Biomimetic Oxidation Reactions of a Naked Manganese(V)–Oxo Porphyrin Complex

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Abstract: The intrinsic reactivity of a manganese(V)-oxo porphyrin complex, a typically fleeting intermediate in catalytic oxidation reactions in solution, has been elucidated in a study focused on its gas-phase ion-chemistry. The naked high-valent Mn^V-oxo porphyrin intermediate **1** ([(tpfpp)Mn^{V}O]$^+$; tpfpp = meso-tetrakis(pentafluorophenyl)porphinato dianion), has been obtained by controlled treatment of [(tpfpp)Mn^{III}]Cl (**2**-Cl) with iodosylbenzene in methanol, delivered in the gas phase by electrospray ionization and assayed by FT-ICR mass spectrometry. A direct kinetic study of the reaction with selected substrates, each containing a heteroatom X (X=S, N, P) including amines, sulfides, and phosphites, was thus performed. Ionic products arising from electron transfer (ET), hydride transfer (HT), oxygen-atom transfer (OAT), and formal addition (Add) may be observed, with a predominance of two-electron processes, whereas the product of hydrogen-atom transfer (HAT), [(tpfpp)Mn^{IV}OH]$^+$, is never detected. A thermochemical threshold for the formation of the product radical cation allows an evaluation of the electron-transfer ability of a Mn^V-oxo complex, yielding a lower limit of 7.85 eV for the ionization energy of gaseous [(tpfpp)Mn^{IV}O]. Linear free-energy analyses of the reactions of para-substituted N,N-dimethylanilines and thioanisoles indicate that a considerable amount of positive charge is developed on the heteroatom in the oxidation transition state. Substrates endowed with different heteroatoms, but similar ionization energy display a comparable reaction efficiency, consistent with a mechanism initiated by ET. For the first time, the kinetic acidity of putative hydroxo intermediates playing a role in catalytic oxidations, [(tpfpp)Fe^{IV}OH]$^+$ and [(tpfpp)Mn^{IV}OH]$^+$, has been investigated with selected reference bases, revealing a comparatively higher basicity for the ferryl, [(tpfpp)Fe^{IV}O], with respect to the manganyl, [(tpfpp)Mn^{IV}O], unit. Finally, the neat association reaction of **2** has been studied with various ligands showing that harder ligands are more strongly bound.

Introduction

High-valent metal–oxo complexes are involved as key intermediates in useful synthetic and biological oxidation processes.[1] Among biomimetic oxidants developed to unveil the mechanistic routes activated by metalloenzymes, iron(IV)-oxo porphyrin π-cation radical species (Cpd I) have been extensively investigated for their role as the competent catalysts of heme based monooxygenases, including cytochromes P450.[2]

Conversely, although endowed with higher reactivity[3] and versatility in various oxidation reactions and implicated in the production of dioxygen at the core of photosystem II,[4] the analogous manganese–oxo species has eluded detection until Groves first reported the synthesis of water-soluble Mn^V-oxo porphyrin complexes and their characterization as low-spin (S=0) ground-state species.[5]

Since then, other high-valent manganese–oxo intermediates based on corrole,[6] salen,[7] corrolazine,[8] and porphyrin ligands[5,9] have been prepared in aqueous or organic solvents and numerous experimental and theoretical studies have explored their electronic structures and reactivity in diverse processes, including olefin epoxidation, C−H bond hydroxylation, hydride-transfer and oxidation of sulfides, amines, halides, and phosphines.[10,11]

Notably, only recently compelling spectroscopic evidence has been able to characterize Mn^V-oxo porphyrin complexes [Mn^V(O)X]$^+$ prepared in basic solvents as a singlet trans-dioxomanganese(V) anions (X=O^{2-}), unreactive with alkenes, but capable of abstracting hydride from NADH analogues.[12] DFT calculations suggest that the remarkable oxidation reactivity of the oxo–hydroxo (X=OH$^-$) and oxo–aqua (X=H$_2$O) complexes that are favored at low pH may

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be related to a decreasing barrier for spin-crossover. In fact, in the series from $X = O^{2-}$ to OH^- and H_2O the barrier separating the unreactive singlet ground state from the reactive high spin states (triplet and quintet), endowed with radical character on oxygen, decreases.[13]

In an effort to elucidate the complex role of environmental factors as distinct from the intrinsic features which govern the chemical behavior of Mn^V-oxo complexes, it has appeared worthwhile using the tools of gas-phase ion chemistry.[14] An access should be allowed to transient intermediates that are elusive species in solution.[15] Previous reports on Cpd I like species, generated either in solution or in the gas phase, and probed by their reactions as naked species towards simple molecules of biological relevance (L), has shown a pronounced reactivity of the iron–oxo intermediates with sulfides, pyridines, and phosphites, and has revealed the ionic intermediates responsible for the activation of amines.[16]

More recently, the access to a ligand-free Mn^V-oxo porphyrin ion, $[(tpfpp)Mn^VO]^+$ (tpfpp = meso-tetrakis(pentafluorophenyl)porphinato dianion), $\mathbf{1}$, prepared in solution and gently transferred in a solvent free environment by electrospray ionization (ESI)[17] has been demonstrated.[18] The so-formed, naked $[(tpfpp)Mn^VO]^+$ ion ($\mathbf{1}$) has been assayed by Fourier transform ion cyclotron resonance (FT-ICR) mass spectrometry,[19] and observed to act as an excellent epoxidation reagent towards olefins, outperforming its iron analogues in the gas phase.[16a]

In view of this result, we have become keenly interested in extending the survey of the oxidant reactivity of $[(tpfpp)Mn^VO]^+$ in the gas phase, void of the complicating effects of solvent, axial donor interactions, and aggregation.

Herein we provide an insight into the ability of $\mathbf{1}$ to mediate selective oxygen atom-transfer (OAT) to a range of reductants containing a heteroatom X (X = S, N, P) by the direct determination of reaction patterns and thermal rate constants.
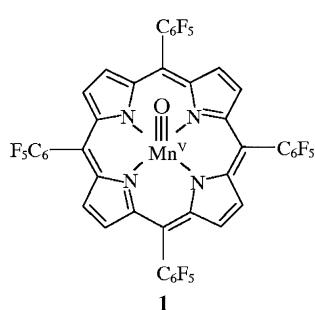
$\mathbf{1}$

zene (PhIO, ca. 0.5 mM) at $-20\,°C$ has been recently described.[18] The reaction mixture sampled by ESI and characterized by high resolution FT-ICR mass spectrometry exhibits an isotopic cluster centered at m/z 1043.0116, revealing the incorporation of one oxygen atom into the reactant species $[(tpfpp)Mn^{III}]^+$ ($\mathbf{2}$) centered at m/z 1027.0148. Unfortunately, upon collision-induced dissociation (CID) experiments, aimed at revealing the structure of the oxo-manganese complex, only trivial hydrogen fluoride losses are obtained.

When trapped in the FT-ICR cell, the mass-selected ion is stable toward unimolecular dissociation ($k_{diss} \leq 0.001\ s^{-1}$) and, when allowed to react with olefins, it behaves as a mixture of two isomeric species. A major fraction of the ion population conforms to a complex bearing a Mn^V-oxo unit, $[(tpfpp)Mn^VO]^+$ ($\mathbf{1}$), able to transfer the manganese-bound oxygen atom to olefins and to regenerate $\mathbf{2}$ displaying O-atom transfer reactivity. A second fraction displays hardly any reactivity with olefins, thereby suggesting that the entered O-atom is rather placed on the porphyrin frame than bound to the metal. This isobaric ion is henceforth described as $[(tpfpp-O)Mn^{III}]^+$ ($\mathbf{3}$). The latter species was found to efficiently add to 2-fluoropyridine (2Fpy) yielding exclusively the $[(tpfpp-O)Mn^{III}(2Fpy)]^+$ adduct, formed by attack of the ligand at a vacant axial site on the four-coordinated manganese center. This binding mode is consistent with the results of a CID experiment, in which the exclusive loss of the ligand 2Fpy has been found.[18] The notably different reactivity observed with the sampled olefins and with 2Fpy has allowed the isomeric population at nominal m/z 1043 to be resolved.[16c,18,20] The relative amount of $\mathbf{1}$ has been consistently found to be $\geq 60\%$. An alternative explanation, namely that the ions at m/z 1043 comprise the same structural isomer in different spin states may not be discarded a priori, given the critical influence of spin state in oxidation reactions involving metal–oxo species.[21]

Reactivity of $[(tpfpp)Mn^V=O]^+$ ions with gaseous substrates: The thermal reactivity of $\mathbf{1}$ toward several reagents (L), including sulfur and phosphorous compounds and amines, is investigated in the gas phase by ESI-FT-ICR mass spectrometry. In all cases, the reaction leads to the complete disappearance of the active intermediate $\mathbf{1}$, which reverts back to the starting $[(tpfpp)Mn^{III}]^+$ complex either releasing an oxygen atom to L [(Eq. (1)], or formally adding a ligand molecule [Eq. (2)]. The branching ratio of the two channels depends on the specific substrate.

Results and Discussion

Preparation and characterization of $[(tpfpp)Mn^V=O]^+$: The preparation of a Mn^V-oxo porphyrin complex by treatment of a methanol solution of the porphyrinatomanganese(III) chloride $[(tpfpp)Mn^{III}]Cl$ (**2-Cl**; ca. 5 µmM) with iodosylben-

$$[(tpfpp)Mn^VO]^+ + L \begin{cases} \xrightarrow{OAT} [(tpfpp)Mn^{III}]^+ + LO & (1) \\ & \mathbf{2} \\ \xrightarrow{Add} [(tpfpp)Mn(O)L]^+ & (2) \\ & \mathbf{1L} \\ \xrightarrow{ET} L^+ + [(tpfpp)Mn^{IV}O] & (3) \\ \xrightarrow{HT} [L-H]^+ + [(tpfpp)Mn^{III}OH] & (4) \\ \xrightarrow{HAT} [(tpfpp)Mn^{IV}OH]^+ + [L-H]^· & (5) \end{cases}$$

In addition, compounds with an ionization potential below 7.85 eV[22] undergo an electron transfer (ET) process that results in radical cation $L^{+\cdot}$ and neutral $[(tpfpp)Mn^{IV}O]$ [Eq. (3)], while aliphatic tertiary amines yield an iminium ion $[L-H]^{+}$ by a formal hydride transfer (HT) route [Eq. (4)]. All these routes [Eqs. (1)–(4)] are independent channels, as evident from the constant ratio of the product ion abundances at any reaction time (see for example the kinetic profile of the reaction between trimethylamine and **1** reported in Figure 1). Notably, the reactivity behavior of **1**
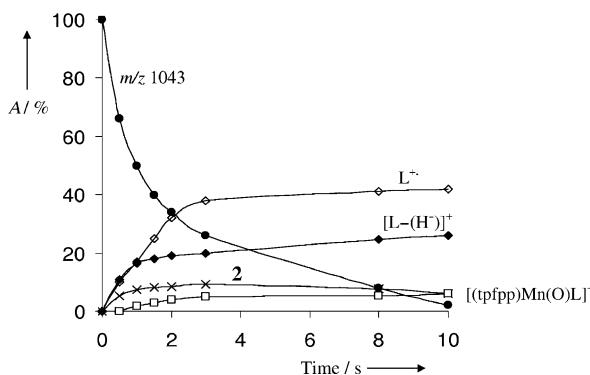
Figure 1. Time dependence of relative ion intensities (A; %) obtained when mass-selected $[(tpfpp)Mn(O)]^{+}$ ions, depleted of the $[(tpfpp-O)Mn^{III}]^{+}$ fraction at m/z 1043 with 2F-py, are allowed to react with $L = N(CH_3)_3$ at 1.6×10^{-8} mbar.

does not display any H-atom transfer (HAT) reactivity [Eq. (5)],[23] and the expected product $[(tpfpp)Mn^{IV}OH]^{+}$ ion at m/z 1044 is never observed, thus suggesting a reaction rate lower than the experimental limit of 10^{-12} cm^3 molecule^{-1} s^{-1}. Lack of H-atom reactivity has similarly been found with compounds with very weak C−H or O−H bonds, including 1,4-cyclohexadiene,[18] cyclobutyl-, and benzyl alcohol. Examples of HAT processes have been reported to be prominent processes by gaseous (non)metal oxides, including MnO^{+},[24] whose chemistry is dominated by radical-abstraction reactions. In a similar way, Mn^V-oxo and Mn^{IV}-hydroxo catalysts are able to promote C−H homolytic cleavage due to their pronounced oxyl character.[11h]

Overall, the decay of the ion abundance of **1** responds to pseudo first order kinetics, as shown by the representative plot of the reaction with thioanisole illustrated in Figure 2.

An insight into the bonding features of L within all the adduct species $[(tpfpp)Mn(O)L]^{+}$ [Eq. (2)] has been gathered from a CID experiment. Not unexpectedly, due to the presence of distinct isomers accounting for the ionic population at m/z 1043, both ions **2** and **3** are cleaved as fragments. The release of **2** reveals the formation of an oxidized substrate LO, by O coupling within the addition complex of L with $[(tpfpp)Mn^{V}O]^{+}$, whereas the release of **3** (and of an intact L) is rather evidence for the formation of an adduct with L bound to four-coordinate $[(tpfpp-O)Mn^{III}]^{+}$ at a vacant axial site. An example of $[(tpfpp)Mn(O)L]^{+}$ complex conforming to the latter behavior is shown in Figure 3 (L =
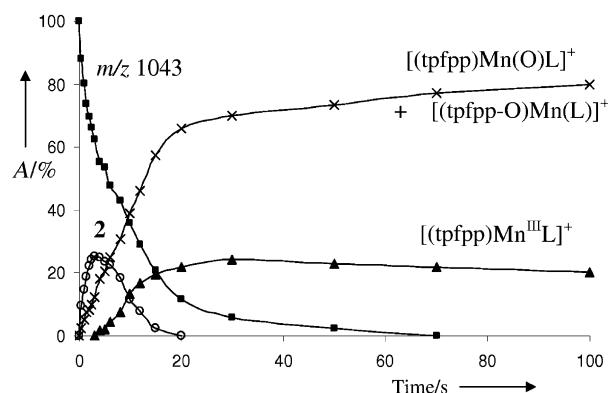

Figure 2. Time dependence of relative ion intensities (A; %) formed after the selection of ions at m/z 1043 (a mixture of $[(tpfpp)Mn^{V}O]^{+}$ and $[(tpfpp-O)Mn^{III}]^{+}$) in L = C$_6$H$_5$SCH$_3$ (L) at 5.5×10^{-8} mbar.
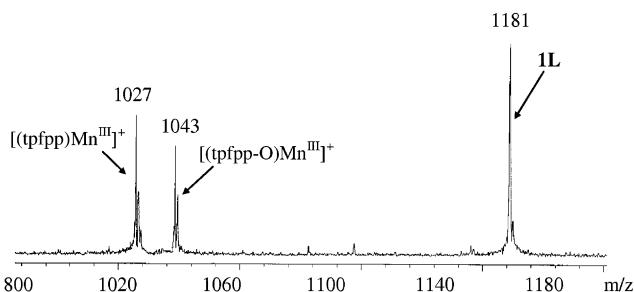
Figure 3. ESI-FT-ICR mass spectrum displaying the formation of ions $[(tpfpp)Mn^{III}]^{+}$ at m/z 1027 and $[(tpfpp-O)Mn^{III}]^{+}$ at m/z 1043 when mass selected adduct ions, $[(tpfpp)Mn(O)L]^{+}$ (L = p-CH$_3$-C$_6$H$_4$-SCH$_3$), at m/z 1181 are submitted to low-energy CID. Methyl p-methylphenylsulfoxide and the intact neutral ligand L are conceivably the neutral fragments released in the dissociation process, respectively.

p-CH$_3$-C$_6$H$_4$SCH$_3$). Ligand-addition reactions to four-coordinate metal porphyrin complexes in the gas phase are well documented.[16a,25,26]

Accordingly, when the ion population at m/z 1043 is depleted of the $[(tpfpp-O)Mn^{III}]^{+}$ fraction by exposure to 2Fpy along the path leading the ions from the ESI source to the FT-ICR cell, to give the adduct $[(tpfpp-O)Mn^{III}(2Fpy)]^{+}$, the remaining ions entering the cell are mainly composed of the metal oxo $[(tpfpp)Mn^{V}O]^{+}$ isomer. As a result, the adduct ions at m/z 1181, formed by reaction with p-CH$_3$-C$_6$H$_4$-SCH$_3$ in the ICR cell, release **2** in far greater amount upon CID. L−O coupling within the addition complex is about complete (Figure 1S in the Supporting Information), thus resulting from an ion population at m/z 1043 mainly accounted by isomer **1**.

Both routes ([Eq. (1)] and [(Eq. (2)]) comply to the oxidative ability of **1** in the gas phase, whereas the $[(tpfpp-O)Mn^{III}]^{+}$ isomer is unable to oxidize any of the investigated L, even in the case of excellent O-acceptors like trimethylphosphite,[27] but rather leads to a five-coordinate $[(tpfpp-O)Mn^{III}L]^{+}$ adduct.

Amine oxidation by [(tpfpp)Mn^{V}O]$^+$ ions: Due to their relevance in chemistry and in the metabolism of xenobiotic amines, the oxidative N-dealkylation reactions of N,N-dialkylamines by heme enzymes and their model compounds has been intensely investigated.[1d,2g–h,28] The active oxidant, thought to be a short-lived Cpd I species, has been proposed to operate by two alternative mechanisms initiated by either a one-electron abstraction (ET), yielding a nitrogen centered radical cation and an iron(IV)-oxo porphyrin species (Cpd II), or by a neat hydrogen atom transfer (HAT), leading to a carbon radical which is then trapped in a rebound step.[28] In the gas phase, recent computational studies on the oxidation of a series of N,N-dimethylanilines with a Cpd I model bound to an SH anionic ligand support a HAT mechanism, which moves to an ET-initiated mechanism in the case of a bare, five-coordinate Cpd I model, devoid of the thiolate ligand.[29]

In a recent mass spectrometric study, the reaction of iron(IV)-oxo porphyrin radical cation, [(tpfpp)$^{+•}$Fe^{IV}=O]$^+$, with a series of *para*-substituted N,N-dimethylanilines (*p*-X-DMAs) has been found to proceed via an electron transfer/proton transfer mechanism, displaying a linear correlation between the rate constants and the ionization energy of DMAs.[16c] ESI-FT-ICR results provided direct experimental evidence for the formation of charged intermediates along the reaction pathway, including the amine radical cation and the iminium ion, the putative intermediates proposed in solution-phase studies.

Also the bare FeO$^+$ cation, lacking any coordination environment, has been found to react by ET and, to a lesser extent, by HT, the latter process displaying a kinetic isotope effect sensitive to the presence and features of an added ligand.[30]

In the present investigation, a kinetic study using FT-ICR mass spectrometry has been performed to evaluate the reactivity and investigate the mechanism of the reaction of a series of amines, including alkylamines, pyridines and *p*-X-DMAs (X=CF$_3$, H, CH$_3$), with [(tpfpp)Mn^{V}O]$^+$, whose high oxidizing power, due in part to the electron-deficient porphyrin ligand,[31] is expected to favor a primary ET process in the gas phase.

The second-order rate constants (k_{exp}), along with the relative kinetic efficiencies ($\Phi = 100 \times (k_{exp}/k_{coll})$ and the product branching ratios, are collected in Table 1.

The data reported in Table 1 show that all sampled amines, spanning a significant range of IE values, undergo oxygen-atom transfer [Eq. (1)] to a large extent, with the exception of pyridine and γ-picoline, which yield only the addition product [Eq. (2)]. Indeed, as already stated, L−O coupling also occurs within the amine adducts, as inferred by the release of [(tpfpp)Mn^{III}]$^+$ upon CID of the adduct and by the occurrence of a ligand substitution reaction replacing an LO unit with a ligand molecule.[16a] Figure 4 shows the time dependence of ion abundances when the mass-isolated ion at m/z 1043 is allowed to react with a stationary pressure of L=*p*-CH$_3$-C$_6$H$_4$N(CH$_3$)$_2$. The profiles of product ion abundances deriving from the routes of Equations (1)–(3)

Table 1. Rate constants (k_{exp}) and efficiencies (Φ) of the reactions of selected amines (L) with [(tpfpp)Mn^{V}O]$^+$ (**1**) formed by the reaction of [(tpfpp)Mn^{III}]$^+$ with PhIO in CH$_3$OH.

| L | IE [eV][a] | k_{exp}[b] | Φ[c] | Product distribution [%][d] | | | |
				ET	HT	OAT	Add
pyridine	9.26	0.48	3.6	–	–	–	100
γ-picoline	9.0	3.0	22	–	–	–	100
(CH$_3$)$_2$NH	8.24	0.65	5.4	–	–	85	15
(CH$_3$)$_3$N	7.85	2.2	22	5	55	30	10
(C$_2$H$_5$)$_3$N	7.53	4.0	35	20	32	48	–
p-CF$_3$-C$_6$H$_4$N(CH$_3$)$_2$	7.52[e]	0.79	5.5	2	–	98	–
C$_6$H$_5$N(CH$_3$)$_2$	7.04[e]	1.8	13.8	13	–	70	17
p-CH$_3$-C$_6$H$_4$N(CH$_3$)$_2$	6.81[e]	3.4	31	17	–	62	21

[a] IE values are experimental values unless stated otherwise.[22] [b] Phenomenological rate constants in units of 10^{-10} cm^3 molecule^{-1} s^{-1}, at the temperature of the FT-ICR cell of 300 K. The estimated error is $\pm 30\%$, while the internal consistency of the data is within $\pm 10\%$. [c] $\phi = (k_{exp}/k_{coll}) \times 100$. Collision rate constants (k_{coll}) evaluated with the parameterized trajectory theory.[54] [d] Product branching ratios associated to electron transfer (ET), hydride loss (HT), oxygen atom transfer (OAT), and addition (ADD) routes. [e] Calculated IE (eV) of the neutral N,N-dimethylanilines determined at B3LYP/6-311+G** level.[16c]
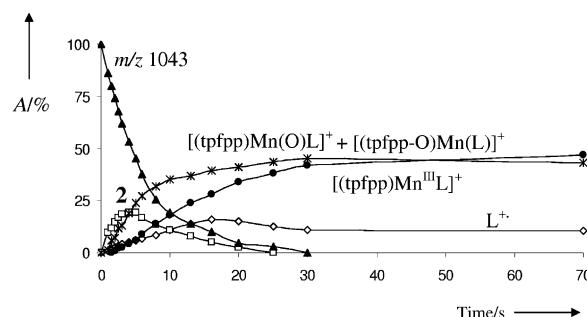

Figure 4. Time dependence of relative ion intensities (A;%) formed after the selection of ions at m/z 1043 (a mixture of [(tpfpp)Mn^{V}O]$^+$ and [(tpfpp-O)Mn^{III}]$^+$) in L=*p*-CH$_3$-C$_6$H$_4$N(CH$_3$)$_2$ at 2.7×10^{-8} mbar.

reveal that OAT, Add and ET processes are independent and characterized by different rates. At longer elapsed time, the OAT product, [(tpfpp)Mn^{III}]$^+$, reacts by ligand association with the neutral in the cell, giving [(tpfpp)Mn^{III}L]$^+$, while the Add product, [(tpfpp)Mn(O)L]$^+$, undergoes a formal ligand displacement eventually forming [(tpfpp)Mn^{III}L]$^+$ concomitant with the release of LO.

Noteworthy, amine radical cations, L$^{+•}$, start to appear with the most oxidizable compounds, namely tertiary aliphatic and aromatic amines, suggesting that ET products are thermochemically allowed for IE values ≤ 7.85 eV.[18] As to the iminium ion, formed only from tertiary aliphatic amines, L=NR$_3$ (R=CH$_3$, C$_2$H$_5$), it may well arise from deprotonation of the initial amine radical cation by the manganyl species, [(tpfpp)Mn^{IV}O], within the reaction complex (**4**; [Eq. (6)]). For example, for L=N(C$_2$H$_5$)$_3$, the pronounced α-C−H acidity of L$^{+•}$ is expected to give the corresponding conjugate base, [L−H]$^•$, which in turn may be readily oxidized to the iminium ion, [L−H]$^+$ [Eq. (6)].[32]

$$[(tpfpp)Mn^VO]^+ + L$$
$$\mathbf{1}$$
$$\downarrow$$
$$[(tpfpp)Mn^{IV}O + L^{+\cdot}] \rightarrow \{[(tpfpp)Mn^{IV}OH]^+ + [L-H]^\cdot\} \rightarrow [(tpfpp)Mn^{III}OH] + [L-H]^+ \qquad (6)$$
$$\mathbf{4}$$

$$L = NR_3 \ (R = CH_3, C_2H_5)$$
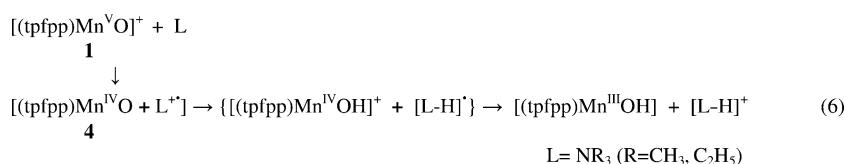
In distinct contrast, the gas phase reaction of amines with iron(IV)-oxo porphyrin radical cation complexes, conforming to the same mechanism described by Equation (6), yields a consistently high amount of HT products with the majority of tested amines,[16c] suggesting a higher basicity for the [(tpfpp)Fe^{IV}O] ferryl species, in comparison with the manganyl complex presently investigated.

To confirm the origin of the observed reactivity behavior, the Brønsted acidity of high-valent metal–hydroxo species, [(tpfpp)M^{IV}OH]$^+$ (M = Mn, Fe) obtained by using either KHSO$_5$ (oxone) or hydrogen peroxide as the oxidant, respectively, has been assayed with gaseous N(C$_2$H$_5$)$_3$, a highly basic reference base B (gas-phase basicity (GB) = 951 kJ mol^{-1}).[22] Due to typically negligible activation barriers, proton-transfer reactions to B may present efficiency values spanning from close to zero, for endoergonic reactions, to nearly unity for exoergonic processes. The efficiency for proton transfer from the iron–hydroxo complex ($k_{exp} = 3.7 \times 10^{-12}$ cm^3 molecule^{-1} s^{-1}; $\Phi = 0.37\%$) is appreciably lower than the one from the manganese–hydroxo species ($k_{exp} = 4.05 \times 10^{-11}$ cm^3 molecule^{-1} s^{-1}; $\Phi = 4.1\%$). This finding reveals that the GB of the conjugate base of [(tpfpp)Fe^{IV}OH]$^+$, namely [(tpfpp)Fe^{IV}O], is distinctly higher than that of the conjugate base of [(tpfpp)Mn^{IV}OH]$^+$, namely [(tpfpp)Mn^{IV}O], thus supporting the suggested basis for the observed reactivity behavior.

The important role of high-valent metal complexes containing a hydroxide ligand has been recently recognized,[33] and a selective HAT reactivity has been reported for [Mn^{IV}-(salen)OH], although distinctly lower if compared to the one of [Mn^{IV}(salen)O].[34]

Notably, the present results allow a direct comparison of the intrinsic basic properties of bare Mn^{IV}=O and Fe^{IV}=O porphyrin complexes, which is often concealed by the use of different solvents, counter ions, or axial ligands.[35]

However, an alternative possibility that the iminium ion may be formed by a direct HAT path within the ion-neutral complex [(tpfpp)Mn^{IV}O+L$^{+\cdot}$] cannot be ruled out a priori, in view of the very low C−H bond dissociation energy (BDE) for the methylene group adjacent to the amino nitrogen.[36] In fact, according to calculations at the B3LYP/6-31+G** level of theory, the BDE of the C−H bond within (C$_2$H$_5$)$_2$N$^+$-C-H(H)(CH$_3$) amounts to 137 kJ mol^{-1}, which may be compared with the C−H BDE of (CH$_3$)$_3$N$^{+\cdot}$ comprised within 223–239 kJ mol^{-1}.

The response of the oxidation reaction to electronic demand has been explored evaluating the dependence of log(Φ) values for the reaction of **1** with p-X-DMAs on the substituent σ^+ constants. A fair linear free energy correlation ($r^2 = 0.980$) is obtained, with a negative ρ^+ value (Fig-

ure 2S in the Supporting Information). Similarly, the reaction efficiency of the sampled amines is found to decrease with increasing IE of the amine.

These results, which denote positive charge development at the nitrogen centre in the transition state of the rate-determining step, suggest a mechanism initiated by an ET event from tertiary aliphatic and aromatic amines to the gaseous Mn^V-oxo ion **1**, lacking any axial ligand. Negative ρ values were also reported in solution for a rate-limiting ET process in the oxidative N-dealkylation of tertiary amines by heme and nonheme oxoiron(IV)-oxo complexes.[28c,d,37]

As to the possible nature of the oxidation products, theoretical studies on the OAT route of DMAs with a CpdI model bearing a SH ligand dismiss the formation of an aniline N-oxide product, while the amine N-oxide is conversely expected when pyridine compounds are sampled.[29]

Oxidation of nitrogen oxides, sulfides, and phosphorous compounds by [(tpfpp)Mn^{V}O]$^+$ ions: Sulfur oxidation is an enantioselective metabolic pathway involved in the detoxification of sulphur-containing drugs and xenobiotics operated by heme enzymes such as peroxidases and cytochrome P450.[38] Insights into these processes at the molecular level may elucidate the formation of reactive metabolites from sulfur containing drugs and aid in developing procedures to bring about selective (asymmetric) sulfide oxidation. From several evidences, including fragmentation and formation of disulfide products from selected sulfides, an ET pathway has been suggested in the sulfoxidation catalyzed by peroxidases, with the exception of chloroperoxidase (CPO), and by biomimetic complexes.[39,40] Alternatively, several experimental and theoretical studies have indicated a concerted, single-step mechanism for biomimetic oxidations of sulfides to sulfoxides by CpdI species, involving myoglobin/heme enzyme mutants and chemical models.[1d,2h,41] However, a bias in favor of the formerly proposed ET mechanism has been suggested for an iron–oxo complex soluble in water, where the substrate oxidation potentials are considerably lower than in organic solvents.[42] Recently, the reactivity of high valent Mn(IV or V)-oxo porphyrin complexes generated in basic aqueous solution have been investigated in the C−H bond activation of alkylaromatics sulfides and in the oxidation of thioanisoles, which were found to involve a hydrogen-atom abstraction (one-electron process) and a direct O-transfer step (two-electron process), respectively.[12c] Table 2 summarizes the second-order rate constants (k_{exp}), together with the efficiencies (Φ) and the product branching ratios for the reaction of **1** with dimethylsulfide and with $para$-substituted thioanisoles (p-XC$_6$H$_4$SCH$_3$) holding electron-donating (X = CH$_3$, OCH$_3$) groups. Data for a trivalent phosphorous compound, P(OCH$_3$)$_3$, and nitrogen oxides are also included. The data reported in Table 2 clearly indicate that sulfur-O coupling is accomplished in all cases, as inferred from the reduction of the reagent ion **1** to the starting

Table 2. Rate constants (k_{exp}) and efficiencies (Φ) of the reactions of [(tpfpp)Mn^{V}O]$^+$ (**1**) with selected nitrogen oxides, sulfides, and phosphorous compounds.

L [IE]	IE [eV][a]	k_{exp}[b]	Φ[c]	Product distribution [%][d]		
				ET	OAT	Add
(CH$_3$)$_2$S	8.69	0.52	4.1	–	70	30
C$_6$H$_5$SCH$_3$	7.94	0.70	6.1	–	37	63
p-CH$_3$-C$_6$H$_4$SCH$_3$	7.9	3.5	28	5	24	71[e]
p-CH$_3$O-C$_6$H$_4$SMe	7.80	5.9	44	6	–	94[e]
P(OCH$_3$)$_3$	8.4	0.57	5	–	89	11
NO	9.26	0.027	0.37	–	100	–
NO$_2$	9.59	0.012	0.20	–	100	–

[a] See footnote [a] in Table 1. [b] See footnote [b] in Table 1. [c] See footnote [c] in Table 1. [d] See footnote [d] in Table 1. [e] CID experiment on the adduct ion yields both [(tpfpp)Mn^{III}]$^+$ and [(tpfpp-O)Mn]$^+$ ions, (in 2:1 ratio).

complex **2** with concomitant formation of the sulfoxide ([[Eq. (7)], path b), and from the CID assay of the association product **1l** ([Eq. (7)], path c), which releases ion **2**. In addition, intermediacy of sulfur-centered radical cations is operative for thioanisoles with comparatively lower ionization energy (X=CH$_3$, OCH$_3$) which react by an initial ET process forming RS$^+$·CH$_3$ ([Eq. (7)], path a). The ET process is consistent with the previously estimated lower limit of 8.1 eV for the IE of gaseous [(tpfpp)Mn^{IV}O].[18]

$$[(tpfpp)Mn^VO]^+ + RSCH_3 \xrightarrow{\quad} \begin{array}{l} \xrightarrow{a} [(tpfpp)Mn^{IV}O] + RS^+\!\cdot CH_3 \\ \qquad\qquad\qquad\downarrow d \\ \xrightarrow{b} [(tpfpp)Mn^{III}]^+ + RS(O)CH_3 \\ \xrightarrow{c} [(tpfpp)Mn(O)RSCH_3]^+ \end{array} \quad (7)$$
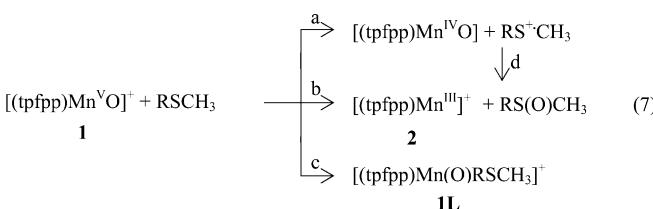
The nature of the *para*-substituent in thioanisoles has an important effect on the reactivity, as evident from the increasing efficiency when the *para*-substituent becomes more electron releasing, with a concomitant bias toward the addition route. At variance with the amine reactions, a free-energy correlation plot with σ^+ values provides poor results, while a more meaningful correlation ($r^2=0.976$) is obtained for σ constants of *para*-substituted thioanisoles. As expected for an electrophilic oxidant, the ρ value is negative (Figure 3S in the Supporting Information), coherent with the electrophilic character of the Mn^V-oxo group of **1** toward the sampled sulfides in the gas phase. This relationship finds an interesting counterpart in the correlation between the IE values of the substrate and the barrier height of the sulfoxidation reaction mediated by Cpd I species.[43]

Although the performance of a correlation of the kinetic data with either σ or σ^+ values has been proposed to support either a one step, concerted oxygen transfer or a two step, electron-transfer mechanism, caution has been suggested against using this kind of evidence as definitive proof of reaction mechanism.[44]

As shown in Table 2, the rate constants for gas-phase sulfoxidation decline from thioanisoles to dimethylsulfide, a trend similarly found in solution and considered to demonstrate a single ET process.[45]

Recent theoretical calculations revealed that Cpd I models with thiolate or imidazole proximal ligands react with dimethylsulfide via a concerted, single-step OAT, with a ligand-dependent spin-state selectivity.[41b]

In the present study, a fast oxygen rebound within the reaction complex ensuing the primary ET step ([Eq. (6)], path d) cannot, however, be excluded when high IE values (≥ 7.9 eV) prevent the formation of the sulfide radical cation.[42]

When the versatility of **1** as an oxidant is assayed in the gas phase toward P(OCH$_3$)$_3$, a major O-atom transfer pathway affords **2** and trimethyl phosphate and an addition process leads to [(tpfpp)Mn(O)P(OCH$_3$)$_3$]$^+$ (Figure 4S in the Supporting Information). The release of **1** when the adduct species is submitted to CID supports a Mn^{III}-trimethylphosphate structure for the ion, which may then be depicted as [(tpfpp)Mn^{III}(OP(OCH$_3$)$_3$)]$^+$.

Although a ΔH_f° difference as large as about 409 kJ mol^{-1} favors OP(OCH$_3$)$_3$ with respect to P(OCH$_3$)$_3$, the reaction of **1** with trimethylphosphite is found to be moderately efficient ($\Phi=4.8\%$), comparing surprisingly well with the value measured for the oxidation of Me$_2$S to dimethylsulfoxide ($\Phi=4.1\%$), a product thermochemically favored by a difference of only about 115 kJ mol^{-1}. In contrast, the reaction of (MeO)$_3$P with [(tpfpp)$^+$·Fe^{IV}O]$^+$, which showed a qualitative correlation between the oxidation rate and the oxophilic character of the active site of L,[28] was among the most efficient ($\Phi=49\%$) among the tested substrates.

However, if an ET initiated mechanism is invoked, the similar oxidation efficiency observed with (CH$_3$)$_2$NH, (CH$_3$)$_2$S, and P(OCH$_3$)$_3$ might be not fortuitous in view of their similar IE values (Table 1 and Table 2, respectively).

Finally, the low rate of net oxygen-atom transfer from **1** to nitrogen oxides NO$_x$ (x=1, 2) as compared to that of the corresponding iron complex, [(tpfpp)$^+$·Fe^{IV}O]$^+$, underlines the relevance of high-valent oxo–iron species in the biochemical reaction of heme enzymes with these natural substrates.

Association reactions of [(tpfpp)Mn^{III}]$^+$ ions: Several ligands were tested as potential substrates of Mn-based (bio)-catalysts with the reduced ion [(tpfpp)Mn^{III}]$^+$ using ESI-FT-ICR. Recently, Mn^{III} complexes have emerged as potent peroxynitrite reductase scavengers with drug-like properties.[46] In analogy with the typical ligand addition reactivity reported for gaseous metal porphyrin ions with vacant axial sites,[16a,b,25,26] the four coordinate species **2** may add the neutral L leaked in the ICR cell to give the adduct [(tpfpp)Mn(L)]$^+$ (**2l**), likely stabilized by collisional and/or radiative cooling.[25,47] All reactions of **2** with selected ligands (L) proceed to the complete consumption of the reagent ion, with the exception of (CH$_3$)$_2$S, where a constant ion abundance ratio is indicative that a reversible process is

established. Table 1S in the Supporting Information presents the kinetics and thermodynamics data of the addition reactions of $[(tpfpp)Mn^{III}]^+$, which are limited to the association of just one ligand molecule, under the prevailing experimental conditions. Only when the sampled neutral is a strong nucleophile, $L = C_6H_5N$, $OP(OCH_3)_3$, a sequential addition step yielding six-coordinated complexes, $[(tpfpp)Mn(L)_2]^+$ (**2l₂**) is also attained (Figure 5S in the Supporting Information illustrates the reaction with OP-$(OCH_3)_3$). The lower efficiency of this route in comparison with the first association step is likely related to the electron-donating performance of the first ligand which reduces the metal reactivity. As to the lack of a second addition route when confronting compounds of higher basicity, like $L = N(CH_3)_3$, but significantly lower dipole moment, it may be likely accounted for by the electrostatic contribution to the coordinative bonding.

On exposure to NO and NO_2, $[(tpfpp)Mn^{III}]^+$ (**3**) proved to be almost inert, at variance with the reactive iron complex.[17a] The lack of an OAT process from NO_2 may suggest that the homolytic Mn–O bond dissociation enthalpy for **1** is lower than $306\ kJ\,mol^{-1}$ (namely, BDE for O-NO),[22] so providing a higher limit for the Mn^VO bond strength. However, the existence of significant kinetic barriers due to the interplay of different spin state surfaces may play an important role as already revealed in the reactions of several metal-oxo complexes.[9b,11c,i,l,26]

Conclusion

High-valent Mn^V-oxo porphyrins are very difficult to select and characterize owing to their inherent instability. A successful route to form $[(tpfpp)Mn^VO]^+$ as naked ion in the gas phase has offered the possibility to explore the oxidation reactivity of a five coordinated Mn^V-oxo species towards a variety of heteroatom-containing substrates (e. g. sulfides, amines, phosphites) using ESI-FT-ICR mass spectrometry. In summary, $[(tpfpp)Mn^VO]^+$ performs as a versatile oxidant, displaying a range of efficient oxygen transfer reactions, with a unique bias towards olefin oxidation.[18] The majority of the reactions of **1** with the substrates studied in this work involve two-electron processes, as evident from the predominance of oxygen-atom transfer, hydride transfer, and addition routes, and from the lack of hydrogen atom transfer products. Several lines of evidence suggest an initial ET event with most of the sampled compounds, which may be followed by either a release of a free radical cation intermediate, for substrates with IE lower than 7.9 eV, or a fast oxygen rebound step within the reaction complex, or a formal hydrogen transfer, comprising stepwise proton–electron transfer. The latter route, observed only from aliphatic tertiary amines, is comparatively less efficient with **1** than with $[(tpfpp)^{+\cdot}Fe^{IV}O]^+$ probably as a result of the lower basicity of a manganyl, $[(tpfpp)Mn^{IV}O]$, with respect to a ferryl, $[(tpfpp)Fe^{IV}O]$, unit.

Whereas the reactivity of $[(tpfpp)^{+\cdot}Fe^{IV}O]^+$ was found to increase in parallel with the oxophilic character of the heteroatom ($S < N < P$), the reactivity of $[(tpfpp)Mn^VO]^+$ correlates with the ionization energy of the substrates.

The binding ability of the reduced species $[(tpfpp)Mn^{III}]^+$ has been examined towards numerous ligands with different functionalities and found to favor harder ligands, endowed with high dipole moments.

Experimental Section

topic pattern, centered at *m/z* 1043, consistent with ion **2**. As already pointed out, the synthetic procedure yields also a certain amount of an isomeric species, presumably oxidized on the porphyrin ligand and unable to deliver an oxygen atom to reductants. The fraction of this four coordinate manganese complex, which may be depicted as [(tpfpp-O)Mn^{III}]$^+$ (**3**), was quantified by the reaction with 2-fluoropyridine (2Fpy) in the FT-ICR cell. 2Fpy selectively traps the isomeric species to give the [(tpfpp-O)Mn^{III}(2Fpy)]$^+$ adduct, which reverts back to **3** losing the 2-Fpy ligand when assayed by low-energy CID.

Acknowledgements

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