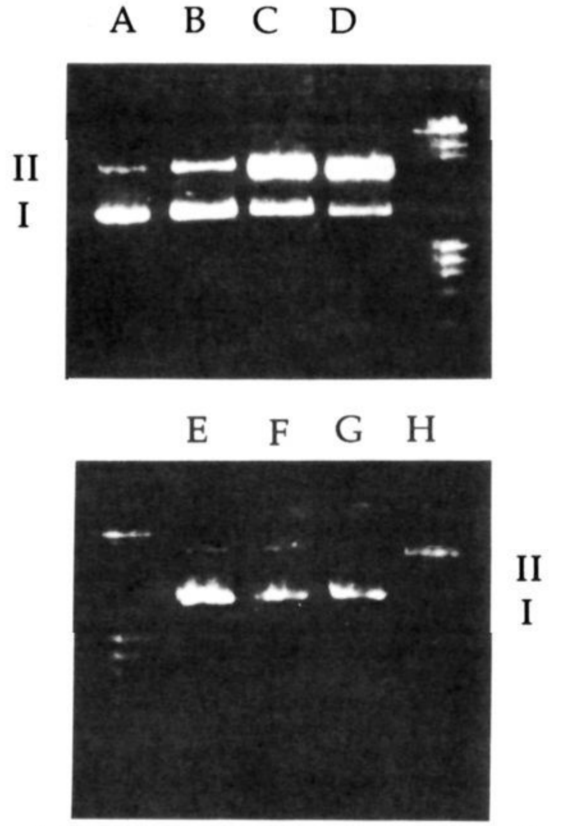

Figure 2. The 1% agarose ethidium bromide gels showing the electrophoresis of solutions containing 60 μM pSport1 DNA with (A) no ruthenium and with 20 μM $\mathrm{[Ru^{II}(tpy)(bipy)OH_2](ClO_4)_2}$ electrolyzed at 0.8 V for (B) 15 min, (C) 30 min, and (D) 1.5 h, (E) shows 60 μM pSport1 with no ruthenium, and (F) shows 60 μM pSport1 that has been electrolyzed at 0.8 V in the absence of metal complex for 2 h, (G) shows 60 μM pSport1 incubated at 25 °C with 0.2 mM $\mathrm{[Ru^{II}(tpy)(bipy)OH_2](ClO_4)_2}$ for 1 h, and (H) shows 60 μM pSport1 incubated with 0.2 mM $\mathrm{[Ru^{IV}(tpy)(bipy)O](ClO_4)_2}$ for 1 h. Molecular weight markers are from DRIgest III (λ DNA-Hind III/*φX174*-Hae III digest) purchased from Pharmacia.

mograms with and without DNA are given in the supplementary material).[9,10] In oxidations of small molecules, controlled potential electrolysis at 0.8 V of $\mathrm{Ru^{II}(tpy)(bipy)OH_2^{2+}}$ leads to electrocatalytic conversions mediated by the Ru(IV) form.[7] Similarly, controlled potential electrolysis at 0.8 V of solutions containing DNA and $\mathrm{Ru^{II}(tpy)(bipy)OH_2^{2+}}$ leads to nearly complete conversion of the supercoiled DNA to the nicked circular form in 1.5 h (Figure 2, lane D).[11,12] Addition of $\mathrm{Ru^{IV}(tpy)(bipy)O^{2+}}$ directly to the DNA effects conversion to form II (lane H). In control experiments, incubation of the DNA with $\mathrm{Ru^{II}(tpy)(bipy)OH_2^{2+}}$ (lane G) or electrolysis of DNA alone for 2 h (lane F) causes no change in the supercoiled/nicked ratio.

The system is ideal for probing the redox pathways of DNA cleavage. Rate constants for cleavage of DNA can ultimately be obtained from electrochemistry and optical measurements. The *quantitative* conversion of $\mathrm{Ru^{IV}(tpy)(bipy)O^{2+}}$ to $\mathrm{Ru^{II}(tpy)(bipy)OH_2^{2+}}$ and the characteristic optical properties of these species present an attractive opportunity for studying concurrently the fate of both the metal complex and the nucleic acid during oxidative DNA cleavage.

Acknowledgment. Helpful discussions with Drs. R. A. Binstead and J. C. Brewer and Professors T. J. Meyer, J. P. Caradonna, D. M. Crothers, S. J. Lippard, and E. F. Bowden are acknowledged. H.H.T. thanks the Camille and Henry Dreyfus Foundation for a New Faculty Award, the National Science Foundation for a Presidential Young Investigator Award (CHE-9157411), and the North Carolina Biotechnology Center for an Academic Research Initiation Grant.

Registry No. $\mathrm{Ru^{IV}(tpy)(bpy)O^{2+}}$, 73836-44-9.

Supplementary Material Available: Cyclic voltammograms of $\mathrm{Ru^{II}(tpy)(bipy)OH_2^{2+}}$ with and without calf thymus DNA and a discussion of the effects of DNA on the electrochemistry (4 pages). Ordering information is given on any current masthead page.

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[9] Cyclic voltammetry was performed at 0.32 cm^2 tin-doped indium oxide working electrodes as previously described (Thorp, H. H.; Brudvig, G. W.; Bowden, E. F. *J. Electroanal. Chem.* **1990**, *290*, 293) with a PAR 273A potentiostat and PAR Model 270 software.

[10] The addition of DNA to solutions of $\mathrm{Ru^{II}(tpy)(bipy)OH_2^{2+}}$ causes decreases in peak currents in the cyclic voltammogram indicative of binding of the complex to the DNA. Importantly, peak currents in the cyclic voltammograms taken with and without DNA exhibit a linear dependence on the square root of the sweep rate, showing that adsorption of the complex or the DNA on the electrode does not occur. For detailed discussions of the effects of DNA binding on the cyclic voltammetry of metal complexes, see: (a) Carter, M. T.; Rodriguez, M.; Bard, A. J. *J. Am. Chem. Soc.* **1989**, *111*, 8901. (b) Carter, M. T.; Bard, A. J. *J. Am. Chem. Soc.* **1987**, *109*, 7528. (c) Carter, M. T.; Bard, A. J. *Bioconjugate Chem.* **1990**, *1*, 257.

[11] Solutions were electrolyzed in the same cell used for cyclic voltammetry and stirred by bubbling buffer-saturated N_2 through the solution. Fractions were loaded onto 1% agarose gels containing ethidium bromide and electrophoresced for 30 min at 44 V and photographed under UV light. pSport1 plasmid DNA was purchased from Bethesda Research Laboratories and used as received.

[12] The electrochemical activation of Fe-bleomycin has been demonstrated: Van Atta, R. B.; Long, E. C.; Hecht, S. M.; van der Marel, G. A.; van Boom, J. H. *J. Am. Chem. Soc.* **1989**, *111*, 2722.

Relative Oxygen Donor Potential of Dioxirane and Carbonyl Oxide. A Theoretical Study

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Although a dioxirane has only recently been isolated and characterized by Murray,[1a] earlier experimental work by Edwards and Curci[1b] stimulated the theoretical community[2] to calculate the chemical and physical properties of the parent dioxirane **1** and its more elusive tautomer, carbonyl oxide **2** (Figure 1). In the relatively short history[3] of this class of oxidant, dimethyldioxirane and several related peroxo species have proven to be powerful oxygen atom transfer reagents of unusual synthetic utility. It is now well established that dioxirane **1** is more stable than its dioxygen ylide **2** and that the respective barriers for their interconversion are sufficiently high that each exhibits its own chemical behavior when independently generated. Calculated[2] energy differences between these isomeric peroxy compounds range from 29.7 to 54.1 kcal/mol while the theoretical estimates of the barrier for ring closure of **2** and **1** range from 20 to 33.6 kcal/mol.[2a,3b] On the basis of a cleverly designed mechanistic probe involving competitive oxidation of sulfides and sulfoxides, Adam[4a] has

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[1] (a) Murray, R. W.; Jeyaraman, R. *J. Org. Chem.* **1985**, *50*, 2847. (b) Curci, R.; Fiorentino, M.; Troisi, L.; Edwards, J. O.; Pater, R. H. *J. Org. Chem.* **1980**, *45*, 4758.

[2] (a) Cremer, D.; Schmidt, T.; Gauss, J.; Radhakrishnan, T. P. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 427. (b) Cremer, D.; Schindler, M. *Chem. Phys. Lett.* **1987**, *133*, 293. (c) Karlström, G.; Engström, S.; Jönsson, B. *Chem. Phys. Lett.* **1979**, *67*, 343. (d) Sawaki, Y.; Kato, H.; Ogata, Y. *J. Am. Chem. Soc.* **1981**, *103*, 3832. (e) Harding, L. B.; Goddard, W. A., III. *J. Am. Chem. Soc.* **1978**, *100*, 7180. (f) Ha, T.-K.; Kühne, H.; Vaccani, S.; Günthard, H. H. *Chem. Phys. Lett.* **1974**, *24*, 172.

[3] (a) Adam, W.; Curci, R.; Edwards, J. O. *Acc. Chem. Res.* **1989**, *22*, 205. (b) Murray, R. W. *Chem. Rev.* **1989**, *89*, 1187. (c) Curci, R. *Advances in Oxygenated Processes*; Baumstark, A. L., Ed.; JAI Press: Greenwich, CT; Vol. 2, Chapter 1, in press.

[4] (a) Adam, W.; Chan, Y.-Y.; Cremer, D.; Gauss, J.; Sheutzow, D.; Schindler, M. *J. Org. Chem.* **1987**, *52*, 2800. (b) Baumstark, A. L.; Vasquez, P. C. *J. Org. Chem.* **1988**, *53*, 3437.

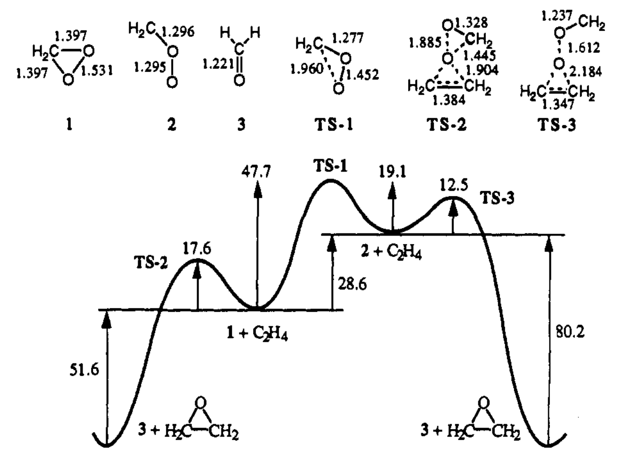

Figure 1. Potential energy diagram for the interconversion for dioxirane and carbonyl oxide and oxygen atom transfer to ethylene. Geometries are MP2/6-31G*, and energies (kcal/mol) are RQCISD(T)/6-31G*//MP2/6-31G*.

suggested that the highly strained cyclic peroxo functionality is more electrophilic than the higher energy open carbonyl oxide structure. However, Baumstark[4b] has cautioned that a clear distinction between nucleophilicity and electrophilicity may be more elusive than initially anticipated. In this report we have calculated the potential energy surface for the interconversion of **1** and **2** and their oxygen atom transfer to the common nucleophile, ethylene. We have employed geometry optimization at a level of theory known to be reliable for these systems[2a,7] (MP2/6-31G*) and computed the energy by a sufficiently accurate method (QCISD(T)/6-31G*) to allow confidence in the calculated barriers.

The activation barrier for ring opening of dioxirane (**1**) to its carbonyl oxide (**2**) is prohibitively high at 47.7 kcal/mol above the global minimum (Figure 1). The geometry of the transition structure (**TS-1**) for this highly endothermic process is consistent with the Hammond postulate and more closely resembles **2** than **1** with the exception of the O–O bond distance, which is only 0.08 Å shorter at the TS. The energy requirements for ring closure of **2** to **1** are also sufficiently high (19.1 kcal/mol) that one should not anticipate a facile equilibration between these two oxidants at room temperature since other, lower activation pathways would surely intervene. Barriers of 54.1 and 22.8 kcal/mol for the interconversions of **1** and **2** have been reported by Cremer (MP4SDQ/6-31G*).[2a]

At first glance the strained but normal covalent structure **1** presents itself as a less nucleophilic reagent than the dioxygen ylide **2**. However, at the MP4SDTQ/6-31G*//MP2/6-31G* level of theory and in the absence of solvent, the activation barriers for oxygen transfer from **1** or **2** to ethylene are indistinguishable, at 13.7 and 13.9 kcal/mol, respectively. Prior experience with reactions involving O–O bond rupture[7a,b] prompted an SCF stability test on both transition structures. The roots of the RHF/UHF stability analysis for **TS-2** and **TS-3** were −0.09 and −0.02, indicating the potential for partial diradical character. Release of the RHF constraint afforded a UHF stable wave function for **TS-3** with an energy decrease of only 0.73 kcal/mol; however, the UHF calculation on **TS-2** was slow to converge. We had anticipated difficulty with **TS-2** since extensive CI calculations were found to be essential to getting correct relative energies of dioxirane and its corresponding bis(oxy)methylene diradical.[2c,3a] Therefore, we decided to use the QCISD(T) method,[6d] which is known to treat adequately partially broken bonds and diradicaloid species. An energy difference of 12.4 kcal/mol (QCISD(T)/6-31G*//QCISD/6-31G*)[8] between ground-state cyclic **1** and its lowest energy open biradical form (2π singlet, $^1A_1$) would tend to exclude a biradical pathway for oxygen atom transfer from **1**. Significantly, the QCISD(T)/6-31G*//MP2/6-31G* barriers for oxygen transfer from **1** and **2** differ by 5 kcal/mol (Figure 1) and the origin of the difference can be traced to an overestimation of the triples contribution at the MP4 level. Reoptimization of the geometries at the QCISD/3-21G level and comparison with the MP2/3-21G structures suggests that the effects of higher excitations on the TS geometries are not significant. Since barriers based upon the QCI calculations ought to be more reliable, we suggest that dioxygen ylide **2** is a more efficient oxygen donor than dioxirane, at least in the gas phase. Despite the appearance of nucleophilicity, oxene transfer from carbonyl oxide to ethylene exhibits a barrier that is actually 2.6 kcal/mol *lower* in energy than epoxidation with peroxyformic acid.[7c] Because of its lower ground-state energy, epoxidation with **1** is less exothermic (51.6 kcal/mol) than oxirane formation from carbonyl oxide (80.2 kcal/mol).

Transition-structure geometries give little indication about the relative position of the TS along the reaction coordinate. The alkene fragment has not been significantly perturbed in either TS while a major geometric distortion is evident in the oxidizing agent. The much shorter C–O bond in spiro **TS-2** at the MP2 level is worthy of note, as is the shorter O–O bond in spiro **TS-3**. Oxygen transfer from **1** is attended by the exothermic formation of a carbon–oxygen double bond and the relief of ring strain (24.7 kcal/mol);[2a] however, both C–O and O–O bond breaking is involved. Epoxidation with the thermodynamically less stable **2** requires breaking a shorter, stronger O–O bond. The O–O bond energy in **1** has been estimated at 36 kcal/mol[2a] while the BDE in **2** is approximately 61 kcal/mol.[9]

Significantly, the "electrophilic" oxygen atom in **TS-3** is essentially a singlet oxygen atom suspended between two fragments, each with a nearly completely formed carbon–carbon or carbon–oxygen double bond. Therefore, one should not expect an energy preference for a spiro or a planar orientation of attack on the double bond. The oxygen lone pairs on the central oxygen are almost degenerate at the TS, and the electron density around an oxenoid oxygen is rather spherical in nature. A similar observation was noted by Cremer,[10] who reported a barrier for **TS-3** of 4.7 kcal/mol (HF/6-31G*). Similarly in the related oxygen atom transfer from an oxaziridine, both spiro and planar orientations of approach to ethylene were first-order saddle points of almost identical energy.[7d] In both cases we suggest that the geometry of the TS will be a reflection of steric interactions and that a special electronic effect is not involved. The more polar carbonyl oxide has a calculated dipole moment of 5.4 while that in **1** is 3.1 D, which should be reflected in a difference in ground-state solvation. Consistent with this observation, the stabilization energies for hydrogen bonding a molecule of water to **1** and **2** are 7.0 and 14.3 kcal/mol, respectively (MP4SDTQ/6-31G*//HF/6-31G*).

From these data, we conclude that optimization at the MP2 level of theory with MP4 correlation correction appears adequate

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(5) The MP2/6-31G* level of theory is essential in order to reproduce the geometry of the O–O bond and to get reliable energies.[2b,7]

(6) (a) Molecular orbital calculations have been carried out by using the GAUSSIAN 90 program system using gradient optimization;[6c] **TS-2** and **TS-3** were optimized in the spiro conformation. (b) GAUSSIAN 90: Frisch, M. J.; Head-Gordon, M.; Trucks, G. W.; Foresman, J. B.; Schlegel, H. B.; Raghavachari, K.; Robb, M. A.; Binkley, J. S.; Gonzalez, C.; DeFrees, D. J.; Fox, D. J.; Whiteside, R. A.; Seeger, R.; Melius, C. F.; Baker, J.; Martin, L. R.; Kahn, L. R.; Stewart, J. J. P.; Topiol, S.; Pople, J. A. Gaussian, Inc., Pittsburgh, PA, 1990. (c) Schlegel, H. B. *J. Comput. Chem.* **1982**, *3*, 214. The three transition structures have been established to be first-order saddle points by a frequency calculation using analytical second derivatives at the HF/6-31G* level. All structures have been optimized at the MP2/6-31G* level of theory with single point calculations at QCISD(T)/6-31G*. (d) Pople, J. A.; Head-Gordon, M.; Raghavachari, K. *J. Chem. Phys.* **1987**, *87*, 5968.

(7) (a) Bach, R. D.; McDouall, J. J. W.; Owensby, A. L.; Schlegel, H. B. *J. Am. Chem. Soc.* **1990**, *112*, 7064. (b) 7066. (c) Bach, R. D.; Owensby, A. L.; Gonzalez, C.; Schlegel, H. B.; McDouall, J. J. W. *J. Am. Chem. Soc.* **1991**, *113*, 2338. (d) Bach, R. D.; Coddens, B. A.; McDouall, J. J. W.; Schlegel, H. B.; Davis, F. A. *J. Org. Chem* **1990**, *55*, 3325.

(8) The C–O bond and O–O bond distances for **1** and its biradical are 1.393 and 1.522 Å and 1.306 and 2.363 Å, respectively.

(9) The BDE of the O–O bond was estimated by calculating (MP4SDTQ/6-31G*//MP26-31G*) the dissociation of H_2COO into a singlet (^1D) oxygen atom and formaldehyde.

(10) Cremer, D.; Bock, C. W. *J. Am. Chem. Soc.* **1986**, *108*, 3375.

for oxygen transfer from dioxygen ylides such as water oxide[7a,b] and carbonyl oxide, but that QCISD(T) calculations are essential for reliable energetics with the highly strained dioxirane. The barrier heights show a remarkable sensitivity to the level of theory, with deviations up to 20 kcal/mol. Although the less stable carbonyl oxide form exhibits the greater reactivity as one might anticipate, the intrinsic gas-phase reactivity of these two isomeric oxygen donors is opposite to that observed in solution.[4a] Since oxygen donation from dioxirane exhibits the higher barrier despite its weaker O–O bond and inherent ring strain, we must look elsewhere for the origin of the difference in reactivity. In addition to steric interactions, solvent effects must play a major role. It has been noted that the presence of water increases the rate of epoxidation of alkenes with dimethyldioxirane[4b] while an increase in solvent polarity has the opposite effect.[1a]

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Registry No. 1, 157-26-6; **2**, 56077-92-0; ethylene, 74-85-1.

Synthesis and Structure of the Chloride and Nitrate Inclusion Complexes of [16-Pyrimidinium crown-4]$^{4+}$

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Anion coordination chemistry has received attention because of its chemical and biological significance.[1,2] Recently it was reported that reflux of a mixture of thiamin iodide and mercuric iodide in acetone produced a cyclic polypyrimidinium cation[3] (see Scheme I). This communication reports the synthesis of another cyclic polymer, [16-pyrimidinium crown-4]$^{4+}$, and the structure of its chloride and nitrate inclusion complexes.

Reflux of a mixture of thiamin chloride hydrochloride and $Ni(OAc)_2{\cdot}4H_2O$ (2:1 molar ratio) in methanol afforded the chloride salt of [16-pyrimidinium crown-4]$^{4+}$,[4] which also was isolated from an aqueous solution of thiamin chloride hydrochloride and $Zn(OAc)_2$. The nitrate salt was prepared as tiny, needle-like crystals by heating thiamin nitrate at 65 °C for 30 min in a 15–50% water–methanol medium.[5,6]

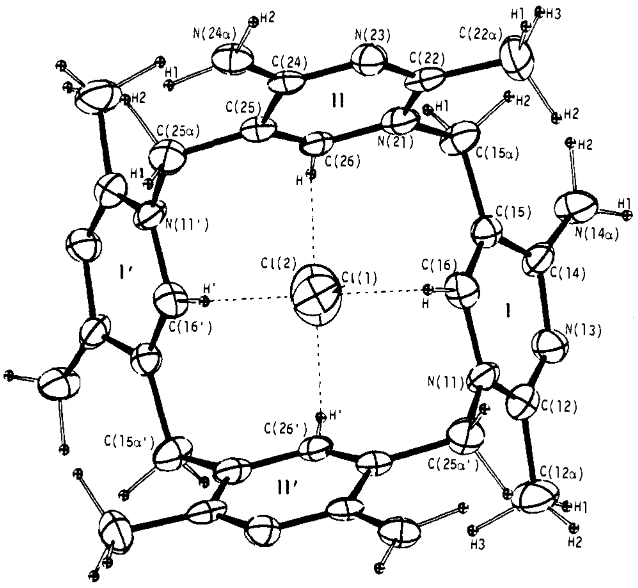


Figure 1. A top view down to 2-fold axis of [16-pyrimidinium crown-4]$^{4+}$. The crystallographic 2-fold axis passes through Cl(1) and Cl(2).

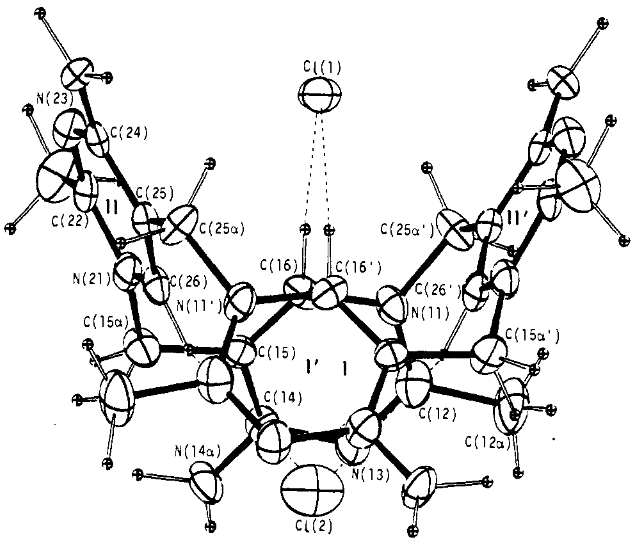
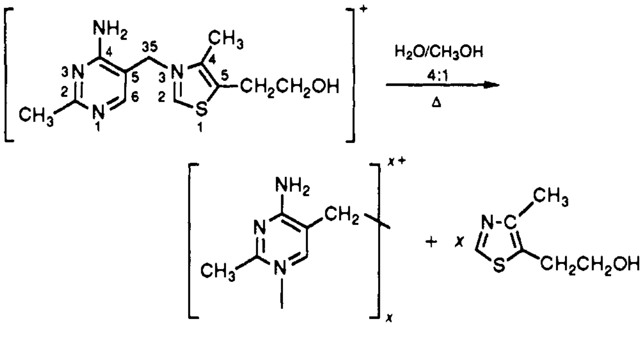


Figure 2. A side view of the [16-pyrimidinium crown-4]$^{4+}$ cation showing its interaction with Cl(1) and Cl(2).

Scheme I



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(1) Lehn, J.-M. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 89–112 and references therein.

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(3) Cramer, R. E.; Carrie, M. J. J. *Inorg. Chem.* **1990**, *29*, 3902–3904.

(4) Cramer, R. E.; Kim, K. E.; Evangelista, R. S.; Kuwabara, E. S. *Abstracts of Papers*, 188th National Meeting of the American Chemical Society, Philadelphia, PA; American Chemical Society: Washington, DC, 1984; INOR 254.

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