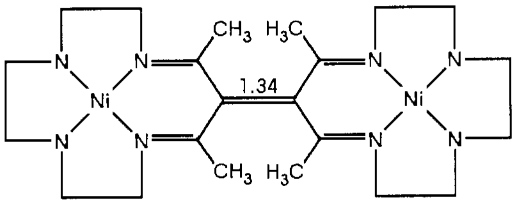
There is one report in the literature of a crystal structure of a related double-bond bridged dimer,[4] a dinickel bis 13-member macrocycle.



An important distinction between the nickel dimer and I is that the methyl groups of the nickel compound interact, causing a displacement of the bridging carbons from the planar array of the nickel and C, N of the imine bonds. This displacement effectively prevents delocalization in the π electron system. Thus, the bond between the bridgehead carbons is 1.34 Å, typical of a localized C–C double bond. Also, the imine N, C distances are within the range expected for a localized C=N, and the bond distance between the bridgehead carbon and the carbon of the imine is 1.50 Å, close to a C–C single bond.

Superficially, then, the nickel dimer structure is a precedent for our new compound. However, in the nickel complex the bonding parameters clearly indicate the presence of alternating, isolated double and single bonds due to interactions of the methyl groups. In I, the planar structure promotes extensive delocalization in the π electron system. We believe this delocalization leads directly to the unusual intense low-energy electronic absorption band (see below).

The iron(II)–nitrogen distances of the complex are also unusual. The iron–imine nitrogen distances of 1.88 and 1.90 Å are the shortest that we could find in a search of the Cambridge Crystallographic Data Base. They are about 0.1 Å shorter than the iron(II)–nitrogen distances observed in porphyrin complexes, and the observed iron(II)–nitrogen distances in 1,10-phenanthroline or bipyridine complexes cluster around 1.97 Å.[5] The iron–nitrogen bond distance in a monomeric tetraene 14-membered macrocycle with two α-diimines is 1.954 Å.[6]

The short iron–nitrogen distances may arise from two independent effects. The first is a constriction imposed by the macrocyclic ligand. However, the iron–aliphatic nitrogen bond distances in the current complex fall within the range found for low-spin iron(II) bound to saturated nitrogen donors. Furthermore, the remaining bond lengths and the angles found throughout the saturated portion of the macrocycle are typical for a fourteen-membered macrocyclic complex. These observations indicate there is no particular strain in fitting the relatively small low-spin iron(II) into the macrocyclic cavity.

A more plausible explanation for the short Fe–N distance is that a strong bond is formed due to extensive overlap which develops between metal and nitrogen orbitals when the nitrogen is in the delocalized electron system of the ligand. Another contribution may be back-bonding of iron(II) to antibonding π orbitals of the delocalized imine moiety. As already noted, the observed C=N bond lengths in I are slightly longer than an isolated imine linkage of about 1.27 Å, which is also consistent with extensive delocalization in the ligand.

There are three prominent bands at 240, 340, and 874 nm in the unusual electronic spectrum of I in acetonitrile. The high intensities of the bands rule out metal-centered d–d transitions. The transitions are then either ligand-centered or involve some type of charge transfer between metal and ligand. It is well-known that complexes containing an imine bonded to iron(II) exhibit an intense absorption band in the visible region.[7] This band has been assigned to an Fe to ligand charge transfer (MLCT).[8] Busch and co-workers in their thorough work on monomeric complexes of iron(II) with unsaturated tetraaza macrocycles observed such MLCT bands with maxima in the 300–550-nm range.[9,10] However, none of their di-, tri-, or tetraimine macrocyclic complexes has an intense electronic band anywhere near the low-energy band for I. In fact, we are not aware of any iron(II) complex that has a similar spectral feature.[11] Therefore, it seems reasonable to assign the near-infrared band to an MLCT that involves transfer of an electron from filled d_{xz}, d_{yz} orbitals of Fe to a particularly low-lying delocalized π^* orbital of the tetraiminoethylene moiety.

Supporting evidence for this assignment comes from the large solvent dependence of the electronic spectrum. Spectra of I in deoxygenated DMF or deoxygenated water also exhibit three prominent bands. The near-infrared band shifts to yet longer wavelengths (λ_{max} 1050 nm in DMF and 1005 nm in water). Also addition of NaSCN to a solution of I in acetonitrile shifts the low-energy band to 1125 nm. We attribute these shifts to ligand exchange with the axial acetonitriles of I. Clearly, the energy of the near-infrared band is very sensitive to the environment around the iron and this is consistent with its assignment as an MLCT.

Further characterization of this interesting new complex is under way.

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Supplementary Material Available: Table SI, listing atomic coordinates for $[Fe_2(C_{20}H_{36}N_8)(CH_3CN)_4](ClO_4)_4\cdot 2CH_3CN$ (1 page). Ordering information is given on any current masthead page.

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Is Intramolecular Hydrogen-Bonding Important for Bleomycin Reactivity? A Molecular Mechanics Study

Bleomycins (BLMs) are a class of natural products which are used clinically as antitumor antibiotics and which have been shown in vitro to bind metal ions.[1] It is believed that a species derived

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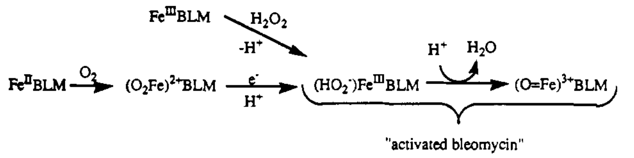
from the reaction of $Fe^{II}BLM$ with dioxygen is responsible for the cellular degradation of DNA[2,3] and that the same species can be generated from reaction of $Fe^{III}BLM$ with hydrogen peroxide as well.[3] The commonly accepted mechanistic pathway is shown as follows.[4,5]



Although intermediates in these reactions have been observed spectroscopically,[3] their identities as well as the coordination chemistry of both Fe^{II}- and $Fe^{III}BLMs$ have not been fully established.[6–10] We are interested in the mechanism of dioxygen and peroxide activation by non-porphyrin–iron complexes and have been intrigued by the observation that, unlike Fe^{III} porphyrin complexes,[11] $Fe^{III}BLMs$ in certain instances give different reactivities toward various organic substrates when ROOH is substituted for H_2O_2.[12] One possible explanation for this difference is that a FeBLM–peroxide complex is responsible for the reactivity with certain substrates. Here we report a qualitative molecular mechanics study of BLM models, which suggests that a peroxide complex might be stabilized by internal hydrogen-bonding with the BLM ligand.

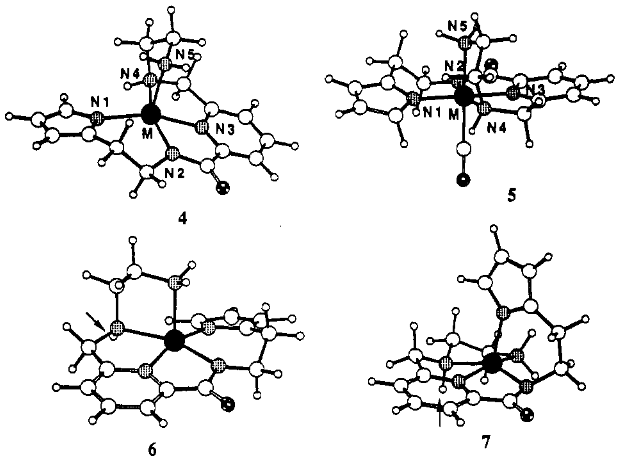


Figure 1. Calculated metal-complex structures of the metal-binding region of BLM. Structures **4** and **5**, with NH_2 axial, are most stable for five- and six-coordinates, respectively, and match reported X-ray structures. (Compare **4** with Figure 1 of ref 13a and **5** with Figure 1 of ref 14.) Structure **6** is another view of **4**. Structure **7** has the imidazole axial. The arrow indicates the position of the NH bond of the secondary amine.

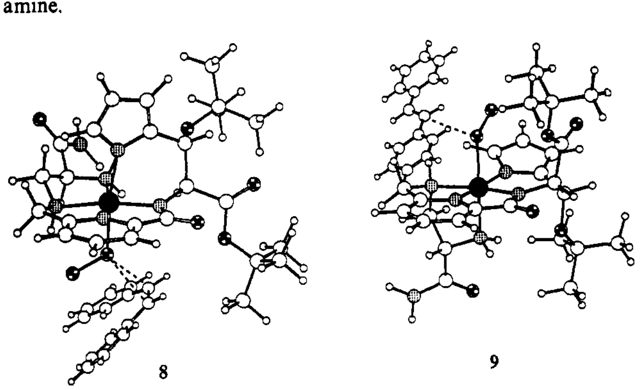
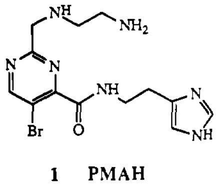
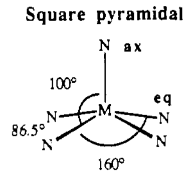


Figure 2. Two modes of coordination of $Fe–PYML–O_2$. In structure **8**, hydrogen-bonding can be achieved, and *cis*-stilbene can approach the oxygen readily. In structure **9**, either *cis*- or *trans*-stilbene can approach the oxygen readily.

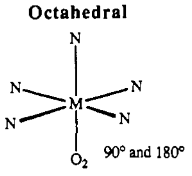
The simplest model for the metal binding side of BLM, PMAH (**1**), has been studied by Mascharak, and X-ray crystal structures of the five-coordinate complex $Cu^{II}PMA$ and the six-coordinate complex $Co^{III}–PMA–OH_2$ have been reported.[13,14] The latter was also shown to degrade DNA in a fashion similar to the Co–BLMs.[14] We performed our initial calculations on both five- and six-coordinate complexes of the PMAH ligand, with the ligands arranged as in **2** and **3**, in order to compare our results with the published structures. Our calculations were carried out with Allinger's MM2 program modified by Raber et al. to 1.5 MM2/MX, which includes coordination numbers greater than 4.[15]



1 PMAH



2



3

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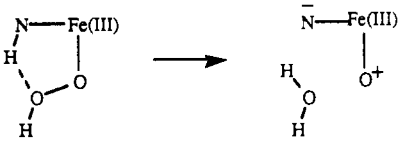
Since no parameters specific to Fe(III) are available,[16] parameters which are generally applicable to metal complexes were applied. The axial M–N bond lengths were set to be 0.1 Å longer than the equatorial ones, and the latter were varied from 1.9 to 2.1 Å. The bond stretching constants for the M–N bonds were set to be 0.4 mdyn/Å. Bending constants were set to 0.1 mdyn/rad for the anti N–M–N angles and were varied from 0.3 to 0.4 mdyn/rad for the remaining N–M–N angles. M–N bond dipoles were set to 0.8 D. The torsional parameters for all X–N–M–N dihedral angles were all set to zero.[17]

Four conformers with the NH_2 axial and two conformers with the imidazole axial were calculated.[18] The most stable structures are **4** and **5** (Figure 1) for the five- and six-coordinate complexes, respectively, both of which have the NH_2 axial. These structures match the X-ray structures reported by Mascharak quite well.[13,14,19] Structure **6** is another view of **4** rotated to show that the NH of the secondary amine is equatorial and is not suitable for hydrogen-bonding to a sixth ligand, O_2 or O_2H^-. Structure **7**, which has the imidazole axial, is calculated to be less stable than **6** by several kcal/mol, primarily due to out-of-plane coordination at the carboxamide N atom. Nevertheless, the NH bond of the secondary amine is axial and is in an ideal position to form hydrogen-bonding with a sixth O_2 or O_2H^- ligand. Therefore, this structure could become more stable with the addition of strong intramolecular hydrogen-bonding to a sixth ligand. Even if **7** does not become the more stable conformer when peroxide is bound, it may nevertheless be required for activation of the bound HOO^- ligand if internal hydrogen-bonding is required to facilitate OH^- loss (eq 1). It has been shown that intramolecular hydrogen-bonding often plays an important role in activating oxygen atom transfer reactions.[20-23] Such hydrogen-bonding is especially important for heterolytic O–O bond cleavage, since negative charge develops on the leaving O.



(1)

This hydrogen-bonding model can also nicely rationalize some puzzling observations reported by Ohno and co-workers concerning the relative yields of epoxidation of *cis*- and *trans*-stilbenes by another Fe–BLM model, Fe–PYML, using H_2O_2 as the oxidant.[7] They found that the reaction of *trans*-stilbene is significantly suppressed by *tert*-butyl groups attached to their PYML ligand. If one assumes either that O–O bond cleavage precedes the reaction with olefin and that the reactive species is a high-valent iron oxo or that O–O bond cleavage is concerted with the reaction with olefin but the peroxide ligand is not pinned down by hydrogen-bonding, it is difficult to understand why *tert*-butyl groups on the ligand would interfere with the reaction with *trans*-stilbene but not *cis*-stilbene (see **9** in Figure 2).[24] On the other hand, in the case where the peroxide ligand is hydrogen-bonded to the PYML ligand and where epoxidation is concerted with O–O bond cleavage,[25] the formation of the hydrogen bond restricts the direction of alkene attack.[26] The attack of *cis*-stilbene may occur readily in this structure, as in **8**, since the Ph groups can orient away from the *tert*-butyl group. However, the approach of *trans*-stilbene is unfavorable, because one of the Ph groups has to be positioned close to the *tert*-butyl group.[27]

Several qualitative conclusions can be derived from the current study: (1) without hydrogen-bonding, the favorable coordination of Fe–BLM is with the NH_2 axial; (2) activation of Fe–BLM by O_2 or H_2O_2 may involve a geometrical change to achieve internal hydrogen-bonding;[28,29] (3) the hydrogen-bonding model can rationalize the relative efficiency of epoxidation of *cis*- and *trans*-stilbenes by PYMLs and BLMs.

Acknowledgment. We are grateful to the National Institutes of Health (K.N.H.) and the National Science Foundation (J.S.V.) for financial support of this research. We thank Professors Pradip Mascharak and Jack Peisach for helpful discussions.

Registry No. BLM, 11056-06-7; Fe–BLM, 71801-37-1; *cis*-stilbene, 645-49-8; *trans*-stilbene, 103-30-0.

Supplementary Material Available: Figure S1, showing calculated structures of five-coordinated metal complexes, and Tables S1 and S2, listing N–M–N bending angles in calculated structures and reported X-ray structures of metal–BLM complexes and the calculated relative energies of metal complexes (2 pages). Ordering information is given on any current masthead page.

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[17] The v.d.w. parameter for the metal is that of C_{sp^3}. The choice of this parameter has little effect on the relative energies of different structures. Upon request, we can provide detailed parameters.

[18] The six structures and relative energies are given in Figure S1 and Table S2 of the supplementary material.

[19] Our calculations for the Cu^{II}–P.3A complex also match the X-ray structure reported by Umezawa.[6a]

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[28] This geometrical change can be achieved easily. Since a five-coordinate intermediate exists in a square-pyramidal conformation, coordination of O_2 from different directions leads to different structures.

[29] Hydrogen-bonding may also play an important role in methane monooxygenase: Green, J.; Dalton, H. *J. Biol. Chem.* **1989**, *264*, 17698.

Kinetics of Formation and Reactions of Thiyl Radicals in Aqueous Solution

Thiyl radicals are formed in biological systems when the sulfhydryl group acts as a radioprotector.[1-6] These radicals are of interest in electron-transfer reactions in inorganic[7-9] and

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