alkane–methylcycloalkene system shows a monotonic sequence of equilibrium constants.[17]

(16) Bigley, D. B.; May, R. W. *J. Chem. Soc. B* **1970**, 1761–1766.
(17) Cope, A. C.; Ambros, D.; Ciganek, E.; Howell, C. F.; Jacura, Z. *J. Am. Chem. Soc.* **1960**, *82*, 1750–1753.

Detection of the Fe–O–O–Fe Intermediate in the Oxidation Reaction of Ferrous Porphyrins by Resonance Raman Spectroscopy

Insook R. Paeng,[1a] Hideaki Shiwaku,[1b] and Kazuo Nakamoto*[1a]

Todd Wehr Chemistry Building
Marquette University
Milwaukee, Wisconsin 53233

Received October 15, 1987

In general, the oxidation reaction of ferrous porphyrins proceeds through the following intermediates:[2]

$$\underset{A}{PFe} \xrightarrow{O_2} \underset{B}{PFeO_2} \xrightarrow{PFe} \underset{C}{PFeOOFeP} \rightarrow \underset{D}{PFeO} \xrightarrow{PFe} \underset{E}{PFeOFeP}$$

Previously, we observed the IR spectra of oxyiron porphyrins (B) in O_2/Ar matrices[3] and resonance Raman (RR) spectra of ferrylporphyrins (D) in O_2 matrices,[4,5] and Balch et al. observed the ^1H NMR signals (pyrrole and phenyl protons of tetraphenylporphyrin (TPP) derivatives) of the Fe–O–O–Fe bridged species (C) and ferrylporphyrins (D) in toluene.[2,6-8]

In this communication, we report the RR spectra of C for the first time. Direct observation of the Fe–O–O–Fe bridge vibration described below provides definitive evidence for the existence of this elusive intermediate in the oxidation process of ferrous porphyrins.

Figure 1 (parts A and B) shows the RR spectra (406-nm excitation) of tetramesitylporphyrinatoiron(II), Fe(TMP), in toluene which were saturated with $^{16}O_2$ and measured at $\sim$ –78 °C and $\sim$ –46 °C, respectively. The experimental techniques used for these and other measurements are basically the same as that reported previously.[9] The most significant features of these spectra are the marked strengthening of the 845-cm^{-1} band and the complete disappearance of the 574-cm^{-1} band when the temperature is raised from $\sim$ –78 °C to $\sim$ –46 °C. Figure 1 (parts C and D) shows the RR spectra of Fe(TMP) in toluene which
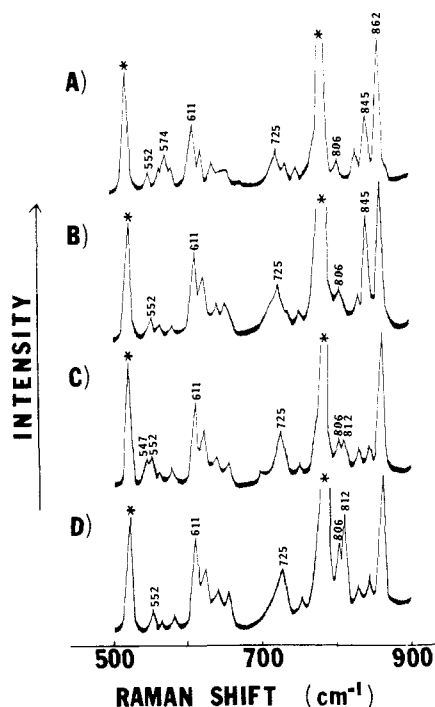
(1) (a) Marquette University. (b) Department of Chemistry, Shimane University, Matsue 690, Japan.
(2) Chin, D.-H.; Del Gaudio, J.; La Mar, G. N.; Balch, A. L. *J. Am. Chem. Soc.* **1977**, *99*, 5486.
(3) Watanabe, T.; Ama, T.; Nakamoto, K. *J. Phys. Chem.* **1984**, *88*, 440.
(4) Bajdor, K.; Nakamoto, K. *J. Am. Chem. Soc.* **1984**, *106*, 3045.
(5) Proniewicz, L. M.; Bajdor, K.; Nakamoto, K. *J. Phys. Chem.* **1986**, *90*, 1560.
(6) Chin, D.-H.; La Mar, G. N.; Balch, A. L. *J. Am. Chem. Soc.* **1980**, *102*, 4344.
(7) Latos-Grazynski, L.; Cheng, R.-J.; La Mar, G. N.; Balch, A. L. *J. Am. Chem. Soc.* **1982**, *104*, 5992.
(8) Balch, A. L.; Chan, Y.-W.; Cheng, R.-J.; La Mar, G. N.; Latos-Grazynski, L.; Renner, M. W. *J. Am. Chem. Soc.* **1984**, *106*, 7779.
(9) Nakamoto, K.; Nonaka, Y.; Ishiguro, T.; Urban, M. W.; Suzuki, M.; Kozuka, M.; Nishida, Y.; Kida, S. *J. Am. Chem. Soc.* **1982**, *104*, 3386.

Figure 1. RR spectra (406-nm excitation) of Fe(TMP) in toluene which were saturated with O_2: (A) $^{16}O_2$, $\sim$ –78 °C; (B) $^{16}O_2$, $\sim$ –46 °C; (C) $^{18}O_2$, $\sim$ –78 °C; (D) $^{18}O_2$, $\sim$ –46 °C. The asterisks denote the solvent bands.

were saturated with $^{18}O_2$ and measured at $\sim$ –78 °C and $\sim$ –46 °C, respectively. In this case, the band at 812 cm^{-1} becomes stronger, and the band at 547 cm^{-1} disappears completely when the temperature is raised from $\sim$ –78 °C to $\sim$ –46 °C. The nature of the bands at 845 and 812 cm^{-1} is well established; these vibrations are due to the $\nu(FeO)$ of Fe(TMP)^{16}O and its ^{18}O analogue, respectively, which are characteristic of five-coordinate ferrylporphyrins.[4,5,10]

The nature of newly discovered bands at 574 and 547 cm^{-1} is of particular interest. Since these bands are relatively weak and partially overlapped by porphyrin bands, we repeated careful measurements to confirm the reproducibility of the spectra. We assign these bands to the symmetric Fe–O stretch, $\nu_s(Fe-O)$, of (TMP)Fe–O–O–Fe(TMP), which is presumably centrosymmetric. The reasons for these assignments are listed below.

(1) These bands cannot be attributed to the $\nu(Fe-O_2)$ of Fe(TMP)O_2 since such a "base-free" O_2 adduct is rapidly oxidized to form (TMP)Fe–O–O–Fe(TMP) in toluene solution at $\sim$ –78 °C.[2,8] Furthermore, the observed frequency of 574 cm^{-1} is too high to assign it to the $\nu(Fe-O_2)$ of a five-coordinate species. For example, Fe(Pc)O_2 (Pc: phthalocyanato anion) in O_2 matrices exhibits the $\nu(Fe-O_2)$ at 488 cm^{-1},[11] whereas the $\nu(Fe-O_2)$ of Fe(TMP)(piperidine)O_2 in toluene ($\sim$ –78 °C) is observed at 568 cm^{-1}.[12] In the case of cobalt porphyrins, the $\nu(Co-O_2)$ of Co(TPP)O_2 in O_2 matrices is at $\sim$345 cm^{-1},[13] while that of Co(TPP)(piperidine)O_2 in toluene ($\sim$ –78 °C) is at 509 cm^{-1}.[14] However, the $\nu_s(Co-O)$ of the peroxo-bridged complex, [(N-H$_3$)$_5$Co(O$_2$)Co(NH$_3$)$_5$](NO$_3$)$_4$ (642 cm^{-1}),[15] is much higher than the $\nu(Co-O_2)$ mentioned above.

(2) According to the NMR studies,[8] (TMP)Fe–O–O–Fe(TMP) is stable near –70 °C in toluene and, upon warming, decomposes

(10) Hashimoto, S.; Tatsuno, Y.; Kitagawa, T. *Proceedings of the Tenth International Conference on Raman Spectroscopy*; Peticolas, W. L., Hudson, B., Ed.; University of Oregon: Eugene, OR, 1986; pp 1–28.
(11) Bajdor, K.; Oshio, H.; Nakamoto, K. *J. Am. Chem. Soc.* **1984**, *106*, 7273.
(12) Paeng, I. R.; Nakamoto, K., to be published.
(13) Kozuka, M.; Nakamoto, K. *J. Am. Chem. Soc.* **1981**, *103*, 2162.
(14) Nakamoto, K.; Paeng, I. R.; Kuroi, T.; Isobe, T.; Oshio, H., to be published.
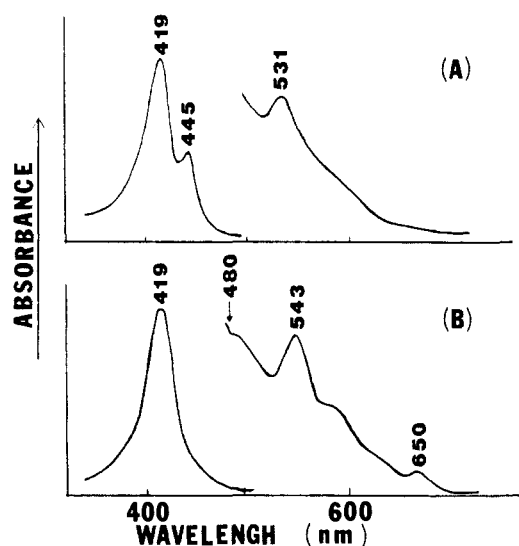(15) Shibahara, T.; Mori, M. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 1374.

Figure 2. Electronic spectra of (A) Fe(TMP) in toluene at ~ -78 °C and (B) Fe(TMP) + O$_2$ in toluene at ~ -78 °C.

into (TMP)FeO and (TMP)FeOH, the latter being the final product at room temperature. (This process which is different from the general scheme shown earlier occurs only for Fe(TMP).)[8] In fact, we observed that the ν(FeO) of (TMP)FeO appears at 845 cm^{-1} in toluene when the solution was warmed from ~ -78 to ~ -46 °C.

(3) These bands cannot be assigned to the ν_s(Fe–O) of the μ-oxo dimer (E) since such a vibration should appear near 360 cm^{-1}.[16]

(4) Figure 2 (parts A and B) show the electronic spectra of Fe(TMP) and Fe(TMP) + O$_2$, respectively, in toluene at ~ -78 °C. These spectra are very similar to those of Fe(TmTP) and Fe(TmTP) + O$_2$, respectively, obtained under similar experimental conditions (TmTP: tetra-m-tolylporphyrinato anion).[2,6] The three λ_{max} values shown in Figure 2B (650, 543, and 480 nm) are close to those of the Fe(TmTP) + O$_2$ system (630, 540, and 480 nm) which were previously attributed to the Fe–O–O–Fe bridged species.[2] These electronic spectra provide further support to our band assignments.

In the centrosymmetric (TMP)Fe–O–O–Fe(TMP), the antisymmetric Fe–O stretch, ν_{as}(Fe–O), is only IR-active, and its frequency is expected to be much lower than ν_s(Fe–O). For example, the ν_{as}(Co–O) (547 cm^{-1}) of the peroxo-bridged amine complex mentioned above is 95 cm^{-1} lower than the ν_s(Co–O) (642 cm^{-1}).[15] Although its ν(O$_2{}^{2-}$) is Raman-active and should appear in the peroxo[2,6-8] region (900-700 cm^{-1}), it was not possible to resonance-enhance this mode with our laser lines (406-676 nm), as are the cases of many other oxyiron porphyrins.[17] It should also be noted that the ν_s(Fe–O) of the bridged species mentioned above can be observed only by excitation in the 406-415-nm region.[12] Thus, this mode must be in resonance with the Soret π-π^*, Fe–O–O–Fe CT transition or a combination of both near 410 nm.

Finally, our RR studies show that (1) (TMP)Fe–O–O–Fe-(TMP) is stable indefinitely in toluene at ~ -78 °C, (2) the step A → C is not reversible, and (3) the ν_s(Fe–O) of the bridged species is observed at ~576 cm^{-1} for analogous TPP and OEP complexes (OEP: octaethylporphyrinato anion).[12]

(16) Burke, J. M.; Kincaid, J. R.; Spiro, T. G. J. Am. Chem. Soc. 1978, 100, 6077.

(17) Yu, N.-T. Methods Enzymol. 1986, 130, 383.

# Characterization of a Crystalline Synthetic Analogue of Copper(II)-Bleomycin

Steven J. Brown and Pradip K. Mascharak*

Department of Chemistry, Thimann Laboratories
University of California, Santa Cruz, California 95064

Douglas W. Stephan[†]

Department of Chemistry and Biochemistry
University of Windsor, Windsor
Ontario, Canada N9B 3P4
Received November 16, 1987

Bleomycins (BLM 1), a family of glycopeptide antitumor drug cause DNA strand cleavage in the presence of metal ions like Fe^{2+} and molecular oxygen. The requirement of a metal ion for the drug action has prompted research in coordination chemistry of BLM and the interaction of metallobleomycins (M-BLMs) with DNA.[1] The coordination structures of various M-BLMs have

R: terminal amine

BLM (1)
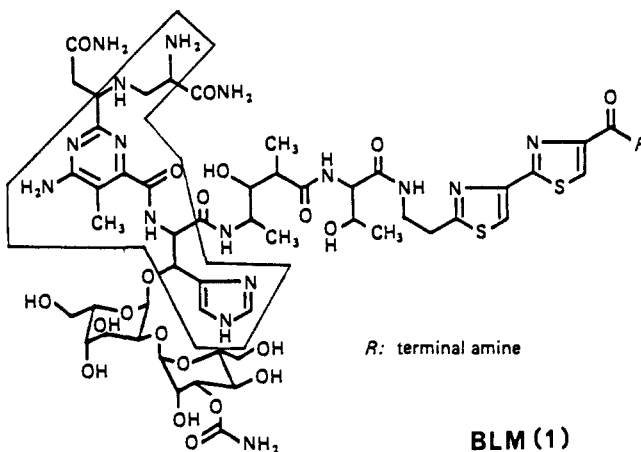
been predicted primarily on the basis of spectroscopic data. The only exception is Cu(II)-BLM in which the assignment of the donor centers around Cu(II) relies on the preliminary crystal structure of a Cu(II) complex of P-3A, a biosynthetic intermediate of BLM.[2,3] Studies on the synthetic analogues of M-BLMs[4,5] reported so far are all restricted to measurements in solutions. In absence of crystallographic studies, precise structure-reactivity correlations with M-BLMs are therefore not available. As part of a systematic synthetic analogue approach to metallo-bleomycins,[6-9] we report here the synthesis, structure, and selected

(1) (a) Stubbe, J.; Kozarich, J. W. Chem. Rev. 1987, 87, 1107. (b) Hecht, S. M. Acc. Chem. Res. 1986, 19, 383. (c) Sugiura, Y.; Takita, T.; Umezawa, H. Met. Ions Biol. Syst. 1985, 19, 81. (d) Dabrowiak, J. C. Adv. Inorg. Biochem. 1983, 4, 69. (e) Povrick, L. F. Molecular Aspects of Anticancer Drug Action; Neidle, S., Waring, M. J., Eds.; MacMillan: London, 1983; p 157. (f) Dabrowiak, J. C. Met. Ions Biol. Syst. 1980, 11, 305. (g) Umezawa, H.; Takita, T. Struct. Bonding (Berlin) 1980, 40, 73. (h) Bleomycin: Chemical, Biochemical and Biological Aspects; Hecht, S. M., Ed.; Springer-Verlag: New York, 1979. (i) Bleomycin: Current Status and New Developments; Carter, S. K., Crooke, S. T., Umezawa, H., Eds.; Academic: New York, 1978.

(2) Iitaka, Y.; Nakamura, H.; Nakatani, T.; Muraoka, Y.; Fuji, A.; Takita, T.; Umezawa, H. J. Antibiot. 1978, 31, 1070.

(3) Certain anomalies have been overlooked in this case. For example, the absorption spectrum, EPR parameters, and half-wave potential of Cu(II)-P-3A are distinctly different from those of Cu(II)-BLM.[4]

(4) (a) Kittaka, A.; Sugano, Y.; Otsuka, M.; Ohno, M.; Sugiura, Y.; Umezawa, H. Tetrahedron Lett. 1986, 27, 3631, 3635. (b) Umezawa, H.; Takita, T.; Sugiura, Y.; Otsuka, M.; Kobayashi, S.; Ohno, M. Tetrahedron 1984, 40, 501. (c) Sugiura, Y.; Suzuki, T.; Otsuka, M.; Kobayashi, S.; Ohno, M.; Takita, T.; Umezawa, H. J. Biol. Chem. 1983, 258, 1328. (d) Otsuka, M.; Yoshida, M.; Kobayashi, S.; Ohno, M.; Sugiura, Y.; Takita, T.; Umezawa, H. J. Am. Chem. Soc. 1981, 103, 6986.

(5) (a) Henichart, J.-P.; Bernier, J.-L.; Houssin, R.; Lohez, M.; Kenani, A.; Catteau, J.-P. Biochem. Biophys. Res. Commun. 1985, 126, 1036. (b) Henichart, J.-P.; Houssin, R.; Bernier, J.-L.; Catteau, J.-P. J. Chem. Soc., Chem. Commun. 1982, 1295.

(6) Brown, S. J.; Tao, X.; Stephan, D. W.; Mascharak, P. K. Inorg. Chem. 1986, 25, 3377.