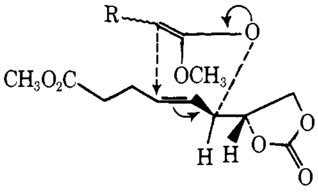
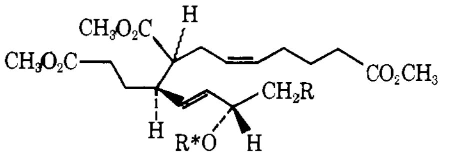
chain R in **5***, and it would therefore be expected that the Claisen product **7** would be a mixture, as shown. In fact, the ^{13}C NMR spectrum of **8** shows doubling of the peaks at ~44, 50, 131, and 133 ppm (attributed to the four starred carbon atoms) with an apparent ratio not far from 50:50. The correctness of the assumption that the epimeric mixture only involves C_8 (which in this particular synthesis is irrelevant because the center is epimerizable to the correct arrangement at the end) follows from the sequel.



5*

The carbinol function in **8**, having served its purpose, was now transformed into an *n*-pentyl group. Semihydrogenation (5% palladium-barium sulfate in methanol (quinoline) of the triple bond, tosylation (1.1 equiv of tosyl chloride in pyridine, 7 days at −20°), and protection of the secondary hydroxyl (ethyl vinyl ether) gave, after purification on florisil (50% ether-hexane), the tosylate **9**, R = OTs, in 79% overall yield (crude) from **8**. Coupling with lithium dibutylcuprate[9] (5 equiv of ether, −40°, 2 h) led to the required **9**, R = butyl in 67% yield as a colorless oil.



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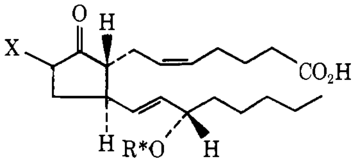
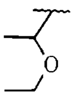


10

R* = 

Cyclization (10 equiv of potassium *tert*-butoxide in tetrahydrofuran, 45 min, 25°) and hydrolysis (0.5 *N* sodium hydroxide, reflux, 10 min), followed by acidification (phosphate buffer), gave the keto acid **10**, X = H,[8] in which the acid chain has now been equilibrated to the correct epimer, in 77% yield from **9**, R = butyl (δ 0.8-2.6 (31 H), 3.3-4.2 (m, 3 H), 4.7 (m, 1 H, O-C*H*-O), 5.2-5.8 (m, 4 H), 8.4 (b s, 1 H, CO_2H); ν (neat) 1740, 1710; mass spectrum P^+ 391 (408 − 17)).

Final transformation to natural PGA_2 became possible when it was found that the selective introduction of the α-phenylseleno group[10] could be carried out on the dianion of the ketoacid **10**, X = H, (2.2 equiv of lithium diisopropylamide, tetrahydrofuran, 1 h, −78°, followed by 3 equiv of phenyl selenyl chloride). Oxidation of the product **10**, X = SePh, with sodium periodate (4 equiv of aqueous methanol, 10 min. 25°) and removal of the ethoxyethyl protecting group gave, after purification (silica gel), the desired PGA_2 (**1**) in 46% overall yield from **10**, X = H. The TLC behavior, uv[11] ($\lambda_{max}^{C_2H_5OH}$ 217 nm, log ϵ 4.03), ^{1}H NMR and, more particularly, the ^{13}C NMR,[12] and rotation[13] ($[\alpha]^{20}{}_D$ + 130 (*c* 1.26, $CHCl_3$)) confirmed the structure of the synthetic natural PGA_2, thus obtained in 7.7% overall yield from **2**.

Acknowledgment. We thank the National Institutes of Health and the National Science Foundation for their support of this work.

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(8) Eluted from silica gel after removal of low polarity impurities with 10–20% ether in hexane.
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Environmental Control of Reactions: Enhancement of μ-Oxo Dimer Formation from Iron(III) Porphyrins in Organized Monolayer Assemblies as a Model for Membrane Catalysis

Sir:

The involvement of metalloporphyrins and related compounds bound in membranes or similar ordered environment has led us to investigate the behavior of simple surfactant metalloporphyrins in the structurally similar environment provided by fatty acid type monolayer films and organized monolayer assemblies.[1-4] In recent studies of other surfactant molecules containing reactive chromophores, we have found that reactivity in the semirigid monolayer assembly is often quite different from behavior of the same compounds in solution. Of particular interest has been the finding that extremely high effective local concentrations of reactive molecules can be obtained, permitting the occurrence of bimolecular phenomena not observable with the same molecules in solution. Among the prominent reactions observed with different systems are dimerization,[5] photodimer formation,[6] and formation of fluorescent excimers.[7] In studies with the dioctadecyl ester of mesoporphyrin IX, we found efficient dimer production when mixed films of the porphyrin and arachidic acid were spread on water surfaces.[5] In the present paper we report an extension of our investigation to a study of surfactant iron(III) porphyrins.

These molecules also show a pronounced preference for formation of dimeric sites when monolayer films or assemblies are generated. Moreover, with these compounds we find a rather dramatic change in their reactivity when incorporated into dimeric monolayer sites.

The reaction under investigation in this study is the formation of μ-oxo dimers of iron(III) porphyrins.[8-12] It has previously been shown that these dimers form in what is essentially a simple acid-base reaction by stirring solutions of iron(III) porphyrins at moderately high concentrations in strongly alkaline medium. The dimer, which is fairly stable once formed, can be decomposed to monomer by treatment with strong acid. For preparation of monolayer films and assemblies the surfactant iron(III) chloride of *meso*-tetra(4-carboxyphenyl)porphine tetra(1-octadecyl) ester, $(\mathrm{Fe^{III}TCP, TOE})^+\mathrm{Cl}^-$ (**1**), was utilized.[13] Films were obtained by spreading chloroform solutions on the monolayer trough water surface (containing 5×10^{-5} M $NaHCO_3$ and 3×10^{-4} M $CdCl_2$) at various surface pressures (5–30 dyn/cm). Monolayer assemblies deposited on glass or quartz microscope slides generated from single or multiple monolayer films of this compound exhibited only the absorption spectrum of the corresponding μ-oxo dimer $(\mathrm{Fe^{III}TCP, TOE})_2\mathrm{O}$, (**2**). The chloroform solutions of pure monomeric **1** used for spreading of the monolayer films were indefinitely stable and showed only monomeric spectra. Attempts to prevent μ-oxo dimer formation on the water surface by dilution with arachidic acid host (up to 1:30 of **1**/arachidic acid) were unsuccessful. To rule out the possibility that the monolayer assemblies exhibited a specific solid-state spectral modification which resulted in the observed visible spectrum, deposited films of monolayer assemblies were dissolved in chloroform and visible spectra were recorded; the solution spectra were nearly identical with those obtained from the assemblies and only transitions assignable to μ-oxo dimer were observed. This unusual, rapid formation of **2** occurred even though the highly purified monolayer trough water was acidic (pH 6.2).

In an attempt to determine whether μ-oxo dimer formation was occurring on the water surface or after deposition on the prepared slides, monolayers were formed on the trough surface (under 5–30 dyn/cm movable barrier pressure as well as with very low external pressure) and subsequently removed from the trough surface by aspiration into a chloroform solution. These chloroform solutions also exhibited only the spectrum of **2**.

To eliminate the possibility that added metal ions contained in the treated trough water could be influencing μ-oxo dimer formation, fresh triply distilled water was utilized as a spreading surface. Again only **2** could be isolated after monolayer films were formed. Similar behavior was observed when films were spread on pH 4 and pH 2 water surfaces. On water surfaces with pH varying from approximately 1.8 to 0.9, mixtures of **2** and **1** were recovered from spread films. Only monomeric metalloporphyrin was recovered from water surfaces having pH below 0.8.

It was also found that stable monolayer films could be formed by spreading chloroform solutions of isolated μ-oxo dimer **2** on purified water surfaces. When solutions of **2** were spread (with and without added arachidic acid host), only **2** was recovered when the pH was 7, 6.2, 4, and 2. Mixtures of **2** and monomer were recovered over the range 1.8 to 0.9 and as with **1**, only monomer was recovered below pH 0.9. Qualitatively similar behavior has been observed with other surfactant iron(III) porphyrins; for example, similar results, though over different pH ranges were observed with the iron(III) chloride of mesoporphyrin IX di(1-octadecyl)ester.

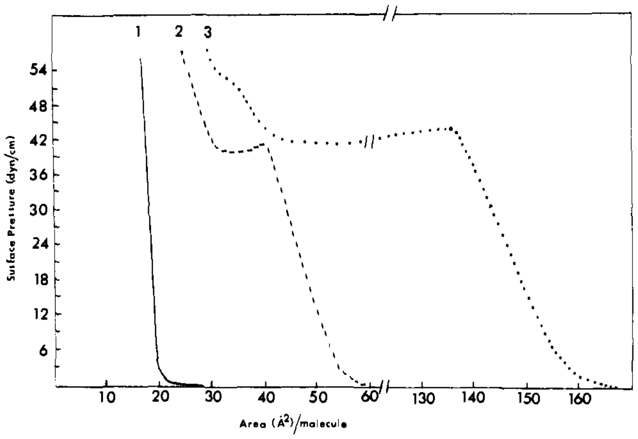

Figure 1. Pressure–area diagram: 1 (—), pure arachidic acid; 2 (- - -), 1:5 solution of **1** arachidic acid; 3 (• • •), calculated area of **1**.

Surface pressure–area isotherms for **1** (Figure 1) indicate[14] as suspected that the porphyrin molecules lie in dimeric sites occupying about half the area expected for closely packed monomers. Thus the area/molecule in the range 10–20 dyn/cm is 145 Å² while an estimation using molecular models indicates a requirement of approximately 253 Å²/molecule. The behavior observed here is similar to that of the free base porphyrin, and it is probably reasonable that in both cases the initial formation of dimeric sites arises from a packing phenomenon, perhaps caused by the imbalance in size between hydrophobic and hydrophilic portions of the surfactant molecules. Although the details of μ-oxo dimer formation in **1** are unclear, the fact that free base porphyrins readily form dimeric sites even where no covalent bond formation occurs suggests that in the case of **1** the first step is formation of dimeric sites from which the μ-oxo dimer is formed in subsequent steps. A plausible reaction sequence for μ-oxo dimer formation in the dimeric sites is schematically outlined in eq 1–3.

$$\mathrm{PFeCl + OH^-} \xrightleftharpoons[k_{-1}]{k_1} \mathrm{PFeOH + Cl^-} \qquad (1)$$

$$\mathrm{PFeOH + OH^-} \xrightleftharpoons[k_{-2}]{k_2} \mathrm{PFeO^- + H_2O} \qquad (2)$$

$$\mathrm{PFeO^- + PFeCl} \xrightleftharpoons[k_{-3}]{k_3} \mathrm{PFeOFeP + Cl^-} \qquad (3)$$

Facile formation of μ-oxo dimer on strongly acidic aqueous surfaces involves both a kinetic phenomenon in which the organized monolayer environment favors dimer formation, as well as a shift of the monomer–dimer equilibrium in favor of dimer. That the equilibrium position at room temperature may be shifted toward dimer formation is indicated by the following results. Chloroform solutions (~10^{-3} M) of nonsurfactant $(\mathrm{Fe^{III}TPP})^+\mathrm{ClO_4}$ (**3**) were stirred with aqueous solutions of known pH. At pH 10, all of **3** was converted to $(\mathrm{Fe^{III}TPP})_2\mathrm{O}$ (**4**) within 2 h. At pH 7, nearly all of **3** was converted to **4** over a period of 3 days. At pH 4, only monomer remained even after 7 days. The reverse process, stirring of chloroform solutions of **4** with aqueous solutions of known pH, gave similar results. At pH 7, mostly μ-oxo dimer remained after several days. At pH 4, nearly all of **4** was converted to monomeric species. Thus the monomer–dimer equilibrium has been shifted toward dimer formation by several orders of magnitude in the monolayer films. Accurate kinetic data for the solution reaction were not obtained because of the occurrence of competing side reactions. However, comparing rates of a reaction in solution with a lower limit estimate for the reaction rate in monolayer films suggests a monolayer acceleration of at least four orders of magnitude.[15] The kinetic acceleration can be readily understood in terms of the extremely high local concentrations in dimeric sites which make step 3 exceedingly rapid. The shift in the equilibrium or rather in the pH dependence of the equilibrium[16] is probably somewhat more complicated; however, a partial explanation may lie in the difficulty of dissociation and/or nucleophilic attack on protonated dimer. In summary, these results indicate that the monolayer environment produces a striking alteration of both rate processes and equilibria in this bimolecular reaction of metalloporphyrins. It will be important to investigate a variety of systems to determine whether in membranes or similar environments the attainment of high local concentrations by such packing phenomena or related interactions[17] may influence or promote the occurrence of reactions not occurring in solution, thus providing a mechanism for biological catalysis.

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(19) Support of this work by a grant from the U.S. Public Health Service (GM 15-238) is gratefully acknowledged. A portion of the work in Göttingen was made possible by a Senior U.S. Scientist Award from the Alexander von Humboldt Foundation.

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Intervalence (Charge-Transfer) Bands in Symmetrical and Unsymmetrical Bispyridinium-Pyridinyl Radical Complexes, $(Py\cdot)_3^{2+}$

Sir:

Inorganic complexes between species which differ by one electron have been studied intensively.[1] More recently, organometallic complexes (biferrocene (II, III),[2] bisruthenium-pyrazine (II, III),[3] etc.) have provided further insight into the ground state and spectroscopic behavior of such complexes.[4] One small, but important, group of organic materials which exhibit an intervalence ("charge-resonance") absorption is that of the TCNQ·⁻ complexes, with at least two distinct classes: the 1:2, $(TCNQ)_2^-$, and 2:3, $(TCNQ)_3^{2-}$, complexes.[5-7] (A closely related complex which appears to exhibit the property is 2TTF·TCM).[8]

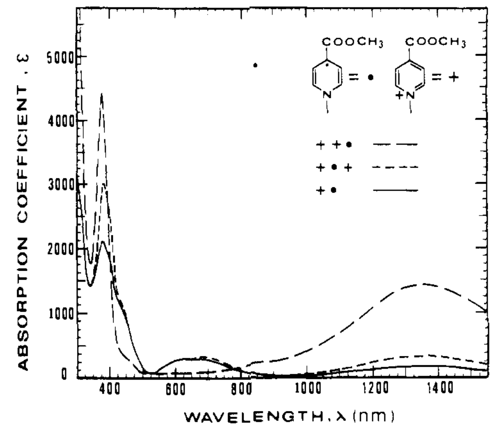
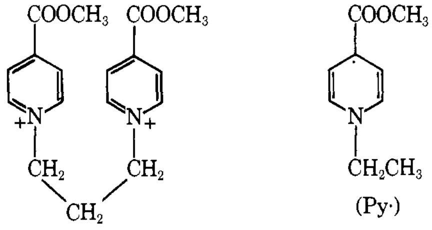


Figure 1. Absorption spectra for 1,1′-trimethylenebis(4-carbomethoxypyridinium) cation radical, (+·), $(Py\cdot)_2^+$ (—); the symmetrical complex of the cation radical (+·) with 1-ethyl-4-carbomethoxypyridinium ion (+), $(Py\cdot)^+$, written as (+·+) or $(Py\cdot)_2^+:(Py\cdot)^+$ or *sym*-$(Py\cdot)_3^{2+}$ (- - -); the unsymmetrical complex of the biscation (++) with 1-ethyl-4-carbomethoxypyridinyl (·), (Py·), written as (++·) or $(Py\cdot)_2^{2+}:(Py\cdot)$ or *unsym*-$(Py\cdot)_3^{2+}$, (- - - -). The visible absorption noted in the spectrum of the cation radical (+·) is assigned to the dimer of the cation radical.

We now report the observation of intervalence bands in complexes produced from (a) 1,1′-trimethylenebis(4-carbomethoxypyridinium) ion, $(Py\cdot)_2^{2+}$, and 1-ethyl-4-carbomethoxypyridinyl radical (Py·), and (b) 1,1′-trimethylenebis(4-carbomethoxypyridinium) cation radical, $(Py\cdot)_2^+$, and 1-ethyl-4-carbomethoxypyridinium ion, $(Py\cdot)^+$.[9] The complexes are more stable than might have been anticipated, and the analogies to the TCNQ complexes are interesting and exciting.



$(Py\cdot)_2^{2+}$ (Py·)

Pyridinyl radical[10] (Py·) in acetonitrile (6.4×10^{-4} M) was added in portions to a solution of $(Py\cdot)_2^{2+}$ in the same solvent.[11] A new broad light absorption appeared at 1360 nm and reached maximum intensity (apparent ϵ_{max} 1500) at a ratio if $(Py\cdot)_2^{2+}$ to (Py·) of about 1:1. (A complete spectrum is shown in Figure 1.) Further additions of (Py·) caused a decrease in the intensity of the new band; at a reactant ratio of 1:2, the new band was almost gone.[12]

The "obvious" choice for the species responsible for the new band, the cation radical $(Py\cdot)_2^+$, had been prepared and studied by Itoh[13] but the spectrum had not been measured past 700 nm. The cation radical was produced[13] and examined in both 2-methyltetrahydrofuran (MTHF) and acetonitrile solution. Only a small 1360-nm absorption could be found ($\epsilon \leq 100$) excluding $(Py\cdot)_2^+$ as the species responsible for the new band. Furthermore, the ultraviolet absorption of the $(Py\cdot)_2^+$ was lower in intensity and somewhat different in shape than that of the species associated with the new band, as the comparison made in Figure 1 shows.

The species responsible for the 1360-nm absorption was