JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

Subscriber access provided by American Chemical Society

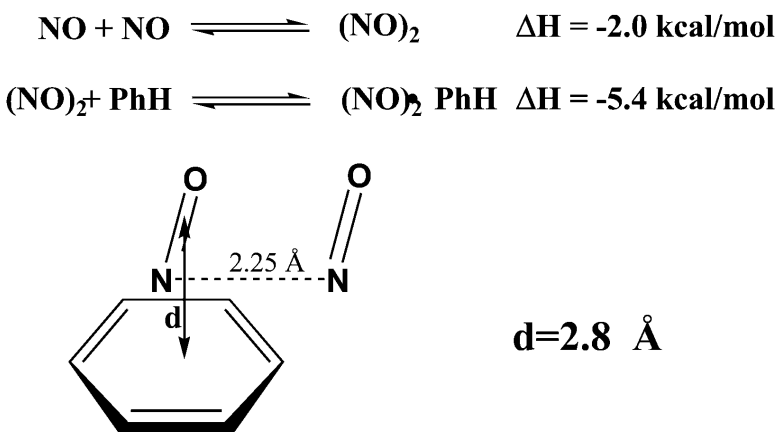
Communication

Theoretical Evidence for Enhanced NO Dimerization in Aromatic Hosts: Implications for the Role of the Electrophile (NO) in Nitric Oxide Chemistry

Yi-Lei Zhao, Michael D. Bartberger, Kei Goto, Keiichi Shimada, Takayuki Kawashima, and K. N. Houk

J. Am. Chem. Soc., **2005**, 127 (22), 7964-7965• DOI: 10.1021/ja042247s • Publication Date (Web): 14 May 2005

Downloaded from http://pubs.acs.org on March 25, 2009



More About This Article

Additional resources and features associated with this article are available within the HTML version:

- Supporting Information
- Links to the 4 articles that cite this article, as of the time of this article download
- Access to high resolution figures
- Links to articles and content related to this article
- Copyright permission to reproduce figures and/or text from this article

View the Full Text HTML

ACS Publications
High quality. High impact.

Journal of the American Chemical Society is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

J|A|C|S
COMMUNICATIONS

Published on Web 05/14/2005

Theoretical Evidence for Enhanced NO Dimerization in Aromatic Hosts: Implications for the Role of the Electrophile $(NO)_2$ in Nitric Oxide Chemistry

Yi-Lei Zhao,[†] Michael D. Bartberger,[‡] Kei Goto,[§] Keiichi Shimada,[§] Takayuki Kawashima,[§] and K. N. Houk*,[†]

Department of Chemistry and Biochemistry, University of California, Los Angeles, California 90095, Department of Molecular Structure and Design, Amgen, Inc., M/S 29-M-B, One Amgen Center Drive, Thousand Oaks, California 91320, and Department of Chemistry, Graduate School of Science, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

Received December 23, 2004; E-mail: houk@chem.ucla.edu

Nitric oxide (NO) is involved in many important reactions in atmospheric, surface, and biological processes. NO is a relatively stable and unreactive radical, except toward O_2 and other radicals. The possibility that the NO dimer, $(NO)_2$, might be involved in reactions has been of interest since the 1950s.[1−3,5,6] For example, the oxidation of triphenylphosphine by nitric oxide follows formally third-order kinetics, k_3 of 10^3 M^{-2} s^{-1} at 294 K.[3]

Here, we present theoretical evidence for the role of the NO dimer in reactions of NO with nucleophiles and show that concentration of $(NO)_2$ increases in aromatic environments.

K_{eq} for the formation of the NO dimer is quite small in the gas phase ($<10^{-4}$ M^{-1}).[3] However, $(NO)_2$ is expected to be much more reactive with nucleophiles since $(NO)_2$ is much easier to reduce: $E_{1/2}$ $(NO/NO^-) = -0.76$ V versus $E_{1/2}$ $[(NO)_2/N_2O_2^-] = -0.38$ V.[4]

It has been proposed that a hydrophobic environment may concentrate nitric oxide;[5] Chan and co-workers have reported that increasing NO concentration in cytochromes weakens the NO EPR signal.[6] Enhanced NO dimerization has been observed by Yates *et al.* for NO trapped inside single-walled carbon nanotubes.[7] It has also been reported that NO, aromatic hydrocarbons, and some Lewis acids form ternary charge-transfer complexes ($NO{\cdot}MX_n{\cdot}ArH$),[8] besides the well-known charge-transfer complexes of $NO^+{\cdot}ArH$.[9]

Many spectroscopic studies have demonstrated that singlet *cis*-O=N···N=O (C_{2v}) is the global minimum in both the gas and condensed phases.[10] The structure has N=O bond lengths of 1.152 Å, a N···N distance of 2.263 Å, an O=N···N angle of 97.2°, and a dissociation energy of 2.0 ± 0.2 kcal/mol.[10]

$(NO)_2$ is also especially intriguing theoretically; the long weak N−N bond formed from overlap of two π^* radicals is hard to predict correctly.[11−14] Semiempirical[11] HF[12] and DFT[13] theories fail to predict the geometry and dissociation energy accurately. Correlated treatments, such as MP2, CPF, CCSD, QCISD(T), CCSD(T), MRCI, and CASPT2, do reproduce the geometry and energies.[14]

Two models, NO−benzene and $(NO)_2$−benzene, were studied to determine the effect of an aromatic environment on the NO dimerization. Ab initio quantum mechanical calculations were performed with the second-order Møller−Plesset perturbation theory (MP2)[15] and the aug-cc-pVDZ basis set in Gaussian 03.[16] Restricted open-shell (for radical) and closed-shell MP2 methods were used since ROMP2 reproduces the global $(NO)_2$ structure and dissociation energy in the gas phase correctly.[17] MP2 is also reasonable for benzene complexes.[18] The different orientations between NO or $(NO)_2$ and benzene were computed, and the global minima were characterized by harmonic frequency analysis.[19] The resulting zero-point energies (ZPEs) at the ROMP2/6-31+G* level were used to correct binding enthalpies. Basis set superposition error (BSSE) was corrected with the counterpoise method.

The resulting minima have similar geometries for both NO−benzene and $(NO)_2$−benzene complexes; one NO lies above the benzene ring with a center−center distance of about 3 Å (Figure 1). In the $(NO)_2$−benzene complex, the NO dimer retains its geometry and the $(NO)_2$ plane is nearly parallel to the phenyl ring, with one NO fragment above the edge of phenyl ring.

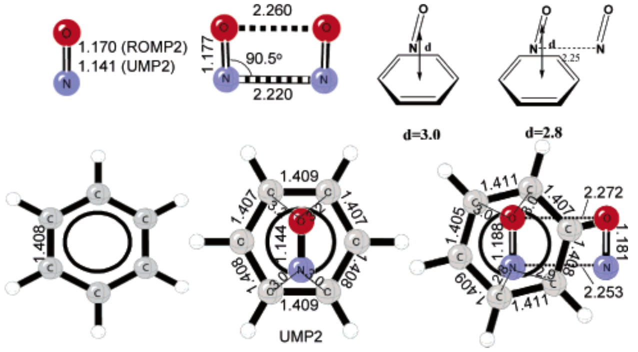


Figure 1. The calculated structures of NO, $(NO)_2$, benzene, NO−benzene, and $(NO)_2$−benzene complexes with MP2/aug-cc-pVDZ (distances in angstroms).

An aromatic environment can be modeled by the following hypothetical equilibria in the gas phase [CPMP2/aug-cc-pVDZ, CPMP2/aug-cc-pVTZ//MP2/aug-cc-pVDZ (in italics)]:[20]

$$NO + NO \rightleftharpoons (NO)_2 \qquad \Delta H = -2.0\ (-\mathit{2.3})\ \text{kcal/mol}$$

$$NO + PhH \rightleftharpoons NO{\cdot}PhH \qquad \Delta H = -2.3\ (-\mathit{2.7})\ \text{kcal/mol}$$

$$(NO)_2 + PhH \rightleftharpoons (NO)_2{\cdot}PhH \qquad \Delta H = -5.4\ (-\mathit{6.5})\ \text{kcal/mol}$$

$$NO + H_2O \rightleftharpoons NO{\cdot}H_2O \qquad \Delta H = -0.4\ (-\mathit{0.4})\ \text{kcal/mol}$$

$$(NO)_2 + H_2O \rightleftharpoons (NO)_2{\cdot}H_2O \qquad \Delta H = -0.7\ (-\mathit{0.8})\ \text{kcal/mol}$$

The binding energy for the $(NO)_2$−π interaction is −3.1 (−*3.8*) kcal/mol stronger than that of the NO−π interaction. The overall enthalpy change from NO monomer and benzene to $(NO)_2{\cdot}PhH$ is −7.4 (−*8.8*) kcal/mol. Although the NO monomer is still favored in aromatic surroundings due to the entropy loss upon dimerization, the dimerization equilibrium constant increases by more than 150 times at room temperature ($\Delta\Delta G > -3$ kcal/mol; $\ln K = -\Delta G/RT$).[20]

The difference is due to charge-transfer and electrostatic interactions between $(NO)_2$ and benzene (Figure 2, data from NIST). The LUMO of $(NO)_2$ is a somewhat π-binding orbital and is lower lying than the singly occupied degenerate π^* orbital of the monomer, providing better charge-transfer stabilization with the HOMO of

---

[†] University of California, Los Angeles.
[‡] Amgen, Inc.
[§] The University of Tokyo.

10.1021/ja042247s CCC: $30.25 © 2005 American Chemical Society

benzene (E_{1g}). These interactions between NO, $(NO)_2$, and aromatic hosts may correlate with UV−vis aromatic solvent onset wavelength increases by nitric oxide.[21]

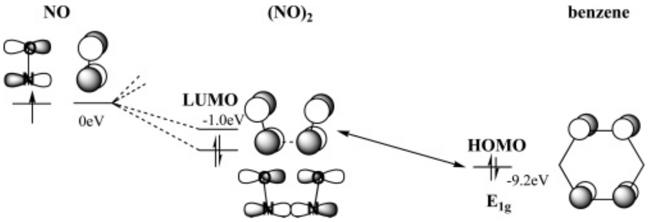


Figure 2. The frontier molecular orbitals of NO, $(NO)_2$, and benzene.

Our calculations also indicate that $(NO)_2$ is the reactive electrophile in NO reactions. The potential energy surface (B3LYP/6-31+G*) for PH_3 plus one molecule of NO is monotonically uphill, and no stable adduct is formed;[17] however, phosphine reacts with $(NO)_2$, easily producing 1,4,2,3,5-dioxadiazaphosphole, a metastable intermediate in the phosphine oxidation. The intermediate undergoes a retro-1,3-dipolar addition to give phosphine oxide and nitrous oxide (Figure 3).

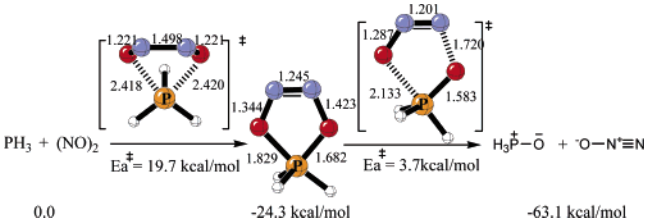


Figure 3. The lowest-energy path of phosphine oxidation by NO (bond lengths in angstroms; energies corrected with zero-point energy).

We have found that the hindered thiol, TrmSH,[22] with many aromatic rings around the SH group, reacts with nitric oxide in a sealed tube, leading to an *S*-nitrosothiol (TrmSNO) at room temperature (Figure 4); *t*-BuSH and nitric oxide do not react in this way.[23]

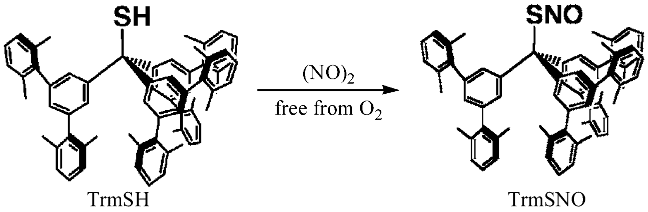


Figure 4. TrmSH *S*-nitrosation with NO under O_2-free condition.

Initial theoretical investigations on CH_3SH and NO also suggest that $(NO)_2$, rather than the monomer, reacts with thiol, leading to *S*-nitrosation (Figure 5). By contrast, thiols and NO form no stable complex.

Aromatic groups in triphenylphosphine and TrmSH may concentrate the highly reactive NO dimer and, subsequently, react with nucleophiles. Thus, the reaction rate ($k_2 = k_3/K_{eq}$) in the triphenylphosphine oxidation by nitric oxide would be in a reasonable range; similarly, this can rationalize that TrmSH reacts with NO much faster than *t*-BuSH does.

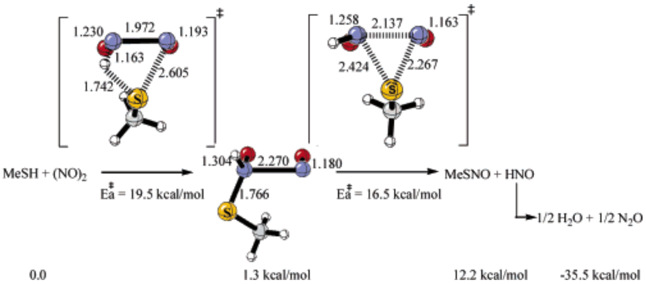


Figure 5. The lowest-energy path of S-nitrosation of thiol by NO (MP2/6-31+G*; details of HNO dimerization[24] are omitted).

Charge-transfer complexation between nitric oxide dimer and aromatic molecules increases the activity of nitric oxide through the enhanced NO dimerization. $(NO)_2$ should not be overlooked in biological processes since many aromatic amino acid residues in proteins can serve as aromatic hosts to induce the NO dimerization, and the resulting NO dimer is a good nitrosating agent and oxidant.[25]

Acknowledgment. We are grateful to the National Institute of General Medical Sciences, National Institutes of Health, for financial support of this research, and to the National Science Foundation and UCLA for computational resources.

Supporting Information Available: Optimized structures and energies for all conformations discussed, binding energy calculations, and harmonic vibrational frequencies (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) Lee, A. S.; Keller, W. E.; Johnston, H. L. *J. Chem. Phys.* **1951**, *19*, 189−192.
(2) Liu, Z.-P.; Jenkins, S. J.; King, D. A. *J. Am. Chem. Soc.* **2004**, *126*, 7336−7340.
(3) Lim, M. D.; Lorkovic, I. M.; Ford, P. C. *Inorg. Chem.* **2002**, *41*, 1026−1028.
(4) (a) Bartberger, M. D.; Liu, W.; Ford, E.; Miranda, K. M.; Switzer, C.; Fukuto, J. M.; Farmer, P. J.; Wink, D. A.; Houk, K. N. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 10958−10963. (b) Poskrebyshev, G. A.; Shafirovich, V.; Lymar, S. V. *J. Am. Chem. Soc.* **2004**, *126*, 891−899.
(5) Liu, X.-P.; Miller, M. J. S.; Joshi, M. S.; Thomas, D. D.; Lancaster, J. R. *Proc. Natl. Acad. Sci. U.S.A.* **1998**, *95*, 2175−2179.
(6) Brudvig, G. W.; Stevens, T. H.; Chan, S. I. *Biochemistry* **1980**, *19*, 5272−5285.
(7) Byl, O.; Kondratyuk, P.; Yates, J. T., Jr. *J. Phys. Chem. B* **2003**, *107*, 4277−4279.
(8) Brownstein, S.; Irish, B. *Polyhedron* **1988**, *7*, 97−101.
(9) (a) Bosch, E.; Kochi, J. K. *J. Org. Chem.* **1994**, *59*, 3314−3325. (b) Gwaltney, S. R.; Rosokha, S. V.; Head-Gordon, M.; Kochi, J. K. *J. Am. Chem. Soc.* **2003**, *125*, 3273−3283 and references therein.
(10) (a) Kukolich, S. G.; Sickafoose, S. M. *Mol. Phys.* **1996**, *89*, 1659−1661. (b) Brookes, M. D.; McKellar, A. R. W.; Amano, T. J. *Mol. Spectrosc.* **1997**, *185*, 153−157. (c) Wade, E. A.; Cline, J. I.; Lorenz, K. T.; Hayden, C.; Chandler, D. W. *J. Chem. Phys.* **2002**, *116*, 4755−4757 and references therein.
(11) Jones, W. H. *J. Phys. Chem.* **1992**, *96*, 594−605.
(12) (a) Skaarup, S.; Skancke, P. N.; Boggs, J. E. *J. Am. Chem. Soc.* **1976**, *98*, 6106−6109. (b) Bardo, R. D. *J. Phys. Chem.* **1982**, *86*, 4658−4659.
(13) (a) Snis, A.; Panas, I. *Chem. Phys.* **1997**, *221*, 1−10. (b) Duarte, H. A.; Proynov, E.; Salahub, D. R. *J. Chem. Phys.* **1998**, *109*, 26−35.
(14) (a) Lee, T. J.; Rendell, A. P.; Taylor, P. R. *J. Phys. Chem.* **1990**, *94*, 5463−5468. (b) East, A. L. L. *J. Chem. Phys.* **1998**, *109*, 2185−2193. (c) Sayos, R.; Valero, R.; Anglada, J. M.; Gonzalez, M. *J. Chem. Phys.* **2000**, *112*, 6608−6624.
(15) Møller, C.; Plesset, M. S. *Phys. Rev.* **1934**, *46*, 618−622.
(16) Frisch, M. J. et al. *Gaussian 03*, revision B.05; Gaussian, Inc.: Pittsburgh, PA, 2003.
(17) Please see details in Supporting Information.
(18) (a) Tsuzuki, S.; Honda, K.; Uchimaru, T.; Mikami, M.; Tanabe, K. *J. Am. Chem. Soc.* **2000**, *122*, 3746−3753. (b) Chalasinski, G.; Szczesniak, M. M. *Chem. Rev.* **1994**, *94*, 1723−1765 and references therein.
(19) Harmonic frequency analysis on NO−benzene complexes uses the unrestricted MP2 method because numerically estimating gradients in the restricted open-shell calculations are very costly.
(20) Calculated solvent effects, using (U)B3LYP(CPCM,UAKS)/6-31+G*//(RO)MP2/aug-cc-pVDZ, indicate that dimers are solvated much better than monomers. Please see details in Supporting Information.

Solvation energies (kcal/mol):	benzene,	ether,	methanol,	water
$2NO \rightarrow (NO)_2$	-0.8	-0.8	-0.7	-1.0
$2NO\bullet H_2O \rightarrow (NO)_2\bullet H_2O$	-1.6	-1.9	-2.6	-3.0
$2NO\bullet PhH \rightarrow (NO)_2\bullet PhH$	-2.3	-2.3	-2.3	-3.1

(21) Grajower, R.; Joshua, J. *J. Am. Chem. Soc.* **1963**, *85*, 512−516.
(22) Goto, K.; Hino, Y.; Kawashima, T.; Kaminaga, M.; Yano, E.; Yamamoto, G.; Takagi, N.; Nagase, S. *Tetrahedron Lett.* **2000**, *41*, 8479−8483.
(23) The reactions were monitored by NMR; also see Supporting Information.
(24) Bartberger, M. D.; Fukuto, J. M.; Houk, K. N. *Proc. Natl. Acad. Sci. U.S.A.* **2001**, *98*, 2194−2198 and references therein.
(25) Liu, Z.-P.; Jenkins, S. J.; King, D. A. *J. Am. Chem. Soc.* **2004**, *126*, 7336−7340.

JA042247S