surrounding the copper atoms were increased above the Norman criteria[12] to compensate for the tendency to overestimate covalency effects. The $-2J$ values of the ground-state exchange interaction were calculated by using the strong valence bond coupling limit with large overlap between metals. However, the end-on cis-μ-1,2 dimer is probably closer to the weak coupling limit which would give values twice as large as that calculated for the singlet-triplet splitting.[10,13]

The orbital energy diagram of **1** is shown in Figure 1, left. The dominant copper-peroxide bond stabilizes the peroxide Π^*_σ (relative to Π^*_v) while destabilizing the antisymmetric combination of Cu d_{xy} orbitals which form the LUMO ($12b_1$) shown in Figure 2A. The HOMO ($14a_1$) shown in Figure 2B is the symmetric combination of Cu d_{xy} orbitals and is also slightly destabilized due to a weak antibonding interaction with the peroxide Π^b_σ ($11a_1$). The bridging hydroxide p_x provides an additional significant destabilizing interaction on the LUMO which combines with the peroxide Π^*_σ in Figure 2A to increase the HOMO-LUMO splitting. This splitting results in a large calculated ground-state exchange interaction of $-2J = 1850$ cm^{-1}.[14]

Broken-symmetry SCF-Xα-SW calculations on **2** produce the orbital energy diagram in Figure 1, right. The dominant copper-peroxide bonding interaction again involves the Cu d_{xy} and peroxide Π^*_σ resulting in a large stabilization of the Π^*_σ ($3b_{1g}$) while destabilizing the antisymmetric combination of Cu d_{xy} orbitals which form the LUMO ($5b_{1g}$) shown in Figure 2C. Due to the larger orbital overlap of both oxygens with the d_{xy} orbitals on each copper, this bonding interaction stabilizes the Π^*_σ to a much deeper energy than in the end-on case, **1**. In addition, the Cu d_{xy} HOMO ($5b_{2u}$) shown in Figure 2D is stabilized due to a bonding interaction with the unoccupied peroxide σ^* ($6b_{2u}$). *To our knowledge this is the first observation of the peroxide σ^* acting as a π acceptor orbital.* The Π^*_σ donor and σ^* acceptor interactions both increase the HOMO-LUMO splitting which is larger than in **1** and has a correspondingly larger ground-state exchange interaction calculated to be $-2J = 5660$ cm^{-1}.[13]

Comparison of the two structures indicates that the dominant bonding interaction in both involves stabilization of the Π^*_σ, with the side-on dimer having a larger stabilization and an additional π accepting interaction with the σ^* orbital. This leads to a more stable peroxide-copper bond and a larger HOMO-LUMO splitting and thus a larger exchange interaction for the side-on structure **2**. The charge on the peroxide is found to be less negative in **2** due to the stronger Π^*_σ donor interaction;[15] however, the additional σ^* acceptor interaction in **2** shifts a small amount of electron density into a strongly antibonding MO. This provides a direct explanation for the low O-O stretching frequency observed in the Raman spectrum of this model complex[16] and possibly of oxyHc.[17] The Π^*_σ of **1** is significantly stabilized with respect to the Π^*_v by 16 500 cm^{-1} and is consistent with the large observed Π^*_v-Π^*_σ splitting of oxyHc. The side-on dimer, **2**, has an even larger Π^*_v-Π^*_σ splitting resulting in the Π^*_σ level being deeper in energy, below the N_σ-Cu bonding levels.[18] Significant mixing between the peroxide Π^*_σ ($3b_{1g}$) and the N_σ ($4b_{1g}$) occurs, destabilizing the N_σ level by $\sim$9000 cm^{-1}, resulting in a Π^*_v-N_σ-(+Π^*_σ) splitting of 25 000 cm^{-1}. This would lead to an alternative possible assignment of the higher energy charge-transfer band in oxyHc based on **2** as a $N_\sigma \rightarrow$ Cu charge transfer which has been lowered in energy due to a large peroxide Π^*_σ mixing. This assignment would provide insight into the UV resonance Raman excitation profiles of oxyHc which exhibit dominant enhancement of Cu-N modes.[17] However, we have found experimentally that the Π^*_σ transition in an end-on trans-μ-1,2 bridging model complex[19] also exhibits this unusual resonance enhancement.[20] These calculations indicate that both structures are viable models for oxyHc, with the side-on dimer providing insight into the vibrational data and the end-on dimer a more direct assignment of the oxyHc charge-transfer spectrum. Single-crystal absorption experiments on oxyHc should distinguish between the two bridging geometries based on the differences in D_{2h} and C_{2v} selection rules of the peroxide charge-transfer transitions.

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Nonexistence of Dianionic Pentacovalent Intermediates in an ab Initio Study of the Base-Catalyzed Hydrolysis of Ethylene Phosphate[†]

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Phosphorus has a broad role in living systems,[1] and the reactions of phosphate esters in solution and in enzymes are of great interest. Pentacovalent phosphorus intermediates or transition states that are formed by nucleophilic attack on the tetracoordinated phosphorus atom[2,3] have been postulated in the nonenzymatic hydrolysis of cyclic and open-chain phosphinates, phosphonates, and phosphates,[4] as well as in the enzymatic hydrolysis of cyclic phosphates.[5] Such intermediates have not been isolated, although there is evidence for pentavalency from ^{31}P chemical shift measurements.[6] A pentacovalent intermediate explains[7] that the acid-catalyzed hydrolysis of hydrogen or methyl ethylene phosphate in water enriched in ^{18}O is accompanied by exchange of ^{18}O into the unreacted ester.[8,9] This exocyclic cleavage with ring

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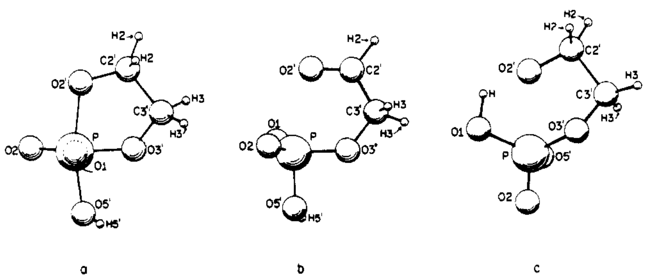

Figure 1. Structures of EP-OH^{2-}. (a) Fully optimized STO-3G geometry of the EP-OH^{2-} intermediate (dashed circle denotes an atom at the back). (b) Nonoptimized 3-21+G* geometry of EP-OH^{2-} which shows ring-opening (P–O_2' = 2.556 Å). (c) Fully optimized 3-21G* structure subject to the constraint that the P–O2′ distance is fixed at 2.25 Å.

retention, along with other results for phosphonate and phosphinate hydrolyses,[7,10] has been interpreted in terms of a trigonal-bipyramidal pentacovalent intermediate that can undergo pseudorotation subject to certain constraints. In contrast, the base-catalyzed hydrolysis of the ethylene phosphate anion is not accompanied by ^{18}O exchange.[8] This can be rationalized by the absence of a dianionic pentacovalent intermediate or by the assumption that the lifetime is too short for pseudorotation. In this communication, we report ab initio calculations for the hydrolysis of ethylene phosphate and show that dianionic pentacovalent phosphorane intermediates do not exist, while singly charged pentacovalent species do form stable intermediates with a distorted trigonal-bipyramidal geometry. These results would explain the experimental observations if the gas-phase calculations apply in solution.

To investigate the behavior of five-membered cyclic phosphate esters, which are hydrolyzed 10^6–10^8 times faster than their acyclic analogues and play a role in enzymes, we have performed ab initio studies for the OH^--catalyzed hydrolysis of the ethylene phosphate ion, EP^-.[11] The reaction profile for the addition of OH^- to EP^- was explored at the Hartree–Fock (HF) level with a STO-3G basis set and refined with a split-valence 3-21G* basis that includes polarization functions (3d orbitals) on the phosphorus atom. Finally, a 3-21 + G* basis set with diffuse functions on the heavy atoms are used; all geometries were fully optimized, unless stated otherwise. The 3-21G* geometries of the cyclic and open-chain tetravalent phosphate molecules are in good agreement with experiment.[12-14]

As the reaction coordinate for the study of the nucleophilic attack of OH^- on the phosphorus atom of EP^-, the hydroxyl O to P distance was employed. In the STO-3G calculations, the reaction was found to proceed via a dianionic pentacovalent intermediate with distorted trigonal bipyramidal geometry (Figure 1a).[11] The STO-3G results obtained here for the cyclic compound are similar to those of Gorenstein et al.[15,16] for the acyclic ester except that the energy of the transition state relative to that of the reactants is 12.6 kcal/mol lower. This is in accord with the hypothesis that ring strain plays an important role in the rate acceleration of the cyclic esters.[8,17]

With the 3-21G* basis set, no stable intermediate was found. The 3-21G* optimization of the STO-3G intermediate (Figure 1a) led to ring-opening; the calculation was terminated when the departing ring O2′ to P distance was greater than 2.55 Å,[11] as compared with 1.96 Å in the intermediate. To confirm this, one of the phosphoryl oxygens was protonated in the EP-OH^{2-} STO-3G structure, and a stable monoanionic intermediate, EHP-OH^-, was obtained with both STO-3G and 3-21G* basis sets. Deletion of the hydrogen bonded to the phosphoryl oxygen in the 3-21G* structure again led to ring opening. The 3-21+G* optimization of a 3-21G* dianionic structure with the smallest repulsive force along the O2′-P coordinate also resulted in ring-opening (Figure 1b).[11] The departure of O2′ is in accord with the hypothesis that apical attack and apical departure (in-line mechanism) is favored over other pathways.[7] An adjacent mechanism, involving equatorial attack and apical departure, would require pseudorotation of a dianionic pentacovalent intermediate to place O2′ in an apical position for departure.[18,3] Thus, the observed stereochemistry of the reaction, which excludes an adjacent mechanism involving pseudorotation, is also consistent with the nonexistence of a dianionic pentacovalent intermediate.

Although the dianionic phosphorane intermediate is not stable, the alkaline hydrolysis product is calculated to be 7.6 kcal/mol more stable than the separated reactants; this dianionic tetravalent open-chain $HO(CH_2)_2OPO_3^{2-}$ compound is stabilized by an internal hydrogen bond between the hydroxyl H and one of the phosphoryl oxygens. It would be of interest to experimentally verify the existence of this species in the gas phase. We have checked whether a dianionic pentavalent trigonal-bipyramidal intermediate may result from ring-closure of the dianionic 2′-hydroxyethyl phosphate by defining the reaction coordinate for ring-closure as the O2′ to P distance. As the reaction coordinate decreases, the energy increases monotonically. When the O2′–P distance becomes shorter than 2.5 Å, the proton (H) is completely transferred to the phosphoryl oxygen, O1; the phosphorus atom remains tetrahedrally coordinated (see Figure 1c).

The present results, which show that monoanionic trigonal-bipyramidal phosphorane intermediates can exist but that dianionic species are unstable, are consistent with the experimental observations by Westheimer et al.[8,9] cited in the introduction. In addition, Brown and co-workers[19] found that, after partial acid hydrolysis of cytidine 3′-(benzyl phosphate), significant phosphoryl migration from 3′ to 2′ occurs; under alkaline hydrolytic conditions, no isomerization occurs. This result was interpreted by postulating a pentacovalent intermediate in the acid hydrolyses. Breslow and co-workers[20,21] found significant isomerization in partial acid hydrolysis of 2′,5′-UpU, but no 2′ to 3′ isomerization in imidazole-catalyzed hydrolysis. They proposed that isomerization and cleavage to 2′,3′-cUMP proceed via pentacovalent monoanionic phosphorane intermediates.

Experimental gas-phase hydrolysis studies of phosphorus esters suggest that the effects observed in solution persist in the gas phase.[22] This supports the present comparison of gas-phase calculations with solution results. A subsequent paper[12] discusses the importance of solvation effects and the relevance of the calculations to the enzyme-catalyzed hydrolysis of cyclic phosphates.

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