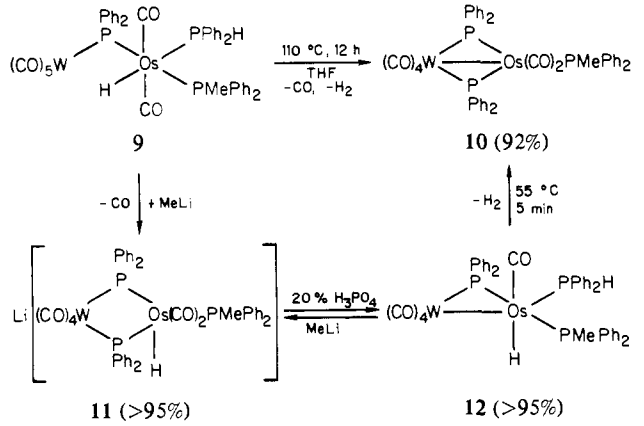
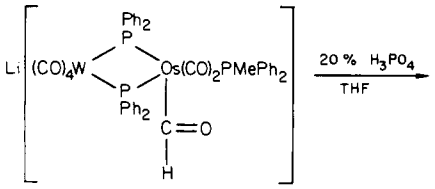
Scheme I

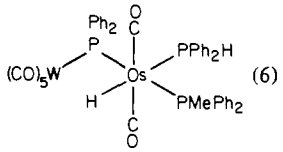


derives by coupling of a μ-PPh_2 ligand with a C(OMe)H carbene ligand generated by methylation of the formyl oxygen. A few other compounds have been prepared containing bridging μ-PR_2CRR' ligands[17] but none by a route such as this.

A phosphido bridge is also eliminated from **7** by protonation with 20% H_3PO_4 to give complex **9**[18] with a terminal PPh_2H ligand (eq 6). Reaction of **7**, labeled with deuterium at the formyl



7



9 (80%) (6)

position, with 20% H_3PO_4 gives **9** with a deuterium label at the hydride position, showing that the PPh_2H hydrogen derives from the added acid. While this product could form via reductive coupling of μ-PPh_2 and hydride ligands, we cannot exclude direct protonation at the phosphorus ligand. The phosphido bridge can be regenerated from **9** by heating to expel H_2 and CO to yield **10** (Scheme I). Alternatively, complex **10** can be obtained by the series of bridge cleavage/formation reactions illustrated in Scheme I, proceeding through complexes **11**[19] and **12**,[20] which can be individually isolated.

The experiments described herein clearly demonstrate that phosphido bridges are not inert and that they can participate in complex reactions. Such bridge elimination reactions may limit the utility of phosphido-bridged complexes in homogeneous catalysis[5,6] and must be considered in the exploration of the chemistry of this class of compounds.

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Supplementary Material Available: Spectroscopic data for complexes **1–12** and crystallographic data for **8** (3 pages). Ordering information is given on any current masthead page.

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(18) ^1H NMR δ 6.6 (dddd, PPh_2H), −6.2 (dddd, OsH); $^{31}P\{^1H\}$ NMR δ −64.9 (dd, μ-PPh_2), −20.5 (dd, PPh_2Me), −11.2 (dd, PPh_2H).

(19) ^1H NMR δ −3.7 (ddd, OsH); $^{31}P\{^1H\}$ NMR δ −119.4 (dd, μ-PPh_2), −128.7 (dd, μ-PPh_2), −3.5 (dd, PPh_2Me).

(20) ^1H NMR δ −12.8 (t, OsH); $^{31}P\{^1H\}$ NMR δ 53.3 (d, μ-PPh_2), −35.0 (dd, PPh_2Me), −13.9 (d, PPh_2H).

Stereoelectronic Effects in the Hydrolysis of Methyl Ethylene Phosphate

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On the basis of a series of molecular orbital calculations, we had predicted that a significant fraction of the 10^6–10^8 rate acceleration of five-membered ring cyclic phosphate esters relative to their acyclic analogues was attributable to a stereoelectronic effect.[1-4] Westheimer and co-workers[5-10] had clearly demonstrated that release of ring strain in forming a trigonal-bipyramidal pentacovalent phosphorane transition state/intermediate was responsible for at most 4–6 kcal/mol of the 10–11 kcal/mol difference in activation energies between the base-catalyzed hydrolysis of methyl ethylene phosphate (**1**) and that of trimethyl phosphate (similar differences exist between ethylene phosphate and dimethyl phosphate).[6,10] As pointed out by Gerlt et al.,[10] ring strain arguments could not be used to explain why the five-membered ring cyclic transition states were still nearly 6 kcal/mol lower in energy than the equally strain-free acyclic pentacovalent transition states.

In the cyclic transition state, **2**, however, the two lone pairs on the basal ring oxygen (assumed sp^3 hybridized)[4] are oriented partially antiperiplanar (app) to the axial ring ester bond leaving group (Figure 1). The MO calculations suggested that this app lone pair orientation could significantly facilitate P–O ester bond cleavage and that proper orbital overlap (stereoelectronic effect) could be responsible for as much as 11 kcal/mol lowering of transition-state energies.[1-3]

However, a major difficulty with the stereoelectronic effect explanation for the remaining 10^3–10^5 rate acceleration (4–6 kcal/mol difference in activation energies) was the observation of significant exocyclic cleavage in the reaction.[8,9] In dilute acid

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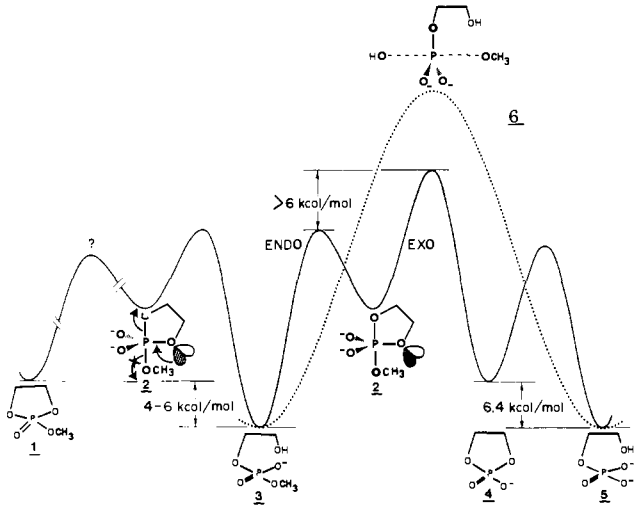

Figure 1. Reaction profiles for base-catalyzed hydrolysis of methyl ethylene phosphate (**1**) and methyl 2-hydroxyethyl phosphate (**3**).

and, in particular, in strong alkali methyl ethylene phosphate hydrolyzed to yield not only the expected endocyclic product, methyl 2-hydroxyethyl phosphate (**3**) but also as much as 1–50% of the exocyclic product, 2-hydroxyethyl phosphate.[8] While the exocyclic cleavage in acid could be reconciled with the stereoelectronic effect (arising from a "reverse anomeric effect"[4] of the protonated leaving group), the 9% and 15% (±5%)[8] exocyclic cleavage in 5 and 10 M alkali, respectively, was at odds with the stereoelectronic effect: note the basal oxygen lone pairs of the ring-constrained pentacovalent transition state are app *only to the apical endocyclic ester bond and not to the exocyclic bond.*

Ethyl ethylene phosphate, however, did not show any exocyclic cleavage (measured accuracy by the ^{31}P NMR method employed ±3%) between pH 8 and 15.[12] We also now find no exocyclic cleavage (0 ± 3%) for methyl ethylene phosphate between pH 8 and 15. Even in 5 M NaOH, a rapid freeze/acid quench (after less than 2 s of reaction)[12,13] lead to 100% endocyclic cleavage product in both methyl and ethyl ethylene phosphate.

Longer incubation periods in strong alkali lead to increased amounts of the exocyclic cleavage product. However, the rate of this secondary reaction was 10^8–10^{12} times slower[14] than the extrapolated rate of the initial endocyclic cleavage reaction of MEP, **1**.[8]

As shown in Figure 2, ^{18}O labeling confirms that this second reaction product, **5**, derives exclusively from a P–O cleavage reaction (as does the primary reaction). The secondary reaction, of the methyl 2-hydroxyethyl phosphate, although quite slow compared to that of MEP, is much faster than the hydrolysis of a simple diester such as dimethyl phosphate.[9,15] This can be attributed to recyclization[16] to reform the pentacovalent intermediate **2**. Most significantly our ^{18}O labeling[17] results (Figure 2) show that even in 5 M NaOH exactly two solvent oxygens appear in the 2-hydroxyethyl phosphate product **5** (and as expected only one solvent oxygen appears in the initially formed methyl 2-hydroxyethyl phosphate (**3**)). Because direct displacement of the methoxy group via **6** is precluded by the very slow hydrolysis of simple dialkyl phosphates,[9,15] we can conclude that **5** is formed via the route **3** → **2** → **4** → **5**.

Because both endocyclic and exocyclic products must be formed through the same transition state/intermediate **2** and since **3** is

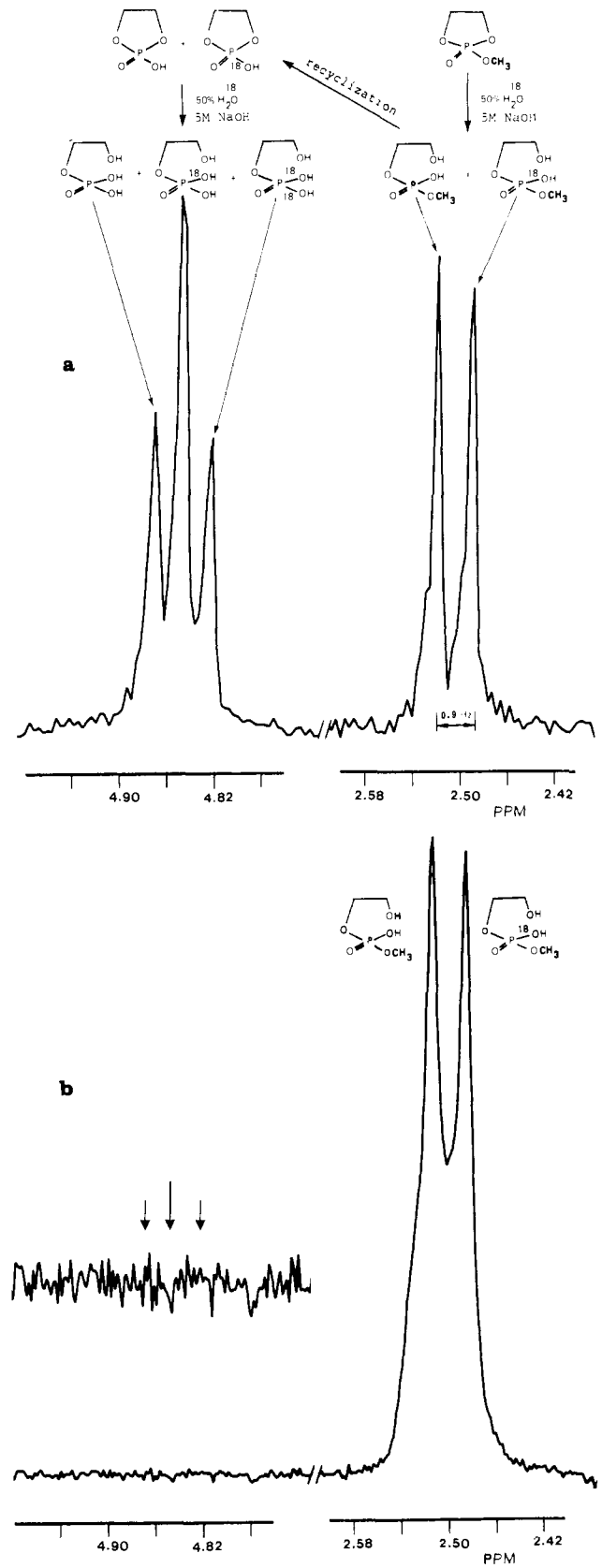

Figure 2. 32.4-MHz ^{31}P NMR spectrum of 2-hydroxyethyl phosphate (triplet, with ^{18}O labeling shown) and methyl 2-hydroxyethyl phosphate (doublet), formed after 23 h (a) or <2 s (b), room temperature hydrolysis of MEP (**1**) in 5 M NaOH (53% $H_2{}^{18}O$).[12,13]

4–6 kcal/mol lower in energy than MEP (**1**) only 10^3–10^4 of the observed 10^8–10^{12} rate acceleration is due to ring-strain effects. Similarly only 4–6 kcal/mol of the difference between the recyclization reaction activation energy for **3** → **2** → **4** and the

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(14) Monitored by ^{31}P NMR. MEP rate data was extrapolated from Kluger et al.[8] to 5 M NaOH and assumed either first-order (10^8 factor) or second-order hydroxide[8] (10^{12} factor) catalyzed hydrolysis of MEP.
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endocyclic reaction activation energy (**1** → **2** → **3**) is attributable to ground-state destabilization of **1**. Thus the rate of partitioning of **2** must favor the endocyclic path by a factor of 10^5–10^8 over the exocyclic path, although a portion of this difference is also attributable to an *increase* in ring strain in forming the strained ethylene phosphate **4** in the exocyclic cleavage path.[18] This factor of 10^5–10^8 we suggest arises at least in part from the stereoelectronic effect.

Acknowledgment. Support of this research by NSF, NIH, and the U.S. Army Research Office is acknowledged.

(18) The transition state, however, will be closer in structure to the high-energy trigonal-bipyramidal pentacovalent intermediate **2**, which is expected to have little bond angle strain (ref 7–9).

Assembly of $[Fe_nS_n(SPh)_4]^{2-}$ (n = 2, 4) in Aqueous-Based Media

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Previous preparations of $[Fe_nS_n(SPh)_4]^{2-}$ (n = 2, 4), which are synthetic analogues of biological iron–sulfur clusters, use nonaqueous solvents.[1-4] We wish to report that these clusters can also be prepared in high yield in aqueous-based (i.e., ≥90 vol % water) media from the same simple reagents used previously. The reaction systems reported here present the possibility of examining questions related to biological iron–sulfur cluster assembly, which cannot be addressed when using nonaqueous solvents.[5-7]

As a starting point, we have chosen media similar to those previously used in this laboratory to solubilize the Et_4N^+ salts of preassembled $[Fe_nS_n(SPh)_4]^{2-}$ (n = 2, 4) in water.[8,9] Thus, under anaerobic conditions, addition of 0.61 g (3.75 mmol) of anhydrous $FeCl_3$ followed by 1.5 mL (15 mmol) of PhSH to 8 mL of acetonitrile results in a light green slurry. Addition of this slurry to an equal volume of the nonionic detergent, Triton X-100, results in no change in appearance. This latter slurry, when transferred with stirring to 144 mL of aqueous buffer (0.5 M sodium *N*-[tris(hydroxymethyl)methyl]-3-aminopropanesulfonate (Na-TAPS), pH 8.5), forms a dark green emulsion. The solvent composition at this point is 90:5:5 vol % aqueous buffer:Triton:CH_3CN. Addition of 0.126 g (3.93 mmol) of solid sulfur to the mixture results in a gradual color change to that of $[Fe_4S_4(SPh)_4]^{2-}$. Figure 1 shows visible absorption spectra of small portions of the reaction mixture diluted fivefold with the same solvent. These diluted solutions are homogeneous and transparent. The fairly featureless spectrum obtained before addition of sulfur contains shoulders at ~335 and 390 nm, both of which are characteristic of the spectrum of $[Fe(SPh)_4]^{2-}$ measured in acetonitrile.[1] The spectrum obtained ~6 h after addition of sulfur has λ_{max} 454 nm and A_{454}/A_{550} = 2.05. These values are both

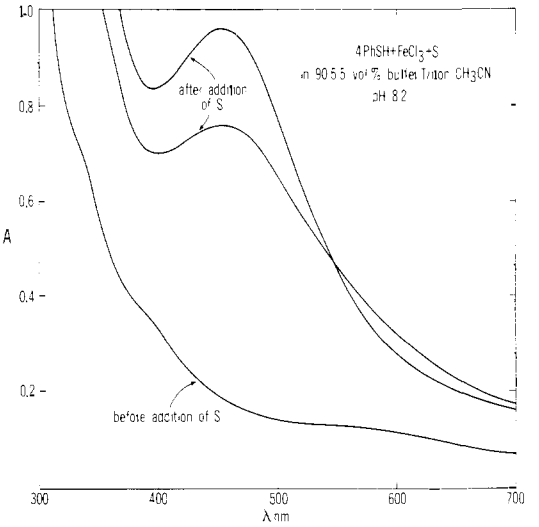

Figure 1. Visible absorption spectra of fivefold dilutions of the reaction mixture described in the text and also listed within the Figure. Cell path length, 0.5 mm. Spectra were obtained ~30 minutes (lower A_{454} and higher A_{600}) and ~6 hours after addition of sulfur. The final pH was 8.2.

characteristic of the spectrum of $[Fe_4S_4(SPh)_4]^{2-}$ measured in the same solvent.[8] By use of ϵ_{454} 17 400 M^{-1} cm^{-1},[8] the spectrophotometric yield of $[Fe_4S_4(SPh)_4]^{2-}$ was calculated to be 96%. The reaction mixture was filtered anaerobically through a celite pad ~7 h after addition of sulfur. To the dark red-brown filtrate were added 4.2 g (20 mmol) of Et_4NBr. The mixture turned cloudy within seconds after dissolution of the quaternary ammonium salt. After ~24 h of stirring at room temperature, the mixture contained a finely divided brown-black solid, which was isolated by filtration and washed with water and ether. After several hours of drying in vacuo, the solid was shown to be analytically pure $(Et_4N)_2[Fe_4S_4(SPh)_4]$ obtained in 82% yield.[10] Another reaction identical with that described above was carried out except that an equal volume of aqueous buffer was substituted for the Triton X-100.[12] In contrast to that described above, this mixture contained solid material throughout the course of the reaction; however, it too gradually assumed the color of $[Fe_4S_4(SPh)_4]^{2-}$. In this case, Et_4NBr (4.0 g) was added after ~7 h without filtering the reaction mixture, which resulted in almost immediate precipitation of a brown-black solid. This crude solid was collected by filtration, washed with water and ether, and dried in vacuo. The solid was then washed through the frit with ~75 mL of warm acetonitrile, the volume reduced to ~25 mL, and ~50 mL of water was added with stirring, which caused crsytallization of $(Et_4N)_2[Fe_4S_4(SPh)_4]$ and of diphenyl disulfide. The latter was removed by washing the filtered crystals with ether. Drying in vacuo resulted in a 71% yield of $(Et_4N)_2[Fe_4S_4(SPh)_4]$ (verified by C, H, N analysis and UV–vis spectra). These two yields compare favorably with those obtained in other solvents.[1,2] Unlike those reactions, NaSPh need not be used in aqueous media since a buffered solution above pH 6.4–6.8 substantially deprotonates the thiol.[13] Thus, the hydrophobia associated with previous preparations of $(Et_4N)_2[Fe_4S_4(SPh)_4]$ is shown to be unwarranted.

In methanol $[Fe_2S_2(SPh)_4]^{2-}$ is an intermediate in the above reaction, and its quaternary ammonium salts have lower solubilities than those of $[Fe_4S_4(SPh)_4]^{2-}$. These properties were exploited

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