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.

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(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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Received August 15, 1983

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 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.

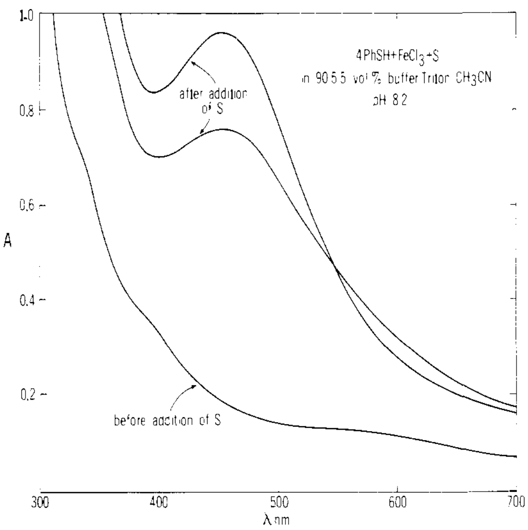

Figure 1. Visible absorption spectra of fivefold dilutions of the reaction mixture described in the text and also listed within the Figure. Cell path length, 0.5 mm. Spectra were obtained ~30 minutes (lower A_{454} and higher A_{600}) and ~6 hours after addition of sulfur. The final pH was 8.2.

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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(10) Anal. Calcd for $C_{40}H_{60}N_2S_8Fe_4$: C, 45.80; H, 5.78; N, 2.67. Found: C, 45.61; H, 5.77; N, 2.64. UV-vis (in DMF) and NMR (in CD_3CN) spectra were also in full agreement with those published for the pure compound.[1,11]

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(12) Buffer was 0.2 *M* Na-TAPS pH 9.0 for these reactions; final pH after reaction was ~7.9.

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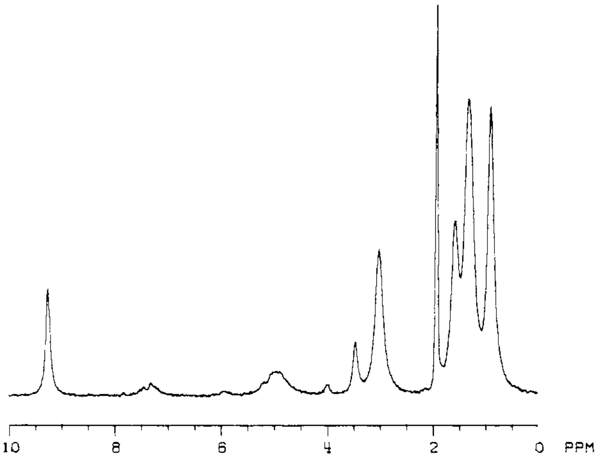

Figure 2. ^1H NMR spectra at 300 MHz in CD_3CN of solid isolated from a reaction mixture similar to that described in Figure 1 but containing 0.1 *M* nPe_4NBr. No additional resonances were seen in the range −60 to +60 ppm.[14]

by Reynolds and Holm to trap the dimer by introduction of the quaternary ammonium halide prior to addition of sulfur.[3] Yields of 50–55% of the $n = 2$ cluster are obtained with much of the remainder being the more soluble $n = 4$ cluster. When this strategy was followed in the aqueous Triton reaction mixture described above by making the buffer 0.1 M in tetra-*n*-pentylammonium bromide (n-Pe_4NBr) a bluish-black emulsion resulted upon introduction of the Triton/CH_3CN slurry.[12] After addition of solid sulfur, the emulsion slowly changed to a purplish-red color. Over the course of 2 days, the emulsion gradually broke down to a dark solid plus a faintly colored solution. Filtration and thorough washing with ether, water, and ether followed by drying in vacuo resulted in a solid which, when dissolved in CD_3CN, gives the ^1H NMR spectrum shown in Figure 2 in the 0–10 ppm range. The isotropically shifted resonances at 9.3 (meta H), 4.9 (ortho H), and 3.4 (para H) ppm are identical with those reported for $[Fe_2S_2(SPh)_4]^{2-}$ in this solvent.[3,14] Analysis of the solid is consistent with that calculated for $(n\text{-}Pe_4N)_2[Fe_2S_2(SPh)_4]$. Anal. Calcd for $C_{64}H_{108}N_2S_8Fe_4$: C, 63.55; H, 9.00; N, 2.32; Fe, 9.23; S, 15.90. Found: C, 63.27; H, 9.13; N, 2.27; Fe, 9.11; S, 15.75. On the basis of the starting amount of iron the yield is 96%. Substitution of increasingly shorter chain tetraalkylammonium salts for n-Pe_4N^+ in the above reaction results in solids contaminated by increasing proportions of $[Fe_4S_4(SPh)_4]^{2-}$. A possible explanation for this selectivity is that ion pairing with the relatively hydrophobic n-Pe_4N^+ inhibits exposure of $[Fe_2S_2(SPh)_4]^{2-}$ to water. Protic solvents including aqueous Triton are known to accelerate conversion of $[Fe_2S_2(SPh)_4]^{2-}$ to $[Fe_4S_4(SPh)_4]^{2-}$.[1,3,8,15] In the presence of Triton, n-Pe_4N^+ could thus function as a "phase-transfer catalyst" by increasing the solubility of $[Fe_2S_2(SPh)_4]^{2-}$ in hydrophobic regions of the Triton micelles or aggregates.[16] Decreased solubility of $[Fe_2S_2(SPh)_4]^{2-}$ in the presence of n-Pe_4NBr may also play a role. Omission of Triton from the above reaction results in essentially complete precipitation within ~2 h. The solid consists of $(n\text{-}Pe_4N)_2[Fe_2S_2(SPh)_4]$ contaminated by 20–25% of $(n\text{-}Pe_4N)_2[Fe_4S_4(SPh)_4]$ based on relative areas of the meta H ^1H NMR resonances of the solid dissolved in CD_3CN.[17]

In these aqueous reaction mixtures, Triton X-100 appears to increase the solubility of FeSPh species resulting in (i) greater contact both among these species and between these species and solid sulfur, which may increase reaction rates, and (ii) greater homogeneity of reaction solutions or dilutions thereof (Figure 1) permitting the use of solution spectroscopies to characterize reaction progress. In this regard ^{19}F NMR could help us to delineate the assembly pathway(s) in aqueous Triton.[18]

In these aqueous-based media, the title clusters can be prepared in yields equivalent to or higher than those obtained in organic solvents. The primary objective of this work is to develop a system that could be used to address synthetic questions stemming from the likely presence of water during at least some stages of biological FeS and MoFeS cluster assembly. The aqueous-based reaction systems described here appear to be sufficiently well-behaved to fulfill this objective.

Acknowledgment. This research was supported in part by NSF Grant PCM-8216447. The NMR spectra were obtained on a NIC-300 spectrometer purchased with funds from NSF equipment Grant CHE-8209709.

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(14) Peaks upfield of 3.4 ppm are due either to nPe_4N^+ or CH_3CN. Multiplet at ~7.5 ppm is due to PhSSPh. The UV–vis spectrum of the solid dissolved in DMF is identical to that published for $(Et_4N)_2[Fe_2S_2(SPh)_4]$ in the same solvent.[11]

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(17) Solid isolated after six days from a mixture of $(Et_4N)_2[Fe_4S_4(SPh)_4]$ and 0.1*M* nPe_4NBr in buffered aqueous Triton gave isotropically shifted ^1H NMR resonances in CD_3CN due only to $[Fe_4S_4(SPh)_4]^{2-}$.

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Eudistomins C, E, K, and L, Potent Antiviral Compounds Containing a Novel Oxathiazepine Ring from the Caribbean Tunicate *Eudistoma olivaceum*[1]

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Received September 29, 1983

Of the 650 marine species assayed during the 1978 Alpha Helix Caribbean Expedition (AHCE 1978)[3] the colonial tunicate *Eudistoma olivaceum*[4] was the most active against *Herpes simplex* virus, type 1 (HSV-1). In the present report we assign structures **1**, **2**, **5**, and **6** (Table I), containing the previously unreported condensed oxathiazepine ring system, to eudistomins C, E, K, and L, respectively, which include the most active antiviral components of *E. olivaceum*. In the following communication[5] we assign the structures of eudistomins A, D, G, H, I, J, M, N, O, P, and Q, additional bioactive components isolated from *E. olivaceum*.

The methanol–toluene (3:1) extract[3] of *E. olivaceum* (IRCE 1-VII-81-3-1, IFE 21-V-82-1-3) was partitioned with toluene and water. The toluene phase yielded eudistomins G, H, and I (see following communication),[5] while extraction of the aqueous phase with chloroform yielded an oil, which was subjected to C_{18} reversed-phase medium-pressure liquid chromatography (MPLC) with methanol–water (7:3) then to silica gel MPLC

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(1) Taken in part from: Harbour, G. C. Ph.D. Thesis, University of Illinois, Urbana, IL, 1983.

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