Oxidative Dehydrogenation of Secondary Amines: The Case of the *N*,*N*,*N′*-Tris(2-pyridylmethyl)-*o*-phenylenediamine Ligand when Coordinated to Iron Dichloride

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We report the preparation and the X-ray crystal structure of the iron complex $[Fe(L^1)Cl][Cl]$ [L^1 = *N*,*N*,*N′*-tris(2-pyridylmethyl)-*o*-phenylenediamine], and its reactivity towards molecular dioxygen. Upon exposure to dry O_2, coordinated L^1 is oxidatively dehydrogenated to the aldimine ligand L^2. The ferric cation $[Fe(L^2)(CH_3CN)]^{3+}$ is thus obtained, and characterized by UV/Vis and EPR spectroscopy, and X-ray diffraction analysis. The free L^2 ligand can be recovered after decomplexation.

Modelling of the active site of non-heme iron-containing oxygenases is one of the main reasons that led to the important development of the chemistry of iron complexes with (aminomethyl)pyridyl-containing ligands.[1–4] Oxygen-atom-transfer processes, however, and all their related chemistry, represent only a part of what Nature is able to carry out. Oxidative dehydrogenation of amines under aerobic conditions is another important process encountered in biochemistry — it is suspected to be one of the possible reasons for cell ageing, and is believed to be catalysed, in some cases, by iron-containing sites.[5] A search of the chemical literature reveals that most of the related published work involves Ni, Ru, Os and Cu complexes, only a limited number of studies being available in the chemistry of iron.[6] Examples taken from the chemistry of iron complexes with (aminomethyl)pyridyl-containing ligands include disproportionation of anionic species under strongly oxidizing conditions, to yield the corresponding coordinated imine as one of the reaction products,[7,8] or, more recently, the indirect demonstration that a tetrapyridine ligand can be desaturated under oxidative conditions.[9] In these cases, however, we could not find any direct evidence that molecular dioxygen is involved during these desaturation process, although O_2 is postulated as one of the key reagents in biologically occurring processes.[5] In the course of our investigations on the biomimetic use of molecular dioxygen with simple iron complexes,[10,11,13] we prepared the new compound $[Fe(L^1)Cl][Cl]$ [L^1 = *N*,*N*,*N′*-tris(2-pyridylmethyl)-*o*-phenylenediamine] and found that, upon exposure to dry dioxygen, $[Fe(L^1)Cl][Cl]$ in solution in acetonitrile smoothly converts to the ferric complex $[Fe(L^2)(CH_3CN)][OH][Cl]_2$, where L^2 is a dehydrogenated form of L^1, i.e. the corresponding imine. This clean reaction, together with the crystal structures of the two new complexes, is reported in this article. This work directly illustrates the fact that molecular dioxygen, as is believed to be the case in natural systems, can, at least at an early stage, induce a clean process of desaturation of acyclic amines by reaction with aferrous complex.

Ligand L^1 was prepared according to a published procedure.[14] The metallation by iron dichloride was carried out anaerobically according to a standard method,[11] and afforded $[Fe(L^1)Cl][Cl]$ almost quantitatively as a stable greenish-yellow solid, as indicated in Scheme 1.[12] The UV/Vis spectrum of $[Fe(L^1)Cl][Cl]$ in an acetonitrile solution displays three maxima $\{\lambda\ (\varepsilon\ [10^3\ \mathrm{mmol{\cdot}cm^2}]) = 258\ (10.24),\ 306\ (\mathrm{sh.})\ \mathrm{and}\ 407\ (2.67)\ \mathrm{nm}\}$.

Single crystals could be obtained by slow diffusion of diethyl ether into an acetonitrile solution of $[Fe(L^1)Cl][Cl]$.[15] An ORTEP diagram of the cation $[Fe(L^1)Cl]^+$ is shown in Figure 1. The X-ray structure analysis reveals that the iron atom is coordinated in a distorted octahedral fashion. The metal−nitrogen distances are all above 2.19 Å, which is indicative of a high-spin state for the metal atom, and are

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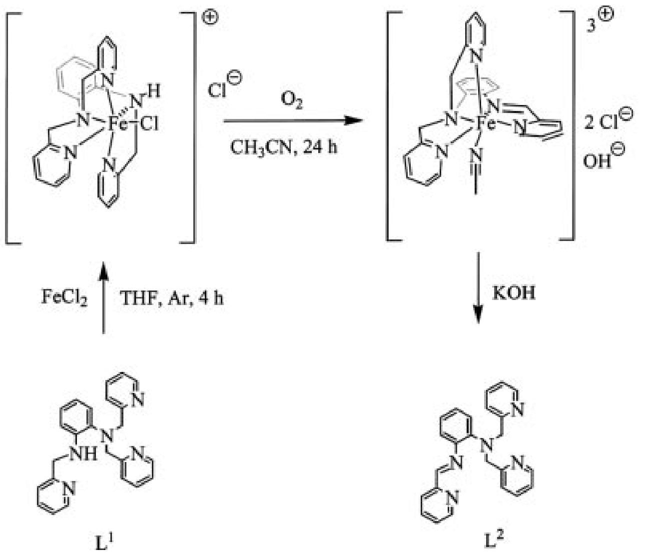

Scheme 1

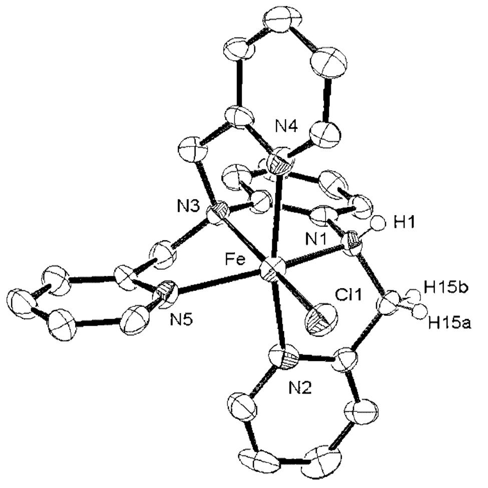

Figure 1. ORTEP diagram of the cation $[Fe(L^1)Cl]^+$ with a partial numbering scheme; all hydrogen atoms except the amine and the H15 methylene ones have been removed for clarity; selected bond lengths [Å] and angles [°]: Fe−Cl1 2.332(2), Fe−N1 2.196(6), Fe−N2 2.238(6), Fe−N3 2.240(6), Fe−N4 2.212(6), Fe−N5 2.195(6); N3−Fe−Cl1 167.83(17), N1−Fe−N5 149.0(2), N4−Fe−N2 159.0(2)

comparable to those reported in another complex with a more flexible pentadentate ligand.[16] The angles belonging to the five-membered metallacycle are found in the range 74−79°, the others being between 93° and 109°.

The addition of dry dioxygen to a solution of $[Fe(L^1)Cl][Cl]$ in acetonitrile resulted in a progressive darkening of its colour, which turned slightly green. Figure 2 displays the spectral variations observed by UV/Vis spectroscopy. A new intense absorption at λ = 322 nm is detected, and a weak and broader one at λ = 694 nm, whose intensities stabilised 24 h after the beginning of the reaction.

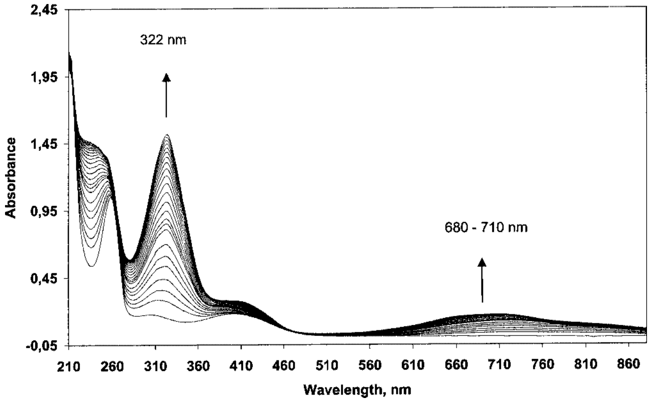

Figure 2. UV/Vis spectral changes observed upon oxygenation of $[Fe(L^1)Cl][Cl]$ at room temperature in acetonitrile solution (one trace per hour over 24 h)

The same experiment was carried out on a preparative scale, and a new complex, formulated as $[Fe(L^2)(CH_3CN)][OH][Cl]_2$, was obtained. The UV/Vis spectrum of this dark-green material in an acetonitrile solution displays several maxima {λ (ε [10^3 mmol·cm^2]) = 252 (sh. in solvent), 322 (17.36), 404 (3.23) and 694 (br., 1.59) nm}. The intensity of the new UV absorption suggested the presence of a new conjugated π system. In the IR spectrum, the ν_{O-H} vibration appears at 3418 cm^{-1}, and the band at 1651 cm^{-1} is assigned to the $\nu_{C=N}$ vibration. The EPR spectrum of an acetonitrile solution recorded at 90 K displays signals at g_x = 2.460, g_y = 2.244 and g_z = 1.874, indicating the presence of a rhombic low-spin iron species. The ^{1}H NMR spectrum displays a complex set of broad and paramagnetically shifted peaks lying between δ = 120 and −15 ppm, consistent with the EPR data.

Attempts to crystallise this new compound as obtained directly after oxygenation were unsuccessful. However, single crystals could be obtained from a solution of the complex to which a small amount of $FeCl_2$ had been added.[17] All spectroscopic data remained unaffected by the presence of $FeCl_2$, whose only function was to help in obtaining single crystals by allowing the formation of the $FeCl_4^{2-}$ counteranion. An ORTEP diagram of the cation $[Fe(L^2)(CH_3CN)]^{3+}$ is shown in Figure 3.

The main feature of this structure is the modification of the ligand: the N7−C6 distance [1.294(4) Å] indicates the presence of an imine bond. Moreover, an almost planar conjugated pyridinyl-*o*-phenylenediamine system is formed, which is responsible for the intense absorption at λ = 322 nm in the UV/Vis spectrum. As expected from the EPR spectrum, the metal−ligand distances are all short (< 1.96 Å), which is consistent with a low-spin state for the metal atom in the solid state. The short N7−Fe distance [1.883(3) Å] corresponds to a strong coordination of the imine to the metal atom. We suggest that the new broad absorption at λ = 694 nm is due to an Fe→N=C metal-to-ligand charge transfer (MLCT) transition. It is noteworthy that the hydroxide is not coordinated to the iron atom — the acetonitrile ligand is preferred by the trication. This preference

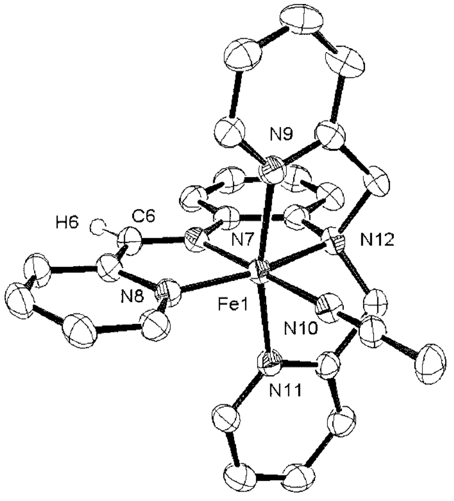

Figure 3. ORTEP diagram of the cation $[Fe(L^2)(CH_3CN)s]^{3+}$ with a partial numbering scheme; all hydrogen atoms except the aldimine one have been removed for clarity; selected bond lengths [Å] and angles [°]: Fe1−N7 1.881(3), Fe1−N8 1.955(3), Fe1−N9 1.972(3), Fe1−N10 1.951(3), Fe1−N11 1.960(3), Fe1−N12 1.989(4), N7−C6 1.294(4); N7−Fe1−N10 178.68(13), N8−Fe1−N12 166.82(14), N9−Fe1−N11 166.17(13)

may derive from the *trans* effect of the strong imine−Fe^{III} bond.[18]

Decoordination of the ligand could be achieved by treatment of a solution of $[Fe(L^2)(CH_3CN)][OH][Cl]_2$ with potassium hydroxide; L^2, obtained as a reddish oil, was characterised by ^1H NMR spectroscopy and mass spectrometry.

Iron complexes with the related pentadentate imine ligand *N*,*N*-bis(pyridin-2-ylmethyl)-*N*′-[(1*E*)-pyridin-2-ylmethylene]ethane-1,2-diamine ($SBPy_3$) have been previously obtained by direct reaction of iron salts with the stable free ligand.[19] In this case the iron(III) state was reported to be unstable, and only the diamagnetic iron(II) complex was fully characterized. At first glance, $SBPy_3$ looks similar to L^2. Thus, $[Fe(L^2)(CH_3CN)][OH][Cl]_2$ might be expected to be unstable. However, this is definitely not the case. This behaviour must be due to a major difference in the structure of $SBPy_3$ and L^2. The presence in the latter of a conjugation between the pyridyl, the imine and the aromatic moieties (from the *o*-phenylenediamine skeleton, absent in $SBPy_3$) seems to be crucial. This obviously provides both a different rigidity of the ligand and modified electronic properties, and, as a consequence, very different spectroscopic properties and stability patterns.

In summary, we provide in this article the first direct evidence for desaturation of a coordinated acyclic secondary amine initiated by the reaction of molecular dioxygen with a stable iron(II) complex. This reaction is certainly related to the peculiar structure of the ligand, and especially the presence of both a secondary amine and a non-innocent benzylic position close to the metal center. From a mechanistic point of view, oxidation of the iron(II) center to iron(III) by molecular dioxygen has been reported in the chemistry of dichlorotris[(2-pyridylmethyl)amino]iron(II) complexes,[13] and seems also to be a reasonable starting hypothesis here. However, the role of dioxygen in the overall reaction is, at present, not completely established. Mechanistic investigations are currently being carried out in our laboratory.

Experimental Section

Metallation of L^1: This reaction was carried out with 100 mg of L^1 according to the procedure detailed in ref.[14] The desired iron complex (130 mg, 90% yield) was obtained in microcrystalline form after workup. $C_{26}H_{26}Cl_2FeN_6$ (549): calcd. C 56.83, H 4.73; found C 57.01, H 4.82. The ^1H NMR spectrum displays a complex set of broad and paramagnetically shifted peaks lying between $\delta = 170$ and -40 ppm. It is provided as Supporting Information.

Oxygenation of $[Fe(L^1)Cl][Cl]$ on a Preparative Scale: After addition of dry dioxygen by syringe to a solution of 100 mg of $[Fe(L^1)Cl][Cl]\cdot CH_3CN$ in acetonitrile, the medium was allowed to stand for 24 h. It was then concentrated and a dark compound precipitated by addition of diethyl ether. The dark-green solid was recrystallised from acetonitrile/diethyl ether, washed with diethyl ether and dried under vacuum (90 mg, 88% yield). $C_{26}H_{25}Cl_2FeN_6O$ $\{[Fe(L^2)(CH_3CN)][OH][Cl]_2\}$ (564): calcd. C 55.32, H 4.43; found C 55.19, H 4.28. The compound was also characterised by ES mass spectrometry. The spectra were recorded in the positive mode without addition of any acidic source because the compounds are somehow sensitive to protonation. High-power conditions were therefore used, and *m*/*z* values differing by −1 unit were generally observed. The traces are provided as Supporting Information. *m*/*z* (%) = 492 (100) $[\{Fe(L^2)(CH_3CN)\}\{OH\}]^{2+}$, 450 (5) $[\{Fe(L^2)\}\{OH\}]^{2+}$, 378 (6) $[L^2 - H]^+$. The EPR spectrum was recorded in solution (CH_3CN) at 30 K (power: 20.2 mW; modulation amplitude: 5.01G; modulation frequency: 100.00 kHz). The ^1H NMR spectrum displays a complex set of broad and paramagnetically shifted peaks lying between $\delta = 120$ and -15 ppm. It is provided as Supporting Information.

Decomplexation: A green acetonitrile solution of $[Fe(L^2)(CH_3CN)][OH][Cl]_2$ (100 mg in 100 mL) was treated with an aqueous solution of KOH. The medium was extracted with dichloromethane, which was subsequently washed, dried and concentrated. The free imine (50 mg) was recovered as a light reddish-brown oil after addition of pentane. We could not avoid the presence of impurities in the decomplexation medium, detected by ^1H NMR as weak signals in the aromatic region. Attempts to purify L^2 by chromatography were unsuccessful, the imine being unstable on the stationary phases. For this reason we could not obtain any satisfactory elemental analysis. ^1H NMR ($CDCl_3$): δ = 8.56, 8.52, 8.44 (broadened doublets, 1 H each, α-pyridyl), 7.80−7.10 (m, 13 H, aromatic), 6.55 (s, 1 H, *H*C=N), 4.46 (s, 4 H, CH_2) ppm; additional weak signals were also present in the aromatic region. ES/MS: *m*/*z* = 378 $[L^2 - H^+]$ ($C_{24}H_{21}N_5$).

X-ray Crystallography: For details, see refs.[15,17]; CCDC-224186 and -224187 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: + 44-1223-336-033; E-mail: deposit@ccdc.cam.ac.uk).

Acknowledgments

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[12] Systematically, dichloroiron(II) complexes are obtained from $FeCl_2$ and ligands in anhydrous conditions, with dried solvents.[11,13] However, a general feature in this kind of chemistry is that, provided the reaction medium is kept under strictly anaerobic conditions, the presence of noticeable amounts of water in the solvent (up to 5% in technical grade CH_3CN for instance) does not induce significant changes in preparation, structure or stability of the complexes. The same observation accounts for complex $[Fe(L^1)Cl][Cl]$.

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[15] Crystal data for $[Fe(L^1)Cl][Cl]\cdot CH_3CN$: yellow crystals, $C_{26}H_{26}Cl_2FeN_6$ (549.28), tetragonal, $P4_3$, $a = b = 9.378(1)$, $c = 29.134(2)$ Å, $V = 2562.2(4)$ Å^3, $Z = 4$, $R = 0.061$, $Rw = 0.120$.

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[17] Crystal data for $[Fe(L^2)(CH_3CN)][OH][FeCl_4]\cdot(CH_3CN)_2$: dark green crystals, $C_{30}H_{30}Cl_4Fe_2N_8O$ (772.12), triclinic, $P\bar{1}$, $a = 12.415(1)$, $b = 12.520(1)$, $c = 13.261(1)$ Å, $V = 1662.5(2)$ Å^3, $Z = 2$, $R = 0.056$, $Rw = 0.174$.

[18] The hydroxide anion lies between one chloride ion of the $FeCl_4^{2-}$ anion and the nitrogen atom of one of the CH_3CN molecules present as solvate in the unit cell. Short contacts are found and support stabilization of OH^- in this position by hydrogen bonding.

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