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Article

Density Functional Study of the O_2 Binding to $[Cu^I(TPA^R)]^+$ (TPA = Tris(2-pyridylmethyl)amine) in THF and EtCN

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Density functional theory using the B3LYP hybrid functional has been employed to study the formation of $[Cu^{II}(TPA^H)(O_2^-)]^+$ and $[Cu^{II}(TPA^{MeO})(O_2^-)]^+$ (TPA = tris(2-pyridylmethyl)amine) in two different solvents, THF and EtCN. The thermodynamics of solvent coordination as well as that of the overall reactions with O_2 has been computed. The formations of $[Cu^{II}(TPA^H)(O_2^-)]^+$ in THF and of $[Cu^{II}(TPA^{MeO})(O_2^-)]^+$ in both THF and EtCN are found to be initiated from the $[Cu^I(TPA^R)]^+$ species, that is, the Cu complex possessing an empty coordination site. In contrast, the formation of $[Cu^{II}(TPA^H)(O_2^-)]^+$ in EtCN is found to be initiated from the $[Cu^I(TPA^H)(EtCN)]^+$ species, that is, one solvent molecule being coordinated to Cu^I. In general, good agreement is found between theoretical and experimental results. The high accuracy of the B3LYP functional in reproducing experimental thermodynamic data for the present type of transition metal complexes is demonstrated by the fact that the differences between measured and computed thermodynamic parameters ($\Delta G°$, $\Delta H°$, and $-T\Delta S°$, in most cases are less than 2.0 kcal mol^{-1}. An attempt was made to investigate the kinetics of the formation of $[Cu^{II}(TPA^H)(O_2^-)]^+$ in THF and EtCN. Computed free energies of activation, $\Delta G^‡$, are in good agreement with experimental results. However, an analysis of the partitioning of the free energy barriers in enthalpic and entropic contributions indicates that the computationally studied reaction pathway might differ from the one observed experimentally.

1. Introduction

Evolution has generated a wide variety of copper containing proteins that interact with and activate O_2. Some of these proteins are oxidases, that is, redox-active enzymes utilizing O_2 as an agent for substrate oxidation, while others function as O_2 carriers, or oxygenases, incorporating oxygen into substrate molecules. To develop a fundamental understanding of the mechanisms of biochemical/biological Cu/O_2 interaction processes, biomimetic systems such as $[Cu^I(TPA^R)]^+$ (TPA = tris(2-pyridylmethyl)amine) (Figure 1) have been studied.

Several experimental studies by Karlin and co-workers have revealed structural, thermodynamic, and kinetic data concerning the $[Cu^I(TPA^R)]^+/O_2$ interaction.[1−6] Effects on the interaction by different R substituents on TPA^R (Figure 1) as well as solvent effects have been investigated. Two recent studies were focused mainly on the solvent effects of THF and EtCN and the electronic effects of the R substituents H− and MeO−.[5,6] Thermodynamic parameters such as free energies, $\Delta G°$, enthalpies, $\Delta H°$, and entropies, $\Delta S°$, were reported for the formation of $[Cu^{II}(TPA^H)(O_2^-)]^+$ and $[Cu^{II}(TPA^{MeO})(O_2^-)]^+$ in EtCN and for $[Cu^{II}(TPA^H)(O_2^-)]^+$ in THF. According to those measurements the reactions are approximately thermo-neutral; that is, $\Delta G°$ is close to 0. Kinetic barriers were found for the formation of $[Cu^{II}(TPA^R)(O_2^-)]^+$ in THF and EtCN. The magnitudes of the barriers differ depending on the chemical nature of the R substituents and the solvents in which the reactions take place. For the formation of $[Cu^{II}(TPA^H)(O_2^-)]^+$, which has been studied in both EtCN and THF, a higher barrier is found when the solvent is EtCN. On the basis of those results the formation of $[Cu^{II}(TPA^R)(O_2^-)]^+$ in EtCN was suggested to

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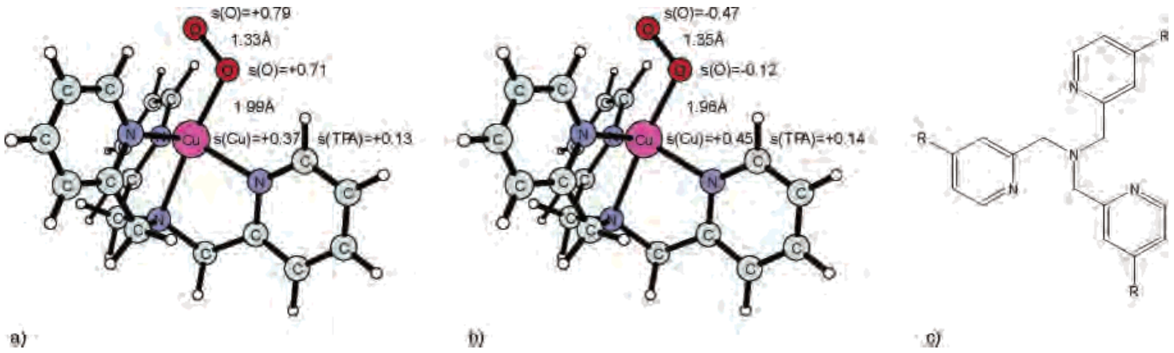

Figure 1. Optimized structure of the complex $[Cu^{II}(TPA^{H})(O_2^{-})]^{+}$. The Mulliken spin populations corresponding to the triplet (a) and the open-shell singlet (b) states are shown on the Cu and O atoms and for the TPA^{H} ligand. (c) The Lewis structure of the general TPA^{R}, R = H− or MeO−.

be initiated from the complex $[Cu^{I}(TPA^{R})(EtCN)]^{+}$, while it is not clear whether the reaction in THF is initiated from the corresponding complex with one THF molecule or from $[Cu^{I}(TPA^{R})]^{+}$ with a vacant coordination site. A general mechanism was proposed in which the solvent, if initially coordinated by the copper atom, is replaced by a dioxygen molecule, a redox process in which Cu^{I} is formally oxidized to Cu^{II}.

The present study is an attempt to model the formation of $[Cu^{II}(TPA^{H})(O_2^{-})]^{+}$ and $[Cu^{II}(TPA^{MeO})(O_2^{-})]^{+}$, in THF and EtCN, using DFT (density functional theory). Thermodynamic and kinetic parameters have been computed to obtain a more detailed understanding of the reaction mechanisms and at the same time to investigate the ability of the B3LYP functional to reproduce this kind of experimental data. The fact that experimental information is available, not only for the free energies but also for the contributions to the free energy from entropy and enthalpy makes these reactions particularly useful for comparisons between experiment and theory. It might seem that to describe these close to thermoneutral reactions, an unreachable accuracy is demanded, but the goal of the calculations is not to determine whether the reactions are exergonic or endergonic, but rather to determine if reaction enthalpies and entropies for this kind of reaction can be described within the normal expected accuracy of the B3LYP functional.

2. Computational Details

a. Methods. Molecular systems have been described by DFT with the B3LYP hybrid exchange-correlation functional (which includes the Becke three parameter exchange and the Lee, Yang, and Parr correlation).[7−9] The quantum chemical software used are Gaussian 98[10] and Jaguar 4.0.[11] Gaussian 98 was used to optimize molecular geometries with respect to energy and to calculate molecular Hessians, that is, second derivatives of the energy with respect to the nuclear coordinates, to compute thermal and entropic corrections at $T = 298$ K. Jaguar 4.0 was used for single-point calculations of the energy with a larger basis set and to compute dielectric effects of solvents. Copper is described by an effective core potential,[12] and for geometry optimizations, all other elements have been described by a double-ζ basis set, designated lacvp in Jaguar 4.0. Molecular Hessians were computed using the lacvp basis set. The single-point calculations of the electronic energy employed a larger basis set with polarization functions on all atoms, designated lacv3p(d,p) in Jaguar 4.0. Thermodynamic parameters computed are changes in free energy (ΔG), enthalpy (ΔH), and entropy (ΔS). Dielectric solvent effects were evaluated using the PCM method implemented in Jaguar 4.0.[13,14] In this method, the solute is modeled as contained in a cavity of a polarizable continuum, characterized by a dielectric constant, ϵ. The dielectric constants used were $\epsilon(\text{EtCN}) = 27.7$ and $\epsilon(\text{THF}) = 7.6$. The cavity was defined by a molecular probe with the radius 2.41 Å for EtCN and 2.64 Å for THF.

The accuracy of the B3LYP functional has been investigated using the G3 benchmark tests on a reference set of molecular properties for a set of small molecules of first- and second-period elements.[15] It has been shown that hybrid DFT methods perform almost as well as the G3 method. The B3LYP functional is less accurate for transition elements and transition states. An overall average error of 3−5 kcal mol^{-1} can be expected for the computed thermodynamic properties of the present system.[16−18] It should also be noted that in all cases we are aware of the binding energies of ligands in complexes are too low in B3LYP calculations. Therefore, if a particular ligand is found to be slightly bound in the calculations, it is quite safe to conclude that it actually is bound. On the other hand, if a ligand is found to be weakly unbound in the calculations,

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it is more difficult to judge, but the ligand still might very well be bound. In some cases there is experimental information that can be used together with the calculations to strengthen the conclusions.

The reparametrized B3LYP* functional which uses 15% Hartree−Fock (HF) exchange compared to the 20% used in the original functional was also used to evaluate bond energies and the difference in electronic energy between different electronic spin states. There are indications that the B3LYP* functional could give a better description of the interaction of O_2 with transition elements.[19]

Density functional methods do not describe open-shell low-spin states accurately. The correct spin states are linear combinations of different spin determinants, and the present DFT implementations are limited to a single determinant. Therefore, low-spin coupled states become spin contaminated by higher spin states. The amount of spin contamination is reflected in the eigenvalue of the S^2 operator. In the case of a pure singlet state this value is 0, while it is 2 for a triplet. If the eigenvalue of the S^2 operator for a singlet state is nonzero, the singlet wave function is spin contaminated by the triplet. The energy of the correct spin states can be approximated by extrapolation of high- and low-spin single determinants employing the broken symmetry approach.[20]

The Mulliken spin population reported for the triplet state in Figure 1 is a qualitative measure of the amount of unpaired α-spin (+ sign) or β-spin (− sign) on each atom. This was computed according to the normal Mulliken population analysis. It is known by experience that Cu^{II} complexes which formally should have one α-spin on Cu have some of the spin delocalized to the ligands and, therefore, typically obtain a spin population of approximately +0.5 on Cu.

b. Models. Free energies of formation, $\Delta G°$, were computed for all complexes of $[Cu^I(TPA^R)]^+$ with O_2, THF, and EtCN. This was done to determine whether the free species or the complexes are the most stable. To model the reactions as taking place in solution, with solvent molecules involved in the reaction, entropy was described in different ways depending on the molecular species and state of aggregation. For the O_2 molecule, computed entropies corresponding to the gas phase were used, assuming that O_2 is in a gas phase/solution equilibrium. The entropy differences between the Cu complexes, $[Cu^I(TPA^R)]^+$, $[Cu^I(TPA^R)(S)]^+$, and $[Cu^{II}(TPA^R)(O_2^-)]^+$, are assumed to be independent of whether the species are in the gas phase or solvated and could, therefore, be described by computed gas phase entropies. Because quantum chemical frequency calculations can only be performed on gas phase models, free energies of the solvent molecules were calculated using experimentally determined absolute liquid-state entropies, $TS°(\mathrm{THF}) = 14.5$ kcal mol^{-1} and $TS°(\mathrm{EtCN}) = 13.5$ kcal mol^{-1} ($T = 298.15$ K).[21,22]

3. Results and Discussion

Quantum mechanical calculations have been performed to investigate the formation of $[Cu^{II}(TPA^R)(O_2^-)]^+$ in the solvents THF and EtCN.

$[Cu^I(TPA^R)]^+$ is a closed-shell d^{10} complex. The electronic structure is hardly affected by coordinating solvent molecules such as EtCN and THF. However, the formation of the copper−oxygen bond in $[Cu^{II}(TPA^R)(O_2^-)]^+$ is a redox process in which electron density is polarized toward O_2. Formally Cu is oxidized from d^{10} to d^9, and O_2 is reduced to a superoxide. The ground-state electronic configuration of $[Cu^{II}(TPA^R)(O_2^-)]^+$ could be either an open-shell singlet (M = 1) or a triplet (M = 3) state. At the B3LYP/lacvp level of theory, the electronic energy of the triplet is 4.9 kcal mol^{-1} lower than for the open-shell singlet. The same splitting was obtained also when the modified B3LYP* functional with reduced HF exchange was used. By employing a larger basis set (lacv3p(d,p)), including thermal and entropic corrections to the electronic energy, and adding dielectric solvent effects, the triplet/singlet splitting was reduced to approximately 4 kcal mol^{-1}. For the open-shell singlet state the eigenvalue of the S^2 operator equals 1.0, which shows that this singlet is severely spin contaminated by a triplet. This spin contamination should be corrected for by applying the broken symmetry approach.[20] However, the Mulliken spin populations show that the computed triplet state does not correspond to the high-spin coupling of this singlet state (Figure 1). It is, therefore, most likely that the singlet is spin contaminated by another triplet. If this other triplet is higher in energy than the singlet, then the energy of the singlet state would be lowered by a spin correction. At present this hypothetical triplet is unknown, and it is not possible to correct for the spin contamination. From the present calculations it is, therefore, not possible to conclude whether the true ground state of $[Cu^{II}(TPA^R)(O_2^-)]^+$ is a singlet or a triplet. However, the triplet shown in Figure 1 was used as the ground state in the following calculations.

Concerning the coordination of O_2 in the $[Cu^{II}(TPA^R)(O_2^-)]^+$ complex both apical coordination and equatorial coordination were tried. The structure with O_2 coordinated in an equatorial fashion was optimized with constraints. The structure was found to be 19 kcal mol^{-1} higher in energy than the complex with apical coordination of O_2. When the constraints were released, optimization led back to the apical coordination without any barrier. Therefore, in the following all structures discussed have O_2 coordinated in an apical fashion and can be considered as trigonal bipyramidal.

Cu^{II} is known to coordinate O_2 either end-on or side-on, as revealed by several experimental and theoretical studies.[23−26] End-on coordination means that Cu binds to one of the O atoms, while side-on means that Cu binds both O atoms in a way that both Cu−O bonds have about the same distance. Whether it is possible for a particular LCu^{II} complex to coordinate O_2 side-on depends on the chemical nature of the complex ligand (L). When the complex ligand is tetradentate and tripodal, as TPA^R, LCu^{II} forms trigonal bipyramidal complexes with ligands such as H_2O, OH^-, and Cl^-. For these kinds of Cu^{II} complexes to coordinate O_2 side-on would

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Table 1. Computed Thermodynamic Parameters for the Binding of $[Cu^{I}(TPA^{R})]^{+}$ to O_2, THF, and EtCN[a]

species	ϵ	reaction	$\Delta H°$	$-T\Delta S°$	$\Delta G°$
O_2	0.0	$[Cu^{I}(TPA^{H})]^{+} + O_2 \rightleftharpoons [Cu^{II}(TPA^{H})(O_2^{-})]^{+}$	−7.34	+9.52	+2.18
	0.0	$[Cu^{I}(TPA^{MeO})]^{+} + O_2 \rightleftharpoons [Cu^{II}(TPA^{MeO})(O_2^{-})]^{+}$	−8.51	+9.79	+1.28
	7.6	$[Cu^{I}(TPA^{H})]^{+} + O_2 \rightleftharpoons [Cu^{II}(TPA^{H})(O_2^{-})]^{+}$	−9.63	+9.52	−0.11
	7.6	$[Cu^{I}(TPA^{MeO})]^{+} + O_2 \rightleftharpoons [Cu^{II}(TPA^{MeO})(O_2^{-})]^{+}$	−12.06	+9.79	−2.27
	27.7	$[Cu^{I}(TPA^{H})]^{+} + O_2 \rightleftharpoons [Cu^{II}(TPA^{H})(O_2^{-})]^{+}$	−10.55	+9.52	−1.03
	27.7	$[Cu^{I}(TPA^{MeO})]^{+} + O_2 \rightleftharpoons [Cu^{II}(TPA^{MeO})(O_2^{-})]^{+}$	−12.79	+9.79	−3.00
THF	7.6	$[Cu^{I}(TPA^{H})]^{+} + THF \rightleftharpoons [Cu^{I}(TPA^{H})(THF)]^{+}$	+4.02	+3.2	+7.2
	7.6	$[Cu^{I}(TPA^{MeO})]^{+} + THF \rightleftharpoons [Cu^{I}(TPA^{MeO})(THF)]^{+}$	+6.43	+3.6	+10.0
EtCN	27.7	$[Cu^{I}(TPA^{H})]^{+} + EtCN \rightleftharpoons [Cu^{I}(TPA^{H})(EtCN)]^{+}$	−2.26	+1.9	−0.4
	27.7	$[Cu^{I}(TPA^{MeO})]^{+} + EtCN \rightleftharpoons [Cu^{I}(TPA^{MeO})(EtCN)]^{+}$	+0.91	+1.7	+2.6

[a] All energies are given in kcal mol^{-1}. Dielectric constants (ϵ) refer to solvents, $\epsilon = 27.7$ refers to EtCN, $\epsilon = 7.6$ refers to THF, and $\epsilon = 0$ corresponds to the gas phase.

require either an octahedral geometry or a tridentate coordination of the tetradentate ligand, but neither of these cases have been observed.[26]

In this study both end-on and side-on $Cu-O_2$ coordination were tried for both $[Cu^{II}(TPA^{H})(O_2^{-})]^{+}$ and $[Cu^{II}(TPA^{MeO})(O_2^{-})]^{+}$. The side-on structures were optimized under the constraint of fixed Cu−O distances. These structures were found to be much higher in energy than the corresponding end-on structures, and when the constraints were released the geometry optimizations for both complexes led to end-on coordination. This investigation was made for both the triplet and the open-shell singlet states, with the result that O_2 is end-on coordinated to Cu^{II} in both states. On the basis of these investigations the end-on coordinated triplet was used in the following calculations.

The remainder of this section is divided into three parts. In the first part the thermodynamics of solvent and O_2 coordination is discussed. On the basis of these results reaction mechanisms are proposed. In the second part the thermodynamics of the suggested mechanisms is discussed and compared to experimental data. The third part is focused on the kinetics of the proposed reaction mechanisms.

Thermodynamics of Solvent and O_2 Coordination. The O_2 binding reaction can occur through different mechanisms depending on how the solvent is involved. To understand whether the solvent is coordinated to $[Cu^{I}(TPA^{R})]^{+}$ or not, the free energy of formation, $\Delta G°$, was computed for the complex $[Cu^{I}(TPA^{R})(S)]^{+}$, where R is H or MeO, and the solvent, S, is THF or EtCN. The results are summarized in Table 1.

The formation of $[Cu^{I}(TPA^{R})(THF)]^{+}$ was found to be endergonic for both R = H and R = MeO. For the hydrogen substituent, the computed $\Delta G°$ was found to be +7.2 kcal mol^{-1}, and for the methoxide substituent it was +10.0 kcal mol^{-1}; that is, the complexes should be regarded as thermodynamically unstable relative to the free species in solution. For the formation of $[Cu^{I}(TPA^{R})(EtCN)]^{+}$, the computed thermodynamics show the same trend depending on the R substituent; that is, the methoxy substituent decreases the bond energy. When the substituent is hydrogen, $\Delta G°$ was found to be −0.4 kcal mol^{-1}; that is., the formation is a slightly exergonic process. Because calculated bond enthalpies are usually too low,[27] this result indicates that the complex is likely to be thermodynamically stable. For the methoxide substituent the formation was found to be an endergonic process, $\Delta G°$ equal to +2.6 kcal mol^{-1}. In general EtCN is expected to coordinate stronger than THF, as a result of back-donation via the π system of Cu^{I} and the nitrile.

In summary, the only case where the calculations clearly indicate a coordinated solvent molecule is in the complex $[Cu^{I}(TPA^{H})(EtCN)]^{+}$. In the THF solvent, the complex $[Cu^{I}(TPA^{R})]^{+}$ has a vacant coordination site both for R = H and for R = MeO. The computed difference in binding energy between the two solvent molecules is almost 8 kcal mol^{-1}, which should be large enough to establish that there exists a qualitative difference between the two solvents. It can be noticed that, for both solvents, the substituent MeO tends to destabilize the coordination of solvent molecules to Cu^{I}, as compared to the substituent H. Going from R = H to R = MeO, $\Delta\Delta G°$ for the formation of $[Cu^{I}(TPA^{H})(THF)]^{+}$ was found to be +2.8 kcal mol^{-1}. The corresponding value of $\Delta\Delta G°$ for EtCN is +3.0 kcal mol^{-1}.

As mentioned above, from previous results calculated bond enthalpies are expected to be too low.[27] This error partly originates from the lack of description of van der Waals interactions in DFT. Correcting for such an error would lead to a stabilization of the solvent complexes. In the case of $[Cu^{I}(TPA^{MeO})(EtCN)]^{+}$, where the computed endergonicity is only 2.6 kcal mol^{-1}, such a stabilization might lead to a thermodynamically stable complex; see below.

For comparison, the formation of $[Cu^{II}(TPA^{R})(O_2^{-})]^{+}$ was first modeled with no involvement of the solvent, giving the intrinsic binding of O_2 to $[Cu^{I}(TPA^{R})]^{+}$. In Table 1, computed thermodynamic data for the gas-phase reactions are presented together with computed dielectric effects on the $Cu-O_2$ bond, using the dielectric constants of THF and EtCN. In the gas phase, O_2 was found to be slightly unbound, mainly due to a large entropy effect of almost 10 kcal mol^{-1}, which is expected when a small molecule goes from the gas phase to a bound complex. The computed $\Delta G°$ values for these endergonic gas-phase processes are in the range 1−2 kcal mol^{-1}, depending on the substituents. Dielectric effects increase the bonding of O_2, as a result of a stabilization of the charge separation occurring in the redox process involved in the bonding. The computed $\Delta G°$ values for the formation of the $Cu-O_2$ bond in these systems are in the range of −3

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Table 2. Formation Pathways of $[Cu^{II}(TPA^R)(O_2^-)]^+$ in THF and EtCN

solvent	reaction
THF	$[Cu^I(TPA^H)]^+ + O_2 \rightleftharpoons [Cu^{II}(TPA^H)(O_2^-)]^+$ $[Cu^I(TPA^{MeO})]^+ + O_2 \rightleftharpoons [Cu^{II}(TPA^{MeO})(O_2^-)]^+$
EtCN	$[Cu^I(TPA^H)(EtCN)]^+ + O_2 \rightleftharpoons [Cu^{II}(TPA^H)(O_2^-)]^+ + EtCN$ $[Cu^I(TPA^{MeO})]^+ + O_2 \rightleftharpoons [Cu^{II}(TPA^{MeO})(O_2^-)]^+$

to 0 kcal mol^{-1} when dielectric effects are included, depending on the substituents and on the solvent.

In contrast to the situation for the solvent molecules, the MeO substituent stabilizes the Cu−O_2 bond in $[Cu^{II}(TPA^R)(O_2^-)]^+$, compared to the H substituent. Going from R = H to R = MeO the computed $\Delta\Delta G°$ for the $[Cu^{II}(TPA^R)(O_2^-)]^+$ formation is −2.2 kcal mol^{-1} in THF (ϵ=7.6), −2.0 kcal mol^{-1} in EtCN (ϵ=27.7), and −1.2 kcal mol^{-1} in the gas phase. The stabilizing or destabilizing effects of the R substituent on the Cu−O_2, Cu−THF, and Cu−EtCN bonds can be explained by the electron donating potential of the two electronically different substituents. The methoxide substituent, having electrons occupying nonbonding lone-pair orbitals, has a higher electron donating potential than the hydrogen substituent, having only the electrons in the covalent bond to carbon. The formation of $[Cu^{II}(TPA^R)(O_2^-)]^+$ is a redox process in which formally one electron is transferred from the copper atom to the dioxygen molecule. This process is thermodynamically stabilized when TPA^R includes substituents with a higher electron donating potential. This trend is reflected in the computed vertical ionization potential of $[Cu^I(TPA^{MeO})]^+$, which is 12 kcal mol^{-1} lower than the corresponding value for $[Cu^I(TPA^H)]^+$. On the other hand, the formation of $[Cu^I(TPA^R)(S)]^+$, where S is THF or EtCN, can be described as an electron donation of lone-pair electrons of the solvent molecule to the copper atom, which explains the computed destabilization of the Cu−THF and Cu−EtCN bonds when TPA^R includes electron rich substituents, such as MeO.

Reaction Thermodynamics. The computed relative free energies of the solvent complexes, $[Cu^I(TPA^R)(S)]^+$, suggest that, for the formation of $[Cu^{II}(TPA^H)(O_2^-)]^+$ in EtCN, one molecule of the solvent is chemically involved in the reaction, which initiates from the reactants $[Cu^I(TPA^H)(EtCN)]^+$ and O_2. For the formation of $[Cu^{II}(TPA^R)(O_2^-)]^+$ in THF, the effect of the solvent is purely electrostatic, and the reaction initiates from the species $[Cu^I(TPA^R)]^+$ and O_2. For the formation of $[Cu^{II}(TPA^{MeO})(O_2^-)]^+$ in EtCN, it is not clear whether EtCN is initially coordinated or not, due to the above-mentioned uncertainty in the calculated bond enthalpies. The proposed reaction mechanisms for O_2 bonding in different solvents and for different substituents are given in Table 2. The suggestions are based on the actually computed binding energies, and the resulting reaction thermodynamics is given in Table 3.

Table 3. Theoretical and Experimental Thermodynamics for the Formation of $[Cu^{II}(TPA^H)(O_2^-)]^+$ and $[Cu^{II}(TPA^{MeO})(O_2^-)]^+$ in THF and EtCN[a]

		R = H		R = MeO	
solvent	thermodynamic parameter	expt[b]	DFT	expt[c]	DFT
THF (ϵ =7.6)	$\Delta G°$	−1.62	−0.1		−2.3
	$\Delta H°$	−11.59	−9.6		−12.1
	$-T\Delta S°$	+9.97	+9.5		+9.8
EtCN (ϵ = 27.7)	$\Delta G°$	+0.57	−0.7	−0.98	−3.0
	$\Delta H°$	−7.12	−8.3	−7.60	−12.8
	$-T\Delta S°$	+7.69	+7.6	+6.62	+9.8

[a] All energies are given in kcal mol^{-1}. [b] Reference 5. [c] Reference 6.

For the overall O_2 binding reactions, there is a good agreement between theoretically and experimentally obtained thermodynamic values, as can be seen in Table 3. The experimental data given here are obtained covering a wide temperature range (183, 223, and 298 K) and are in all cases very accurate ($\Delta H°$ values having uncertainties less than 1 kcal mol^{-1} and $\Delta S°$ values having uncertainties less than 3 cal mol^{-1} K^{-1}).[6] The reactions are in all cases close to thermo-neutral, and the deviation between measured and computed $\Delta G°$ is in no case more than 2 kcal mol^{-1}, thus well within the uncertainty of the B3LYP functional. For the formation of $[Cu^{II}(TPA^H)(O_2^-)]^+$ in THF and EtCN, experimentally obtained $\Delta S°$ values are accurately reproduced by the calculations, and the main part of the error in $\Delta G°$ is enthalpic in origin. These results indicate that the procedure used to estimate the entropy effects on the reaction, as described in the computational details section, is valid. In the case of the THF solvent, the computed entropy effect of 9.5 kcal mol^{-1} comes solely from the loss of entropy of the O_2 molecule going from the gas phase to the bound complex. The experimental value is very similar, 9.97 kcal mol^{-1}. In the case of the EtCN solvent, the loss of O_2 entropy is partly balanced by the gain in entropy when the solvent molecule is released. However, because the EtCN molecule in solution has a much lower entropy than the O_2 molecule in the gas phase, the computed net entropy loss is 7.6 kcal mol^{-1} for the O_2 binding reaction. The experimental value is 7.69 kcal mol^{-1}. The difference between the two solvents, THF and EtCN, in the experimentally measured entropy effects on the O_2 binding reaction indicates the same difference that the calculations show in the interaction between the copper complex and the two solvent molecules, namely, that EtCN is bound and THF is not. The calculated reaction enthalpies are also in good agreement with experiment. In the case of THF the calculated value is approximately 2 kcal mol^{-1} too small, while in the case of EtCN the calculated value is 1.3 kcal mol^{-1} too large. Both these deviations are well within the uncertainty of the B3LYP method.

For the formation of $[Cu^{II}(TPA^{MeO})(O_2^-)]^+$ in EtCN, the experimental data are also accurately reproduced, the computed $\Delta G°$ being only 2.0 kcal mol^{-1} from the experimental value. It should be noted that the computed Cu−EtCN bond energy of $[Cu^I(TPA^{MeO})(EtCN)]^+$ is close to 0, and it is, therefore, not clear whether the EtCN molecule should be regarded as bound to the complex or not. The values given in Table 3 are calculated assuming that EtCN is not bound. The computed entropy effect is almost 3 kcal mol^{-1} larger than the experimental value, which indicates that the computed result that this solvent is unbound is most likely wrong. If it is instead assumed that EtCN is bound also in

Table 4. Theoretical and Experimental Kinetics for the Formation of $[Cu^{II}(TPA^{H})(O_2^{-})]^{+}$ in THF and EtCN[a]

solvent	$\Delta H^{\ddagger}$ expt[b]	$\Delta H^{\ddagger}$ DFT	$\Delta G^{\ddagger}$ expt[b]	$\Delta G^{\ddagger}$ DFT
THF ($\epsilon = 7.6$)	+1.8	−1.4	+5.0	+7.0
EtCN ($\epsilon = 27.7$)	+7.6	+2.3	+6.8	+7.5

[a] All values are presented in kcal mol^{-1}. [b] Reference 5.

this complex, the computed entropy effect on the O_2 binding reaction would be 8.1 kcal mol^{-1}, closer to the experimental value of 6.62 kcal mol^{-1}. At the same time, the computed reaction enthalpy is larger than the experimental value by about 5 kcal mol^{-1}. Also, this error could be decreased if it is assumed that EtCN is bound.

In summary, it can be concluded that the B3LYP functional well reproduces the experimental thermodynamic data for the present type of transition metal complexes.

Reaction Kinetics. Since there is experimental information available also about the kinetic parameters for the O_2 binding reactions in the different solvents, an attempt was made to model these. Computed results are compared with experimental data in Table 4. Concerning the reaction in EtCN the experimental data given here are as accurate and reliable as the thermodynamic data reported above.[6] The experimental kinetic data for the reaction in THF are obtained by measuring at 193 and 298 K but are reported without any uncertainties.[5] It was found to be much more difficult to model and reproduce the kinetic data, as compared to the thermodynamic data, but a short discussion of the results is given below.

The formation of $[Cu^{II}(TPA^{H})(O_2^{-})]^{+}$ in THF was modeled as if no solvent molecule is initially coordinated to the copper atom, that is, the formation of the complex is the pure formation of the Cu−O_2 bond. This assumption is based on the computational results for the coordination of THF to $[Cu^{I}(TPA^{H})]^{+}$, which is found to be endergonic. By scanning the Cu−O distance an energy profile was obtained for the pure electronic energy. This profile shows that the electronic energy decreases continuously and without barriers as the Cu−O distance decreases. From the Mulliken spin population it was noted that the electron transfer occurred gradually as the Cu−O distance was decreased. Thermal corrections to the enthalpy and the entropy were then computed for each Cu−O distance and added to this energy profile. For the enthalpy, as well as the pure electronic energy, there is no barrier in the profile, and the enthalpy decreases as the Cu−O distance decreases. However, the free energy profile obtained in this way has a maximum at a Cu−O distance of 3.8 Å. At this point the spin population on Cu is 0.02 electrons. Taken as the difference between this point and the infinitely separated species, the free energy of activation, $\Delta G^{\ddagger}$, was found to be +7.0 kcal mol^{-1}. The experimental value is slightly lower, +5.0 kcal mol^{-1}.[5] Concerning the partition of the free energy of activation into ethalpic and entropic contributions, it is noted that no enthalpy barrier was found for the formation of the Cu−O_2 bond in the calculations. In fact, the enthalpy is lower ($\Delta H^{\ddagger} = -1.4$ kcal mol^{-1}) at the transition state Cu−O_2 distance than for the infinitely separated species. In contrast, a small activation enthalpy of $\Delta H^{\ddagger} = +1.8$ kcal mol^{-1} was found experimentally.[5] In light of the barrier-less energy profile obtained from the calculations it is not clear what causes the experimentally observed enthalpy barrier. The most likely explanation is that a lower free energy path can be found by not following the lowest enthalpy path. Such a reaction path cannot be described by the present type of calculations. Because the experimental enthalpy barrier is so low and the computed free energy barrier is only 2 kcal mol^{-1} higher than the experimental one, it can still be said that experimental data for this process are quite well-reproduced in these calculations.

The formation of $[Cu^{II}(TPA^{H})(O_2^{-})]^{+}$ in EtCN has been described in a different and more complicated way, assuming that one EtCN molecule is initially coordinated to the copper atom of the complex. This assumption is based on the computational results that the formation of $[Cu^{I}(TPA^{H})(EtCN)]^{+}$ is an exergonic process. The reaction was modeled as dissociative, that is, the EtCN molecule dissociates before the association of the O_2 molecule starts. This kind of mechanism is indicated by the result that the formation of the initially required complex of an associative mechanism, $[Cu(TPA^{H})(EtCN)(O_2)]^{+}$, was found to be endergonic in the calculations. The trial structures for such a complex were found to be very high in energy. On the electronic level ΔE for the formation was computed to be +1.9 kcal mol^{-1}, which indicates that thermal corrections would result in a large positive $\Delta G°$ on the order of +15 kcal mol^{-1}. For the dissociation of EtCN from $[Cu^{I}(TPA^{H})(EtCN)]^{+}$, $\Delta H°$ was found to be +2.3 kcal mol^{-1}, and $\Delta G°$ was found to be +0.4 kcal mol^{-1}. These values contribute to the ethalpy and free energy of activation, $\Delta H^{\ddagger}$ and $\Delta G^{\ddagger}$, for the formation of $[Cu^{II}(TPA^{H})(O_2^{-})]^{+}$ in EtCN. The second step in the reaction is the association of the O_2 molecule to the copper complex. As in the case of THF, the formation of $[Cu^{II}(TPA^{H})(O_2^{-})]^{+}$ in EtCN was computed by scanning the Cu−O bond distance and computing thermal corrections to enthalpy and entropy in each optimized point. In fact, these energy profiles are based on the same calculations as in the THF case, with the only difference being that the dielectric constant is changed in the calculations of the solvent effect on the energy. The change in dielectric constant has only minor effects, and just as in the THF case no enthalpy barrier was found, while a free energy barrier of +7.1 kcal mol^{-1} was found at 3.8 Å. Adding the free energy of activation corresponding to the dissociation of the EtCN molecule to the free energy barrier for the formation of the Cu−O_2 bond, the computed free energy of activation for the formation of $[Cu^{II}(TPA^{H})(O_2^{-})]^{+}$ in EtCN is equal to +7.5 kcal mol^{-1}. Experimentally, $\Delta G^{\ddagger}$ is found to be quite similar, +6.8 kcal mol^{-1}.[5] Because no enthalpic barrier was found computationally for the formation of the Cu−O_2 bond, the enthalpy of activation originates completely from the dissociation of the coordinated EtCN molecule. In this way the computed $\Delta H^{\ddagger}$ is equal to +2.3 kcal mol^{-1}, while the experimental value is +7.6 kcal mol^{-1}.[5] Thus, even if the calculated free energy barrier agrees very well with the experimental one, the difference between computational and experimental results is substantial for the

EtCN solvent regarding the contributions from enthalpy and entropy. The computed enthalpy barrier is about 5 kcal mol^{-1} too low compared to experiment. Further, the calculations indicate that entropy increases the barrier by about 5 kcal mol^{-1}, while according to the experiments, entropy lowers the barrier by 0.8 kcal mol^{-1}. As for the reaction in the THF solvent, it is again likely that the reaction pathway with the lowest free energy barrier is not the one with the lowest enthalpy barrier.

4. Summary and Conclusions

Quantum mechanical calculations have been performed on the formation of $[Cu^{II}(TPA^H)(O_2^-)]^+$ and $[Cu^{II}(TPA^{MeO})(O_2^-)]^+$ in two different solvents, THF and EtCN. The thermodynamics of solvent coordination to $[Cu^I(TPA^R)]^+$ was computed at the B3LYP/lacv3p(d,p) level of theory. To estimate the Gibbs free energy, experimentally obtained liquid-state entropies of the solvents were used. The free energies computed in this way indicate that EtCN is coordinated to $[Cu^I(TPA^H)]^+$ ($\Delta G° < 0$), while THF is not ($\Delta G° > 0$), and that neither THF nor EtCN is coordinated to $[Cu^I(TPA^{MeO})]^+$ ($\Delta G° > 0$). On the basis of these results, the formation of $[Cu^{II}(TPA^H)(O_2^-)]^+$ in THF and of $[Cu^{II}(TPA^{MeO})(O_2^-)]^+$ in both THF and EtCN is described as a pure formation of the copper−oxygen bond under the dielectric influence of the solvents. In contrast, the formation of $[Cu^{II}(TPA^H)(O_2^-)]^+$ in EtCN is described as a dissociation of the copper−nitrile bond followed by the formation of the copper−oxygen bond in a completely dissociative mechanism. It can be concluded that the B3LYP functional accurately reproduces experimentally obtained thermodynamic data. For the $[Cu^I(TPA^H)]^+$ complex, where experimental results are available for both solvents, the differences between the computed and the measured thermodynamic parameters ($\Delta G°$, $\Delta H°$, and $-T\Delta S°$) are in fact less than 2.0 kcal mol^{-1}. In this case the combined computational and experimental results clearly show that the two solvents lead to different mechanisms for the O_2 reaction. For the $[Cu^I(TPA^{MeO})]^+$ complex, where there is experimental data available only for the EtCN solvent, the combined experimental and computational results indicate that most likely the computed binding energy of the solvent molecule to the complex is underestimated by 3−5 kcal mol^{-1} and that in fact also in this case the reaction mechanism with O_2 most likely involves the solvent molecule.

Concerning the kinetics of the investigated reactions, the formation of $[Cu^{II}(TPA^H)(O_2^-)]^+$ in THF and EtCN, the computed free energies of activation, $\Delta G^‡$, are also in quite good agreement with experimentally determined free energy barriers. The trend found experimentally, that the O_2 binding is faster in THF than in EtCN, is found also theoretically. However, the quantum chemical analysis of the partitioning of the free energy of activation in enthalpic ($\Delta H^‡$) and entropic ($\Delta S^‡$) contributions is not in agreement with experimental data. An explanation could be that the reaction pathway having the lowest enthalpy barrier, that is, the one described in these calculations, is not the same as the pathway with the lowest free energy barrier, that is, the one observed experimentally. However, it is interesting to note that because the computed free energies of activation are only slightly higher than the experimental values, the gain in free energy by following a higher enthalpic path is not very large.

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