Syntheses of Covalently-Linked Porphyrin-Quinone Complexes (1)

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A synthetic route for the preparation of covalently-linked porphyrin-quinone and metalloporphyrin-quinone complexes as models for the phototrap in bacterial photosynthesis is described. 5-(4-Carboxyphenyl)-10,15,20-tritolylporphyrin, prepared by a mixed aldehyde approach, was attached to a benzoquinone center with a propanediol bridge by means of ester linkages. The starting point for the benzoquinone moiety was 2,5-dihydroxyphenylacetic acid, whose hydroquinone function was first protected by preparing its dimethyl ether. The spacing between the two centers of the complex could be altered simply by varying the length of the bridging group (a diol) employed. Boron tribromide was used to unmask the quinol derivatives in the final coupled products. The zinc(II) derivative of porphyrin-quinone complex was prepared by addition of a saturated solution of zinc acetate in methanol to a solution of the corresponding porphyrin-hydroquinone complex in dichloromethane at room temperature. The structures of these complexes were confirmed by nmr spectroscopy, uv-visible absorption, and mass spectroscopy. Oxidation of the quinol moiety in the covalently-linked complex to its corresponding quinonoid derivative was accomplished by treating a solution of the complex in dichloromethane with a stoichiometric amount of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, a high potential benzoquinone.

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Introduction.

Over the last ten years, much has been learned about the components which play a major role in the primary photochemical events of photosynthesis (2-4). For example, it is known that several bacteriochlorophyll molecules cooperate to serve as the primary electron donor. Another bacteriochlorophyll molecule and/or a bacteriopheophytin molecule may serve as very short-lived electron acceptor(s) (5-7). In *R. rubrum* and *R. spheroides*, a ubiquinone molecule is the first stable electron acceptor, and very likely the next redox center in secondary electron transport (8-10). In spite of this important knowledge, there is little understanding of the actual mechanism of the primary photochemical event, the three-dimensional relationship of these molecules, or why this particular set of molecules has been selected over many millions of years to best accomplish this important act.

At this juncture, synthetic models whose structure and three-dimensional relationship are well understood and whose properties can be systematically varied, can be extremely helpful - even necessary - to fully understand this energy conversion step. For several years we have been synthesizing complexes which we felt would allow us to systematically probe appropriate structure-function relationships. Thus, we have prepared well-defined covalently-linked porphyrin dimers and trimers (11) as models for the multiple bacteriochlorophyll that constitute the primary electron donor and also as models for antenna complexes to study the transfer of excited state energy (12).

In this paper we wish to report the details of the synthesis of covalently-linked porphyrin-quinone complexes which will serve as models for the systematic examination of porphyrin-quinone photochemistry. This represents, of course, a key part of the reaction center components. Although porphyrin and chlorophyll photochemistry has been much studied (13-19), these have always been in monomeric solutions or in aggregrated systems. Important information has been obtained from these systems but several problems exist. For example, when the quinone concentration is sufficiently high to interact with the porphyrin excited singlet state, charge separated products are not obtained (oxidized porphyrin and reduced quinone) presumably because the two species are so close together that charge recombination is exceedingly fast. Since the charge separation in the *in vivo* process occurs from the excited singlet state, this is an important shortcoming of past models. In the case of frozen or aggregated systems, these are not well defined structurally and it is difficult to systematically probe structure-function relationships. We hope that covalently-linked porphyrin-quinone complexes will be helpful in overcoming some of these difficulties.

A preliminary report of this work has been given (20).

Results and Discussion.

In earlier work from this laboratory (21,22), useful methods for the successful preparation of a series of unsymmetrically substituted tetraarylporphyrins were developed. One of these porphyrin derivatives, the 5-(4-carboxyphenyl)-10,15,20-tritolylporphyrin (I), was used for synthesis of the covalently-linked porphyrin-quinone compounds in this study. Compound I contains a monocarboxy functional group to which extended linking groups as well as quinone analogues can be attached. Synthesis of I involves carrying out the porphyrin condensation reaction with a 5:1 ratio of *p*-tolualdehyde:*p*-carboxybenzaldehyde and 6 equivalents of pyrrole. This gives rise

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to a mixture of mono, di, tri, and tetra-(4-carboxyphenyl)-substituted arylporphyrins. Purification of each component was best achieved in their methyl ester forms, obtained by treating the mixture with diazomethane. Column chromatography on silica gel followed by preparative thin layer chromatography and then recrystallization from chloroform-methanol afforded compound II, the 5-(4-carbomethoxyphenyl)-10,15,20-tritolylporphyrin in 4.2% yield. Base catalyzed hydrolysis of compound II in an aqueous potassium hydroxide/tetrahydrofuran solvent system gave the free carboxyporphyrin I, after acidification, in greater than 90% yield.

For the quinone half of the complexes, a commercially available quinone precursor molecule (III), 2,5-dihydroxyphenylacetic acid (Homogentisic acid) was employed. In order to overcome the instability of the hydroquinone functional group during linking reactions, the hydroxy groups of homogentisic acid were blocked by converting them to methyl ethers. Extension of the side chain of the dimethoxyhydroquinone compound (IVa) was then affected by activating IVa with thionyl chloride, followed by condensation with a diol. Alternately, *trans*-esterification of compound IVb with a diol under acidic conditions also yielded the same product (Figure 1). Isolation and

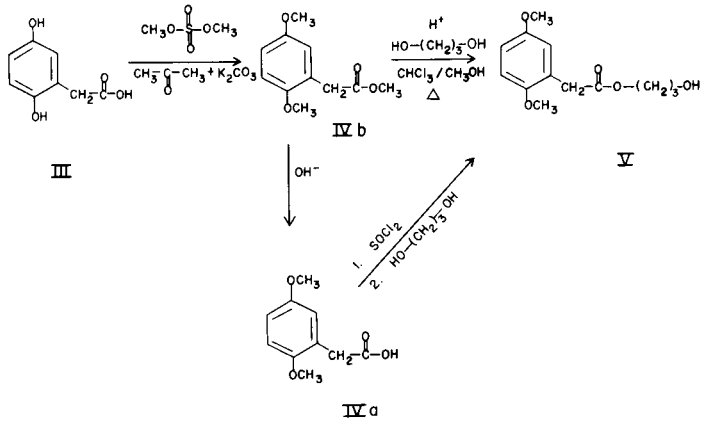

Figure 1. Side chain extension of 2,5-dimethoxyphenylacetic acid and methyl 2,5-dimethoxyphenylacetate.

purification were by means of column chromatography on silica gel and preparative thin layer chromatography.

As outlined in Figure 2, the coupling of compound V, γ-hydroxypropyl 2,5-dimethoxyphenylacetate, with porphyrin I was effected by treating the acid chloride of I with an excess of V. The expected condensation product, VI (5-(*p*-benzoyloxypropyl 2,5-dimethoxyphenylacetate)-10,15,20-tri(*p*-tolyl)porphyrin), was obtained in approximately 65% yield after column and preparative thin layer chromatography.

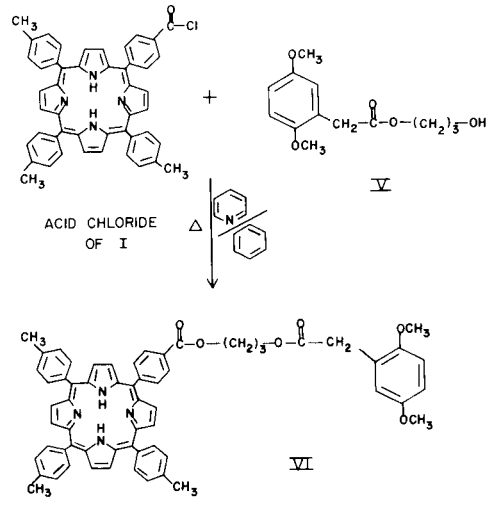

Figure 2. Condensation of hydroxyalkyl ester of 2,5-dimethxoyphenylacetic acid with the acid chloride of porphyrin I.

In order to unmask the quinonyl functionality, compound VI was demethylated using boron tribromide. At dry ice acetone temperature and in methylene chloride solution, this reagent was observed to preferentially cleave the methyl ether of compound VI and after 5 hours yielded the monomethyl ether product (VII), 5-(*p*-benzoyloxypropyl 2-hydroxy-5-methoxyphenylacetate)-10,15,20-tri-(*p*-tolyl)porphyrin. If the solution was allowed to attain room temperature with stirring for another two hours, compound VIII (5-(*p*-benzoyloxypropyl 2,5-dihydroxyphenylacetate)-10,15-20-tri(*p*-tolyl)porphyrin), the hydroquinone derivative of VI, was isolated in good yield (see Figure 3). Characterization and verification of structures were by means of nmr, mass spectra and uv-visible absorbance.

The nmr spectra of compounds VI, VII and VIII are shown in Figure 4. These spectra were recorded by time-averaging either on a Varian CFT-20 (80 MHz) spectrometer, or on a WP-60 Bruker (60 MHz) spectrometer (23). The solvent used was 99.8% deuteriochloroform. The chloroform-H peak is marked with an asterisk on all three spectra. Tetramethylsilane was used as an internal standard and has an assigned δ value of 0.00 ppm. The nmr data support unambiguously the assigned structures. The chemical shifts and integration area for all peaks were as expected. No interaction between the two entities of the covalently-linked complexes was indicated. Note that the spectra differ from each other only in the methoxy region. See the experimental section for more detailed analyses of nmr spectra.

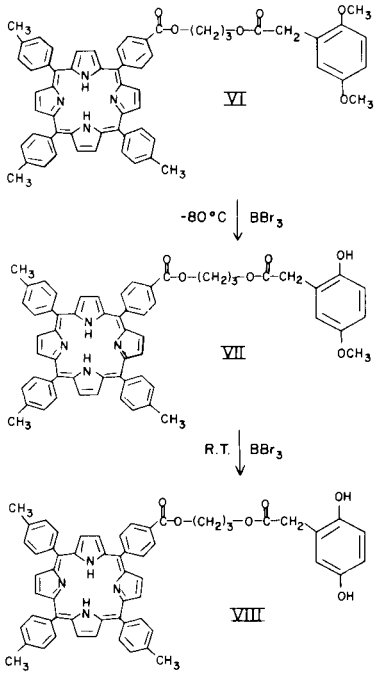

Figure 3. Demethylation of 5-(*p*-benzoyloxypropyl 2,5-dimethoxyphenylacetate)-10,15,20-tri(*p*-tolyl)porphyrin using boron tribromide as reagent.

The mass spectral data of compounds 5-(*p*-benzoyloxypropyl 2,5-dimethoxyphenylacetate)-10,15,20-tri(*p*-tolyl)porphyrin, 5-(*p*-benzoyloxypropyl 2-hydroxy-5-methoxyphenylacetate)-10,15,20-tri(*p*-tolyl)porphyrin, and 5-(*p*-benzoyloxypropyl 2,5-dihydroxyphenylacetate)-10,15,20-tri(*p*-tolyl)porphyrin are listed in Table I (24). Both compounds 5-(*p*-benzoyloxypropyl 2,5-dimethoxyphenylacetate)-10,15,20-tri(*p*-tolyl)porphyrin and 5-(*p*-benzoyloxypropyl 2-hydroxy-5-methoxyphenylacetate)-10,15,20-tri(*p*-tolyl)porphyrin showed the expected parent peaks 936 and 922, respectively. Although no parent mass was observed for compound 5-(*p*-benzoyloxypropyl 2,5-dihydroxyphenylacetate)-10,15,20-tri(*p*-tolyl)porphyrin, analyses of its fragmentation pattern were completely consistent with the assigned structure and constitute further proof of structure. When the hydroxy groups on the hydroquinone half were blocked with methyl ethers (5-(*p*-benzoyloxypropyl 2,5-dimethoxyphenylacetate)-10,15,20-tri(*p*-tolyl)porphyrin), breaking of the covalently-linked complex occurred predominantly at the O-C linkage near the dimethoxyhydroquinone end, yielding the fragment of mass = 740 [parent minus 2,5-dimethoxyphenylacetate]$^{+\cdot}$ as the major ion. If one or both of the methoxy groups were demethylated, a major peak at m/e = 758 was obtained, corresponding to the loss of the monomethoxyhydroquinone or hydroquinone part of the molecule from the parent compound with breakage occurring at the O-C=O bond of the ester linkage near the monomethoxyhydro-

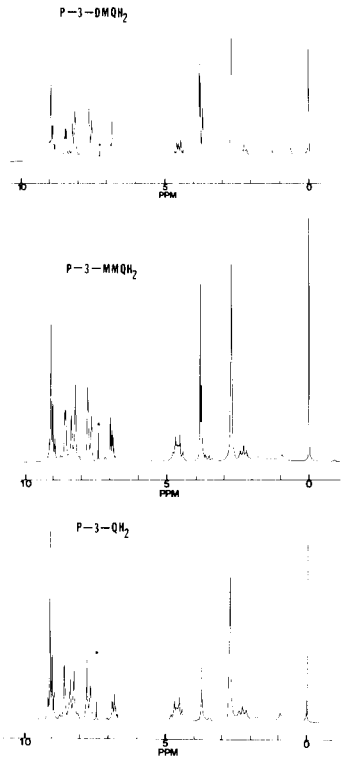

Figure 4. ^{1}H nmr spectra of 5-(*p*-benzoyloxypropyl 2,5-dimethoxyphenylacetate)-10,15,20-tri(*p*-tolyl)porphyrin, 5-(*p*-benzoyloxypropyl 2-hydroxy-5-methoxyphenylacetate)-10,15,20-tri(*p*-tolyl)porphyrin and 5-(*p*-benzoyloxypropyl 2,5-dihydroxyphenylacetate)-10,15,20-tri(*p*-tolyl)porphyrin in deuteriochloroform. The reference is tetramethylsilane. For detailed peak assignments, see the experimental section. Note that the spectra are very similar except for the methoxy region (3.80-3.70 ppm). The asterisk indicates the location of the proton in chloroform.

Table 1

Mass Spectrometer Fragmentation Patterns of 5-(*p*-benzoyloxypropyl 2,5-dimethoxyphenylacetate)10,15,20-tri(*p*-tolyl)porphyrin, 5-(*p*-benzoyloxypropyl 2-hydroxy-5-methoxyphenylacetate)10,15,20-tri(*p*-tolyl)porphyrin and 5-(*p*-benzoyloxypropyl 2,5-dihydroxyphenylacetate)10,15,20-tri(*p*-tolyl)porphyrin

P-3-DMQH$_2$ (MW = 936)	P-3-MMQH$_2$ (MW = 922)	P-3-QH$_2$ (MW = 908)
m/e	m/e	m/e
936	922	—
740	758	758
699	699	699
654	654	654
	164	150
	136	122
	108	94
	93	
	78	

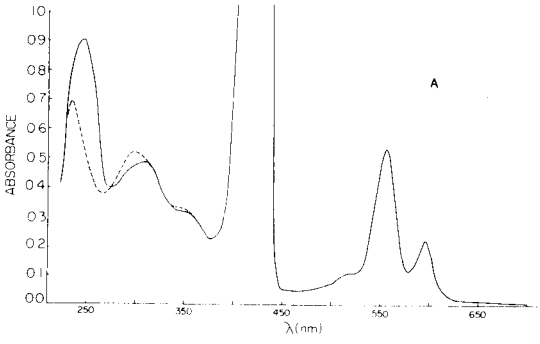

Figure 5A. Absorbance spectrum of covalently-linked 5-(*p*-benzoyloxypropyl 1,4-benzoquinonylacetate)-10,15,20-tri-(*p*-tolyl)porphyrinatozinc complex (solid line) in dichloromethane containing 2% ethanol. Potassim borohydride was added to obtain the spectrum of the reduced form, 5-(*p*-benzoyloxypropyl 2,5-dihydroxyphenylacetate)-10,15,20-tri(*p*-tolyl)porphyrin (dashed line). The solution concentration was $2.5 \times 10^{-5}M$, 1 cm cuvets, room temperature.

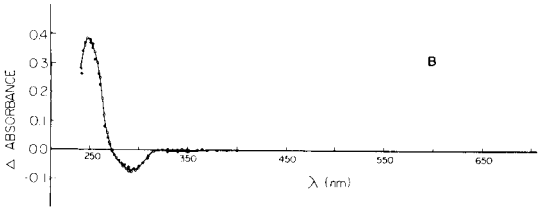

Figure 5B. The difference spectrum of 5-(*p*-benzoyloxypropyl 1,4-benzoquinonylacetate)-10,15,20-tri(*p*-tolyl)porphyrinatozinc and 5-(*p*-benzoyloxypropyl 2,5-dihydroxyphenylacetate)-10,15,20-tri(*p*-tolyl)porphyrinatozinc (●) in dichloromethane containing 2% ethanol and the oxidized-reduced difference spectrum of homogentisic acid (○) in the same solvent system. The solution concentration was $2.5 \times 10^{-5}M$ in each case, 1 cm cuvets, room temperature.

quinone or hydroquinone end of the molecule. This fragmentation behavior strongly suggests the tendency for the formation of a γ-lactone structure by the hydroquinone part of the molecule and is thus taken as direct support for the assignment of structure proposed for compound VII (5-(*p*-benzoyloxypropyl 2-hydroxy-5-methoxyphenylacetate)-10,15,20-tri(*p*-tolyl)porphyrin). A major peak of m/e = 699 was observed for all three compounds studied; this fragment was readily identified to be the 5-(4-carboxyphenyl)-10,15,20-tritolylporphyrin species. Several other low m/e fragments were also detected and their structural assignments were consistent with the hydroquinone half of the covalently-linked species.

Optimal conditions for the boron tribromide reaction were first determined by preparing a simpler derivative of homogentisic acid, ethyl 2,5-dimethoxyphenylacetate. Because this derivative does not contain the porphyrin moiety, there was no interference in the uv-visible spectral characterization of the benzoquinone and hydroquinone products. The appropriate demethylated products isolated after the boron tribromide cleavage reaction were thus readily prepared and well characterized by their nmr and uv-visible spectra. The demethylation reaction conditions worked out for this analogue were found to be quite appropriate for application to 5-(*p*-benzoyloxypropyl 2,5-dimethoxyphenylacetate)-10,15-20-tri(*p*-tolyl)-porphyrin.

Preparation of the zinc porphyrin-hydroquinone complex was accomplished by addition of a saturated solution of zinc acetate in methanol to a solution of VIII in dichloromethane at room temperature with stirring. The progress of metal insertion was followed by visible spectroscopy. This is a very facile reaction requiring only about 30 minutes for quantitative metal insertion. In fact, this reaction goes so well that free base porphyrins often pick up zinc from glass surfaces when dissolved in organic solvents such as dichloromethane. At the end of metallation reaction, the excess zinc acetate was removed by washing the reaction solution several times with water. The solution was then dried and purification of the Zn^{++} porphyrin-hydroquinone complex IX (5-(*p*-benzoyloxypropyl 2,5-dihydroxyphenylacetate)-10,15,20-tri(*p*-tolyl)-porphyrinatozinc) was by means of preparative thin layer chromatography. Nmr and mass spectra of complex IX were recorded, and the spectral data were consistent with the expected structure.

To convert compounds VIII and IX into their corresponding quinone complexes, 5-(*p*-benzoyloxypropyl 1,4-benzoquinonylacetate)-10,15,20-tri(*p*-tolyl)porphyrin (X) and 5-(*p*-benzoyloxypropyl 1,4-benzoquinonylacetate)-10,15,20-tri(*p*-tolyl)porphyrinatozinc (XI), various oxidants were evaluated. Potassium ferricyanide, ferric sulfate, or ferric chloride were used with limited success. The main problem seemed to be that beside oxidizing the quinol moieties, these oxidants, which had to be used in excess, also caused oxidation of the porphyrin ring systems yielding a series of degradation products. High potential quinones such as chloranil and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, on the other hand, when used in near stoichiometric quantities in dichloromethane, efficiently converted the hydroquinones to their corresponding benzoquinone forms without causing degradation of the porphyrin or metalloporphyrin centers. Based on chromatographic characteristics, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone was chosen as the preferred oxidant because this compound moves only very slowly on silica gel, making it easy to separate. Indeed, separation of the desired covalently-linked porphyrin-quinone, metalloporphyrin-quinone complexes from the oxidant was accomplished quickly (5-10 min) and efficiently by simply

passing the reaction solution through a column of silica gel at the end of the reaction. The 5-(*p*-benzoyloxypropyl 2,5-dihydroxyphenylacetate)-10,15,20-tri(*p*-tolyl)porphyrin, 5-(*p*-benzoyloxypropyl 1,4-benzoquinolylacetate)-10,15,20-tri(*p*-tolyl)porphyrin, 5-(*p*-benzoyloxypropyl 2,5-dihydroxyphenylacetate)-10,15-20-tri(*p*-tolyl)porphyrinatozinc, and 5-(*p*-benzoyloxypropyl 1,4-benzoquinolylacetate)-10,15,20-tri(*p*-tolyl)porphyrinatozinc complexes are highly photolabile so that extreme care must be taken to exclude light from all operations. Also, the compounds are more stable in the absence of oxygen so that anaerobic conditions were used whenever possible.

The uv-visible absorbance spectra of the covalently-linked zinc porphyrin quinone (5-(*p*-benzoyloxypropyl 1,4-benzoquinonylacetate)-10,15,20-tri(*p*-tolyl)porphyrinatozinc) complex and its reduced form are shown in Figure 5A. The oxidized form differs from the reduced form only at wavelengths below 370 nm. The solvent used was 2% ethanol in dichloromethane. Borohydride was added to obtain the spectrum of the reduced form. Exactly the same spectrum was recorded by separately preparing a solution of compound IX, 5-(*p*-benzoyloxypropyl 2,5-dihydroxyphenylacetate)-10,15,20-tri(*p*-tolyl)porphyrinatozinc, in the same solvent. Over the concentration range studied (10^{-4} – 10^{-7} *M*), spectra of compounds VIII and IX were observed to obey Beer's law; thus, no specific aggregration effects in this solvent system were found. The absorbance spectra of appropriate monomeric species, the 1,4-benzoquinonylethanoic acid and its reduced form, and the 5-(4-carbomethoxyphenyl)-10,15,20-tritolylporphyrinatozinc were also taken in the same solvent system. Depicted in Figure 5B are the difference spectra of the covalently-linked 5-(*p*-benzoyloxypropyl 1,4-benzoquinonylacetate)-10,15,20-tri(*p*-tolyl)porphyrinatozinc and 5-(*p*-benzoyloxypropyl 2,5-dihydroxyphenylacetate)-10,15,20-tri(*p*-tolyl)-porphyrinatozinc complexes compared with the difference spectra of the 1,4-benzoquinonylethanoic acid and homogentisic acid. Note that the two difference spectra were almost identical, indicating the spectra of the two covalently-linked species are simple 1:1 additions of the two monomer spectra. No evidence of interaction between the two moieties was observed in this solvent system. Such an observation is consistent with similar spectral data from this laboratory on covalently-linked porphyrin centers (11,12).

Thus, we have synthesized in pure form a covalently-linked porphyrin-hydroquinone complex and its corresponding oxidized form (5-(*p*-benzoyloxypropyl 1,4-benzoquinonylacetate)-10,15,20-tri(*p*-tolyl)porphyrin) and also their zinc containing analogues. These complexes are quite soluble in a variety of organic solvents and should lend themselves to systematic physical studies including fluorescence properties, electrochemical behavior and photochemical activity. In addition, the length of the connecting bridge can be readily varied so that the properties of a series of analogues can be compared.

EXPERIMENTAL

All reactions and chromatography were carried out in minimum room light. Benzene used in the reactions was distilled from phosphorus pentoxide and stored over sodium wire. Pyridine was distilled from *p*-toluenesulfonyl chloride and stored in the dark over sieves. Other solvents used were spectral grade or better quality. All compounds were used without further purification.

The silica gel used for dry column chromatography was "Silica Gel Woelm for Dry Column Chromatography" #04526 obtained from ICN pharmaceuticals. The plates used for preparative thin layer chromatography were Quantum 1000 micron PLQ5F and PLQ5 silica gel plates. Analytical thin layer plates were Q5F silica, 250 micron thickness, Quantum Industries.

Absorbance spectra were taken using a Cary 14 Recording Spectrophotometer. Nmr data were obtained using either a Perkin-Elmer R-20-B nmr spectrometer (60 MHz), a CFT-20 nmr spectrometer (80 MHz, Varian Associate), or a WP-60 Bruker nmr spectrometer (60 MHz). Tetramethylsilane (Aldrich) was used as internal standard.

Elemental analyses were performed at Micro-Tech Laboratories, Inc., Skokie, Illinois and at Chemalytics, Inc., Tempe, Arizona. All analytical samples were recrystallized and dried *in vacuo* at 70° for 24 hours.

Methyl 2,5-Dimethoxyphenylacetate.

A solution of 1.0 g. of homogentisic acid (0.006 mole) in 60 ml. of anhydrous acetone was treated with 1.6 ml. (0.018 mole) of dimethylsulfate and 2.6 g. (0.02 mole) of potassium carbonate under nitrogen. The solution mixture was refluxed for about 8 hours, during which time the solution mixture turned into a bright yellow color. After cooling, the inorganic salt was filtered off and washed three times with a few ml. of acetone. The combined filtrates were taken to dryness under reduced pressure and the residue appeared as a yellow syrup. This residue was purified by column chromatography on silica gel (110 g.) using chloroform as eluant. The first yellow band, which travelled almost with the solvent front, contained the desired product. Evaporation of the solvent from the eluate left a residue which solidified readily. After recrystallizing twice from 1:1 ethanol-water, the desired compound was obtained as pale yellow, fluffy flakes. The yield was 0.81 g. (65%), m.p. 40°; uv (ethanol): λ max 295 nm, 227 nm sh; ^{1}H nmr (deuteriochloroform): δ 6.70 (s, 3H, Arom.), 3.80-3.75 (2s, 9H, $-OCH_3$), and 3.60 ppm (s, 2H, benzylic CH_2).

Anal. Calcd. for $C_{11}H_{14}O_4$: C, 62.85; H, 6.71. Found: C, 62.94; H, 6.83.

2,5-Dimethoxyphenylacetic Acid.

To 1.0 g. of methyl 2,5-dimethoxyphenylacetate dissolved in 50 ml. of benzene was added 50 ml. of 2*N* aqueous potassium hydroxide solution and the reaction mixture was allowed to reflux for 4 hours. The solution was then diluted with 300 ml. of water, neutralized with 2*N* aqueous hydrochloric acid and extracted three times with diethylether. The combined etheral extracts were washed with 2% sulfuric acid, twice with water and dried over magnesium sulfate. Evaporation of the solvent under reduced pressure and recrystallization of the residue from 1:1 ethanol-water yielded 2,5-dimethoxyphenyl acetic acid as an off-white powder, m.p. 123°, comparable with an authentic sample obtained from Aldrich Chemical Company; uv (ethanol): λ max 293 nm, 227 nm sh; ^{1}H nmr (deuteriochloroform): δ 6.75 (s, 3H, aromatic), 3.73 (s, 6H, $-OCH_3$), 3.60 ppm (s, 2H, benzylic CH_2).

2,5-Dimethxoyphenylacetyl Chloride.

2,5-Dimethoxyphenylacetic acid (500 mg.) was added to 50 ml. of benzene containing 6 ml. of thionyl chloride under nitrogen. The solution was allowed to reflux for 3 hours, during which time the solution turned into a bright yellow color. The solvent was removed under reduced pressure and the residue was redissolved in another 30 ml. of benzene.

The solvent was once again taken to dryness to remove traces of thionyl chloride. The acid chloride was then used without further purification.

Ethyl 2,5-Dimethoxyphenylacetate.

Ethanol (4 ml.) dissolved in 6 ml. of pyridine was added slowly with stirring to a solution of the acid chloride prepared above in 50 ml. of benzene. The solution mixture was refluxed for 8 hours and the solvent was removed under reduced pressure. The residue was redissolved in 30 ml. of chloroform and washed with water, 2% sulfuric acid, water, 8% sodium bicarbonate and water again. Evaporation of the solvent left a colorless oil. This colorless oil was dissolved in about 2 ml. of chloroform and chromatographed on a column of silica gel (110 g.) using chloroform as eluant. Fractions of 30 ml. were collected until about 300 ml. of chloroform was used. Only the fractions which showed a spot (under uv lamp) with R_f = 0.75 on analytical tlc plates using chloroform as eluant were combined and the solvent evaporated. The residue was recrystallized from 1:1 ethanol-water to give the desired compound as an off-white solid material in 77% yield (0.44 g.); uv (ethanol): λ max 292 nm, 230 nm sh; ^{1}H nmr (deuteriochloroform): δ 6.67 (s, 3H, aromatic), 4.32-3.92 (quartet, 2H, O-CH_2-), 3.65 (s, 6H, -OCH_3), 3.55 (s, 2H, benzylic CH_2), and 1.27-1.02 ppm (triplet, 3H, terminal CH_3).

Anal. Calcd. for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.30, H, 7.40.

γ-Hydroxypropyl 2,5-Dimethoxyphenylacetate.

(a).

Condensation of 2,5-dimethoxyphenylacetyl chloride with 1,3-propanediol by a method analogous to that described for formation of ethyl 2,5-dimethoxyphenylacetate yielded a yellow oil as residue after the solvent was removed under reduced pressure. Further purification by column chromatography on silica gel with 2% acetone in chloroform as eluant gave a fast moving yellow band which was not the product of interest. The column was further eluted with 5% acetone-chloroform. Fractions of 30 ml. were collected until the eluate that came off the column was colorless. Only the fractions which showed a spot (under uv lamp) with R_f = 0.57 on analytical tlc plates using 3% acetone-chloroform as eluant were combined and the solvent evaporated. The residue which was the desired product was a viscous yellow oil, yield 0.41 g. (70%).

A solution of 0.5 g. of methyl 2,5-dimethoxyphenylacetate in 20 ml. of chloroform, 50 ml. of 1,3-propanediol, 2 ml. of methanol and 2 ml. of concentrated sulfuric acid was refluxed overnight. On the following morning, this reaction mixture was poured into 250 ml. of water, neutralized with 4% aqueous sodium hydroxide solution and extracted with chloroform (3 × 30 ml.). The combined extracts were washed with water, 2% sulfuric acid, water, 8% sodium bicarbonate and water again. The residual yellow oil was purified as described above to give γ-hydroxypropyl 2,5-dimethoxyphenylacetate in 54% yield (0.32 g.) which was found to be indentical with material prepared by method (a); ^{1}H nmr (deuteriochloroform): δ 6.68 (s, 3H, aromatic), 4.18-3.97 (m, 4H, -O-CH_2-C-CH_2-O-), 3.65 (s, 6H, -OCH_3), 3.53 (s, 2H, benzylic CH_2), 2.43 (broad, OH), and 2.1-1.77 ppm (m, 2H, -C-CH_2-C-).

Anal. Calcd. for $C_{13}H_{18}O_5$: C, 61.41; H, 7.14. Found: C, 61.13; H, 7.28.

Ethyl 2-Hydroxy-5-methoxyphenylacetate.

Ethyl 2,5-dimethoxyphenylacetate (0.2 g.) was dissolved in 30 ml. of methylene chloride in a 100 ml. round bottom flask fitted with a condenser and was placed in an acetone-dry ice bath at −80°. A solution of approximately 3 g. of boron tribromide in 10 ml. of methylene chloride was added dropwise through a condenser to the stirred solution. A drying tube was fitted to the top of the condenser in order to protect the reaction mixture from moisture. The reaction mixture was kept at −80° for 8 hours and then allowed to attain ice temperature. The remaining boron tribromide in the reaction mixture was then hydrolyzed by carefully adding 15 ml. of water over a 10 minute period. A white precipitate appeared but later redissolved. The solution was extracted with diethyl ether (3 × 20 ml.) and the combined etheral extracts were washed with water (2 × 10 ml.) and then dried over magnesium sulfate. After evaporation of the solvent, the residue was chromatographed on a column of silica gel (85 g.) using chloroform as eluant. Fractions of 30 ml. were collected and only the fractions which showed a spot (under uv lamp) with R_f = 0.40 using chloroform as eluant were combined. Removal of solvent left the product as a yellow oil, yield 0.13 g. (70%); ^{1}H nmr (deuterioacetone): δ 6.65 (s, 3H, aromatic), 4.30-3.94 (quartet, 2H, -O-CH_2-), 3.66 (s, 3H, -OCH_3), 3.57 (s, 2H, benzylic CH_2), and 1.32-1.08 ppm (triplet, 3H, terminal CH_3).

Anal. Calcd. for $C_{11}H_{14}O_4$: C, 62.85; H, 6.71. Found: C, 62.67; H, 6.76.

Ethyl 2,5-Dihydroxyphenylacetate.

The conditions for the preparation of the dihydroxy derivative using boron tribromide as cleavage reagent were similar to those described for the monohydroxy compound. In this case, the reaction mixture was allowed to attain room temperature for 3 hours before water was added. 10% Acetone in chloroform was used as eluant for a subsequent column chromatography on silica gel. The product was purified further by prepartive tlc using 4% acetone in chloroform as the developing solvent to give an off-white solid material in good yield (50%), m.p. 117°, identical with literature reported value (25); ^{1}H nmr (deuterioacetone): δ 6.63 (s, 3H, aromatic), 4.31-3.96 (quartet 2H, -O-CH_2-), 3.56 (s, 2H, benzylic CH_2), and 1.33-1.10 ppm (triplet, 3H, terminal CH_3).

Anal. Calcd. for $C_{10}H_{12}O_4$: C, 61.22; H, 6.17. Found: C, 61.01; H, 6.00.

Ethyl (1,4-Benzoquinonyl)acetate.

Ethyl 2,5-dihydroxyphenylacetate (50 mg.) dissolved in 5 ml. of acetonitrile was added to a 10 ml. saturated solution of ferric sulfate in 5% aqueous acetonitrile. The solution mixture was shaken for 5 minutes and then diluted with 25 ml. of water. The solution was then extracted with diethyl ether (3 × 15 ml.). The combined etheral extracts were washed with 15 ml. of saturated sodium chloride solution and dried over magnesium sulfate. Removal of the solvent left a greyish yellow oil which was chromatographed on a column of silica gel (6 g.) with chloroform as eluant. Evaporation of the solvent gave the quinone as a yellow solid; uv (ethanol): λ max 248 nm, 300 sh.

Anal. Calcd. for $C_{10}H_{10}O_4$: C, 61.85; H, 5.19. Found: C, 61.38; H, 5.54.

5-(*p*-Benzoyl Chloride)-10,15,20-tri(*p*-tolyl)porphyrin.

The acid chloride was prepared by dissolving 100 mg. of 5-(4-carboxyphenyl)-10,15,20-tri(*p*-tolyl)porphyrin (11) in a mixture of 50 ml. of benzene and 6 ml. of thionyl chloride. The solution was brought to reflux for 3 hours and the solvent was removed under reduced pressure. The acid chloride was redissolved in about 20 ml. of benzene and once again taken to dryness under reduced pressure to remove traces of thionyl chloride. The acid chloride was then used without further purification.

5-(*p*-Benzoyloxypropyl 2,5-Dimethoxyphenylacetate)-10,15,20-tri(*p*-tolyl)-porphyrin (VI).

A solution of 115 mg. of the acid chloride of I (prepared as above) in 50 ml. of benzene and 200 mg of γ-hydroxypropyl 2,5-dimethoxyphenylacetate in 20 ml. of pyridine were mixed and refluxed overnight. The solvent was removed under reduced pressure and the residue redissolved in 30 ml. of chloroform, washed with water, 2% sulfuric acid, water, 8% sodium bicarbonate and water again. The excess γ-hydroxypropyl 2,5-dimethoxyphenylacetate was removed from the crude mixture by recrystallization of the crude product from chloroform-methanol. The crude purple crystalline product was then chromatographed on a column of silica gel (85 g.) using chloroform as eluant. After 2 faint impurity bands were collected, the column was eluted with 2% acetone in chloroform in order to collect the desired product which moved as a major, dense purple band. This band was further purified by preparative tlc using 1% acetone in chloroform as eluant. Recrystallization of the purified product from chloroform-methanol gave the expected coupled compound as purple crystals for a yield of 65% (100 mg.); uv-visible (ethanol): λ max 647, 591, 550, 514, 416, 300 and 227 nm sh; ^{1}H nmr (deuteriochloroform): δ 8.91-8.75 (m, 8H, β-pyrrole), 8.39-8.34 (AB quartet, 4H, carboxyphenyl-2,3,5,6), 8.12-8.02 (d, 6H, tolyl-2,6), 7.55-7.45 (d, 6H, tolyl-3,5), 6.76-6.73 (m, 3H, dimethoxyphenyl-3,4,6), 4.53-4.40 (m, 4H, -O-CH_2-C-

CH_2-O-), 3.75-3.72 (2s, 6H, -OCH_3), 3.64 (s, 2H, benzylic CH_2), 2.65 (s, 9H, methyl), 2.30-2.22 (m, 2H, -C-CH_2-C-), and −2.80 ppm (s, 2H, pyrrole N-H) (compare with Figure 4).

Anal. Calcd. for $C_{61}H_{52}N_4O_6$: C, 78.18; H, 5.59; N, 5.98. Found: C, 77.81; H, 5.68; N, 5.79.

5-(*p*-Benzoyloxypropyl 2-hydroxy-5-methoxyphenylacetate)-10,15,20-tri(*p*-tolyl)porphyrin (VII).

5-(*p*-Benzoyloxypropyl 2,5-dimethoxyphenylacetate)-10,15,20-tri(*p*-tolyl)porphyrin (70 mg.) was dissolved in 30 ml. of dichloromethane in a round bottom flask fitted with a condenser and placed in an acetone-dry ice bath at −80°. A solution of approximately 2 g. of boron tribromide in 10 ml. of methylene chloride was added dropwise to the stirred solution. The solution changed from purple to a clear green color. A drying tube was then fitted to the top of the condenser to protect the reaction mixture from moisture. The reaction mixture was kept at −80° for 5 hours and then allowed to attain ice temperature. Water (15 ml.) was added over a 10 minute period to terminate the reaction. A white precipitate appeared but redissolved during this time. The reaction mixture was extracted with diethyl ether (3 × 20 ml.), and the combined etheral extracts were washed with water (2 × 20 ml.), dried and evaporated. The product was then purified by preparative tlc using 2% acetone in chloroform as eluant (R_f = 0.41). Recrystallization of the monomethyl ether complex from chloroform-methanol yielded the product as purple crystals for a yield of 65% (45 mg.); uv-visible (ethanol): λ max 647, 591, 550, 514, 416, 300 and 227 nm sh; ^{1}H nmr (deuteriochloroform): δ 8.93-8.71 (m, 9H, β-pyrrole), 8.37-8.34 (AB quartet, 4H, carboxyphenyl-2,3,5,6), 8.15-8.02 (d, 6H, tolyl-2,6), 7.59-7.46 (d, 6H, tolyl-3,5), 6.82-6.72 (m, 3H, monomethoxyphenyl-3,4,6), 4.58-4.42 (m, 4H, -O-CH_2-C-CH_2-O), 3.73 (s, 3H, -OCH_3), 3.66 (s, 2H, benzylic CH_2), 2.68 (s, 9H, methyl), 2.25 (m, 2H, -C-CH_2-C-), and −2.76 ppm (s, 2H, pyrrole, N-H) (compare with Figure 4). Repeated attempts at purification did not yield a product which gave better CHN data.

Anal. Calcd. for $C_{60}H_{50}N_4O_6$: C, 78.07; H, 5.46; N, 6.07. Found: C, 77.23; H, 5.79; N, 5.80.

5-(*p*-Benzoyloxypropyl 2,5-dihydroxyphenylacetate)-10,15,20-tri(*p*-tolyl)porphyrin (VIII).

Preparation of the quinol derivative of compound VI using boron tribromide utilizing conditions similar to those described for the preparation of VII led to isolation of VIII. In this case, the reaction mixture was allowed to attain room temperature for about 2 hours before water was added. Acetone in chloroform (4%) was used as eluant for preparative tlc (R_f = 0.31). Recrystallization from chloroform-methanol gave a yield of 56%; uv-visible (ethanol): λ max 647, 591, 550, 514, 416, 300 and 227 nm sh; ^{1}H nmr (deuteriochloroform): δ 8.92-8.70 (m, 8H, β-pyrrole), 8.36-8.32 (AB quartet, 4H, carboxyphenyl-2,3,5,6), 8.15-8.01 (d, 6H, tolyl-2,6), 7.58-7.44 (d, 6H, tolyl-3,5), 6.70-6.58 (m, 3H, dihydroxyphenyl-3,4,6), 4.66-4.30 (m, 4H, -O-CH_2-C-CH_2-O-), 3.63 (s, 2H, benzylic), −2.67 (s, 2H, pyrrole N-H) (compare with Figure 4).

Anal. Calcd. for $C_{59}H_{48}N_4O_6$: C, 77.95; H, 5.32; N, 6.16. Found: C, 78.02; H, 5.50; N, 6.53.

5-(*p*-Benzoyloxypropyl 2,5-dihydroxyphenylacetate)-10,15,20-tri(*p*-tolyl)porphyrinatozinc (IX).

Saturated zinc acetate in methanol (1 ml.) was added with stirring to a solution of 20 mg. of 5-(*p*-benzoyloxypropyl 2,5-dihydroxyphenylacetate)-10,15,20-tri(*p*-tolyl)porphyrin (VIII) in 20 ml. of dichloromethane. The solution was stirred at room temperature in the dark for about a half hour. Progress of conversion to the zinc complex was followed by visible spectroscopy. The solution was washed well with water (3 × 15 ml.), dried and evaporated. The zinc complex was purified by preparative thin layer chromatography using 4% acetone in chloroform as eluant. The material was removed from the silica gel with 10% acetone in chloroform and recrystallized from chloroform-hexane to give 15 mg. for a yield of 70%; uv-visible (ethanol): λ max 598, 558, 424 and 300 nm; (dichloromethane): 587, 549, 421 and 298 nm; ^{1}H nmr (deuteriochloroform): δ 8.89-8.85 (m, 8H, β-pyrrole), 8.33-8.28 (AB quartet, 4H, carboxyphenyl-2,3,5,6), 8.13-8.01 (d, 6H, tolyl-2,6), 7.58-7.46 (d, 6H, tolyl-3,5), 6.64-6.55 (m, 3H, hydroquinonoid-3,4,6), 4.45-4.35 (m, 4H, -O-CH_2-C-CH_2-O-), 3.61 (s, 2H, benzylic CH_2), 2.68 (s, 9H, methyl) and 2.43-2.20 ppm (m, 2H, -C-CH_2-C-). This derivative is derived directly in solution from the fully characterized precursor as indicated above and is thermally and photochemically unstable. Therefore, we have not attempted to obtain CHN analytical data.

5-(*p*-Benzoyloxypropyl 1,4-Benzoquinonylacetate)-10,15,20-tri(*p*-tolyl)-porphyrinatozinc (XI).

5-(*p*-Benzoyloxypropyl 2,5-dihydroxyphenylacetate)-10,15,20-tri(*p*-tolyl)-porphyrinatozinc (2 × 10^{-5} mole) in 5 ml. of dichloromethane was treated with 1 ml. of 2 × 10^{-2}*M* solution of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone in dichloromethane at room temperature for 5 minutes. The solution was chromatographed on a short column of silica gel (4 g.) with 4% acetone in methylene chloride as eluant and the pigmented band was evaporated to dryness under reduced pressure. The sample was stored under nitrogen in the dark. Reduction of the quinone moiety to the quinol derivative was observed to occur spontaneously when dissolved in ethanol. It appeared stable in chloroform containing 2% ethanol; uv-visible (dichloromethane): λ max 587, 548, 412, 300 and 248 nm. This derivative is derived directly in solution from the fully characterized precursor as indicated above and is thermally and photochemically unstable. Therefore, we have not attempted to obtain CHN analytical data.

5-(*p*-Benzoyloxypropyl 1,4-Benzoquinonylacetate)-10,15,20-tri(*p*-tolyl)porphyrin (X).

This was prepared from 5-(*p*-benzoyloxypropyl 2,5-dihydroxyphenylacetete)-10,15,20-tri(*p*-tolyl)porphyrin (VIII) using 2,3-dichloro-5,6-dicyano-1,4-benzoquinone as oxidant by a method similar to that described above for oxidation of compound IX to compound XI. Sensitivity to reduction in ethanol was also observed for this compound; uv-visible (dichloromethane): λ max 647, 593, 552, 518, 420, 302 and 248 nm. This derivative is derived directly in solution from the fully characterized precursor as indicated above and is thermally and photochemically unstable. Therefore, we have not attempted to obtain CHN analytical data.

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REFERENCES AND NOTES

(1) This investigation was supported by research grants from the National Science Foundation (PCM 74-12588 and PCM 78-16669) and the National Institutes of Health (GM 11741).

(2) P. A. Loach, in "Progress in Bioorganic Chemistry", Vol. 4, E. T. Kaiser and F. J. Kezdy, Eds., Wiley-Interscience, N. Y., 1976, p. 89.

(3) G. Feher and M. Okamura, in "The Photosynthetic Bacteria", R. K. Clayton and W. R. Sistrom, Eds., Plenum, New York, N. Y., 1978, p. 349.

(4) R. E. Blankenship and W. W. Parson, *Annu. Rev. Biochem.*, **47**, 635 (1978).

(5) J. Fajer, D. C. Brune, M. S. Davis, A. Forman and L. D. Spaulding, *Proc. Natl. Acad. Sci. U. S. A.*, **72**, 4956 (1975).

(6) K. J. Kaufman, P. L. Dutton, T. L. Netzel, J. S. Leigh and P. M. Rentzepis, *Science*, **188**, 1301 (1975).

(7) V. A. Shuvalov, B. Ke and E. Dolan, *Proc. Natl. Acad. Sci. U.S.A.*, **76**, 770 (1979).

(8) M. Y. Okamura, R. A. Issacson and G. Feher, *ibid.*, **72**, 3491 (1975).

(9) C. A. Wraight, *Biochim. Biophys. Acta*, **459**, 525 (1977).

(10) L. Morrison, J. Runquist and P. Loach, *Photochem. Photobiol.*, **25**, 73 (1977).

(11) J. A. Anton, J. Kwong and P. A. Loach, *J. Heterocyclic Chem.*, **13**, 717 (1976).

(12) J. A. Anton, P. A. Loach and Govindjee, *Photochem. Photobiol.*, **28**, 235 (1978).

(13) J. J. Katz, L. L. Shipman, T. M. Cotton and T. R. Janson, in "The Porphyrins", Vol. 5, Part C, D. Dolphin Ed., Academic Press, New York, N. Y., 1978, p. 401.

(14) T. M. Cotton, P. A. Loach, J. J. Katz and K. Ballschmiter, *Photochem. Photobiol.*, **27**, 735 (1978).

(15) W. I. White, in "The Porphyrins", Vol. 5, Part C, D. Dolphin, Ed., Academic Press, New York N. Y., 1978, p. 303.

(16) J. R. Harbour and G. Tollin, *Photochem. Photobiol.*, **19**, 147 (1974).

(17) A. A. Lamola, M. L. Manion, H. D. Roth and G. Tollin, *Proc. Natl. Acad. Sci. U.S.A.*, **72**, 3265 (1975).

(18) D. Huppert, P. M. Rentzepis and G. Tollin, *Biochim. Biophys. Acta*, **440**, 356 (1976).

(19) G. R. Seely in "The Chlorophylls", L. P. Vernon and G. R. Seely, Eds., Academic Press, New York, N. Y., 1966, p. 67.

(20) J. Kong and P. A. Loach, in "Frontiers of Biological Energetics: From Electrons to Tissues", Vol. 1, P. L. Dutton, J. S. Leigh and H. Scarpa, Eds., Academic Press, New York, N. Y., 1978, p. 73.

(21) R. G. Little, J. A. Anton, P. A. Loach and J. A. Ibers, *J. Heterocyclic Chem.*, **12**, 343 (1975).

(22) J. A. Anton and P. A. Loach, *ibid.*, **12**, 573 (1975).

(23) Spectra recorded on the WP-60 Bruker nmr spectrometer were obtained by Mr. Arthur G. Kostka of the Chemistry Division, Argonne National Laboratory.

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(25) M. C. Kloetzel, R. P. Dayton and G. Y. Abadir, *J. Org. Chem.*, **20**, 38 (1955).