reasoning will be useful in understanding the mechanisms of reactions catalyzed by structurally uncharacterized enzymes such as glyoxalase I,[45] proline racemase,[46] and both vitamin K dependent[47] and biotin-dependent[48] carboxylases.

Acknowledgment. This research was supported by GM-34572 (to J.A.G.) and GM-40570 (to J.A.G., G.L.K., and J.W.K.) from the National Institutes of Health and by the National Science Foundation (to P.G.G.).

---

(44) Although our arguments are based upon reasonable estimates for both the pK_a values for carbonyl-bound protons of carbonyl-protonated carbon acids and the pK_E values, the errors in our estimates are not expected to alter our conclusions.

(45) Chari, R. V. J.; Kozarich, J. W. *J. Biol. Chem.* **1981**, *256*, 9785.

(46) Albery, W. J.; Knowles, J. R. *Biochemistry* **1986**, *25*, 2572.

(47) Dowd, P.; Ham, S. W.; Geib, S. J. *J. Am. Chem. Soc.* **1991**, *113*, 7734.

(48) Knowles, J. R. *Annu. Rev. Biochem.* **1989**, *58*, 195.

(49) The "libido" rule that the change in pK_a of the substrate during a concerted general acid-general base catalyzed reaction must result in a favorable proton transfer to the active site base predicts that the pK_a of the protonated enol will be less than that of the active site base: Jencks, W. P. *J. Am. Chem. Soc.* **1972**, *94*, 4731. That this requirement is not quite achieved in our analyses of carboxylic acid substrates may reflect the uncertainties in the various pK_as and pK_Es.

Gas-Phase Reactions of Iron Porphyrins with NO_2: Oxygen Atom Transfer to Anionic and Cationic Iron Porphyrins

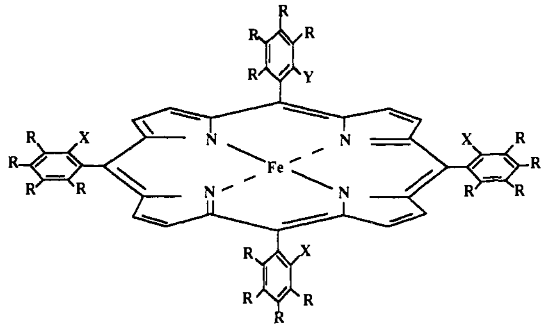
H. L. Chen, T. E. Hagan, S. E. Groh, and D. P. Ridge*

Department of Chemistry and Biochemistry and
Center for Catalytic Science and Technology
University of Delaware, Newark, Delaware 19716

Received August 7, 1991

We report the observation of bimolecular O atom transfer reactions between NO_2 and ionic iron porphyrins in the gas phase. Both molecular anions (iron(I)) and cations (iron(III)) of iron(II) porphyrins accept an O atom from NO_2, forming species which are nominally iron(III) and iron(V), respectively. Species of this kind have not been previously observed in the gas phase and are thought to be important in a number of oxidative processes catalyzed by iron porphyrins and related species.[1] These processes include the oxidative processes catalyzed by cytochrome P450[2] and the selective air oxidation of alkanes.[3]

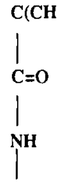
The reactant ions were introduced into the ion trap of a Fourier transform ion cyclotron resonance (FT-ICR) spectrometer[4] (FTMS-2000 Extrel, Madison, WI) using previously described methods involving a heated sample probe and an electron beam[5,6] or laser desorption.[7] Ions were generated from iron(II) tetraphenylporphyrin (**1**), iron(II) tetrakis(pentafluorophenyl)porphyrin (**2**), iron(II) tetrakis(*o*-pivalamidophenyl)porphyrin (**3**),[8] and iron(II) (*o*-(5-imidazol-1-ylvaleramido)phenyl)triphenylporphyrin (**4**).[9] Typically NO_2 was present at a pressure of 10^{-7} Torr. Under these conditions bimolecular reactions can be unambiguously identified.



1. R=X=Y=H

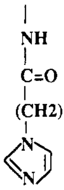
2. R=X=Y=F

3. R=H, X=Y=



$$\mathrm{-NH-C(=O)-C(CH3)3}$$

4. R=X=H, Y=



The anion of **3** reacts according to eqs 1 and 2. The primary

$$[3]^{\bullet-} + NO_2^{\bullet} \xrightarrow{k_1} [3O]^{\bullet-} + NO^{\bullet} \qquad (1)$$

$$[3]^{\bullet-} + NO_2^{\bullet} \xrightarrow{k_2} [3NO_2]^{-} \qquad (2)$$

products react further to form $[3(NO_2)_2]^{\bullet-}$. Intermediates in the conversion of $[3O]^{\bullet-}$ to $[3(NO_2)_2]^{\bullet-}$, $[3NO_3]^-$ and $[3(NO_3)(NO_2)]^{\bullet-}$, occur at small steady-state concentrations. We note that $3(NO_2)_2^-$ also results from the condensed-phase reaction between NO_2^- and **3**.[10] The observation of reaction 1 suggests that $NO_2^{\bullet}$ is bound to $3^{\bullet-}$ through an O atom.

The reactions of $4^{\bullet-}$ with $NO_2^{\bullet}$ are essentially the same as those of $3^{\bullet-}$, giving $[4O]^{\bullet-}$, $[4(NO_2)]^-$, and finally $[4(NO_2)_2]^{\bullet-}$. $1^{\bullet-}$ and $2^{\bullet-}$, on the other hand, are *not* observed to form $[1O]^{\bullet-}$ and $[2O]^{\bullet-}$. Instead they form $NO_2^{\bullet}$ adducts and transfer an electron to $NO_2^{\bullet}$. This suggests that the oxo moieties in $[3O]^{\bullet-}$ and in $[4O]^{\bullet-}$ are stabilized by the ortho amido substituents in those species.

On exposure to $NO_2^{\bullet}$, $2^{\bullet+}$ disappears exponentially with time and is eventually completely converted to products. The ratio of $[2NO]^+$ product to $[2OH]^+$ product is independent of reaction time but proportional to the ratio of $NO_2^{\bullet}$ pressure to **2** pressure. These observations are consistent with reactions 3 and 4[11] where $[2-H]^{\bullet}$ is the radical formed by H atom transfer from **2**. The

$$2^{\bullet+} \xrightarrow[-NO]{NO_2^{\bullet}} [2O]^{\bullet+} \xrightarrow[[2-H]^{\bullet}]{2} [2OH]^{+} \qquad (3)$$

$$[2O]^{\bullet+} \xrightarrow[-O_2]{NO_2^{\bullet}} [2NO]^{+} \qquad (4)$$

rate constant for the first step of reactions 3 and 4 is much smaller than the combined rate constants for the second steps of 3 and

---

(1) (a) Groves, J. T.; Watanabe, Y. *J. Am. Chem. Soc.* **1988**, *110*, 8443-8452. (b) Groves, J. T.; Nemo, T. E. *J. Am. Chem. Soc.* **1983**, *105*, 6243-6248. (c) Guengerich, F. P.; Macdonald, T. L. *Acc. Chem. Res.* **1984**, *17*, 9-16.

(2) McMurry, T. J.; Groves, J. T. In *Cytochrome, Structure, Mechanism and Biochemistry*; Ortiz de Montellano, P. R., Ed.; Plenum: New York, 1986; Chapter 1.

(3) (a) Nappa, M. J.; Tolman, C. A. *Inorg. Chem.* **1985**, *24*, 4711-4719. (b) Ellis, P. E., Jr.; Lyons, J. E. *Coord. Chem. Rev.* **1990**, *105*, 181-193.

(4) Buchanan, M. V.; Comisarow, M. B. In *Fourier Transform Mass Spectroscopy*; Buchanan, M. V., Ed.; American Chemical Society: Washington, DC, 1987; pp 1-20.

(5) Chen, H. L.; Pan, Y. H.; Groh, S.; Hagan, T. E.; Ridge, D. P. *J. Am. Chem. Soc.* **1991**, *113*, 2766-2767.

(6) Chen, H. L.; Hagan, T. E.; Groh, S. E.; Ridge, D. P. *Org. Mass Spectrom.* **1991**, *26*, 173-174.

(7) (a) Nuwaysir, L. M.; Wilkins, C. L. *Anal. Chem.* **1989**, *61*, 689-694. (b) Forest, E.; Marchon, J.-C.; Wilkins, C. L.; Yang, L.-C. *Org. Mass Spectrom.* **1989**, *24*, 197-200. (c) For an alternative procedure, see: Irikura, K. K.; Beauchamp, J. L. *J. Am. Chem. Soc.* **1991**, *113*, 2767-2768.

(8) Prepared as described in the following: Collman, J. P.; Brauman, J. I.; Doxsee, K. M.; Halbert, T. R.; Bunnenberg, E.; Linder, R. E.; LaMar, G. N.; DelGaudio, J.; Lang, G.; Spartalian, K. J. *J. Am. Chem. Soc.* **1980**, *102*, 4182.

(9) Prepared as described in the following: Collman, J. P.; Gagne, R. R.; Reed, C. A.; Halbert, T. R.; Lang, G.; Robinson, W. T. *J. Am. Chem. Soc.* **1975**, *97*, 1427.

(10) (a) Finnegan, M. G.; Lappin, A. G.; Scheidt, W. R. *Inorg. Chem.* **1990**, *29*, 181-185. (b) Nasri, H.; Goodwin, J. A.; Scheidt, W. R. *Inorg. Chem.* **1990**, *29*, 185-191.

(11) Reaction 4 may be viewed as a reaction between the O atom in $[2O]^{\bullet+}$ and $NO_2^{\bullet}$ to form O_2 and $NO^{\bullet}$. The details of the mechanism, which presumably leaves NO bound to the metal, are not known.

0002-7863/91/1513-9669$02.50/0 © 1991 American Chemical Society

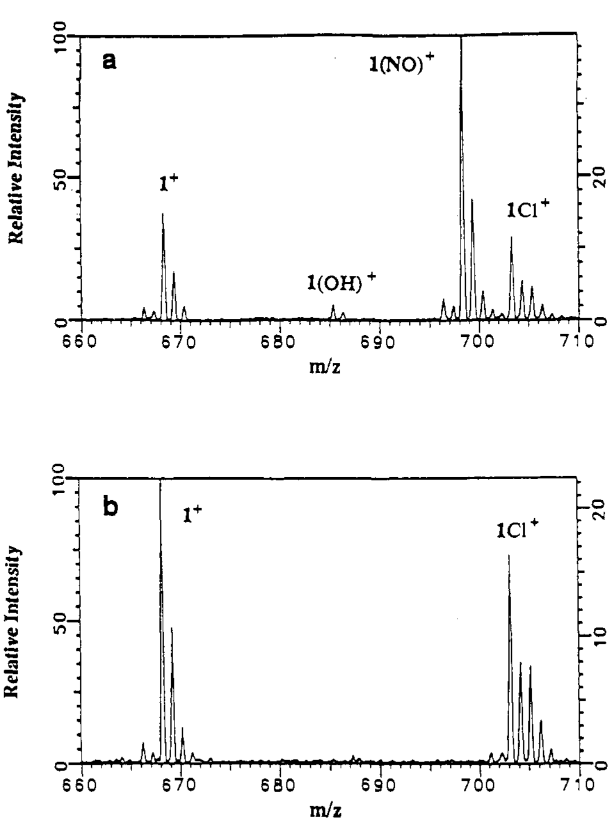


Figure 1. (a) Spectrum of ions formed by laser desorption of 1Cl after exposure to NO_2. Naturally occurring isotopes (^{13}C, ^{37}Cl, ^{54}Fe, etc.) give each chemical species several isotopic variants. The right-side axis is absolute intensity in arbitrary units. (b) Spectrum identical with a except that ions of the mass of 1O$^+$ ejected continuously during the exposure to NO_2.

4. Consequently, $[2O]^{\bullet+}$ is not directly observed. The intermediacy of $[2O]^{\bullet+}$, however, is implied both by the kinetics of the reactions and by the results of ion ejection experiments. Such an experiment is illustrated in Figure 1 for the reaction of $1^{\bullet+}$ with $NO_2^{\bullet}$, which is analogous to the $2^{\bullet+}$ reaction with $NO_2^{\bullet}$. The reactant ion is produced by pulsed laser desorption and stored in the ion trap. A pulsed valve[12] then opens and admits a burst of $NO_2^{\bullet}$ following which spectrum 1a is obtained revealing a substantial $[1NO]^+$ product. Spectrum 1b is obtained under identical conditions except that an rf voltage is applied to the cell to eject ions of the mass of $[1O]^{\bullet+}$ continuously during the $NO_2^{\bullet}$ burst.[13] Even though $[1O]^{\bullet+}$ cannot be detected, it can be ejected.[14] Obviously from spectrum 1b, eliminating $[1O]^{\bullet+}$ eliminates $[1NO]^+$, supporting the intermediacy of the former in producing the latter.

The reactions of $3^{\bullet+}$ with $NO_2^{\bullet}$ are analogous to those of $1^{\bullet+}$ and $2^{\bullet+}$. On the other hand, $4^{\bullet+}$ does not react with $NO_2^{\bullet}$. We have previously shown that the "tethered" imidazole base in $4^{\bullet+}$ is coordinated with the metal.[8] The failure of $4^{\bullet+}$ to react thus suggests that the efficiency of O atom transfer from $NO_2^{\bullet}$ is sensitive to the nature of any axial ligand in the complex and that the O atom adds to the metal.

Acknowledgment. Jim Lyons and Asgeir Bjarnason are acknowledged for helpful discussions and Sun Co. and the Delaware Research Partnership for financial support.

---

[12] (a) Sack, T. M.; Gross, M. L. *Anal. Chem.* **1983**, *55*, 2419–2421. (b) Carlin, T. J.; Freiser, B. S. *Anal. Chem.* **1983**, *55*, 571.

[13] Comisarow, M. B.; Grassi, V.; Parisod, G. *Chem. Phys. Lett.* **1978**, *57*, 413–416.

[14] Bjarnason, A. *Org. Mass Spectrom.* **1989**, *24*, 847–848. The resolution of the ejection in this case corresponds to ca. ±2 amu so that ions within 2 amu of the most abundant isotopic mass of $1O_2^+$ (m/z = 684) are also ejected.

Pinched-Cone Conformers of Calix[4]arenes[1]

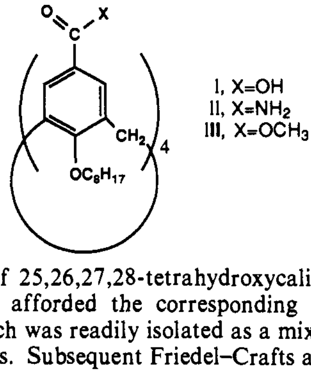
Mark Conner, Vaclav Janout,[2] and Steven L. Regen*

Department of Chemistry and
Zettlemoyer Center for Surface Studies
Lehigh University, Bethlehem, Pennsylvania 18015

Received August 30, 1991

Calix[4]arenes are cyclic tetramers of phenol that exist as cone, partial cone, 1,2-alternate, and/or 1,3-alternate conformational isomers.[3-6] Currently, it is the *cone* isomer that is receiving the greatest attention as a framework for constructing molecular hosts, templates, and pores.[3-9] Although the ^1H NMR spectra that have been reported for all homo-tetrasubstituted calix[4]arene cones are consistent with C_{4v} symmetry, recent theoretical calculations predict that such a conformation can represent a saddle-point structure, where the corresponding C_{2v} isomers ("pinched cones") are thermodynamically favored (Figure 1).[6] The fact that pinched-cone conformers have not yet been detected *in solution*[9] has been rationalized in terms of a rapid interconversion between two equivalent C_{2v} isomers.[6] Experimental support for this hypothesis, however, is lacking.

During the course of our studies dealing with the construction of perforated monolayers,[7,8] we had need for the tetrasubstituted calix[4]arenes I and II. While the synthesis of these compounds proved to be straightforward, it soon became apparent that both compounds showed unusual spectral properties. Our principal findings, which are reported herein, provide the first direct evidence that pinched-cone conformers can play a major role in the overall structure and dynamics of the calix[4]arene framework.



Alkylation of 25,26,27,28-tetrahydroxycalix[4]arene[10] with 1-bromooctane afforded the corresponding tetra-*n*-octyloxytetraether, which was readily isolated as a mixture of cone and noncone isomers. Subsequent Friedel–Crafts acylation (CH_3COCl) or reaction with NBS afforded a stereoisomeric mixture of acetylated and brominated derivatives, respectively, from which

---

[1] Supported by the Division of Basic Energy Sciences and the Department of Energy (DE-FG02-85ER-13403) and by Air Products and Chemicals, Inc., Allentown, PA.

[2] On leave from the Institute of Macromolecular Chemistry, Czechoslovak Academy of Sciences, Prague, Czechoslovakia.

[3] Gutsche, C. D. *Calixarenes*; The Royal Society of Chemistry: Thomas Graham House, Science Park, Cambridge, 1989.

[4] Vicens, J.; Bohmer, V. *Calixarenes: A Versatile Class of Macrocyclic Compounds*; Kluwer Academic Publishers: Boston, 1991.

[5] Groenen, L. C.; van Loon, J.-D.; Verboom, W.; Harkema, S.; Casnati, A.; Ungaro, R.; Pochini, A.; Ugozzoli, F.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1991**, *113*, 2385.

[6] Grootenhius, P. D. J.; Kollman, P. A.; Groenen, L. C.; Reinhoudt, D. N.; van Hummel, G. J.; Ugozzoli, F.; Andreetti, G. D. *J. Am. Chem. Soc.* **1990**, *112*, 4165.

[7] Markowitz, M. A.; Bielski, R.; Regen, S. L. *J. Am. Chem. Soc.* **1988**, *110*, 7545.

[8] Markowitz, M. A.; Janout, V.; Castner, D. G.; Regen S. L. *J. Am. Chem. Soc.* **1989**, *111*, 8192.

[9] Homo-tetrasubstituted calix[4]arene cones having C_{2v} symmetry have previously been observed in the *solid state*: (a) Ungaro, R.; Pochini, A.; Andreetti, G. D. *J. Inclusion Phenom.* **1984**, *2*, 199. (b) McKervery, M. A.; Seward, E. M.; Ferguson, G.; Ruhl, B.; Harris, S. J. *J. Chem. Soc., Chem. Commun.* **1985**, 388. (c) Arduini, A.; Pochini, A.; Reverberi, S.; Ungaro, R.; Andreetti, G. D.; Ugozzoli, F. *Tetrahedron* **1986**, *42*, 2089. (d) Ferguson, G.; Kaitner, B.; McKervery, M. A.; Seward, E. M. *J. Chem. Soc., Chem. Commun.* **1987**, 584. (e) Calestani, G.; Ugozzoli, F.; Arduini, A.; Ghidini, E.; Ungaro, R. *J. Chem. Soc., Chem. Commun.* **1987**, 344.

[10] Gutsche, C. D.; Lin, L. G. *Tetrahedron* **1986**, *42*, 1633.