 mmol.cm2. In some cases ($F_3TPAFeCl_2$, for example), the absorptions are almost invisible. The question of the conservation of the geometry between the solid state and the solution could be approached [9-12]. The possibility of decoordination of a chloride ion could also induce a change in geometry. In this case, there would be the formation of a charged metallic species. Molar conductometric measurements can answer this question. Almost generally, all the complexes of structure $LFeCl_2$ in which L is a ligand with a simple TPA motif exhibit a neutral electrolytic behaviour, in the concentration ranges usually used for reactivity studies (Figure 7).



$20 < \Lambda < 50$ S.cm^2.mol^{-1}

$3 < C < 5$mM

Figure 7: Average molar conductivity values measured on dichloroferrous complexes.

It should be noted that this is valid in pure solvent (CH_3CN). The situation is quite different when conditions involving high salinity (such as the presence of a supporting electrolyte in cyclic voltammetry) are used. There can then be dissociation of the chloride ions and reorganization of the complex into a bimetallic derivative. Thus, the combined study of the complexes by ^{1}H NMR, UV-visible and conductimetry makes it possible to predict the geometries of the complexes, which we will see later play a significant role in reactivity. It should be noted that in general, the structures observed in the solid state by X-ray diffraction are preserved in solution. A priori, the chlorine is therefore maintained on the metal even when the complex is in solution. Questions relating to the measurement of $Fe^{(II)}/Fe^{(III)}$ redox potentials are well known in the laboratory:

$TPAFeCl_2$, with a deformed Oh geometry, is the only complex to present a well-defined and unique redox couple, at $E_{1/2} = 195$ mV/SCE.

It has previously been shown in the laboratory that the complexes of the electrode-deficient ligands dissociate when they are dissolved in a strongly dissociating medium such as that used for cyclic voltammetry measurements. Very often, however, the voltammograms are usable, and the torque values are always positive. Note, however, that the deformed Oh geometries induce much more positive torques (E > 200 mV/ECS) than the TBP geometries, whose potentials are weakly positive ($0 < E < 100$ mV). Finally, it should be noted that certain derivatives, such as F3TPA, for example, do not seem to be stable under the conditions of electrochemical studies: multiple waves are observed, but always at positive potential (Figure 8).

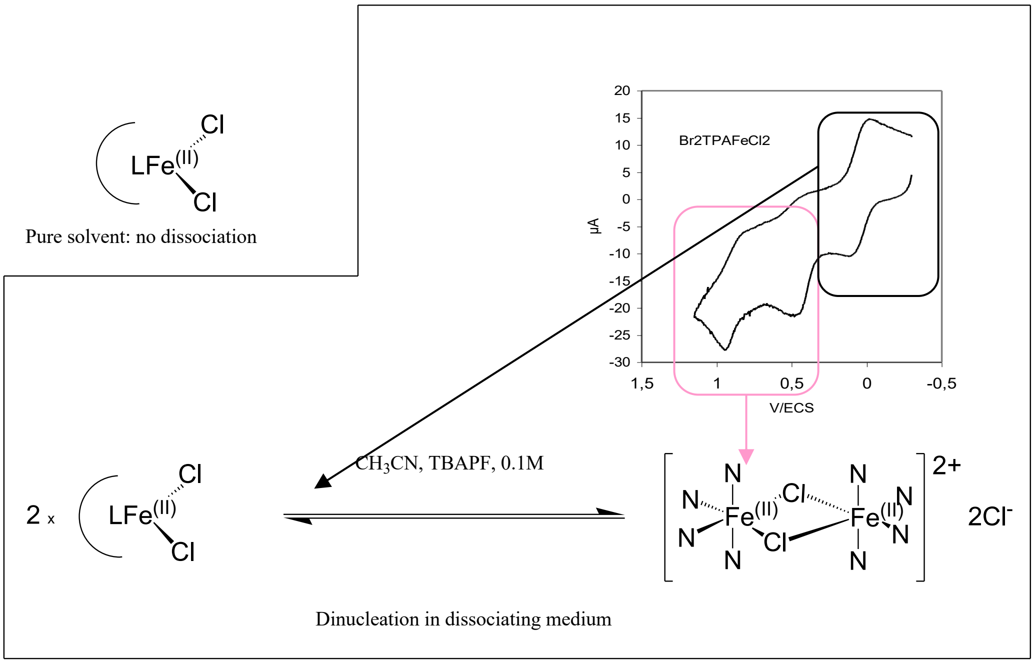


Figure 8 : Behavior of Complexes in Solution, and Electrochemical Detection of Mono Versus Binuclear Equilibrium.

At the preparatory level, the achievements of the laboratory reside in the mastery of the preparation and study of very stable and perfectly characterized complexes. It remains to be seen whether the stability provided by the chloride ions will come at the expense of future reactivity.

II. MOLECULAR OXYGEN REACTIVITY ON FERROUS DERIVATIVES IN THE CHEMISTRY OF TPA AND RELATED LIGAND COMPLEXES.

The first mention of a possible biomimetic mechanism of dioxygen coordination followed by its homolytic cleavage was published a dozen years ago by the group of L. Que Jr. [5]. The $[TPAFe(Sar)]^+$ derivative, Sar = mesityl thiolate, Figure 9, reacts with air at low temperature to generate a metastable blue-green species corresponding to the formation of a ferric compound [5]. The latter was characterized as such by EPR and visible UV spectroscopy, and the fact that only 26% molar equivalent in dioxygen is necessary for the reaction led the authors to postulate the following mechanism:

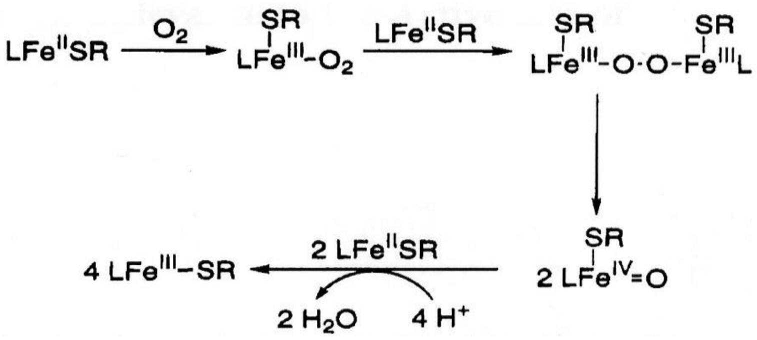


Figure 9 : Reaction of [TPAFe(Sar)]+ with Dioxygen, According to Reference [5].

This is only a postulated mechanism: none of the intermediate steps are characterized. Even the final derivative is unstable and evolves into a poorly described species. It has been suggested that the latter may be a diferric μ-oxo compound based on the fact that: i) two absorptions are observed in visible UV spectroscopy at λ = 500 and 600 nm (but this argument seems unconvincing to us), and ii) that signals are present in a range of 30 ppm in ^{1}H NMR.

What is certain is that the starting product, of bipyramid geometry with a trigonal base, and coordinated by a thiolate (itself in itself reactive with respect to dioxygen) reacts rapidly with molecular oxygen in the proportion of 4 equivalents of complex for 1 equivalent of O_2.

The complex $[LFe(BF)]^+$, BF = benzoylformate, L = 6-Me$_3$TPA, 5-Me$_3$TPA and TPA, Figure 10, also reacts with dioxygen [4-6]. Here, decarboxylation of an α-keto benzoate ligand occurs, allowing such a system to mimic the reactions at the active sites of non-heme iron enzymes of the α-ketoglutarate-dependent type.

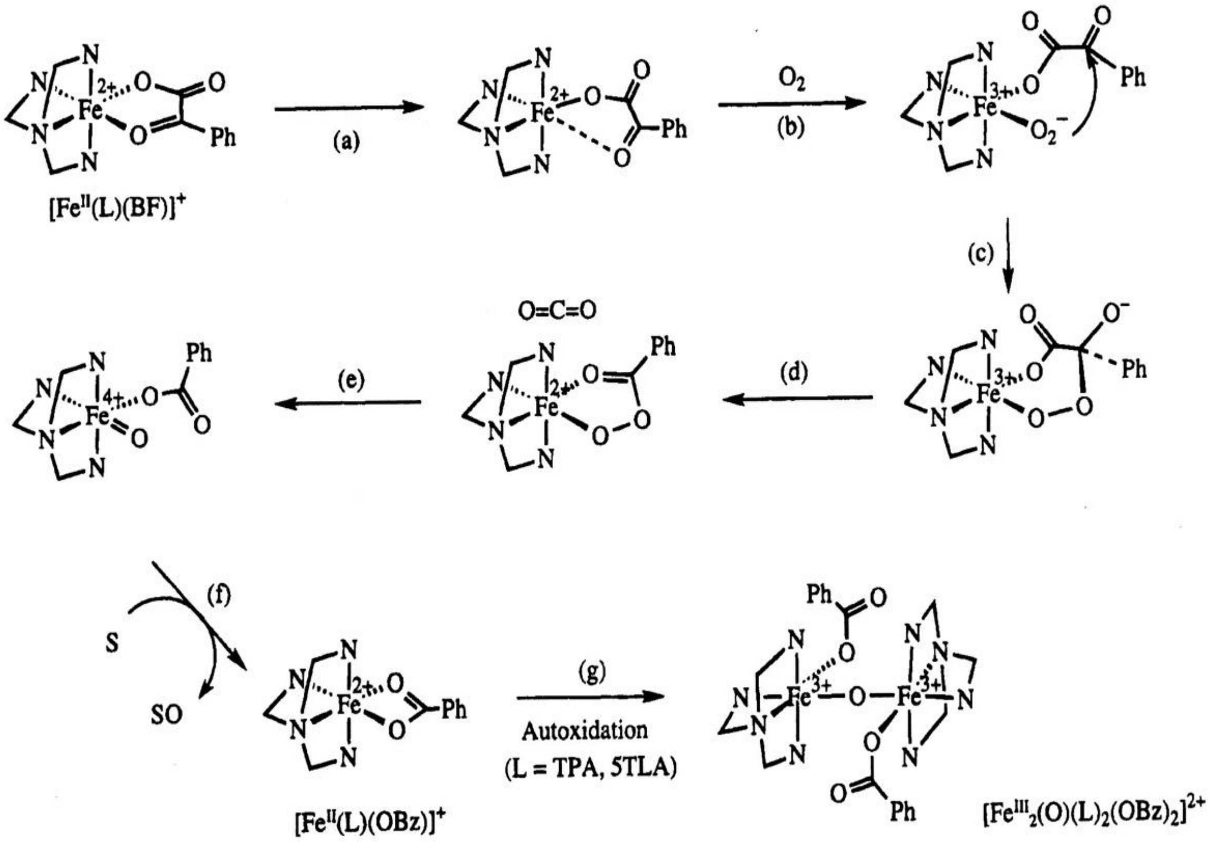


Figure 10 : Postulated Mechanism of the Reaction of [LFe(BF)]+ with Dioxygen, According to Reference [5]. S = PPh3.

The reaction is slow: with L=6-Me$_3$TPA, this reaction, followed by ^{1}H NMR, takes a week, and the final product obtained is the ferrous derivative coordinated by a benzoate. In other cases, it only takes two days of reaction time to detect the presence of a μ-oxo diferric derivative finally.

Once again, this mechanism is a postulated mechanism. The oxo ferryl derivative obtained after step (e, Figure 10) has not been characterised. Still, its structure is assumed on the basis that it reacts with PPh_3 to give the corresponding phosphine oxide. The use of oxygen brand $^{18}O_2$ results in a maximum incorporation rate of 60 to 85% of ^{18}O in the phosphine oxide. Further studies showed that in the presence of water, there could be exchange between the oxygen atoms of the benzoate ligand, but not at the level of the phosphine oxide. The third example cited here concerns the reactivity of the derivative [6-Me$_3$TPAFe (DBCH)]+, and of its analog $[6\text{-}Me_3TPAFe(CatH)]^+$, Cat = catecholate. These compounds, yellow-orange in color, react rapidly with oxygen to simply generate the corresponding ferric complexes [4].

Here there is a simple conversion into a ferric monocation $[6\text{-}Me_3TPAFe\ (DBC)\ (\text{or Cat, respectively})]^+$ and this reaction takes place quite quickly (time scale of a few tens of minutes).

A little later, a variation of this reaction was published, Figure 11, which involves an identical complex with the ligand TPA bis(6-methyl substituted)[12-17]. The originality of this work results in the reaction of the coordinated catechol, and the distribution of the reaction products, resulting from both an intradiol and extradiol type cleavage. The reaction time here is a few hours, and the postulated mechanism is shown below.

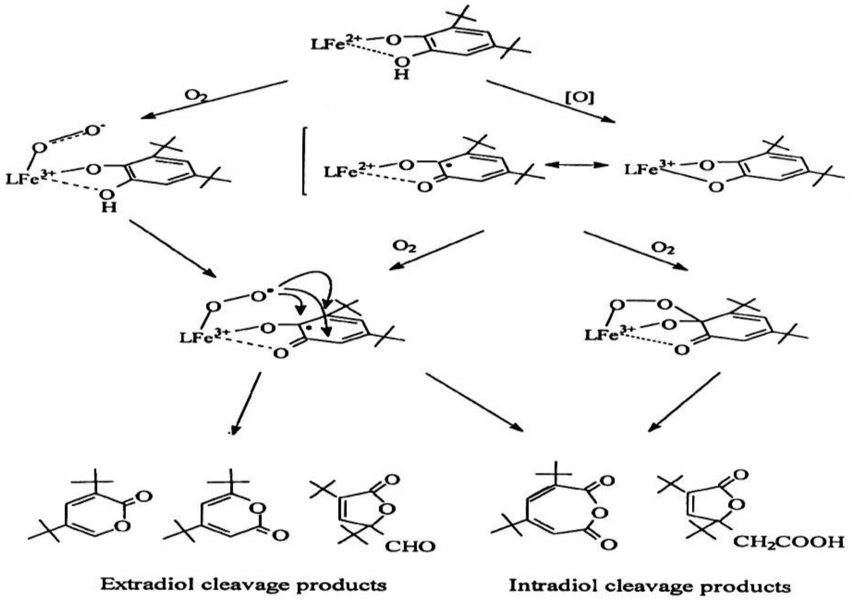


Figure 11 : Complex with bis (6-methyl substituted) TPA ligand.

Finally, let us mention that the coordination of catechols in dianionic form allows the ferric ion to also react with dioxygen[15-18]. This is a now well-known reaction whose mechanism involves the presence of a [semi-quinone]/$Fe^{(II)}$ form. We can insist on the following two points: 1) the ligands used are anionic and are not innocuous. For example, tetramesityl thiolate oxidizes very well in solution without adding metal to give the corresponding disulphide. Could the same result have been observed with tetraflurophenyl thiolate? and : 2) In the case of [LFe(BF)]+, the reactions are slow, taking two days to one week.

III. CONTRIBUTION OF OUR LABORATORY IN REACTIVITY VIS-A-VIS MOLECULAR OXYGEN

When we started our work, the laboratory had already published the preparation of dichloroferrous derivatives, Figure 12, and developed the bases for studying these complexes [4-13]. In particular, the dibrominated ligand derivative was reported to be oxygen sensitive. Following this work, the oxygenation reaction of the compound $F_3TPAFeCl_2$, leading to the majority formation of a μ-oxo diferric derivative had been described.

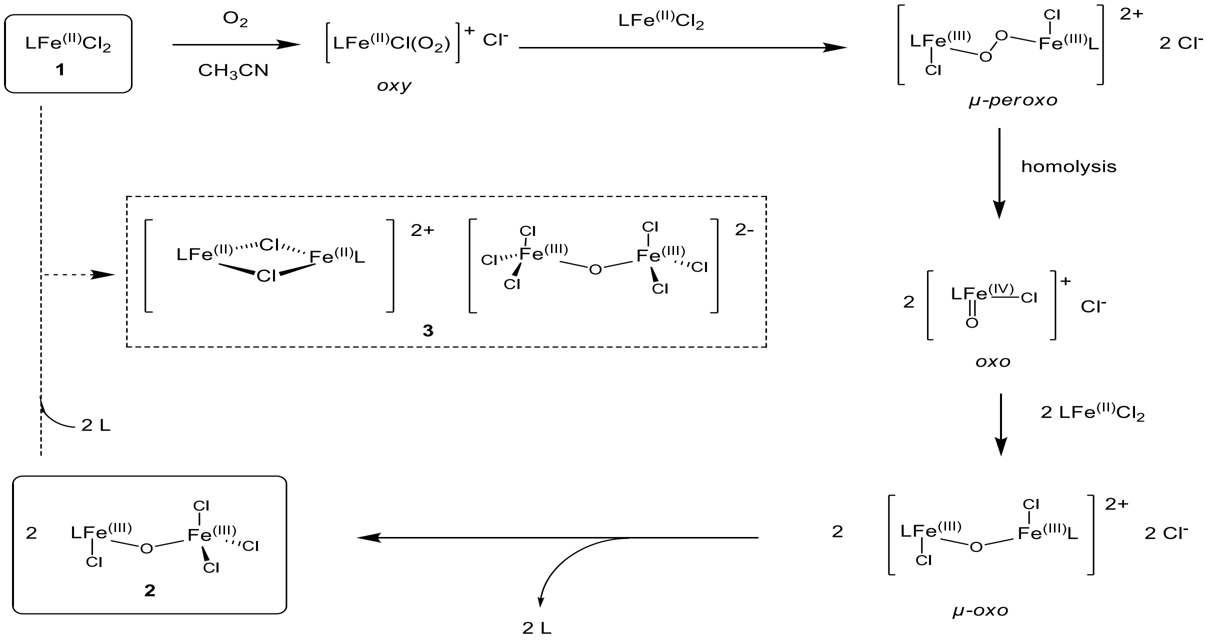


Figure 12: Conversion of the F3TPAFeCl2 Compound Into a μ-oxo Diferric Complex by Reaction with Dioxygen. From Reference [8,17-29].

A mechanism based on that well known in porphyrin chemistry [11, 20-28] had been postulated, involving potentially oxidizing species. The speed of reaction of dioxygen on ferrous compounds was then attributed to the geometry of the starting compounds, in particular to the fact that the metal is in a coordinately unsaturated environment. We will see later that this is only partially true. Alongside the chemistry of TPA ligands, an example of oxidative dehydrogenation (Figure 13) had also been described [18,28-37]:

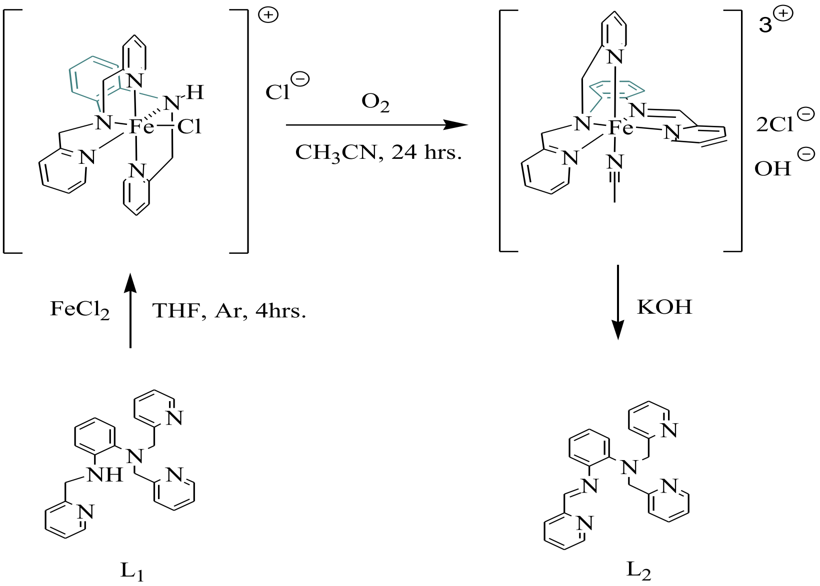


Figure 13: Oxidative Dehydrogenation Reaction Triggered by the Action of Oxygen on a Secondary Amine Complex, According to Reference [14].

Here too, a ferrous derivative reacts with oxygen, cleanly and slowly (the reaction takes 24 hours). The secondary amine of the ligand is converted into an imine which can be recovered after decomplexation. The question of the reaction mechanism has not been addressed in this article. However, monitoring by UV-visible spectroscopy suggests the presence of an oxygenated form of the metal, a transient absorption being detected around $\lambda = 800$ nm. It is the possibility of manufacturing substituted ligands in a variety of ways in TPA chemistry that led us to undertake a systematic study of the reactivity of the corresponding dichloroferrous complexes.

IV. PEROXIDES, OXYGEN DONORS AND OTHER REDUCED FORMS OF OXYGEN: PRACTICAL TOOLS

Biomimetic inorganic oxidation chemistry, all forms of ligands combined, is dominated by the use of peroxides. Historically, porphyrin chemistry contributed a lot to the later development of biomimetic catalysis[28, 32-44], through the use of diverse and varied oxygen donors (Figure 14). The chemistry of TPA series iron complexes and methylated analogues has undergone the same evolution, and the field is now very well documented [1,35-50]. The use of peroxides is undoubtedly because in the absence of biomimetic ligands such as thiolates, catechols or α- keto benzoates, the ferrous complexes in this series react little or poorly with oxygen. The reactions studied are essentially of the hydroxylation of alkanes, epoxidation of olefins, and cis-dihydroxylation of olefins type. In general, the number of cycles or turnovers is relatively low and does not allow the exploitation of these complexes for preparatory purposes. The generation of ferric-hydroperoxide species is now entirely accepted [1,3,16,48-60]. Their characterization has been extensively studied, and it is postulated that there is a relationship between the spin state

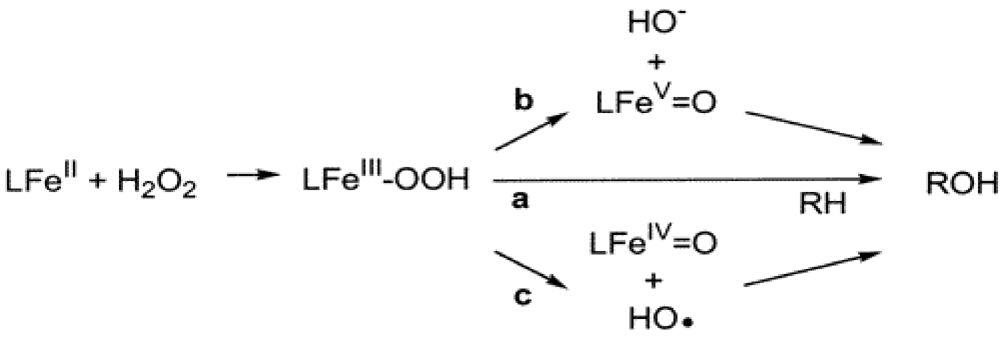


Figure 14: The Different Mechanistic Pathways Followed by Iron Hydroperoxides. According to Reference [1-20].

The iron hydroperoxide species can react directly with the substrate, but it can also undergo cleavage, which can be either homolytic or heterolytic in nature. In these two cases, there is the generation of species with a high degree of iron oxidation, analogous to one of the postulated intermediates during the catalytic cycle of Isopenicillin N-synthase. Numerous studies have been carried out and demonstrate the exchangeable nature of the iron–oxo bond depending on the nature of the ligands used. During this thesis, we wanted to focus more on the reactivity towards dioxygen. For this reason, we limit ourselves here to mentioning these few general characteristics concerning the main postulated reaction and intermediate paths, knowing that a very abundant literature is available on the subject [19,59,60].

V. CONCLUSION

This paper examines the coordination chemistry of iron with TPA-like nitrogenous tripod ligands and their derivatives, focusing on their interactions with molecular oxygen. The complexes of this series exhibit general characteristics, including a low-spin Fe2+ ion, a relatively large ligand field strength, and a relatively small coordination number, which enables a wide range of applications in various chemical and biological systems. Our findings highlight the effect of steric constraints on the spin state of the metal, as well as the conservation of geometry between the solid state and the solution, providing insight into the coordination chemistry of iron to these ligands and their reactivity towards dioxygen.

DECLARATION

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Conflicts of Interest/ Competing Interests	No conflicts of interest to the best of our knowledge.
Ethical Approval and Consent to Participate	No, the article does not require ethical approval or consent to participate, as it presents evidence.
Availability of Data and Material/ Data Access Statement	Not relevant.
Authors Contributions	I am the sole author of the article.

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