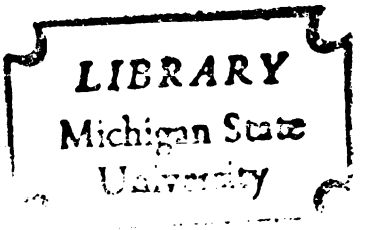

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SYNTHESIS OF PORPHYRINS AND DIPORPHYRINS
AND THEIR BIOMIMETIC APPLICATIONS

presented by

Ching-Bore Wang

has been accepted towards fulfillment
of the requirements for

Ph.D. degree in Chemistry

Chi K. Chang

Major professor

Date May 15, 1981

SYNTHESIS OF PORPHYRINS AND DIPORPHYRINS AND THEIR BIOMIMETIC APPLICATIONS

By

Ching-Bore Wang

A DISSERTATION

Submitted to
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1981

ABSTRACT

SYNTHESIS OF PORPHYRINS AND DIPORPHYRINS
AND THEIR BIOMIMETIC APPLICATIONS

By

Ching-Bore Wang

A series of difunctional C_2h symmetry porphyrins were synthesized by condensation of pyrrole aldehydes and pyrrole acids. The porphyrins can be obtained in large scale by this method. Some porphyrins with one, two, three and four carboxyester side chains were prepared by condensation of 5,5'-dibromopyrromethene and 5,5'-dimethylpyrromethene. Most of the porphyrins can be obtained from the simple 5-methyl-2-carbonylpyrrole ester.

From the C-13 nmr chemical shift of the β-carbons, the structure of porphyrins can be determined. The Cβ-Me's chemical shift were affected by their neighbor substituents.

Several cofacial and slipped diporphyrins were synthesized by coupling of 1,5-difunctional porphyrins with 1,5- and 1,4-difunctional porphyrins in amide bonds. The application of dimers as a photosynthesis reaction center model and sterically binded myoglobin binding site model were discussed.

A series of porphyrin- and chlorin-quinone compounds were prepared. Their photopotentials were compared with chloroplast on bilayer lipid membrane.

ACKNOWLEDGMENTS

I wish to express my sincere appreciation to Professor C. K. Chang for his encouragement, guidance and confidence throughout the course of this study.

I am very grateful to Dr. J. Fajer for the financial support for me to stay at Brookhaven National Laboratory. Many thanks also go to the colleagues at BNL for the help, discussion and friendship.

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1

INTRODUCTION

A great deal of effort has been expended over the past few years in elucidating the nature of active sites in metalloenzymes using well-defined model compounds. Of the many areas in which biomodeling has been undertaken, metalloporphyrin chemistry has been and continues to be, one of the most fruitful. A large number of studies have centered around simple porphyrin and metalloporphyrin system, such as complexes of protoporphyrin IX and synthetic octaethylporphyrin (OEP) and tetraphenylporphyrin (TPP) [1]. While studies of these readily available molecules have provided important information concerning the basic chemical and structural properties of metalloporphyrins, these simple models do have serious limitations in mimicking complex biomolecules. For example, it would be extremely difficult, if not impossible, for the monomeric metal chelate to function as a multinuclear metal catalysts. Clearly there is a need for more elaborate, tailor-made model system designed to model specific features of biological system.

The objectives of this research are:

(1) to synthesize a wide variety of dimeric cofacial porphyrins with predetermined geometry such that they can serve as biomimetic models for the

reaction centers in photosynthetic units.

(2) to synthesize a series of quinone-porphyrin and chlorin complexes to serve as models for studying electron transport phenomenon in photosynthesis.

(3) to develop synthetic methods for large-scale preparations of pyrrol and porphyrin precursors required for the above studies.

During the course of this study, we have also used mixed metal Cu-Fe cofacial diporphyrins as an example to show how oxygen and carbon monoxide binding to a heme can be modulated by local nonbonding steric effects.

(I) Photosynthesis

All photosynthetic organisms except bacteria use water as electron or hydrogen donor to reduce carbon dioxide or other electron acceptor; as a consequence they evolve molecular oxygen. Photosynthesis developed by plants and algae, can be simply represented as

$$nH_2O + nCO_2 \xrightarrow{h\nu} (CH_2O)_n + nO_2$$

It should be appreciated that in addition to carbon, hydrogen, and oxygen, the plants also incorporate nitrogen and sulfur into organic material via light-dependent reactions.

There are, basically, two types of photosynthesis: (a) the water splitting variety seen in all plants and algae, and (b) the photosynthetic bacterial type which cannot use water as an electron donor but instead uses compounds such

as sulfide, organic acids, etc. In both types of photosynthesis, the important processes are the same: 1. light absorption by chlorophyll-containing membrane; 2. a charge separation across the membrane; and 3. donation and acceptance of electron on either side of the membrane.

(a) Bacterial Photosynthesis [2]:

A typical reaction center isolated from the membrane of red and green photosynthetic bacteria has molecular weight about 70,000 and contains four molecules of bacteriochlorophyll, two molecules of bacteriopheophytin, one atom of iron, two quinone molecules, and three hydrophobic proteins of molecular weight 20,000-30,000. Within these reaction centers, the primary photochemistry occurs. In addition, there are the light-harvesting or antenna bacteriochlorophylls (about 40 per reaction center) and their associated proteins which are involved in the capture of light energy and the funnelling of it to a specific reaction center.

A scheme for electron transport is shown in Fig. 1-1, which emphasizes the redox potentials. Light channeled by the light-harvesting bacteriochlorophylls to the reaction center is captured by a bacteriochlorophyll dimer (P870) and within 10 ps a radical pair is formed between P870 and bacteriopheophytin[$(P870)^{+}(BPheo)^{-}$]. Within another 200 ps, an electron is passed to the primary quinone (Q_1) which is associated with a nonheme iron atom; the quinone forms a semiquinone but then transfers the electron to the secondary

quinone (Q_2). The electron then reduces a pool of ubiquinones (UQ) which span the membrane and shuttle protons

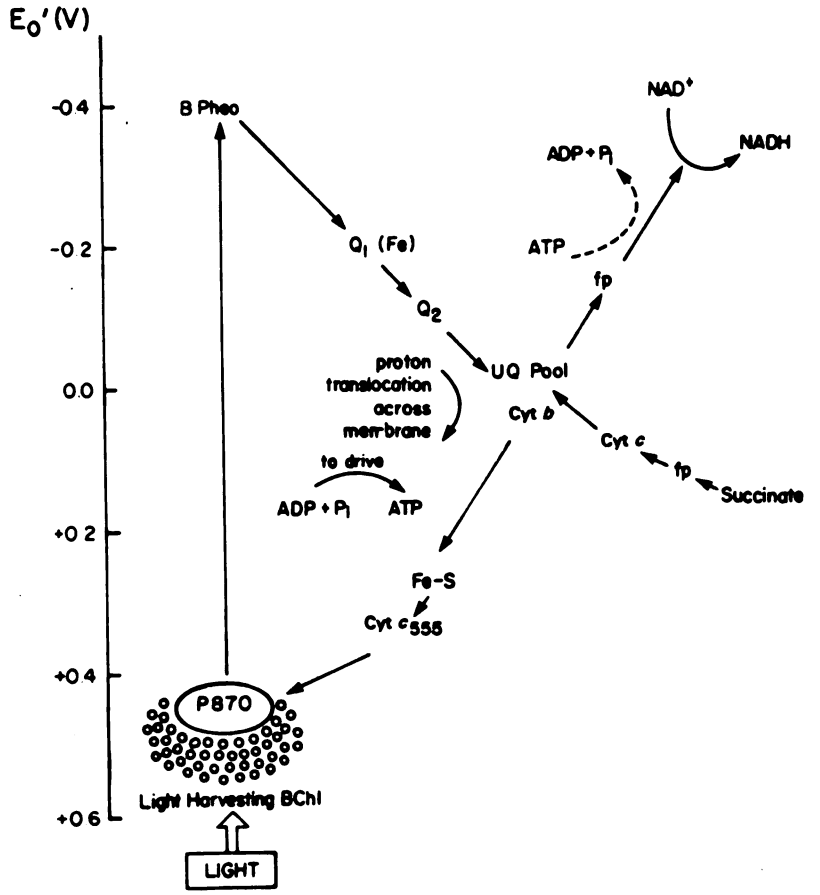


Fig. 1-1. Electron transfer pathway of Bacterial Photosynthesis.

back and forth across the membrane. These protons are used for ATP formation via a chemiosmotic mechanism. The electron completes the cycle by returning to the P870 via an Fe-S protein (Reiske-type) and a high potential cytochrome c. This last step probably occurs within 270 ns of the initial light reactions, while the other reactions are occurring simultaneously. The overall result from this cyclic process is ATP formation, but under certain conditions an external

electron donor such as succinate or sulfide can donate electrons and, using the ATP formed in the cyclic reaction, reduce NAD to NADH which is required for subsequent carbon fixation.

(b) Plant Photosynthesis [2]:

The unique ability of plant (and algae) chlorophyll-containing membranes to split water was postulated by Hill and Bendall [3] as the so-called "Z Scheme," Fig. 1-2. Nature has evolved a marvellous system whereby four quanta are collected as positive charges (Z^+) from four successive photoacts; these "holes" are then used to remove electrons from H_2O to produce oxygen (and protons). The light-generated Z^+ probably represents a Mn-containing complex

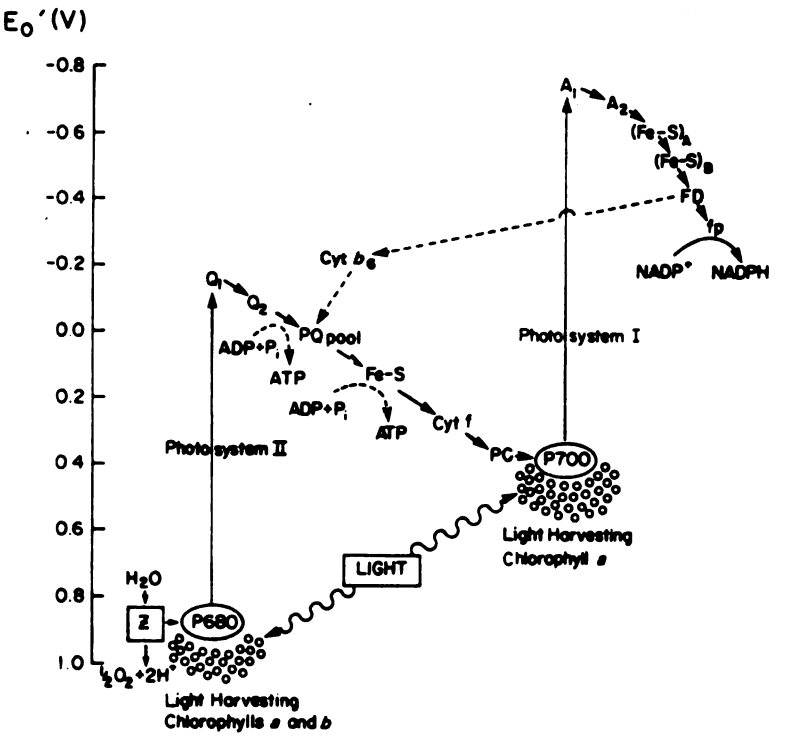


Fig. 1-2. Electron transfer pathway of Plant Photosynthesis.

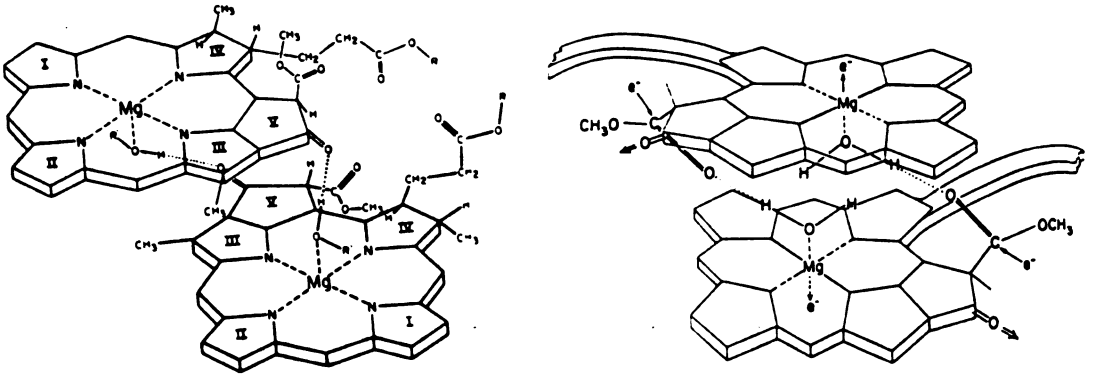
(enzyme?) which can transfer an electron to $P680^+$ in less than 1 μs - possibly within 30 ns in chloroplasts. (The oxidized $P680^+$ is generated in the initial photoact when each photon causes one electron to be extracted from the P680 dimer and donated within 1 ns to the primary electron acceptor-anion of pheophytin or quinone Q_1.)

The primary electron acceptors of photosystem II (pheophytin, Q_1 and Q_2) pass electrons singly within a millisecond to a plastoquinone pool which then shuttles protons and electrons across the membrane. In this way, a proton gradient is built up (often as high as 2.5-3.5 pH units from the outside to the inside of the membrane) which is subsequently used for ATP synthesis via a chemiosmotic mechanism, as in photosynthetic bacteria. The overall stoichiometry is thought by some to approach one ATP molecule formed for each photosystem.

The reduced plastoquinone at the inside of the membrane passes its electron to the oxidized $P700^+$ chlorophyll dimer (reaction-center trap of primary photoact results in a charge separation across the membrane, with one electron moved per photon. The primary electron acceptors of photosystem I have been well explored using a variety of physicochemical techniques. It is believed that a redox potential of -0.73 V, or even more negative, is generated and that A_1 may be a chlorophyll anion and A_2 an Fe-organic complex with the organic part being possibly a chlorophyll *a*. This primary reaction occurs in about 20 ns and then the

electrons are passed within 100 ns to two membrane-bound Fe-S proteins with redox potentials of -0.59 and -0.55 V, and thence to ferrodoxin, to flavoprotein, and finally to $NADP^+$ to form NADPH, which is used along with the ATP for CO_2 reduction.

The orientation of specific pigments within the membrane and the reaction centers is an active field of research at present. The structure of the reaction center chlorophyll is somewhat related to the hydrated chlorophyll aggregates. Currently, it is believed that the Photosystem I reaction center consists of a special pair of chlorophylls bridged by two water ligands. Several models have been proposed for P700, Fig. 1-3 [4, 5].



(a) (b)

Fig. 1-3. P700 model proposed by (a) Katz (b) Fong

Our study of dimeric porphyrins would shine light on the basic photochemistry in the charge separation process and would further allow us to assess the influence of spatial configuration and redox potential differences in driving and controlling charge transfer kinetics.

(II) Pyrrole and Porphyrin Synthesis

The synthetic aspect of porphyrin chemistry has been treated extensively in Hans Fischer's classic work "Die Chemie des Pyrrols" (1934-40) [6]. Newer methods for synthesis of porphyrins and related compounds have been surveyed in excellent reviews in Dolphin's "The Porphyrins" [7].

(a) Porphyrin from pyrroles

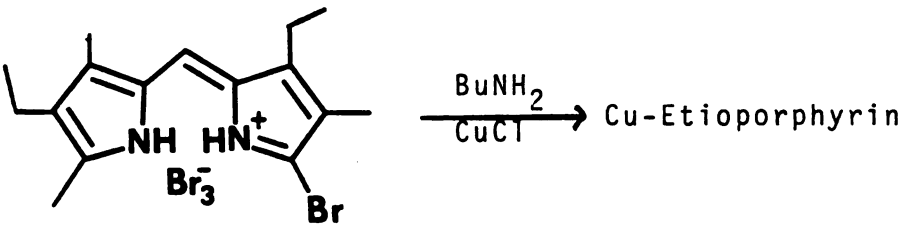
The first synthesis of a porphyrin directly from the self-condensation of a pyrrole was the formation of etioporphyrin from 3-methyl-4-ethyl pyrrole (opsopyrrole) [8]. In spite of the high yield and the ease of preparation this route cannot be applied when the pyrrole has 2 different substituents at 3 and 4 position, isomeric porphyrins will be obtained. However, this is the method of choice in preparing octaethylporphyrin (OEP).

(b) Porphyrins from dipyrromethenes

A widely used porphyrin synthesis is the condensation of dipyrromethene in a melt of succinic or tartaric acid which was developed by Fischer [9] in 1920. In general the yield of porphyrins obtained by this method are low. This method involved the condensation of hydrobromides of two 5-bromo-5'-methyldipyrromethene or the condensation of the

hydrobromides of a 5,5'-dimethyldipyrromethene with a 5,5'-dibromodipyrromethene. The drastic reaction conditions, (e.g. high temperature in acid melt) do not permit the survival of labile substituents. Nevertheless, this route represents the most straightforward method to prepare porphyrins with C_2h or C_2v symmetry required in our dimer synthesis.

These methods have been improved by Corwin and Sydow by using milder conditions. Etioporphyrin copper complex was synthesized by treatment of the dipyrromethene with boiling



t-butylamine in the presence of cuprous chloride [10].

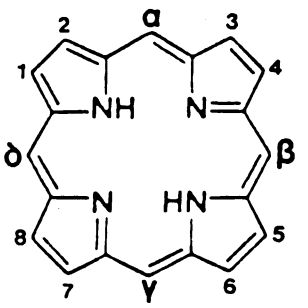
Smith [11] recently reported that 5-methyl-5'-bromo-dipyrromethenium bromide gave high (40-60%) of type I porphyrins when refluxed in anhydrous formic acid. In our study, we have further simplified the procedures and made it adaptable to large-scale manipulations.

Nomenclature of Porphyrins

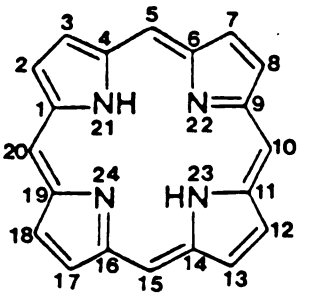
Two systems [12] for numeration of the porphyrin ring are currently in use. The IUPAC system is shown in structure B, which was designed to achieve consistency between porphyrins and corrins. The major disadvantage of the IPUAC recommended system is that it may divorce contemporary

research from the monumental body of early work which used the Fischer system, A. In the classical system of nomenclature the peripheral positions are numbered from 1 to 8 and the "interpyrrolic" methine positions, usually called "meso", are designated α, β, γ and δ. The rings are usually lettered A, B, C and D, although Roman numerals were preferred in some earlier texts. In this thesis, we chose to use the Fischer system to name the porphyrins.

There are four possible arrangements of the two different side chains; two of them are naturally occurring uroporphyrin I with A,P; A,P; A,P;, A,P and uroporphyrin III with A,P; A,P; P,A; A,P; (A = carboxymethyl and P = 2-carboxyethyl). When three different types of substituents are present (four of one kind, and two pairs of others) then fifteen isomers are possible. For detailed discussion, see the Fischer's classical work "Die Chemie des Pyrrols."



A



B

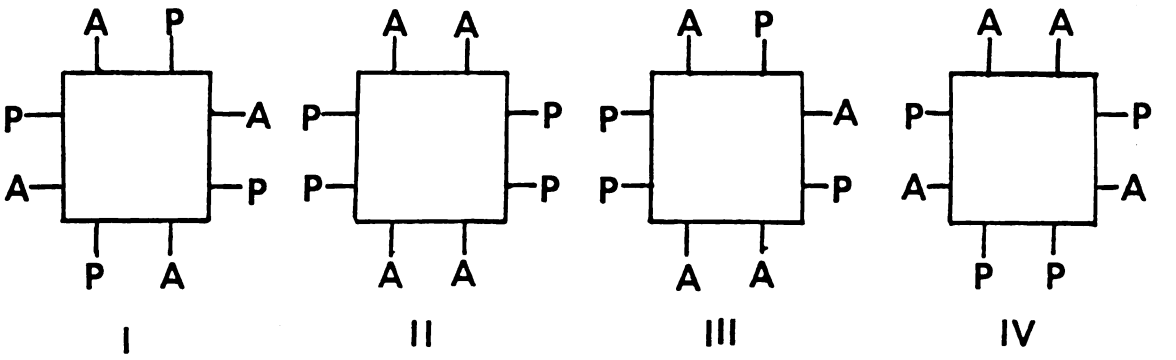


Fig. 1-4. Isomers of Uroporphyrin.

CHAPTER 2

SYNTHESIS OF PYRROLES AND PORPHYRINS

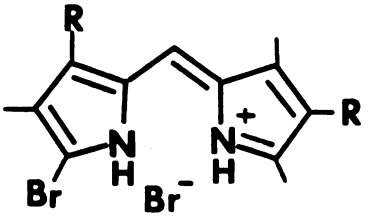
Introduction

Strategically, the synthesis of stacked-porphyrins is best achieved by a modular approach. Individual porphyrins are synthesized first, functional groups are introduced to the two substituted side chains and the two chains can then be condensed with another bifunctional molecule. Porphyrins having difunctional groups as carboxy or amine groups are required for the synthesis of diporphyrins which are linked by amide bonding.

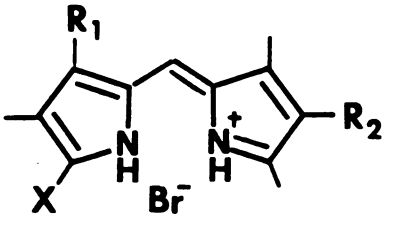
Preparation of the desired β-linked face-to-face dimer requires the synthesis of monomeric porphyrins with suitably functionalized side chains at positions 1 and 5 (see Chapter 1). Dialkyldeuteroporphyrin II is chosen for elaboration mainly because of its high solubility in organic solvents, which is essential for successful coupling and purification of the diporphyrins or other cyclophane porphyrins. Such type II substituted porphyrins are available by using variations of Fischer's original dipyrromethene route [6].

Traditionally the yields of porphyrins obtained by Fischer's method are low, but Smith [11] recently reported that 5-methyl-5'-bromodipyrromethenium perbromide 1 gives high yield (40-60%) of type I porphyrin when refluxed in

anhydrous formic acid, and further noted that small amounts of water partially diverted the reaction to biliverdins of head-to-head symmetry. It was found [13] that the carboxydipyrromethene 2b, which is more conveniently prepared than the unsubstituted analog 2c, can be brominatively decarboxylated and cyclised, without isolation, to porphyrin with equally good yield.



1a R=Et
b R=P



2a X=Br R1=Et
b X=COOH, R2=P
c X=H

Monomeric porphyrins with dicarboxylic ester side chains can be converted into diamines and diacid chlorides (see Chapter 3) which are then coupled to give the dimers under high dilution condition [14].

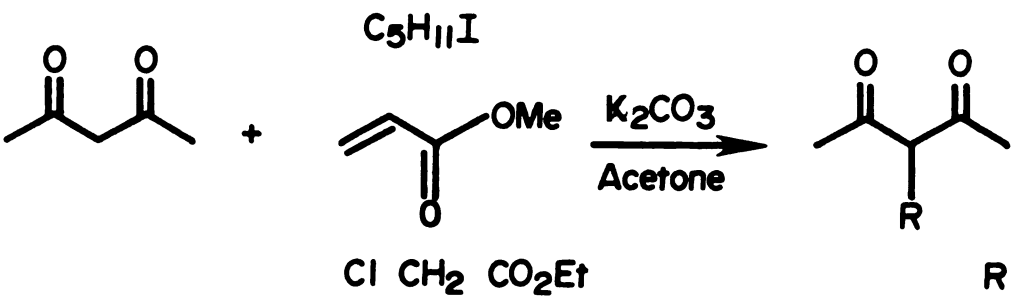
For the preparation of the "slipped dimer", porphyrins with 5,8 disubstituents are necessary. These porphyrins can be obtained by the reaction between 5,5'-dibromodipyrromethenes and 5,5'-dimethyldipyrromethenes, to give porphyrins of type II, III or IV symmetry (see Chapter 1). Using this approach, porphyrins substituted with one to four functional groups can also be obtained. The single functionalized porphyrin can be used to couple an imidazole or a quinone

moiety for the purpose of oxygen binding or photosynthesis model studies. This approach to porphyrin synthesis is especially useful in that both precursors are readily available form the 5-methylpyrrole-2-carboxylate ester [15].

Results and Discussion

I. Pyrrole synthesis

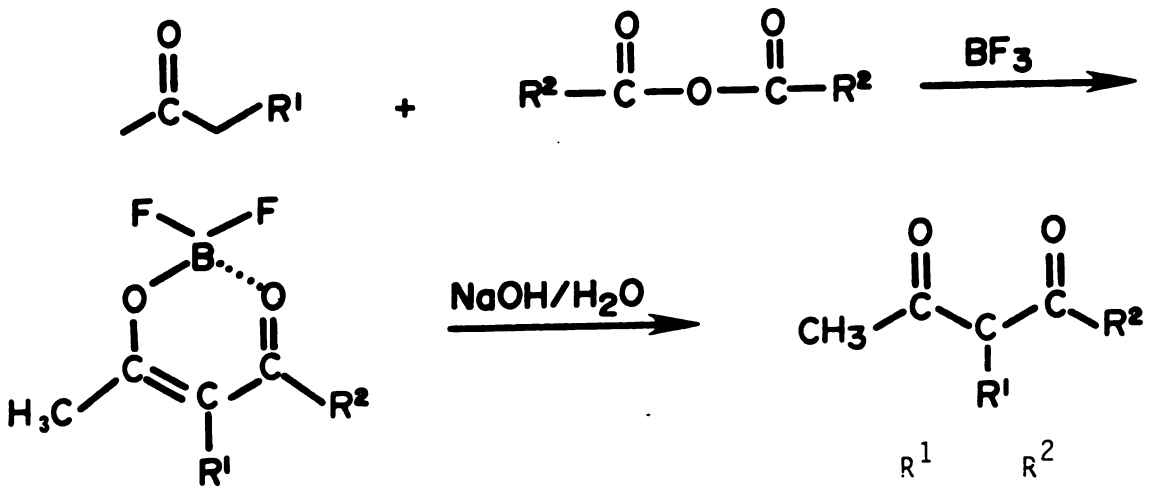
Most of the pyrroles required in our porphyrin synthesis were 5-methylpyrrole-2-carboxylate esters. The preparation follows the established method [7] of the Knorr-type condensation of benzyl oximinoacetoacetate and 3-substituted 2,4-pentanedione 3. 2,4-Pentanedione derivatives can be obtained by condensation with alkyl halide or by Michael addition with methyl acrylate. 3-Pentyl-2,4-pentanedione



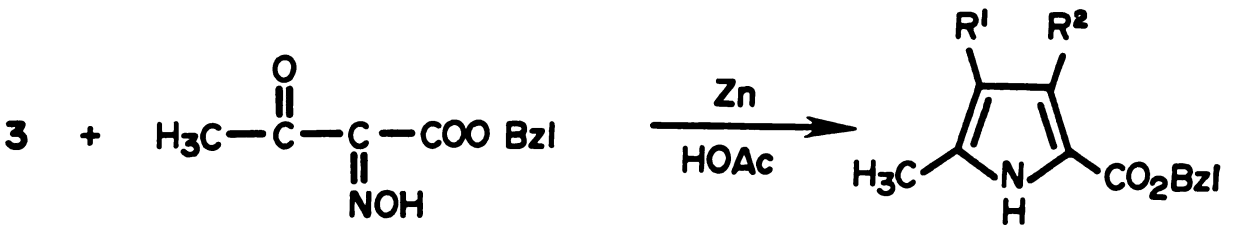
3 a C_5H_{11}
b CH_2-CH_2-COOMe
c CH_2-COOEt

3a can also be prepared by the hydrolysis of the BF_2 complex [16] from the condensation of acetic anhydide and 2-octanone. Through the same procedure,

3-ethyl-2,4-hexanedione 3d was obtained from propionic anhydride and 2-pentanone. Pyrroles 1 were obtained in 40-50% yield when 3-alkyl-diketones condensed with benzyl oximinoacetoacetate in acetic acid use zinc powder as reduction agent.

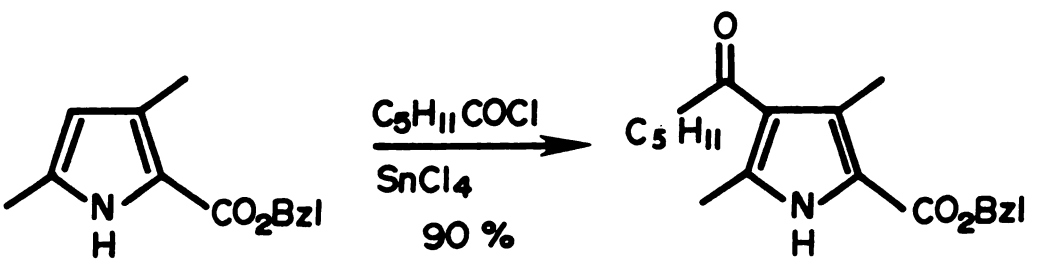


		R^1	R^2
3	a	C_5H_{11}	CH_3
	b	Et	Et

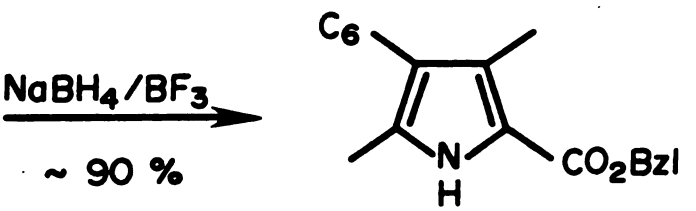


		R^1	R^2
4	a	C_5H_{11}	CH_3
	b	P	CH_3
	c	A	CH_3
	d	Et	Et

The hexyl side chains was introduced to 4e by Friedel-Craft acylation in the presence of $SnCl_4$, followed by diboran reduction of the resulting carbonyl pyrrole 5 to obtain 6.

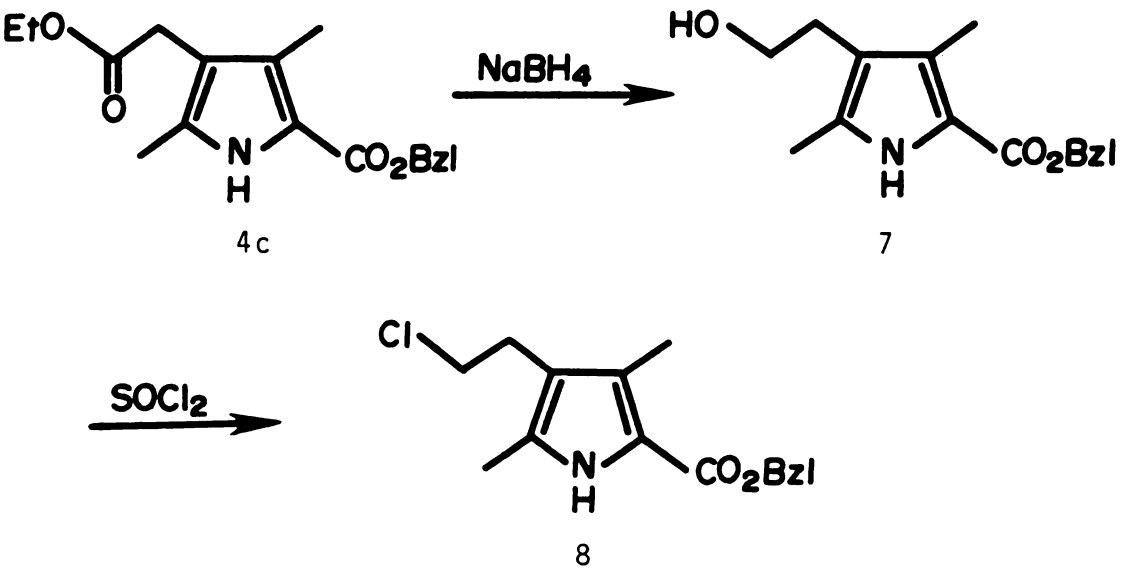


4e 5



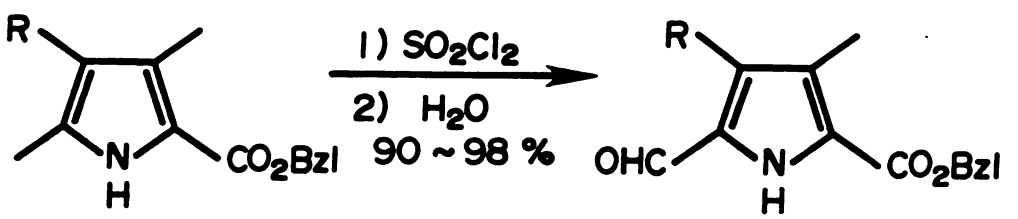
6

The ethoxycarbonylmethyl pyrrole was reduced with diborane to form 2-hydroxyethyl pyrrole 7 [17] and then converted to 2-chloroethyl pyrrole 8 by thionyl chloride [18].



4c 7 8

In dilute dichloromethane solution sulfuryl chloride smoothly brought about dichloroination of the 5-methyl group without attack on other positions. Hydrolysis then afforded the pyrrole aldehyde in good yield.



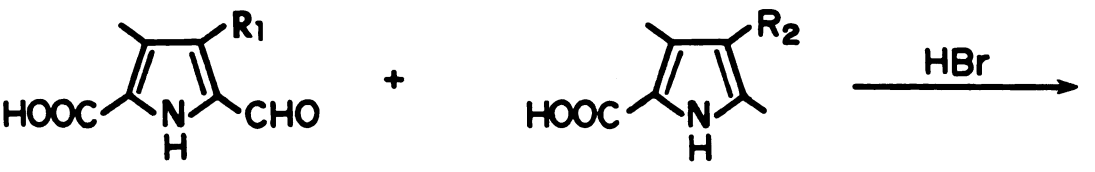
		R
9	a	Hexyl
	b	Pentyl
	c	P

Hydrogenolysis of the pyrrole benzyl esters was conducted in THF with 10% Pd/C catalyst. When hydrogen uptake was complete (3-24 h) the THF solution of pyrrole carboxylic acid 10 or 11 was filtered from the catalyst and evaporated to dryness in vacuo. Recrystallization was unnecessary; the acids may be stored in the refrigerator for several months without significant decomposision.

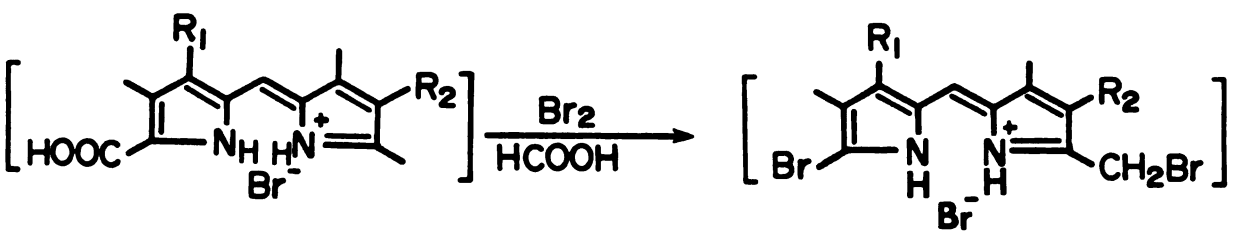
II. C_2h (Type II) Porphyrins Synthesis

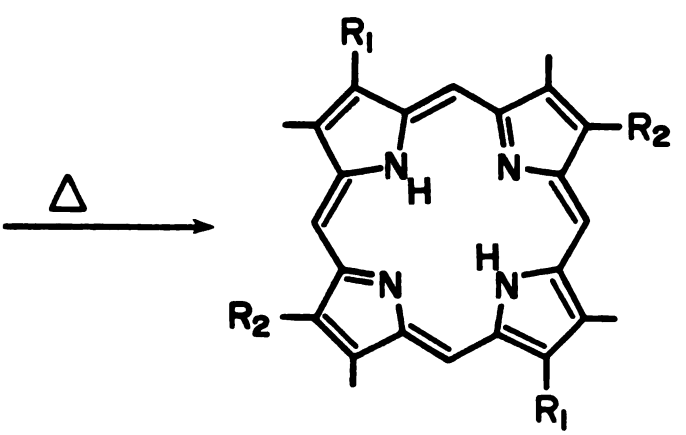
C_2h porphyrins were obtained by the condensation of suitable pyrroles, in the strongly acidic media, with the pyrrole aldehyde to afford the intermediate dipyrromethenes. Brominative decarboxylation and cyclization of dipyrromethenes without isolation of any of the intermediates then afforded the desired porphyrins with very good yield. This method is especially attractive in that the cyclization can be performed in large scales (0.2 mole) and suffers no decrease in yield. The porphyrins listed in Table 2-1 have been prepared and the yields are quoted for the crystalline products.

Small amounts of tripentyl, trihexyl and trichloroethyl porphyrins 13, 14 and 15 were found in the synthesis of 12d, 12a, and 12e. These side products may come from the self condensation of 10 or 11 during the porphyrin synthesis. The structure of 13 can be determined by C-13 nmr.



10 11





12

Table 2-1. C_2h Porphyrins.

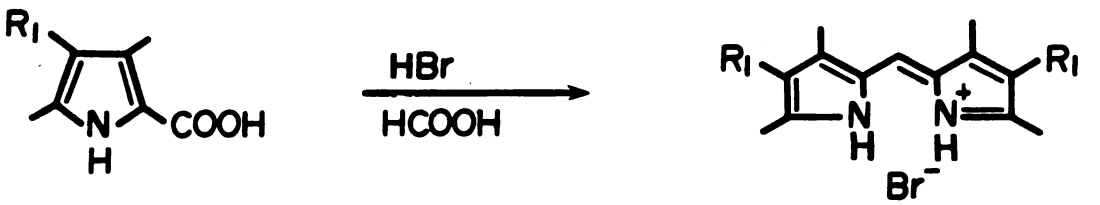
	R1	R2	yield (%)
10a+11a=12a	hexyl	A	16
10a+11b=12b	hexyl	P	20
10b+11a=12c	pentyl	A	15
10b+11b=12d	pentyl	P	20
10c+11d=12e	C-C-Cl	A	10
12f	octyl	P	
12f	octyl	A	

III. Synthesis of porphyrins with one, two (C_2v), three and four carboxylic acid side chains

A. Synthesis of symmetrical dipyrrolmethenes:

(i) 5,5'-Dimethyldipyrromethenes

The symmetric 5,5'-dimethyldipyrromethenes were obtained from the self-condensation of α-free acid pyrroles to give the dipyrromethenes 16.



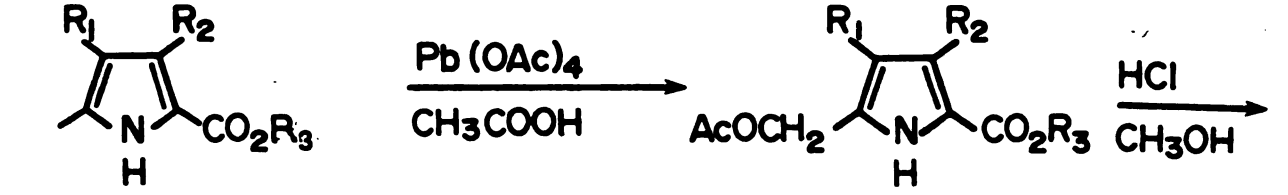
16

	R1
16a	A
16b	P
16c	C-C-C1

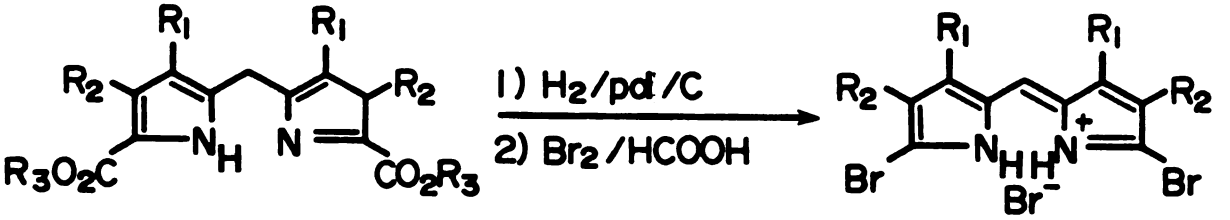
(ii) 5,5'-Dibromodipyrromethenes

5,5'-Dibromodipyrromethenes 19 were obtained in several steps from corresponding pyrroles. 5-Methyl pyrroles were treated with lead tetracetate in acetic acid to give the acetoxy methylpyrroles 17, which were then heated on a steam bath in acidic alcoholic solution to yield the dipyrromethanes 18. Dipyrromethanes upon catalytic hydrogenolysis, provided the very insoluble 5,5-dicarboxy-dipyrromethanes. Addition of this diacid to a formic acid solution with excess of bromine brought about rapid oxidation and

bromination before acid-catalysed rearrangement or decomposition [19]. The products 19 (which may be obtained as perbromide salts) can be converted to the bromide salt by treatment with cyclohexene in dichloromethane [15].



17



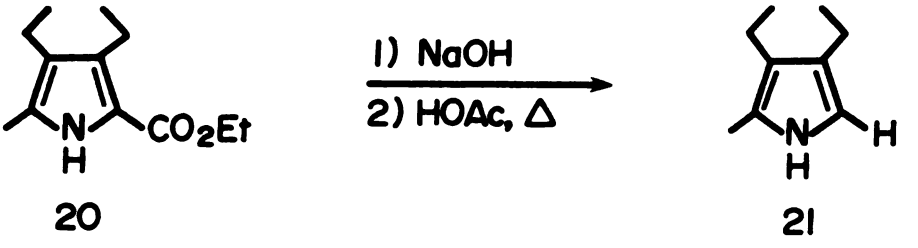
18 19

	R1	R2	R3
a	Et	Et	Et
a'	Et	Et	Bzl
b	P	Me	Bzl
c	C-C-Cl	Me	Bzl
d	hexyl	Me	Bzl
e	pentyl	Me	Bzl

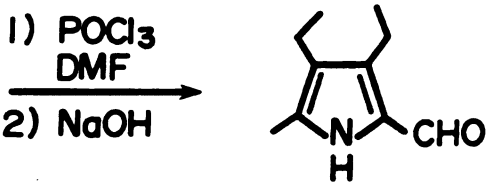
B. Synthesis of unsymmetric 5,5'-dimethyldipyrromethene

In order to make an unsymmetric porphyrin, at least one of the dipyrromethene should be unsymmetric.

The ethyl ester pyrrol 20 was saponified with sodium hydroxide, then neutralized with acetic acid, followed by steam distillation. The α-free pyrrole 21 in the distillate was immediately dried, and formylated with an excess of phosphorus oxychloride in N,N-dimethylformamide. After hydrolysis of the iminium salt, the aldehyde 22 was obtained in moderate yield [1].

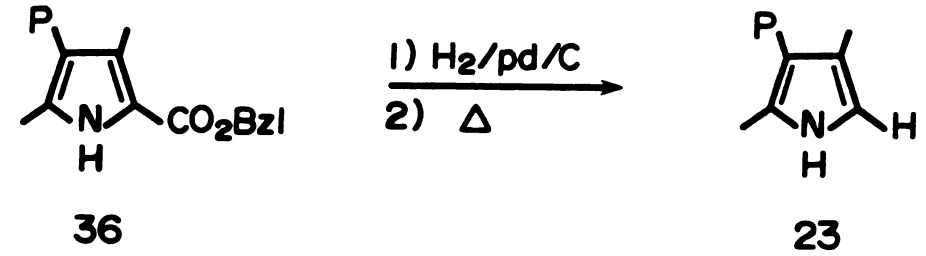


20 21

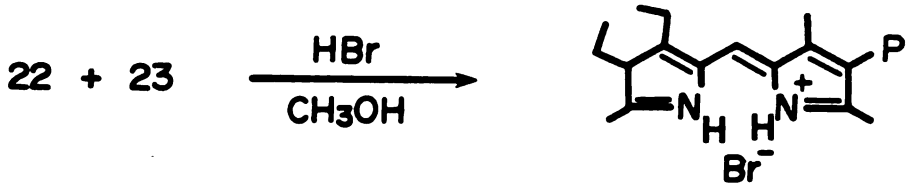


22

The α-free propionic acid pyrrole 23 was prepared by hydrogenolysis of pyrrole benzyl ester, and dry distillated vacuum. The aldehyde 22 and α-free pyrrole 23 was condensed in methanol with 48% HBr to form the unsymmetric dipyrromethene 24.



36 23



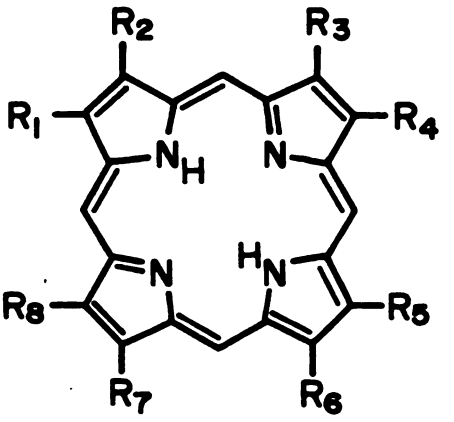
24

C. Synthesis of porphyrins

The condensation step was carried out in a manner similar to that reported previously [15], only one equivalent of bromine in formic acid was used. The mechanism of the reaction is still unclear. The porphyrins and their yield were listed on Table 2-2.

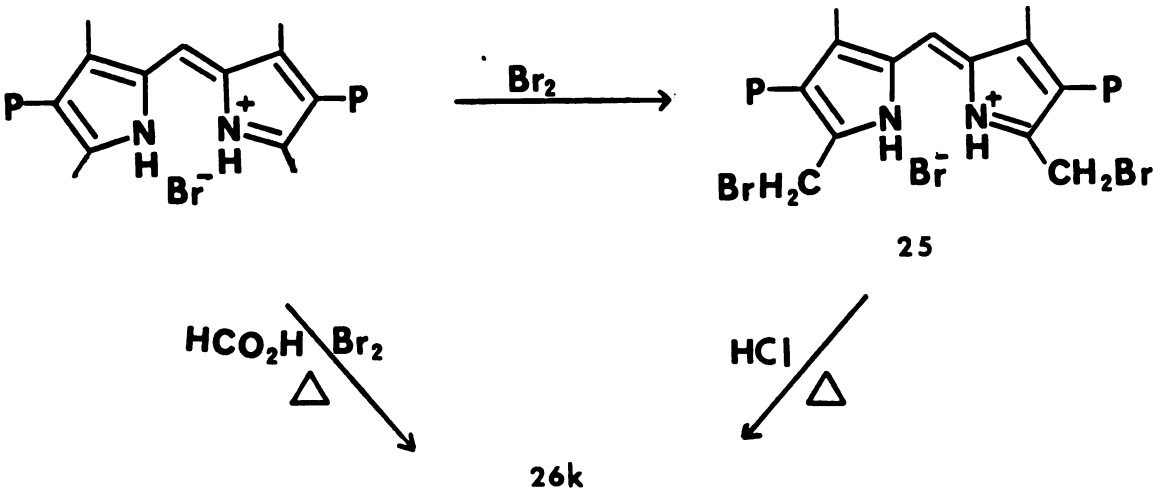
Instead of using bromine, saturated HBr-formic acid solution was also effective to bring about dipyrromethene condensation. This can be shown the porphyrin 26d in 30% yield. The tetracarboxylic porphyrin was obtained in self-condensation by 5,5'-dimethyl dipyrromethene in bromine or 5,5'-dibromomethyl dipyrromethene in HCl solution, but the yield was very low (only 4%).

Table 2-2



	R1	R2	R3	R4	R5	R6	R7	R8	%
19a+24 =26a	P	Me	Et	Et	Et	Et	Et	Et	31
19a+16b=26b	P	Me	Me	P	Et	Et	Et	Et	24
19a+16b=26c	A	Me	Me	A	Et	Et	Et	Et	5
19d+16b=26d	P	Me	Me	P	Me	C6	C6	Me	30
									44*
19d+16a=26e	A	Me	Me	A	Me	C6	C6	Me	10
19h+24 =26f	Et	Et	Me	P	Me	P	P	Me	40
19b+16c=16g	EtC1	Me	Me	EtC1	Me	P	P	Me	28
19c+16b=26h	P	Me	Me	P	Me	EtC1	EtC1	Me	23
26i	Vinyl	Me	Me	Vinyl	Me	P	P	Me	
26j	P	Me	Me	P	Me	Vinyl	Vinyl	Me	
16b+16b=26k	P	Me	Me	P	P	Me	Me	P	4
26l	A	Me	Me	A	Me	C5	C5	Me	
26m	Et	Et	Et	Et	Me	P	P	Me	
26n	Me	C8	C8	Me	Me	P	P	Me	
26o	Me	C5	C5	Me	A	Me	Me	A	

* in HBr/HCOOH



The 2-chloroethyl porphyrin 26i and 26j can be readily converted into vinyl groups by elimination under base conditions [20]. The iron complexes derived from these synthetic porphyrins can be combined with globin and other apoproteins. Reconstitution experiments with these hitherto unavailable hemes would shine light on the heme structure-enzyme function relationship of hemoproteins [21].

IV. C-13 Nuclear Magnetic Resonance of Porphyrins

The C-13 nmr spectra of porphyrins [22] and other related compounds [23] are of considerable current interest. The studies concern the electron delocalization pathway in the porphyrin ring [24], pathways of biosynthesis [25] and mechanisms of unpaired spin delocalization in paramagnetic metalloporphyrins [26]. All previous C-13 nmr studies have dealt with natural occurring porphyrins, such as copro-porphyrins, deuteroporphyrin-IX [27] and protoporphyrin-IX [28]. The only synthetic porphyrins previously studied were octaethyl porphyrin and tetraphenyl porphyrin [27].

We have recorded natural abundance C-13 nmr spectra of porphyrins with C_2h and C_2v symmetry as well as many other compounds. The complete spectral assignments for the C-13 nmr spectra of porphyrins were presented in Table 2-3.

(i) The assignment of α-carbon chemical shift

The α-carbons were found in the region between 143 to 147 ppm. The broadening of the signal was caused by the N-H tautomerism of the porphyrin ring [29]. The α-carbons appeared as sharp signals in the spectra of free base porphyrins dissolved in trifluoroacetic acid and of the Zn and Th complexes.

(ii) The assignments of β-carbons

The β-carbons appeared as sharp resonances between 130-140 ppm. The β-carbons in previous reports [27] were separated into those bearing methyl, propionic ester, and ethyl substituents. In the case of coproporphyrins the

Table 2-3. C-13 NMR Data of some Porphyrins

	C_α	C_β-Me	C_β-P	C_β-Alkyl	meso	CH_3	CH_2	CH_2	CO	OCH_3	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8
12d	141.26	139.89	137.43	134.72	96.63	11.70	22.00	37.16	173.73	51.72	26.37	32.71	32.14	22.73	14.10			
	147.02	139.21			96.27													
12b	146.88	139.69	137.26	134.44	96.48	11.60	21.93	37.13	173.68	51.68	26.29	32.93	29.60	31.93	22.71	14.12		
	147.67	139.01			96.14													
	141.44																	
	140.91																	
12f	146.98	139.83	137.38	134.60	96.63	11.72	22.02	37.16	173.67	51.75	26.30	33.03	29.98	29.68	29.35	31.94	22.66	14.07
	147.59	139.12			96.26													
	141.08																	
12c	150.56	139.98	137.38	133.48	96.79	11.52		32.62	172.35	52.23	26.26	32.88	32.12	27.70	14.10			
	149.56	139.09				11.95												
	138.91																	
	138.66																	
12a	138.52	139.76	133.78	133.29	96.59	11.40		32.83	172.31	52.23	26.18	31.86	29.60	31.86	22.70	14.15		
	149.08	138.91				11.78												
12g	150.01	140.04	134.03	133.58	96.87	11.59		32.96	172.36	52.27	26.37	32.96	29.99	29.68	29.35	31.95	22.67	14.06
	150.09	139.16				12.00												

Table 2-3. (cont'd.)

	C_α	C_β-Me	C_β-P	C_β-Alkyl	meso	CH_3	CH_2	CH_2	CO	OCH_3	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8
26b	144.16	136.14	137.80	141.64	96.53	11.53	21.90	37.04	173.56	51.68	19.76	18.48						
				141.76	96.25													
26d	144.95	140.91	137.85	135.73	96.67	11.71	21.94	37.09	173.65	51.70	26.58	33.19	29.77	32.02	22.72	14.14		
	138.46	136.19			96.22	11.57												
26e	144.86	140.68	130.81	135.75	96.30	11.29		32.65	172.03	52.14	26.45	33.11	29.78	31.98	22.74	14.12		
	143.36	137.33			96.83	11.52												
26o	144.91	140.81	131.10	135.92	96.52	11.56		32.46	172.04	52.26	26.43	32.77	32.26	22.75	14.10			
	143.61	137.60			97.09													
26f	146.40	136.96	138.91	141.29	96.19	11.62	21.87	36.99	173.54	51.64	19.67	18.44						
	145.29	135.93	138.72		96.28													
	142.90		137.79															
26m	144.26	136.15	138.15	141.65	96.62	11.62	21.87	37.00	173.59	51.65	19.73	18.47						
					96.05													
26n	144.56	140.92	138.21	135.58	96.61	11.65	21.96	37.04	173.63	51.69	26.44	33.09	30.00	29.70	29.38	31.96	22.69	14.09
	145.23	136.18			96.16													
Meso	144.88	136.15	138.13	142.26	96.34	11.46	21.87	37.00	173.61	51.67	19.76	17.62						
	145.11	135.12		142.19	96.13	11.64												
13	142.84	141.34	138.42	134.86	96.48	11.69	22.03	37.17	173.71	51.71	26.45	32.79	22.74	14.12				
	146.10	140.18		134.98	96.21													
		136.66																
		136.04																
Copro	143.83	136.63	138.33		96.57	11.72	21.94	37.06	173.53	51.76								
Etio	147.33	134.97		142.13	96.25	11.57					19.87	17.67						
	144.33																	

Cβ-Me's were assigned to higher field, around at 136 ppm by comparison with toluene (C-1 = 137.3 ppm). The Cβ-P shifts were assigned to lower field at 138 ppm (C-1 of methyl-3-phenylpropionate = 140.1 ppm).

From the β-carbon chemical shifts of the compounds shown in the Table, the Cβ-Me were separated into two groups, those with a P or A chain on the same pyrrole ring, and those with an alkyl group on the same ring. The chemical shift of Cβ-Me's of proto- or deuteroporphyrin cannot be applied to these compounds. From the data in the Table, we assigned the chemical shift by their substituent environment. Those Cβ-Me's between P (or A) and alkyl groups appeared in the 140 ppm region, but the Cβ-Me between P (or A) and methyl or P and P (26f) appeared at 136±1 ppm. From the chemical shift of Cβ-Me we can determine the environment of the Cβ-Me. The Cβ-P appeared around the 137-138 ppm region as reported with C_2h symmetry compounds. In porphyrins with C_2v symmetry such as 26e, 26f the Cβ-A were shifted to high field by about 3 ppm to 130 ppm. The assignment of the Cβ-A was based on the similar analogous C-1' of methyl phenyl acetate at 134.4 ppm. The Cβ-alkyls appeared in the 133-134 ppm region for the C_2h compounds, and at 165 ppm region for C_2v compounds. The Cβ-ethyl were found around 141-142 ppm by comparing with meso- and deuteroprophyrins.

(iii) <u>The meso carbons</u>

The meso-carbons were assigned unambiguously from the literature [27] in the region around 96 ppm. The environment

of the meso-carbon has little effect on their chemical shift. The splitting of meso-carbon signals were dependent on the symmetry of the molecule. Compounds 12c, 12f, 12g as well as coporporphyrin and deuteroporphyrin exhibited only one meso signal.

(iv) The methyl carbons

The methyl group chemical shift appeared at 11-12 ppm as reported in the literature [27]. In compounds 12b, 12d, and 12f, there was only one methyl signal, in spite of the difference of these two symmetry.

(v) The methyl propionate and acetate carbons

The assignment of the methyl propionate was based on the literature [27]: C-1' (22 ppm); C-2' (37 ppm); carbonyl (173 ppm); methoxy (51 ppm). There was no report about the acetate. From the chemical shift of the methyl phenyl acetate [30], C-1' was assigned at 41.1 ppm, the C-1' of acetate of porphyrin derivatives was assigned at 32 ppm. The 10 ppm difference of the porphyrin and benzene nucleus was also evident in the propionated 21 ppm in porphyrin and 31 ppm in benzene.

(vi) The alkyl group carbons

The assignments of alkyl carbons were based on the literature [31]. Long chain alkyl carbons were assigned on the basis of benzene analogues and octaalkyl porphyrins.

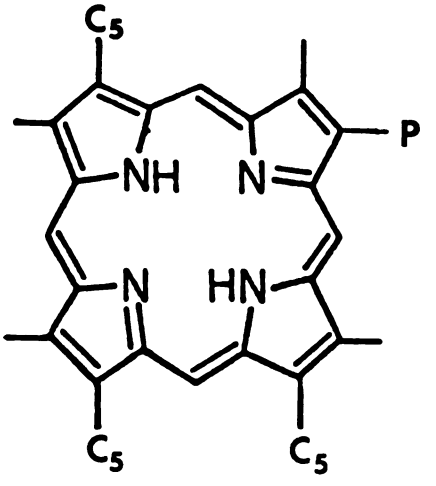
The assignment of the β-carbons in the porphyrins were very difficult, only a few simple porphyrins have been assigned completely. We assigned the synthetic porphyrin

β-carbons based upon their substituent environment, from this, it is also possible to determine the structure of porphyrin.

(vii) Structure determination of porphyrin side product by C-13 nmr

A side product was obtained during the synthesis of porphyrin 12d. The structure of this compound was proved to have one methyl propionate ester and three pentyl side chains by pmr and the mass spectrum. However the relationship between these side chains and the four methyl groups could not be elucidated from pmr. The C-13 nmr of 13, measured in $CDCl_3$ showed that the Cβ-Me's have chemical shifts at 141.34, 140.18, 136.66, 136.04 ppm. From the C-13 chemical shift data obtained from known porphyrins discussed previously, the signals were assigned as below.

The two peaks at 140.18 and 141.34 were assigned to be the Cβ-Me between pentyl and propionate, the two signals at 136.66 and 136.04 belonged to the Cβ-Me between methyl and pentyl. From the arrangement of these four methyl groups, the structure of 13 can be elucidated.



The north hemisphere then must be from the original dipyrromethene, the other dipyrrolemethene arises from the head to head condensation of two C5 pyrroles.

Experimental

Reagents and Solvents

All solvents and reagents were of reagent grade quality, purchased commercially, and used without further purification except noted. Methylene chloride was distilled from calcium hydride. Sulfuryl chloride was redistilled. Silica gel for column chromatography (60-200 mesh) was from J. T. Baker (3405). Preparative silica gel plates were from Analtech, Inc. For analytical TLC, Eastman 13181 chromatography sheet was used.

Physical and Spectroscopic Methods

Melting points were obtained on an Electrothermal melting point apparatus and are uncorrected. Visible spectra were obtained on a Cary 17 or 219 spectrophotometer. The infrared spectra were recorded on a Perkin-Elmer Model 237 B spectrophotometer. The PMR spectra were obtained on a Varian T-60 and Bruker WM250 spectrometer with chemical shifts reported in δ-units measured from tetramethylsilane as the internal standard. A Varian CFT-20 spectrometer was used for C-13 NMR spectra. Mass spectra were obtained in a Hitachi Perkin-Elmer Instrument RMU-6 mass spectrometer and Finnigan 4000 GC/MS system using the direct inlet mode, at 70 ev ionization energy. Field absorption mass spectra were obtained from Varian CH-5 mass spectrometer. Elemental

analyses were done by Spang Microanalytical Laboratory, Eagle Harbor, Michigan.

General procedures for the synthesis of 3-alkyl-2,4-pentanedione, 3-Ethyl-2,4-hexanedione-BF_2 Complex

Boron trifluoride gas was slowly bubbled through a mixture of 2-pentanone (43 g, 0.5 mol) and propanoic anhydride (130 g, 1.0 mol) in such a manner that the temperature of the mixture was kept below 50°C. After the absorption of boron trifluoride has ceased the mixture was poured into ice/water (500 ml). The solid product was collected by filtration and recrystallized from methanol; yield: 85 g (89%); m.p. 75-77°C; p.m.r. 1.08 (t, J = 8 Hz, 3H), 1.22 (t, J = 8 Hz, 3H), 2.32 (s, 3H), 2.33 (q, J = 8 Hz, 2H), 2.60 (q, J = 8 Hz, 2H).

3-Ethyl-2,4-hexanedione 3d

3-Ethyl-2,4-hexanedione-BF_2 complex (11 g) was dissolved in methanol (50 ml). This solution was brought to PH 9 by adding 50% aqueous sodium hydroxide. The mixture was refluxed on a steam bath for 15 min, methanol was removed in a rotary evaporator, and the residue was taken up in ether (50 ml). The solution was dried with sodium sulfate, the ether evaporated, and the residue distilled; yield: 6.5 g (80%); b.p. 191-193°C; p.m.r. 0.37 (t, J = 7 Hz, 3H), 1.02 (t, J = 7 Hz, 3H), 1.80 (t, J = 7 Hz, 2H), 2.08 (s, 3H), 2.44 (q, J = 7 Hz, 2H), 3.52 (t, J = 7 Hz, 1H), 16.3 (s, broad, 15% of 1H).

3-Pentyl-2,4-pentanedione BF_2 Complex

This compound was prepared as above, b.p. 155-157°/2 mmHg; p.m.r. 0.9 (braod, 3H, $-(CH_2)_4-\underline{CH_3}$), 1.33 (broad, 6H, $-(\underline{CH_2})_3-CH_3$), 2.20 (t, J = 8 Hz, 2H, $-\underline{CH_2}-C_4H_9$), 2.30 (s, 6H, $-CH_3$).

3-Pentyl-2,4-pentanedione 3a

3a was obtained as above, b.p. 123-125°/20 mmHg; p.m.r. 0.87 (broad, 3H, $-(CH_2)_4-\underline{CH_3}$), 1.26 (broad, 6H, $-CH_2-(\underline{CH_2})_3-CH_3$), 1.67-2.00 (broad, 2H, $-\underline{CH_2}-C_4H_9$), 2.17 (s, 6H, $-CH_3$), 3.57 (t, J = 7.0 Hz, methine proton), 16.3 (s, enol form, -OH).

Ethyl-3-acetyl-4-oxopentanoate 3c

Ethyl chloroacetate (551 g) was added slowly to a stirred mixture of acetylacetone (450 g), anhydrous potassium carbonate (570 g), and dry acetone (500 ml). During the addition the mixture was heated to reflux. When all the acetate was added, the mixture was kept refluxing for a further 1 hr. The mixture was filtered when cool, and the acetone removed under reduced pressure. The residual oil was fractionated twice under vacuum. Yield: 500 g (60%); b.p. 110-5°/0.1 mmHg; p.m.r. 1.27 (t, J = 7.0 Hz, $-CH_2\underline{CH_3}$), 2.17 (s, $-CH_3$ enol form), 2.27 (s, $-CH_3$ keto form), 2.86 (d, J = 7.0 Hz, $-\underline{CH_2}$-COOEt, keto form), 3.25 (s, $-\underline{CH_2}$-COOEt, enol form), 4.10 (t, J = 7.0 Hz, methene proton), 4.13 (q, J = 7.0 Hz, $-\underline{CH_2}CH_3$). The ratio of enol:keto = 1:3. M^+ = 186.

The general procedure of the synthesis of pyrroles (4a-e)

Benzyl 3,5-dimethylpyrrole-2-carboxylate 4e

1030 g (5 mol) of benzyl acetoacetate [32] in 1080 g (18 mol) acetic acid were kept at room temperature with stirring, 1242 g of sodium nitrite in 1560 ml water were added through a peristatic pump into the acetic acid solution during 20 hrs. After the addition, the upper (organic) layer of benzyl oximinoacetoacetate was separated, no further purification was necessary.

In a three neck 12 l round bottom flask equipped with mechanical stirrer, 6 moles of diketone and 3000 ml acetic acid were added. The benzyl oximinoacetoacetate was slowly added to the flask by a pump while 200 g of zinc dust were added gradually. The temperature rose to around 90-95^{o}C. More zinc dust was added during the reaction to keep the temperature at 90-95^{o}C. After the reaction was over (6 hrs), excess zinc and zinc acetate was allowed to precipitate. The brown liquid, still hot, was decanted to a bucket containing 10 l water. After cooling the product of pyrrole was collected by filtration and washed by water. The solid was dissolved in methylene chloride and filtered. The methylene chloride solvent was removed under reduced pressure. The pyrroles were recrystalized from methanol to give a slightly yellow crystal; p.m.r. 2.2 (s, 3H, CH_3), 2.3 (s, 3H, CH_3), 5.2 (s, 2H, $\underline{CH_2}$Ø), 5.7 (broad, 1H), 7.2 (s, 5H, phenyl protons).

Benzyl 4-pentyl-3,5-dimethylpyrole-2-carboxylate (4a)

M.P. 65-66°C; p.m.r. 0.83 (broad triplet, 3H, $-CH_3$), 1.27 (broad, 6H, $-CH_2-(\underline{CH_2})_3-CH_3$), 2.10 (s, 3H, $-CH_3$), 2.20 (s, 3H, $-CH_3$), 2.20 (broad, 2H, $-\underline{CH_2}-C_4H_9$), 5.17 (s, 2H, $-CH_3$), 7.20 (s, 5H, -Ø), 8.50 (broad, 1H, -NH). M^+ = 289.

Benzyl 4-methylcarboxyethyl-3,5-dimethylpyrrole-2-carboxylate [33] 4b

Yield: 47%; m.p. 96-98°C.

Benzyl 4-ethylcarboxymethyl-3,5-dimethylpyrrole-2-carboxylate 4c

Yield: 45%; m.p. 74-76°C.

Benzyl 3,4-diethyl-5-methyl-2-carboxylate [34] 4d

Yield: 43%; m.p. 72°C.

Benzyl 4-(1-oxo-hexane)-3,5-dimethyl-2-carboxylate-pyrrole 5

57.3 g of pyrrole 4e was dissolved in 300 ml dry methylene chloride. This solution was cooled to 10°C in an ice bath and 35 ml of hexanoyl chloride was added. To this mixture 40 ml of $SnCl_4$ was added dropwise through a pressure-equalizing dropping funnel. The reaction temperature was kept below 15°C. After all $SnCl_4$ was added, the mixture was kept stirring for 1 hr in the ice bath. A sample was withdrawn and mixed with 2 ml of methylene chloride and 10 ml water. The organic solution was spotted on silica gel TLC and developed in CH_2Cl_2. When there was no starting material left, the reaction mixture was poured into 200 ml of cold water, the organic layer was separated and washed twice with

sodium carbonate solution, and water. The solvent was removed under reduced pressure. A white crystalline solid was obtained after recrystalized in methanol; m.p. 86°C; p.m.r. 0.87 (broad, 3H, $-CH_3$), 1-00-1.60 (broad, 6H, $-CH_2-(\underline{CH_2})_3-CH_3$), 2.43 (s, 3H, $-CH_3$), 2.56 (s, 3H, $-CH_3$), 2.67 (t, J = 7.0 Hz, 2H, $-\underline{CH_2}-CO-$), 5.20 (s, 2H, $-\underline{CH_2}\emptyset$), 7.23 (s, 5H, phenyl protons), 9.00 (broad, 1H, -NH).

Benzyl 4-hexyl-3,5-dimethylpyrrole-2-carboxylate 6

In a 250 ml flask, 32 g of pyrrole 5 was dissolved in 100 ml THF, 8 g of sodium borohydride was added. The mixture was cooled to 10°C with stirring in an ice bath. To this mixture, 35 ml of trifluoroborane-etherate was added dropwise such that the temperature of the mixture was below 15°C. After the addition of BH_3 was completed, the mixture was kept in ice bath for another 2 hr. The mixture was poured into 200 ml ice water, 50 ml concentrated HCl and 200 ml chloroform were added. The organic layer was separated and washed first with 200 ml 0.5 N HCl, then water. 50 ml of methanol was added to the methylene chloride solution before it was evaporated to dryness. The residue was recrystalized with methanol to afford pyrrole 13.5 g (yield 43%); p.m.r: 0.87 (broad, 3H, $-(CH_2)_5-\underline{CH_3}$), 1.33 (broad, 8H, $-CH_2-(\underline{CH_2})_4-CH_3$), 2.13 (broad, 2H, $-\underline{CH_2}-C_5H_{11}$), 2.16 (s, 3H, $-CH_3$), 2.27 (s, 3H, $-CH_3$), 5.20 (s, 2H, $-CH_2\emptyset$), 7.23 (s, 5H, phenyl protons), 8.50 (broad, 1H, NH).

Benzyl 4-(2-hydroxyethyl)-3,5-dimethylpyrrole-2-carboxylate 7

Benzyl-4-(2-methoxycarboxymethyl)-3,5-dimethylpyrrole-2-carboxylate (5 g, 0.02 mole) was dissolved in 100 ml dry THF and 1 M solution of borane-tetrahydrofuran complex 50 ml was added dropwise during 45 min. Methanol was then carefully added until the vigorous reaction ceased. The solvent was removed on a rotary evaporator, and the hydroxyethylpyrrole 7, 4.5 g (99%) was crystallized from benzene-petroleum ether to give white needle; m.p. 120-121°C; p.m.r. 2.16 (s, 3H, $-CH_3$) 2.23 (s, 3H, $-CH_3$), 2.60 (t, J = 7.0 Hz, 2H, $-\underline{CH_2}-CH_2-OH$), 3.71 (t, J = 7.0 Hz, 2H, $-CH_2-\underline{CH_2}-OH$), 5.23 (s, 2H, $-\underline{CH_2}\emptyset$), 7.27 (s, 5H, phenyl protons).

Benzyl 4-(2-chloroethyl)-3,5-dimethylpyrrole-2-carboxylate 8

Benzyl-4-(2-hydroxyethyl)-3,5-dimethylpyrrole-2-carboxylate 7 (2.8 g) in 20 ml dry methylenechlordie and 1 ml pyridine was heated at 50°C, 1 ml thionyl chloride was rapidly added. Dry nitrogen was then passed through the solution at 50°C for 1 hr. 100 ml of methylene chloride was added and the solution washed with 2N HCl, saturated aqueous sodium bicarbonate solution, and then water. The organic layer was dried over sodium sulfate and evaporated to dryness. The residue was recrystallized from methanol to give 8 (2.5 g, 84%); m.p. 120-121°C. p.m.r. 2.17 (s, 3H, $-CH_3$), 2.23 (s, 3H, $-CH_3$), 2.77 (t, J = 7.0 Hz, 2H, $-\underline{CH_2}Cl$), 3.43 (t, J = 7.0 Hz, 2H, $-\underline{CH_2}CH_2-Cl$), 5.17 (s, 2H, $-\underline{CH_2}\emptyset$), 7.22 (s, 5H, phenyl H), 10.90 (broad, 1H, NH).

Benzyl 5-formyl-4-hexyl-3-methylpyrrole-2-carboxylate 9a

Pyrrole 6 (23 g) was dissolved in 250 ml dry methylene chloride and 21 g of sulfuryl chloride in 200 ml dry methylene chloride was added to the stirring pyrrole solution at $0^{o}C$ in an ice/salt bath. The addition of sulfuryl chloride took about 4 hr. After completion of addition, the solution was stirred for additional 30 minutes at room temperature, and 300 ml 50% aqueous methanol was added and the mixture was stirred overnight. The organic layer was separated and reduced to 200 ml. The brown solution was shaked with 100 ml 50% aqueous methanol, the methylene chloride layer was separated and washed with sodium bicarbonate solution, then washed with water. Evaporation of the solvent afforded a brown oil which solidified on standing, the solide was recrystallized from 95% MeOH to give a pale yellow product. p.m.r. 0.83 (broad, 3H, $-CH_3$), 1.30 (broad, 8H, $-(\underline{CH_2})_4-CH_3$), 2.27 (s, 3H, $-CH_3$), 2.67 (t, J = 7.0 Hz, 2H, $-\underline{CH_2}-C_5H_{11}$), 5.27 (s, 2H, $-CH_2\emptyset$), 7.33 (s, 5H, phenyl protons), 9.70 (s, 1H, aldehyde proton). m.p. $55^{o}C$.

Benzyl 5-formyl-4-pentyl-3-methylpyrrole-2-carboxylate 9b

This compound was obtained using the procedure for 9a. p.m.r. 0.83 (broad, 3H, $-CH_3$), 1.33 (broad, 6H, $-(\underline{CH_2})_3-CH_3$), 2.23 (s, 3H, $-CH_3$), 2.67 (t, J = 7.0 Hz, 2H, $-\underline{CH_2}-C_4H_9$), 5.27 (s, 2H, $-\underline{CH_2}-\emptyset$), 7.24 (s, 5H, phenyl protons), 8.70 (broad, 1H, NH), 9.60 (s, 1H, aldehyde proton). m.p. $62-63^{o}C$. M^{+} = 313.

Benzyl 5-formyl-4-methoxycarbonylethyl-3-methylpyrrole-2-carboxylate 9c

This compound was obtained as above, p.m.r. 2.27 (s, 3H, $-CH_3$), 2.50 (t, J = 6.0 Hz, 2H, $-\underline{CH_2}-COOCH_3$), 3.00 (t, J = 6.0 Hz, 2H, $-\underline{CH_2}-CH_2-COOCH_3$), 3.57 (s, 3H, OCH_3), 5.23 (s, 2H, $-\underline{CH_2}\emptyset$), 7.23 (s, 5H, phenyl protons), 9.67 (s, 1H, aldehyde proton). m.p. 75°C. M^+ = 329.

Catalytic hydrogenolysis of benzyl ester pyrroles or dipyrromethanes

The identical procedure was used for all benzyl esters. The appropriate pyrrole ester (0.1 mol) was dissolved in 200 ml dry THF and a few drops of triethylamine and 1 g of 10% palladized charcoal was added. The mixture was stirred under 1 atm of hydrogen until hydrogen uptake had ceased (3-24 hr). The filtrated solution was evaporated to dryness in vacuo, to give the pink pyrrole acid in almost quantitative yield. The pyrrole acids can be stored in freezer for months without decomposition.

General synthesis procedure of the C_2h porphyrins

2-Methyl-5-carboxylic acid pyrrole 11, 15 mmol, and 5-carboaldehyde-2-carboxylic acid pyrrole 10, 15 mmol, were dissolved in 80 ml methanol and 80 ml acetonitrile. The solution was heated on a steam bath for 5 min then 2.5 ml of 48% HBr solution was added. The mixture was kept refluxing for 30 min and then evaporated under reduced pressure. The dark brown residue was dried under vacuum overnight. The dipyrromethene was dissolved in 15 ml anhydrous formic acid and heated on an oil bath to 80°C for 5 min, bromine (0.9 ml,

20 mmol) was added slowly and the oil bath temperature was raised to 120-125°C. The mixture was refluxed for 2-2.5 hr. The solvent was then boiled off by blowing air into the flask. The black residue was dissolved in 100 ml methanol and 5 ml concentrated sulfuric acid was added, followed by 20 ml trimethyl orthoformate. After standing overnight, the mixture was basified with triethylamine and evaporated to dryness. The crude methyl esters were chromatographed on silica gel, using methylene chloride as eluent, a dark non-fluorescent fraction was discarded, the porphyrin fraction was concentrated and precipitated with methanol. Yield: 10-20% from pyrroles. The physical properties of porphyrins are listed below.

Porphyrin 12a

m.p. 208-210°C. p.m.r. 0.90 (broad, 6H, $-(CH_2)_5-\underline{CH_3}$), 1.50 (broad, 12H, $-CH_2-(\underline{CH_2})_3-CH_3$), 2.13 (broad, 4H, $-\underline{CH_2}-C_4H_9$), 3.42 (s, 6H, $-CH_3$), 3.47 (s, 6H, $-CH_3$), 3.67 (s, 6H, $-OCH_3$), 3.83 (t, 4H, $-\underline{CH_2}-C_5H_{11}$), 4.80 (s, 4H, $-\underline{CH_2}-COOCH_3$), 9.70, 9.73 (s, 4H, meso protons), -3.96 (broad, NH). VIS: 397, 497, 532, 566, 620 nm. M^+ = 678.

Porphyrin 12b

m.p. 146-148°C. p.m.r. 0.90 (broad, 6H, $-(CH_2)_5-\underline{CH_3}$), 1.60 (broad, 12H, $-(\underline{CH_2})_3-CH_3$), 2.27 (broad, 4H, $-\underline{CH_2}-C_4H_9$), 3.20 (t, J = 7.0 Hz, 4H, $-\underline{CH_2}-COOCH_3$), 3.53 (s, 6H, $-CH_3$), 3.56 (s, 6H, $-CH_3$), 3.67 (s, 6H, $-OCH_3$), 3.97 (t, J = 6.0 Hz, 4H, $-\underline{CH_2}-C_5H_{11}$), 4.30 (t, J = 7.0 Hz, 4H, $-\underline{CH_2}-CH_2-COOCH_3$), 10.0 (s, 4H, meso protons). VIS: 400, 498, 536, 565, 620 nm. M^+ = 706.

Porphyrin 12c

m.p. 190°C. p.m.r. 0.96 (broad, 6H, $-(CH_2)_5-\underline{CH_3}$), 1.60 (broad, 8H, $-(CH_2)_2-CH_3$), 2.17 (broad, 4 H, $-\underline{CH_2}-C_3H_7$), 3.17 (t, 4H, $-\underline{CH_2}-COOCH_3$), 3.57 (s, 6H, $-CH_3$), 3.60 (s, 6H, $-CH_3$), 3.63 (s, 6H, $-OCH_3$), 4.0 (t, J = 7.0 Hz, $-\underline{CH_2}-C_4H_9$), 4.33 (t, J = 7.0 Hz, $-\underline{CH_2}-CH_2-COOCH_3$), 9.93 (s, 4H, meso protons). VIS: 398, 496, 532, 566, 618 nm. M^+ = 650.

Porphyrin 12d

m.p. 221°C. p.m.r. 0.93 (broad, 6H, $-(CH_2)_4-\underline{CH_3}$), 1.57 (broad, 8H, $-(\underline{CH_2})_2-CH_3$), 2.37 (b, 4H, $-\underline{CH_2}-C_3H_7$), 3.43 (s, 6H, $-CH_3$), 3.47 (s, 6H, $-CH_3$), 3.70 (s, 6H, $-OCH_3$), 3.83 (t, 4H, $-\underline{CH_2}-C_4H_9$), 4.8 (s, 4H, $-\underline{CH_2}-COOCH_3$), 9.70, 9.77 (s, 4H, meso protons). VIS: 400, 500, 516, 534, 620 nm. M^+ = 622.

Porphyrin 12e

p.m.r. 3.68 (s, 12H, $-CH_3$), 3.90 (s, 6H, $-OCH_3$), 4.24 (t, J = 8.0 Hz, 4H, $-CH_2-\underline{CH_2}-Cl$), 4.56 (t, J = 8.0 Hz, 4H, $-\underline{CH_2}-CH_2-Cl$), 5.12 (s, 4H, $-\underline{CH_2}-COOCH_3$), 10.08, 10.24 (s, 4H, meso protons), -4.06 (b, 2H, NH). VIS: 400, 495, 530, 565, 620 nm.

Porphyrin 13

m.p. 139-140°C. p.m.r. (250 MHz): 0.95 (t, 9H, $-(CH_2)_4-\underline{CH_3}$), 1.55 (m, 6H, $-(CH_2)_3-\underline{CH_2}-CH_3$), 0.70 (m, 6H, $-(\underline{CH_2})-C_2H_5$), 2.28 (m, 6H, $-\underline{CH_2}-C_3H_7$), 3.28 (t, 2H, $-CH_2-\underline{CH_2}-COOCH_3$), 3.59 (broad, 12H, $-CH_3$), 3.70 (s, 3H, OCH_3), 4.02 (m, 6H, $-\underline{CH_2}-C_4H_9$), 4.40 (t, 2H, $\underline{CH_2}-CH_2-COOCH_3$), 10.03 (s, 4H, meso protons). M^+ = 622.

Porphyrin 14

p.m.r.: 0.90 (b, 9H, $(CH_2)_5$-$\underline{CH_3}$), 1.50 (b, 18H, -$(\underline{CH_2})_3$-CH_3), 2.23 (b, 6H, -$\underline{CH_2}$-C_4H_9), 3.5 (s, 12H, -CH_3), 3.67 (s, 6H, -OCH_3), 3.90 (b, 6H, -$\underline{CH_2}$-C_5H_{11}), 4.67 (s, 2H, -$\underline{CH_2}$-$COOCH_3$), 9.80 (s, 4H, meso protons), -3.73 (b, 2H, NH).

Porphyrin 15

p.m.r.: 3.64 (s, 12H, -CH_3), 3.88 (s, 3H, -OCH_3), 4.24 (t, J = 8.0 Hz, 6H, -CH_2-$\underline{CH_2}$-Cl), 4.48 (t, J = 8.0 Hz, 6H, -$\underline{CH_2}CH_2$-Cl), 5.08 (s, 2H, -$\underline{CH_2}$-$COOCH_3$), 10.12 (s, 3H, meso protons), 10.28 (s, 1H, meso proton), -4.16 (b, 2H, NH). VIS: 402, 500, 532, 568, 622 nm.

3,3'-(2-Hydroxycarbonylmethyl)-2,2',4,4'-tetramethyl-5,5'-dipyrromethenium bromide 16a

2-Methoxycarbonylmethyl pyrrole 4c (16 g) was hydrogenolyzed with 10% Pd/C in THF. The α-acid pyrrole was refluxed in 100 ml formic acid plus 20 ml 48% HBr on a steam bath for 4 hr. After cooling, 12 g (60%), Of 16a was obtained. p.m.r. ($CDCl_3$/TFA): 2.33 (s, 6H, -CH_3), 2.57 (s, 6H, -CH_3), 3.57 (s, 4H, -$\underline{CH_2}$-COOH), 7.17 (s, 1H, methine proton).

3,3'-(2-Methoxycarbonyl)-2,2',4,4'-tetramethyl-5,5'-dipyrromethenium bromide 16b

2-Methoxycarbonylmethyl pyrrole 20 g was catalytically hydrogenolyzed to acid. After reacted with 48% HBr, 13.4 g (99%) of 16b was obtained. m.p. 206-207°C. p.m.r.: 2.23 (s, 6H, -CH_3), 2.50 (t, J = 6.0 Hz, 4H, CH_2-$\underline{CH_2}$-$COOCH_3$), 2.63 (s, 6H, -CH_3), 2.70 (t, J = 6.0 Hz, -$\underline{CH_2}CH_2$ $COOCH_3$),

3.57 (s, 6H, $-OCH_3$), 6.90 (s, 1H, methine proton), 9.63 (b, 2H, NH).

3,3'-(2-Chloroethyl)-2,2',4,4'-tetramethyl-5,5'-dipyrromethenium bromide 16c

m.p. 217-219°C. p.m.r.: 230 (s, 6H, $-CH_3$), 2.67 (s, 6H, $-CH_3$), 2.93 (t, J = 6.0 Hz, 4H, $-CH_2\underline{CH_2}Cl$), 3.37 (s, J = 6.0 Hz, 4H, $-\underline{CH_2}-CH_2Cl$), 6.97 (s, 1H, methine proton), 9.67 (b, 2H, NH).

5-Acetoxymethyl-2-ethoxycarbonyl-3,4-diethylpyrrole 17a

2-Ethoxycarbonyl-3,4-diethyl-5-methylpyrrole 4d (20.9 g) was dissolved in 100 ml acetic acid containing 2 ml acetic anhydride and lead acetate (48 g) was added all at once. The mixture was stirred by magnetic stirrer and after a brief induction period, the mixture dissolved, reacting exothermically. The mixture was warmed briefly to 60°C to ensure completion of reaction. 5-10 ml of ethylene glycol was added to reduce any remaining lead (IV) followed by 400 ml water. The precipitates were throughly washed with water and filtered to yield 19.5 g solid which were pure enough for further reactions. m.p. 70-72°C. p.m.r. 1.07 (t, J = 7.0 Hz, 3H, $-CH_3$), 1.10 (t, J = 7.0 Hz, 3H, $-CH_3$), 1.32 (t, J = 7.0 Hz, 3H, $-CH_3$), 2.00 (s, 3H, $COCH_3$), 2.41 (q, J = 7.0 Hz, 2H, $-\underline{CH_2}CH_3$), 2.67 (q, J = 7.0 Hz, 2H, $-\underline{CH_2}CH_3$), 4.23 (q, J = 7.0 Hz, 2H, $-OCH_3$), 4.93 (s, 2H, $-\underline{CH_2}OAc$), 8.8 (b, 1H, NH). M^+ = 267.

Benzyl 5-acetoxymethyl-4-(2-chloroethyl)-3-methyl-pyrrole-2-carboxylate 17c

Lead tetraacetate 4.0 g was added in portions during 2 hr to a stirred solution of 2-chloroethylpyrrole 2.6 g in 100 ml acetic acid and 2 ml acetic anhydride. After stirring at room temperature overnight, water (200 ml) was added to form precipitates. The solid was collected by filtration, washed with water and then dried under vacuum. The acetoxymethyl-pyrrole 17c (2.9 g, 97%) was recrystallized from methanol; m.p. 166-169°C. p.m.r. 2.00 (s, 3H, $-CH_3$), 2.23 (s, 3H, $-CH_3$), 2.85 (t, J = 7.0 Hz, 2H, $-\underline{CH_2}Cl$), 3.45 (t, J = 7.0 Hz, 2H, $-\underline{CH_2}CH_2Cl$), 4.93 (s, 2H, $-\underline{CH_2}OAc$), 5.20 (s, 2H, $-\underline{CH_2}\emptyset$), 7.23 (s, 5H, phenyl protons), 9.00 (broad, 1H, NH).

Benzyl 5-acetoxymethyl-4-hexyl-3-methylpyrrole-2-carboxylate 17d

4-Hexylpyrrole 34 g was dissolved in 200 ml acetic acid and 10 ml acetic anhydride. Lead tetraacetate (50 g) was added in portions during 2 hrs. The mixture was stirred at 50°C overnight. 500 ml water was added to precipitate the product. The solid was collected by filtration. m.p. 83-85°C (98%). p.m.r. 0.83 (broad, 3H, $-(CH_2)_5-\underline{CH_3}$), 1.27 (s, 8H, $-(\underline{CH_2})_4-CH_3$), 2.00 (s, 3H, $COCH_3$), 2.23 (s, 3H, $-CH_3$), 2.35 (broad, 2H, $-\underline{CH_2}-C_5H_{11}$), 4.90 (s, 2H, $-\underline{CH_2}-OAc$), 5.20 (s, 2H, $-\underline{CH_2}\emptyset$), 7.23 (s, 5H, phenyl protons), 8.87 (broad, NH), M^+ = 371.

5,5'-Diethoxycarbonyl-3,3'4,4'-tetraethyl-2,2'-dipyrromethane 18a

17a (15 g, 0.057 mol) dissolved in 95% ethanol (100 ml) was heated to boiling on a steam bath. Concentrated HCl (1 ml) was added and the heating was continued for an hour. The solution was then allowed to cool overnight; light yellow chunky solid crystallized out. 11 g was collected (96%). m.p. 84-85°C. p.m.r. 1.16 (t, J = 7.0 Hz, 6H, $-CH_2\underline{CH_3}$), 1.30 (t, J = 7.0 Hz, $-CH_2\underline{CH_3}$), 2.70 (q, J = 7.0 Hz, 4H, $-\underline{CH_2}CH_3$), 3.80 (s, 2H, methene protons), 4.20 (q, J = 7.0 Hz, $-COO\underline{CH_2}-CH_3$), 8.58 (broad, 2H, NH). M^+ = 402.

2,2'-Dibenzyl-3,3',4,4'-tetraethyl-2,2'-dipyrromethane dicarboxylate 18a'

11 g of 18a was added to 50 ml refluxing benzyl alcohol under nitrogen. 10 ml of sodium benzylate solution prepared by dissolving a small piece of sodium (1 g) in benzyl alcohol (20 ml) was added into the mixture and the refluxing was continued for 3 hrs. The reaction mixture was cooled to about 100°C and poured into icewater (500 ml). The solid was collected by filtration. The product of 13 g 18a' (91%) was pure enough for further reactions. p.m.r. 0.80-1.40 (two sets of triplet, J = 8.0 Hz, 12H, $-CH_2\underline{CH_3}$), 2.40 (q, J = 8.0 Hz, 4H, $-\underline{CH_2}CH_3$), 2.73 (q, J = 8.0 Hz, 4H, $-\underline{CH_2}CH_3$), 3.78 (s, methene proton), 5.20 (s, 4H, $-\underline{CH_2}\text{Ø}$), 7.20 (s, 5H, phenyl protons), 7.23 (s, 5H, phenyl protons). M^+ = 526.

2,2'-Dibenzyl-3,3'-di(2-chloroethyl)-4,4'-dimethyl-5,5'-dipyrromethane dicarboxylate 18c

The 4-(2-chloroethyl)-5-acetoxypyrrole 2.9 g was dissolved in a mixture of 100 ml ethanol and 20 ml concentrated HCl, and the solution was heated under reflux on a steam bath for 5 hr. After cooling, methylene chloride (100 ml) was added and the solution was washed first with 5% aqueous sodium bicarbonate solution, then with water, separated, and dried over sodium sulfate, and evaporated to dryness. After recrystalized from methanol, 2.35 g of the dipyrromethane 18c (50%) was obtained. m.p. 134-135°C. p.m.r. 2.21 (s, 6H, $-CH_3$), 2.77 (t, J = 7.0 Hz, 4H, $-CH_2\underline{CH_2}Cl$), 3.33 (t, J = 7.0 Hz, 4H, $-\underline{CH_2}CH_2Cl$), 3.77 (s, 2H, methylene protons), 5.10 (s, 4H, $-\underline{CH_2}\emptyset$), 7.10 (s, 10H, phenyl protons), 9.70 (broad, 2H, NH).

2,2'-Dibenzyl-4,4'-dihexyl-3,3'-dimethyl-5,5'-dipyrromethane dicarboxylate 18d

m.p. 93-95°C. p.m.r. 0.87 (b, 6H, $-(CH_2)_5-\underline{CH_3}$), 1.32 (b, 16H, $-(\underline{CH_2})_4-CH_3$), 2.20 (s, 6H, $-CH_3$), 2.33 (b, 4H, $\underline{CH_2}-C_5H_{11}$), 3.70 (s, 2H, methene protons), 5.10 (s, 4H, $-\underline{CH_2}\emptyset$), 7.10 (s, 10H, phenyl protons), 9.02 (broad, 2H, NH). M^+ = 610.

2,2'-Dibromo-3,3',4,4'-tetraethyl-5,5'-dipyrromethenium bromide 19a

13 g of 18a was hydrogenolyzed with pd/c catalyst in THF as described above. A solution of bromine (10 g) in dry formic acid (100 ml) was poured into the dicarboxylic acid

solution and the mixture swirled until mixing was complete. The solution was allowed to stand overnight. The crystals were collected by filtration, washed with ether to give pure 13 g (100%) of product. m.p. 145-147°C. p.m.r. 1.10 (t, J = 7.0 Hz, 6H, $-CH_2\underline{CH_3}$), 1.23 (t, J = 7.0 Hz, 6H, $-CH_2\underline{CH_3}$), 2.43 (q, J = 7.0 Hz, 4H, $-\underline{CH_2}CH_3$), 2.70 (q, J = 7.0 Hz, 4H, $-\underline{CH_2}CH_3$), 7.10 (s, 1H, methine proton).

5,5'-Dibromo-3,3'-di(2-methoxycarbonylethyl)-4,4'-dimethyl-2,2'-dipyrromethenium bromide 19b

19b was obtained as described in reference 15.

2,2'-Dibromo-4,4'-(2-chloroethyl)-3,3'-dimethyl-5,5'-dipyrromethenium bromide 19c

The compound 19c was prepared as above. m.p. >300°C. Yield: 20%. p.m.r. ($CDCl_3$/TFA), 2.07 (s, 6H, $-CH_3$), 3.13 (t, J = 6.0 Hz, $-CH_2\underline{CH_2}Cl$), 3.62 (t, J = 6.0 Hz, 4H, $-\underline{CH_2}CH_2-Cl$), 7.20 (s, 1H, methine proton).

2,2'-Dibromo-4,4'-dihexyl-3,3'-dimethyl-5,5'-dipyrromethenium bromide 19d

The compound 19d was prepared as above. m.p. 198-200°C. Yield: 53%. p.m.r. 0.87 (b, 6H, $-(CH_2)_5-\underline{CH_3}$), 1.33 (b, 16H, $-(\underline{CH_2})_4-CH_3$), 2.00 (s, 6H, $-CH_3$), 2.67 (b, 4H, $-\underline{CH_2}-C_5H_{11}$), 7.00 (s, 1H, methine proton).

4'-(2-Hydroxycarbonylethyl)-3,4-diethyl-3',5,5'-trimethyl-2,2'-dipyrromethenium bromide 24

3-(2-Methoxycarbonylethyl)-2,4-dimethylpyrrole 3b (1.87 g 0.11 mole) and 2-formyl-3,4-diethyl-5-methylpyrrole 22 (2.06 g 0.11 mole) were heated in 20 ml methanol on a steam

bath. 48% HBr (15 ml) was added in one portion to the hot solution and heating was continued for 80 minutes until gas evolution (carbon dioxide) ceased. On standing at room temperature overnight, brown needle crystallized. The product was collected by filtration, washed with ether and air dried to give 4.23 g (95%). m.p. 183-184^{o}C. p.m.r. 1.06 (t, J = 8.0 Hz, 3H, $-CH_2-\underline{CH_3}$), 1.20 (t, J = 8.0 Hz, 3H, $-CH_2-\underline{CH_3}$), 2.23 (s, 3H, $-CH_3$), 2.63 (s, 6H, $-CH_3$), 2.40-3.00 (b, 4H, $-\underline{CH_2}CH_2COOH$), 6.90 (s, 1H, methine proton), 12.8 (b, 2H, NH).

Porphyrin Synthesis from Dipyrromethenium bromide

2,2'-Dimethyldipyrromethenium bromide (1.0 mmol) and 2,2'-dibromodipyrromethenium bromide (1.0 mmol) were suspended in formic acid (5.0 ml, 100%). The mixture was refluxed in an oil bath (120^{o}C), the 50.1 ul of bromine was added. The solution was refluxed for 2.5-3 hrs. The solvent was then allowed to boil off. The residue was dissolved in 20 ml methanol and then 1 ml concd. sulfuric acid and 10 ml trimethyl orthoformate were added. After standing overnight, 30 ml dichloromethane and 100 ml water were added to the mixture. The organic layer was washed, separated, and evaporated to dryness. The crude product was purified by chromatography on silica gel TLC plates, using dichloromethane: methanol 95:5, as the developing solvent. The porphyrin band was collected and rinsed off with methanol:methylene chloride 5:95. After removal of solvent, the solid was dissolved in minimum amount of methylene chloride and diluted with methanol to precipitate the crystals.

Methyl-1,2,3,4,5,8-hexaethyl-6-methyl-7-propionate porphyrin 26a

m.p. 185-186°C. p.m.r. 1.85 (t, J = 7.5 Hz, 18H, $-CH_2-\underline{CH_3}$), 3.08 (t, J = 7.5 Hz, 2H, $-CH_2\underline{CH_2}COOCH_3$), 3.40 (s, 3H, $-CH_3$), 3.50 (s, 3H, $-COOCH_3$), 3.93 (q, J = 7.5 Hz, 12H, $-\underline{CH_2}-CH_3$), 4.17 (t, J = 7.5 Hz, 2H, $-\underline{CH_2}CH_2COOCH_3$), 9.73, 9.77, 9.83, 9.85 (s, 4H, meso), -3.77 (b, 2H, NH). VIS: 397, 496, 530, 565, 618 nm. M^+ = 578. Anal. Calcd. for $C_{37}H_{46}N_4O_2$: C, 76.78; H, 8.01, Found: C, 77.04; H, 7.81.

Methyl-1,2,3,4-tetraethyl-6,7-dimethyl-5,8-dipropionate porphyrin 26b

m.p. 150-152°C. p.m.r. 1.87 (t, J = 7.5 Hz, 12H, $-CH_2CH_3$), 3.17 (t, J = 8.0 Hz, 4H, $-CH_2\underline{CH_2}COOCH_3$), 3.53 (s, 6H, $-CH_3$), 3.57 (s, 6H, $-OCH_3$), 4.03 (t, J = 8.0 Hz, 4H, $-\underline{CH_2}CH_2COOCH_3$), 4.27 (q, J = 7.5 Hz, 8H, $-\underline{CH_2}CH_3$), 9.86 (b, 4H, meso protons), -3.70 (b, 2H, NH). VIS: 398, 496, 530, 566, 620 nm. M^+ = 622; Anal. Calcd. for $C_{38}H_{46}N_4O_4$: C, 73.28; H, 7.45, Found: C, 74.40; H, 7.46.

Methyl-1,2,3,4-tetraethyl-6,7-dimethyl-5,8-diacetate porphyrin 26c

m.p. 295°C. p.m.r. 1.83 (t, J = 7.5 Hz, 12H, $-CH_2\underline{CH_3}$), 3.23 (s, 6H, $-CH_3$), 3.60 (s, 6H, $-OCH_3$), 3.93 (q, J = 7.5 Hz, 8H, $-\underline{CH_2}CH_3$), 4.67 (s, 4H, $-\underline{CH_2}COOCH_3$), 9.40, 9.76 (s, 2H, meso H), 9.67 (s, 2H, meso H), -4.00 (b, 2H, NH). VIS: 399, 497, 532, 566, 620 nm. M^+ = 694 for $C_{36}H_{42}N_4O_4$.

Methyl-1,4,6,7-tetramethyl-2,3-dihexyl-5,8-dipropionate porphyrin 26d

m.p. 183-185°C. p.m.r. 0.88 (t, J = 5.0 Hz, 6H, $-(CH_2)_5\underline{CH_3}$), 1.10-1.90 (b, 12H, $-(\underline{CH_2})_3-CH_3$), 2.00-2.50

(b, 4H, -$\underline{CH_2}C_4H_9$), 3.15 (t, J = 8.0 Hz, 4H, -$\underline{CH_2}$-$COOCH_3$), 3.46, 3.53 (s, 6H, -CH_3), 3.60 (s, 6H, -$COOCH_3$), 3.92 (t, J = 7.0 Hz, 4H, -$\underline{CH_2}C_5H_{11}$), 4.26 (t, J = 8.0 Hz, 4H, -$\underline{CH_2}CH_2COOCH_3$), 9.78 (b, 4H, meso H), -3.83 (b, 2H, NH). VIS: 402, 498, 531, 565, 622 nm. M^+ = 706; Anal. Calcd. for $C_{44}H_{58}N_4O_4$: C, 74.96; H, 8.01; Found: C, 74.69; H, 7.90.

Alternative synthesis of 26d by saturated HBr formic acid

292 mg of 19d and 213 mg of 16b was dissolved in 10 ml HBr-saturated dry formic acid and refluxed at 140°C for 2.5 hr. After purification 30.3% of 26d was obtained.

Methyl-1,4,6,7-tetramethyl-2,3-dihexyl-5,8-diacetate porphyrin 26e

m.p. 240-242°C. p.m.r. 0.87 (poorly resolved triplet, 6H, -$(CH_2)_5$-$\underline{CH_3}$), 1.20-2.00 (b, 12H, -$(\underline{CH_2})_3$-CH_3), 2.00-2.60 (b, 4H, -$\underline{CH_2}$-C_4H_9), 3.40, 3.46, 3.63 (s, 6H, 6H, 6H, -CH_3, -OCH_3), 3.90 (t, J = 8.0 Hz, -$\underline{CH_2}$-C_5H_{11}), 4.77 (s, 4H, -$\underline{CH_2}$-$COOCH_3$), 9.73, 9.80 (s 1H, 3H, meso H), -3.67 (b, 2H, NH). VIS: 397, 496, 530, 565, 620 nm. M^+ = 678; Anal. Calcd. for $C_{42}H_{54}N_4O_4 \cdot$ 1 1/2 H_2O: C, 71.48; H, 8.08, Found: C, 71.31; H, 7.61.

Methyl-2,5,8-trimethyl-3,4-diethyl-1,6,7-tripropionate porphyrin 26f

m.p. 148-150°C. p.m.r. 1.80 (t, J = 8.0 Hz, 6H, -$CH_2\underline{CH_3}$), 3.10 (poorly resolved triplet, 6H, -CH_2-$\underline{CH_2}COOCH_3$), 3.40 (b, 9H, -CH_3), 3.60 (s, 3H, -$COOCH_3$), 3.86 (q, J = 8.0 Hz, 4H, -$\underline{CH_2}CH_3$), 4.10 (t, J = 8.0 Hz, 6H, -$\underline{CH_2}$-CH_2COOCH_3), 9.70

(b, 4H, meso H), -3.60 (b, 2H, NH). VIS: 396, 496, 530, 564, 617 nm. M^+ = 666; Anal. Calcd. for $C_{39}H_{46}N_4O_4$: C, 70.25; H, 6.95, Found: C, 70.20; H, 6.86.

1,4-Bis(2-chloroethyl)-2,3,5,8-tetramethyl-6,7-bis(2-methoxycarbonylethyl) porphyrin 26g

m.p. 200-202°C. p.m.r. 3.17 (t, J = 7.0 Hz, 4H, $-\underline{CH_2}-COOCH_3$), 3.30 (s, 3H, $-CH_3$), 3.32 (s, 3H, $-CH_3$), 3.60 (s, 6H, $-OCH_3$), 3.80-4.50 (m, 12H, $-\underline{CH_2}\underline{CH_2}Cl$, $-\underline{CH_2}CH_2COOCH_3$), 9.57, (broad, 3H, meso proton), -4.07 (broad, 2H, NH). MS, field desorption, M^+ = 662.

2,3-Bis(2-chloroethyl)-1,4,6,7-tetramethyl-5,8-bis(2-methoxycarbonylethyl) porphyrin 26h

m.p. 215-217°C. p.m.r. 3.07 (t, J = 7.0 Hz, 4H, $-\underline{CH_2}-COOCH_3$), 3.33 (s, 6H, $-CH_3$), 3.33, 3.43, 3.50 (s, 18H, $-CH_3$, $-OCH_3$), 3.90-4.40 (m, 12H, $-\underline{CH_2}\underline{CH_2}Cl$, $-\underline{CH_2}CH_2COOCH_3$), 9.53, 9.57, 9.63 (s, 1H, 1H, 2H, meso protons), -4.00 (broad, 2H, NH). VIS: 416, 500, 528, 566, 619 nm. M^+ = 662

Methyl-1,4,5,8-tetrapropionate 2,3,6,7-tetramethyl porphyrin 26k

I. 425 mg of 5,5'-dimethyldipyrromethenium bromide 16b was dissolved in 100 ml dry formic acid and heated to 100°C in an oil bath (130°C) for 5 min. 0.15 ml bromine was added and the mixture refluxed for another 2 hrs. After isolation and esterification, 2% of porphyrin 26k was obtained. m.p. 183-185°C. p.m.r. 3.20 (t, J = 8.0 Hz, $-\underline{CH_2}-COOCH_3$), 3.60 (s, 24H, $-CH_3$, $-CH_3$), 4.30 (t, J = 8.0 Hz, 8H, $-\underline{CH_2}CH_2COOCH_3$), 7.81 (s, 4H, meso H), -3.66 (broad, 2H, NH). VIS: 400, 498, 533, 367, 622 nm M^+ = 710.

II. 1 g of 3,3',5,5'-tetramethyl-4,4'-dimethoxycarbonylethyl dipyrromethene 16b was dissolved in 5 ml acetic acid followed by 0.8 ml of bromine. The mixture was allowed to stand overnight at room temperature. Crystals formed in the mixture were filtrated and washed with hexane to give 0.92 g of 25. 200 mg of 25 was dissolved in 10 ml formic acid mixed with 1 ml conc. HCl. The mixture was refluxed at 140°C for 15 hrs. After purification, 10 mg of 26k was obtained in 4% yield.

The dehydrochlorination of 2-chloroethyl porphyrins to vinyl porphyrins. General procedure [20]:

Bis(2-chloroethyl)porphyrin 10 mg was dissolved in a mixture of 4.5 ml pyridine and 10 ml 3% NaOH and the mixture was refluxed for 1.5 hr. The solution was neutralized with 6H acetic acid before extracting with methylene chloride. The organic layer was separated and dried over sodium sulfate and evaporated under reduced pressure. The residue was dissolved in a mixture of 10 ml methanol, 5 ml trimethyl orthoformate and 3 drops of concd. sulfuric acid, and was allowed to stand overnight. After removal of the solvent, and dried under vacuum, the solid was recrystallized from methylene chloride-methanol.

1,4-Divinyl-2,3,5,8-tetramethyl-6,7-bis(2-methoxycarbonylethyl) porphyrin 26i

Yield: 56%. m.p. 208-210°C. VIS: 408, 506, 548, 576, 630 nm. M^+ = 590.

2,3-Divinyl-1,4,6,7-tetramethyl-5,8-bis(2-methoxy-carbonylethyl) porphyrin 26j

Yield: 60%. m.p. 260-262°C. VIS: 402, 502, 536, 570, 625 nm. MS: field desorption, M^+ = 590.

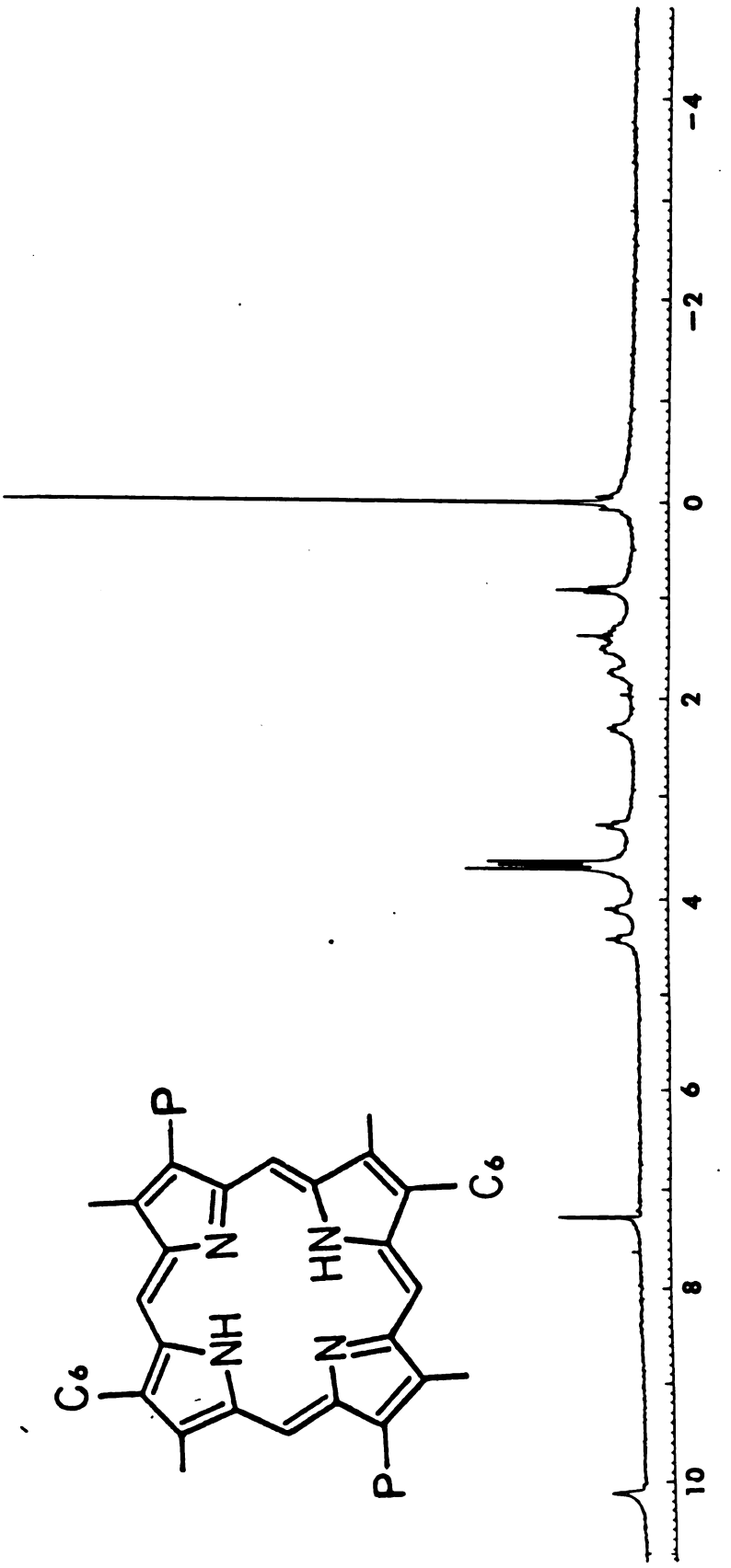


Fig. 2-1. PMR Spectrum of Porphyrin 12b

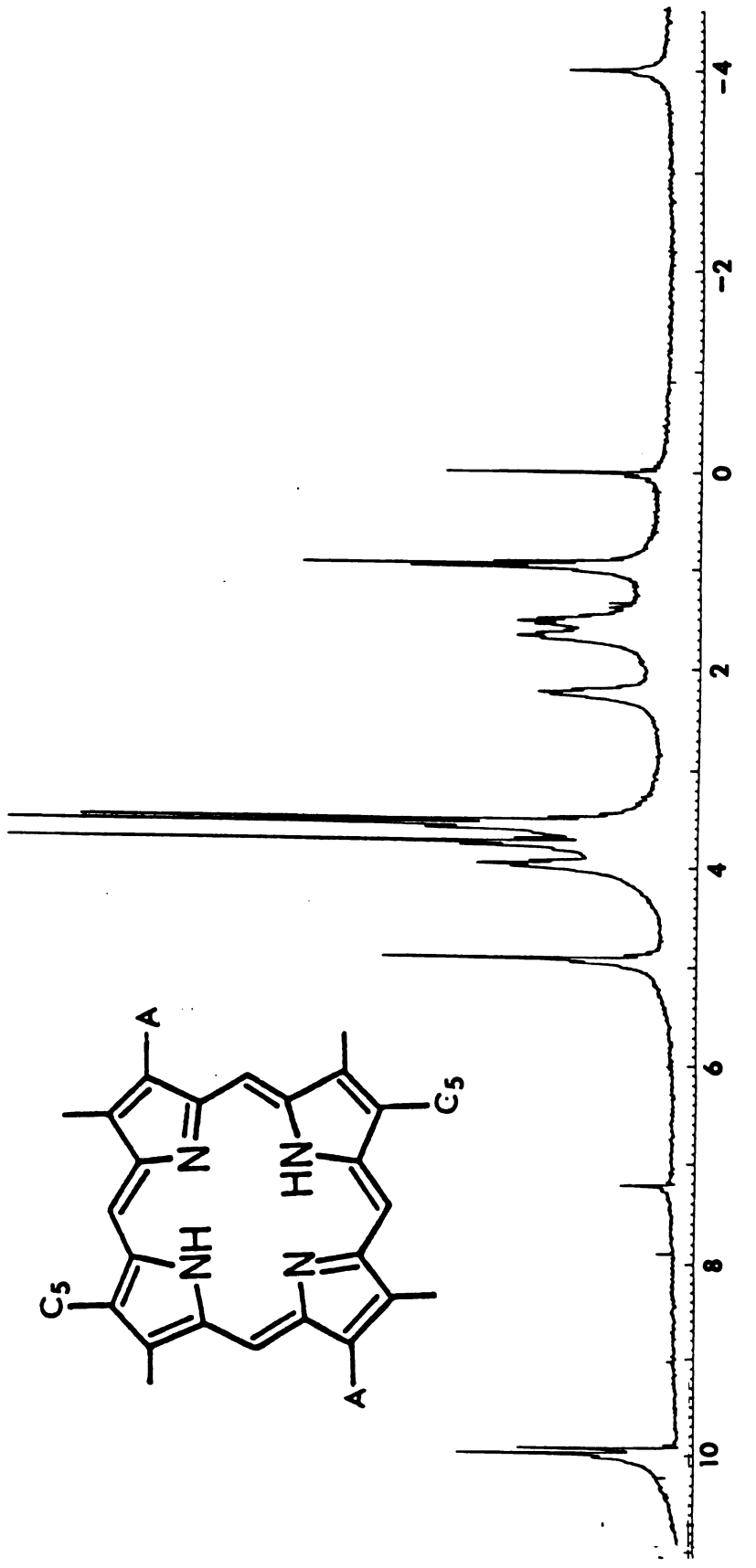


Fig. 2-2. PMR Spectrum of Porphyrin 12c

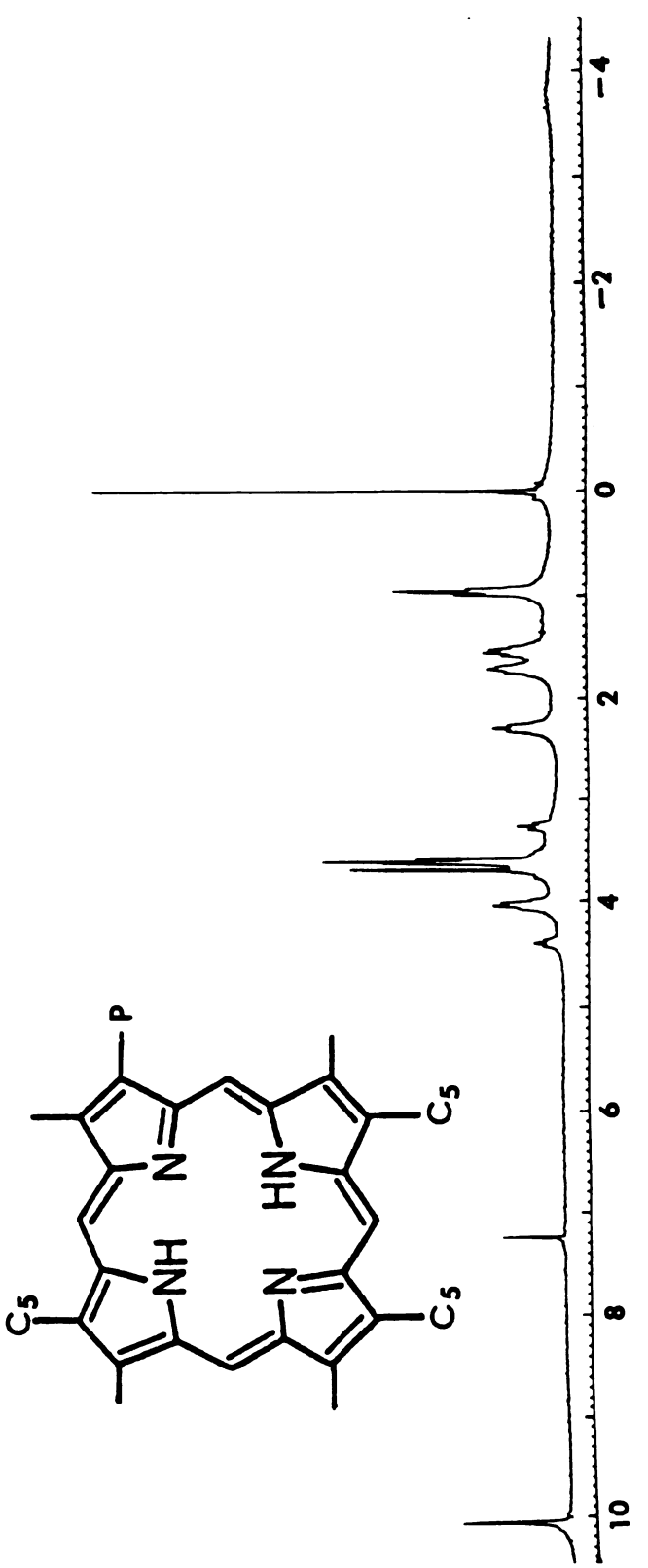


Fig. 2-3. PMR Spectrum of Porphyrin 13

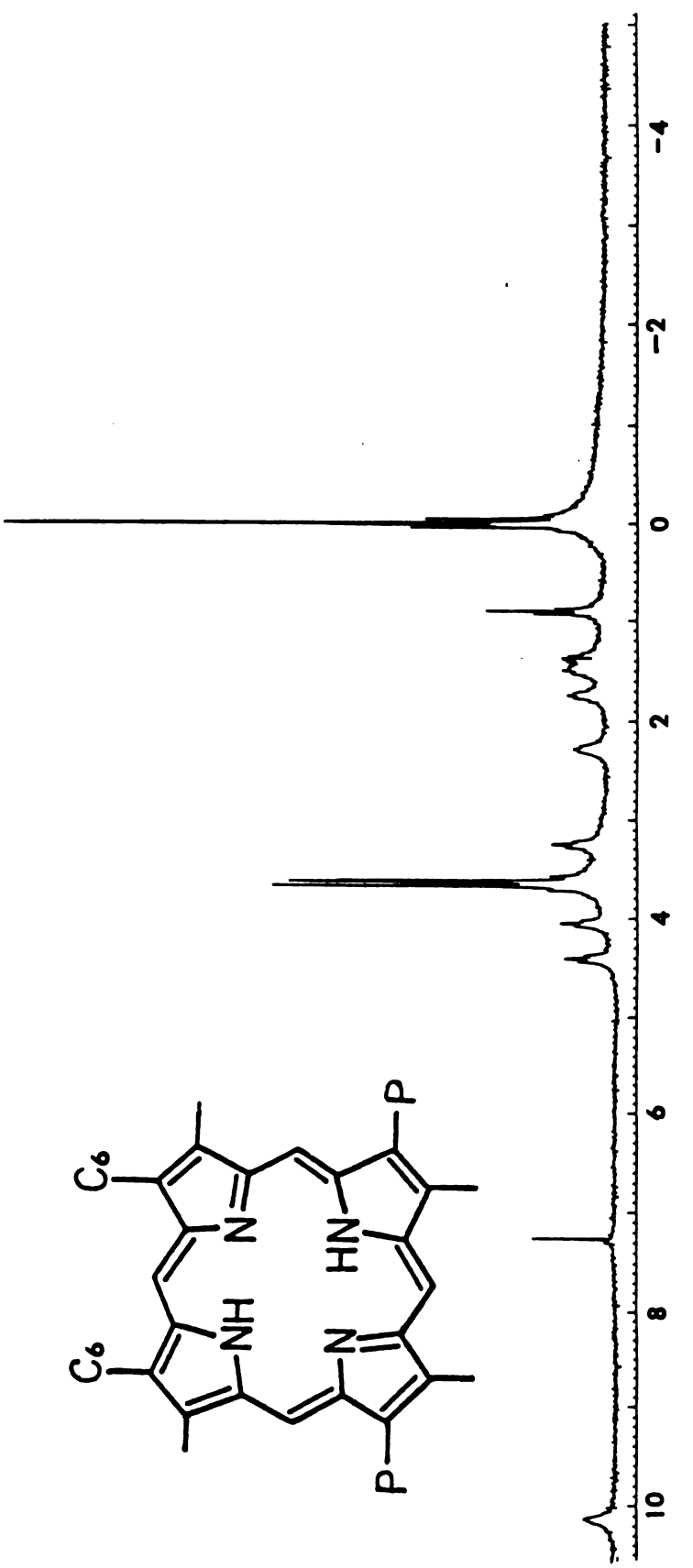


Fig. 2-4. PMR Spectrum of Porphyrin 26d

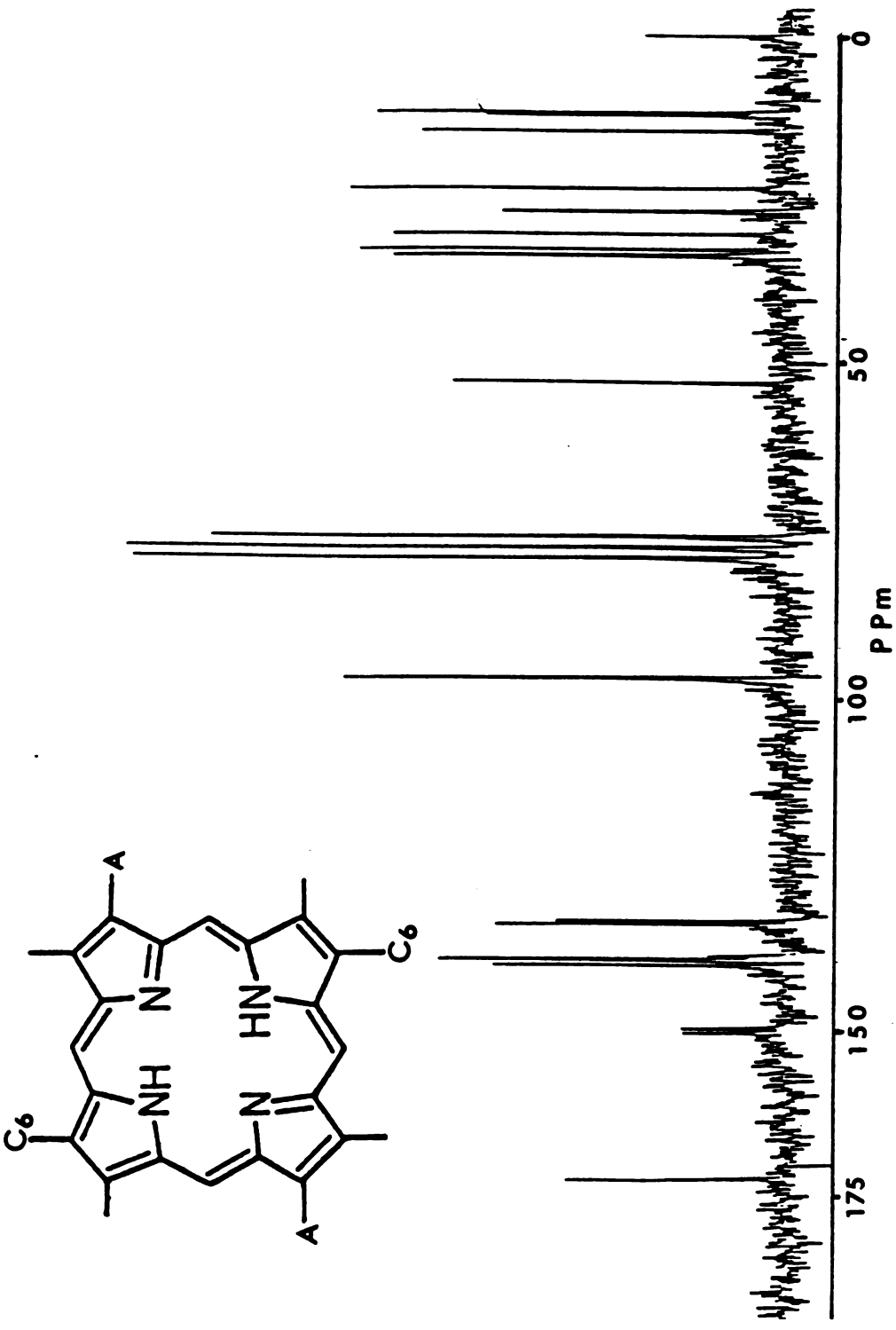


Fig. 2-5. CMR Spectrum of Porphyrin 12a

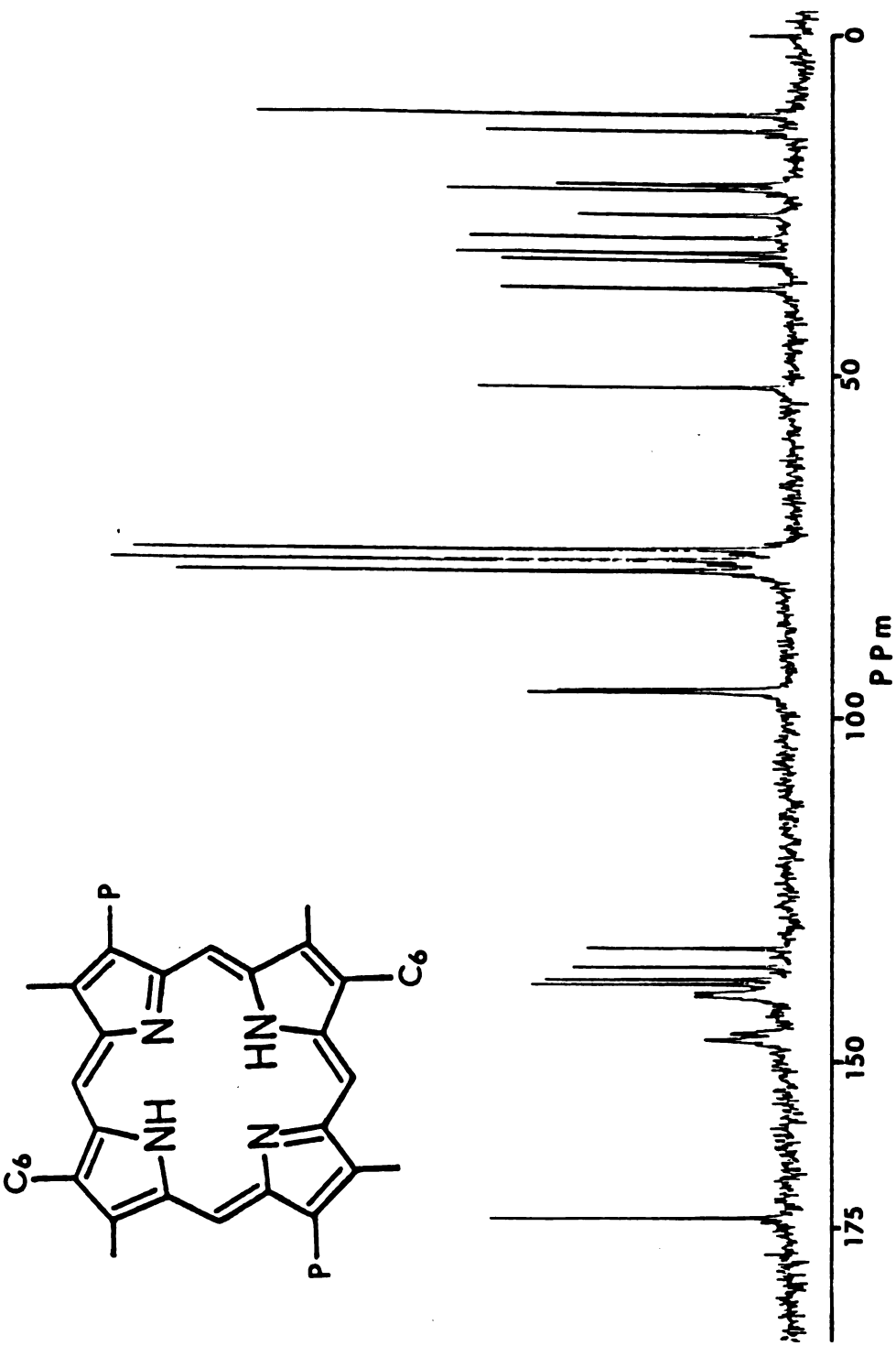


Fig. 2-6. CMR Spectrum of Porphyrin 12b

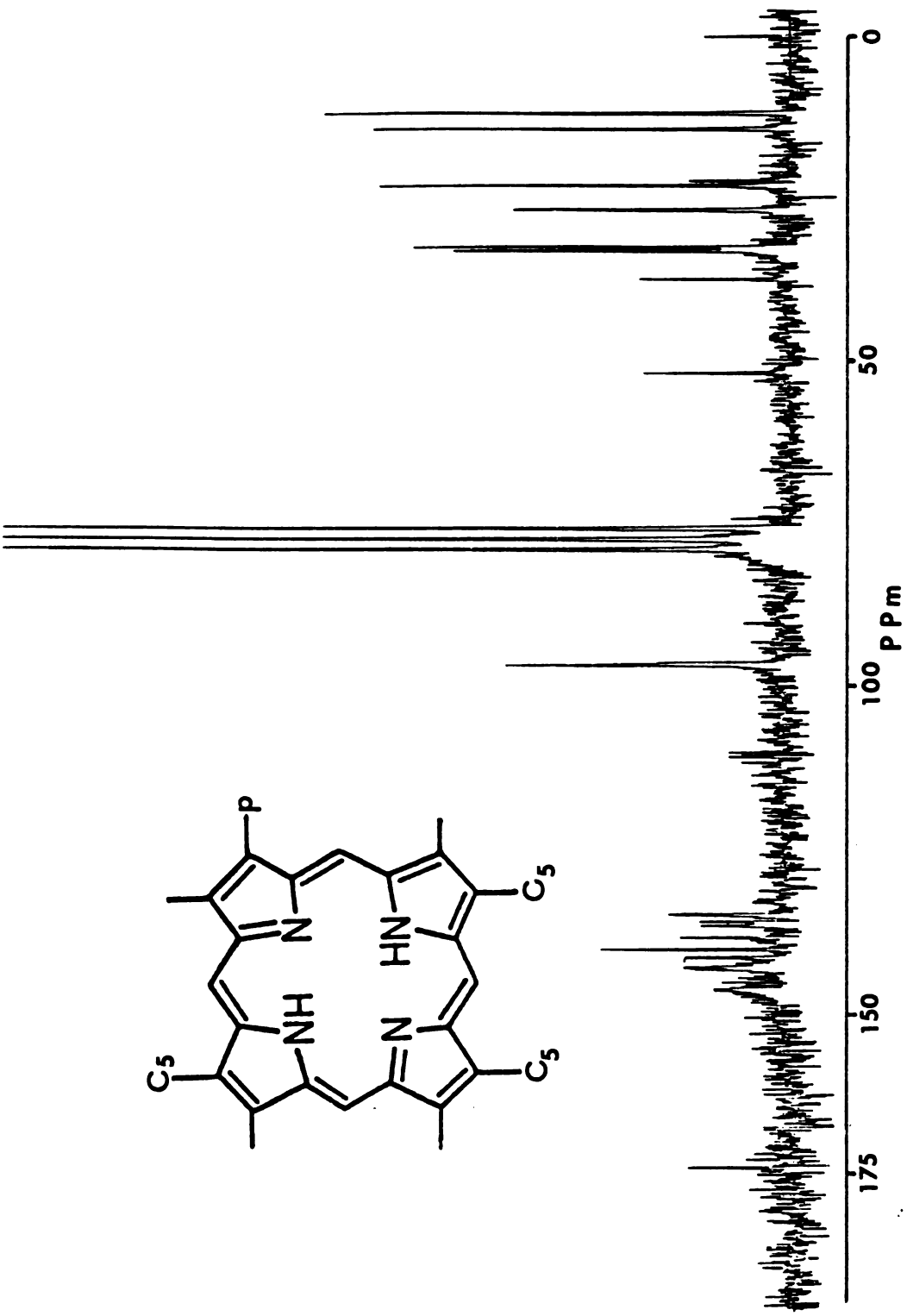


Fig. 2-7. CMR Spectrum of Porphyrin 13

CHAPTER 3

SYNTHESIS OF COFACIAL AND SLIPPED DIPORPHYRINS

Introduction

In the past few years, several types of diporphyrins have been synthesized. These cofacial diporphyrins have great significance in many branches of chemistry. As organic molecules, in addition to being challenging synthetic targets, they can present a multitude of properties by the mere token of their size and by the resulting interaction of the two 18 π-electron porphyrin ring. As inorganic compounds, they have the unusual capability of containing two metal ions at selected distance and thus can display interesting properties arising from metal-metal interaction. Furthermore from the point of view of biochemistry, they represent a class of elaborately designed bioinorganic models for many essential biological systems; among these were:

(1) "special pair" chlorophyll model in photosynthetic unit.

(2) cytochrome oxidase model capable of multielectron reduction of oxygen.

(3) polynuclear complexes with certain catalytic activity.

Collman and his coworkers [35] in 1977, synthesized a face-to-face porphyrin by the dimerization of two functionalized meso-tetraphenylporphyrin derivatives. We have also

reported, in the same year, a series of diporphyrins [27,36, 37]. These dimers were linked by two amide bonds at the pyrro-β-positions. The distance between the porphyrins can be varied by changing the bond length. Ogoshi et al. [38] also reported the preparation of a β-linkage diporphyrin. However, the absorption spectra of their diporphyrin suggest that the compound may not be a cofacial dimer. Wasielewski et al. [39] prepared a chlorophyll dimer as a model of special pair chlorophyll. Kagen et al. [40] prepared a dimer by linking para-substituted meso-tetraphenylporphyrins.

Recently Collman [41,42] reported several diporphyrins linked at either the meso positions, or at the pyrrole β-positions, using the same synthetic approach reported by us. The interplanar distance was varied from 6.5 Å to 4 Å. A dramatic 4-electron electrocatalytic reduction of oxygen was observed with one of the cobalt-cobalt diporphyrins [43].

In this chapter we describe the synthesis of several cofacial diporphyrins as well as a "slipped" diporphyrins. Unusual properties of the diporphyrins and the experiments using diporphyrins as a photosynthetic reaction center model are also discussed.

Results and Discussion

A. Synthesis of Diporphyrins

(1) Synthesis of dimers

With the large variety of difunctionalized porphyrins described in Chapter 2, at least 2 types of cofacial diporphyrins can be synthesized. The first is a true face-to-face

dimer resulting from the coupling of two 1,5-difunctionalized monomers (32 and 30 or 35). The other is a "slipped" dimer obtained from the coupling of a 1,4- and a 1,5-disubstituted porphyrins (36 and 30 or 35) (see Fig. 3-1).

The coupling of the diamine and diacid chloride was affected with a high dilution, mixing procedure, using equmolar solutions concentration ca. 5 mM of the porphyrin diamine and diacid chloride in dichloromethane. Triethylamine was added to the solution of porphyrin diamine, in order to increase the solubility and catalyze amide bond formation. Work-up consists of removal of the solvent on a rotary evaporator, dissolution of the residue in dichloromethane, and passage through a short silica gel pad to remove the polymer and unreacted amine. The dimer fraction was further purified on preparative TLC plat.

The dimers prepared by this route may give two isomers, designated as "syn" and "anti" (Fig. 3-2). Attempts to separate them on TLC plates have been unsuccessful.

Metal ions such as Cu, Co, Mg were inserted in the diporphyrins by standard procedure [12]. Mixed dimetal system were prepared by coupling the metal complex of an acid chloride with the free base diamine, followed by subsequent metal insertion. Using this approach, Cu-Fe and Mg-H_2 diporphyrins have been successfully prepared. Upon chromatographing on silica gel plate, the Mg-Mg dimer also demetalizes to give a Mg-H_2 dimer. The physical properties of these dimers were listed on Table 3-1.

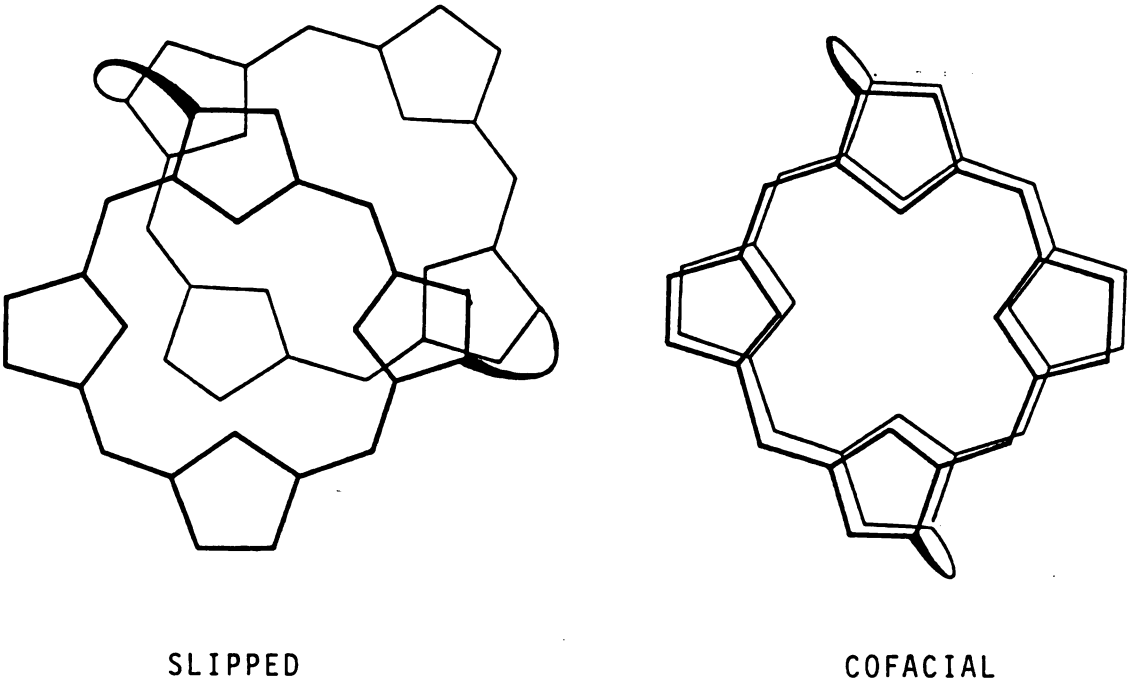


Fig. 3-1. Cofacial and Slipped Diporphyrin

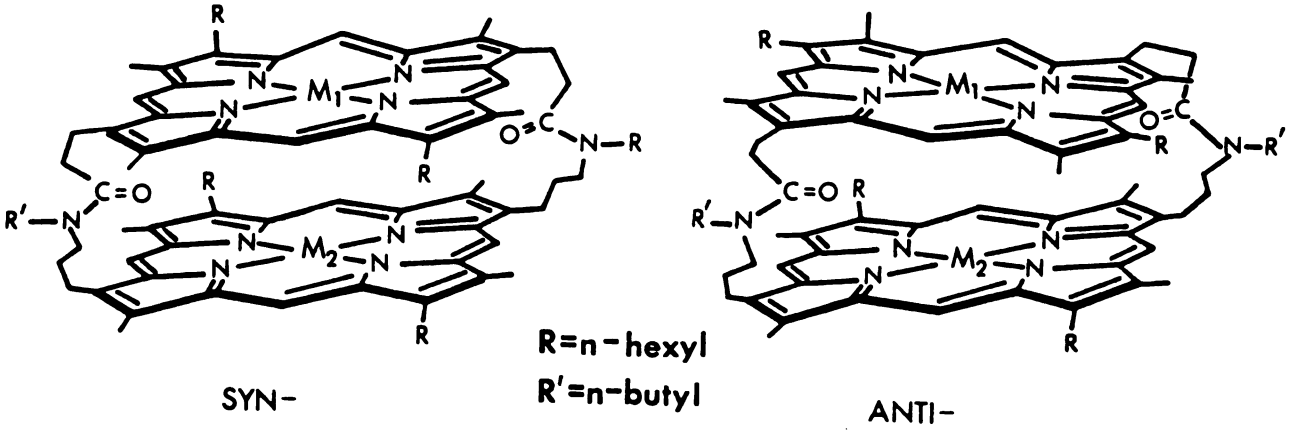


Fig. 3-2. Syn and Anti Configuration of Diporphyrins

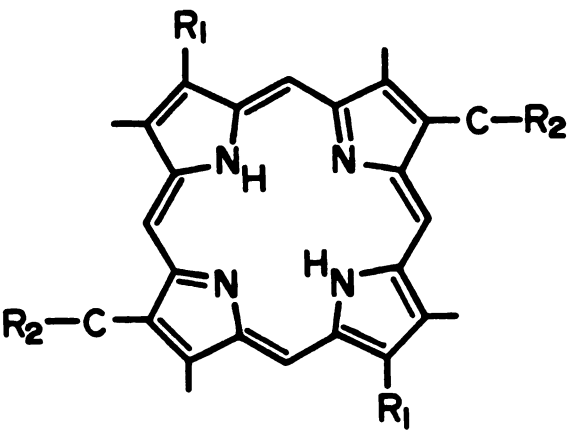
(2) Preparation of secondary porphyrin diamines

The diester porphyrins 27 are reduced by lithium aluminium hydride in THF to the diols 28 which, in turn, are converted to their mesylates 29 by treating with methanesylfonyl chloride in dichloromethane/triethylamine. Refluxing with n-butylamine gave the diamine 30 in almost quantitative yield from 27.

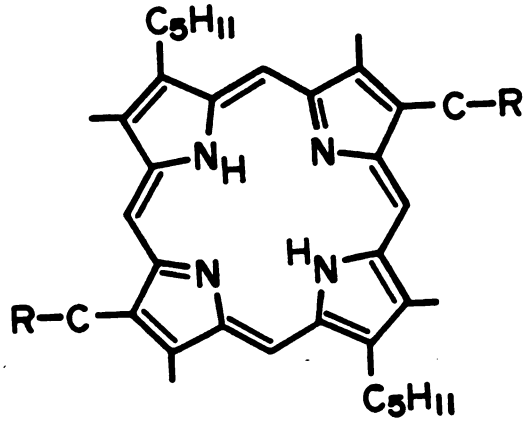
(3) Preparation of primary porphyrin diamines

The diester porphyrin 27 was hydrolyzed to diacid dihydrochloride 31 and these could be converted to the diacid chloride 32 with oxalyl chloride. The diacid 31d was insoluble in methylene chloride and oxalyl chloride. The presence of a small amount of phosphorus oxychloride was necessary to achieve the conversion. Treatment of the acid chloride in methylene chloride with sodium azide in water using tetrabutylammonium bromide as phase transfer catalyst, gave diacid azide 33. Upon heating in dry benzene, these were converted to the diisocyanate derivatives 34 without further purification. IR was used to monitor the progress of the rearrangement, which was complete in 4 hrs.

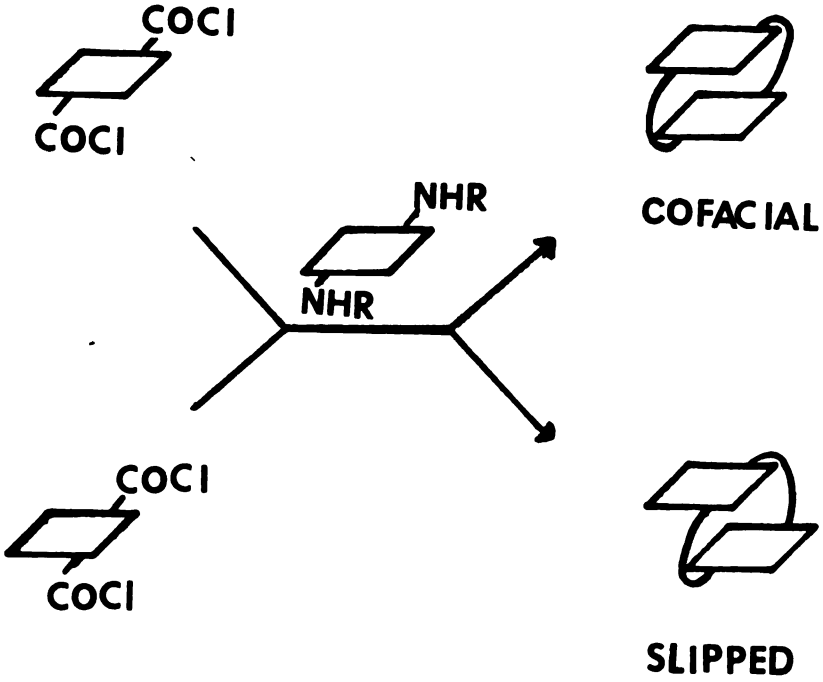
The diisocyanate was used without isolation to give the primary diamine porphyrin 35 by acid hydrolysis. The diamine was purified by passing through a silica gel pad, using a methylene chloride:methanol:triethylamine 100:10:0.5 solvent mixture as elutent. The diamine can be stored in freezer for months without decomposition.



27a	R1=C8	R2=$COOCH_3$	31a	R1=C6	R2=CH_2COOH
b	R1=C6	R2=CH_2COOCH_3	b	R1=C6	R2=COOH
c	R1=C6	R2=$COOCH_3$	c	R1=C5	R2=CH_2COOH
d	R1=C5	R2=CH_2COOCH_3	d	R1=C5	R2=COOH
e	R1=C5	R2=$COOCH_3$			
28a	R1=C8	R2=CH_2OH	32a	R1=C6	R2=CH_2COCl
b	R1=C6	R2=CH_2CH_2OH	b	R1=C6	R2=COCl
c	R1=C6	R2=CH_2OH	c	R1=C5	R2=CH_2COCl
			d	R1=C5	R2=COCl
29a	R1=C8	R2=CH_2OMs	33a	R1=C5	R2=CON_3
b	R1=C6	R2=CH_2CH_2OMs	b	R1=C5	R2=CH_2CON_3
c	R1=C6	R2=CH_2OMs			
30a	R1=C8	R2=CH_2NBu	34a	R1=C5	R2=NCO
b	R1=C6	R2=CH_2CH_2NBu	b	R1=C5	R2=CH_2NCO
c	R1=C6	R2=CH_2NBu			
			35a	R1=C5	R2=NH_2
			b	R1=C5	R2=CH_2NH_2



36a	R1=C6	R2=CH_2CH_2COCl
b	R1=C6	R2=CH_2COCl
c	R1=C5	R2=CH_2COCl



B. Nuclear Magnetic Resonance Spectroscopy

NMR spectroscopy is a particularly useful technique for establishing the integrity of a porphyrin dimer. If one porphyrin ring is positioned atop another, the ring current of the second porphyrin can cause additional shifts of the proton resonance, in particular, the NH signals [35].

The diporphyrins prepared by this route consists of two isomers. The meso protons have a chemical shift in the region at 8 $\sim$10 ppm. More than 4 peaks were observed in this region indicating a mixture of the syn and anti isomers (Fig. 3-3). In a similar dimer reported by Collman [41] obtained from a different approach only 4 peaks were found.

The nitrogen protons of the monomeric porphyrin were observed at -4 ppm, while those of dimers were shifted to higher field by the ring current interaction. The shift of NH protons seem to reflect the distance between the two porphyrins; the closer the dimer, the larger the shift. The slipped dimer SD5 has a smaller shift than the face-to-face FD5 dimers. The tertiary amide linked dimers FD6(NBu), FD5 (NBu) were shifted further than the secondary amide linked dimers FD6(NH), FD5(NH). This may indicate that the secondary amide linked dimers are more flexible than the tertiary amide linked dimers. Indeed, the x-ray structure of Cu-Cu dimer FD7 has been shown to have a slipped structure [44].

Nmr signals of all peripheral alkyl substituents in the region of 4.5-0.5 ppm could not be resolved because of the isomeric nature and flexibility of the dimers. The sharper

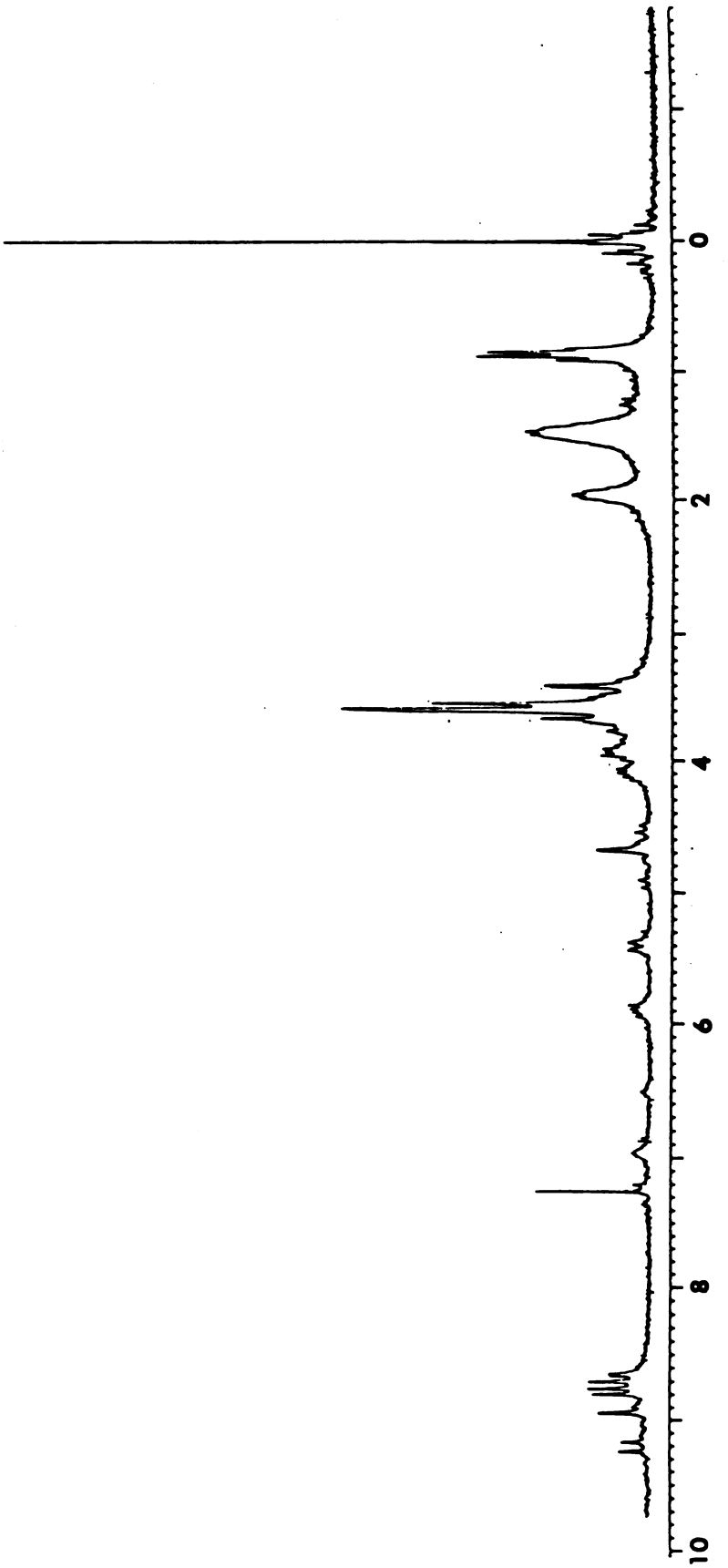


Fig. 3-3. PMR Spectrum of Diporphyrin FD4

Table 3-1. PMR and Vis Spectra Data of Dimers

DIMER	N-R	NH	MESO	SORET	IV	III	II	I	%
32a+30b=FD*7	Bu	-6.2	8.8- 9.8	383	502	535	571	624	60
36a+30b=SD*7	Bu	-4.0	8.2- 9.8	390	503	536	570	624	55
32a+30b=FD6	Bu	-6.6		381					50
32c+35b=FD6	H	-5.4	7.9- 8.8	390	500	536	570	623	50
Cu-Cu				390		528	564		
32b+30c=FD5	Bu	-8.5		373					30
Mg-H_2									
32a+35a=FD5(3+1)*	H	-7.3	8.5- 9.5	380	505	541	570	626	25
Cu-H_2				382	510	540	570	628	
Cu-Fe				386		526	562		
32b+35b=FD5(2+2)*	H	-7.7	8.3- 8.8	380	504	540	570	622	25
36b+30a=SD5	Bu	-6.8	8.4-10.5	381	500	534	570	622	20
Mg-Mg				408		543	582		
Mg-H_2				392	500	540	578	620	
Co-Co				383		525	555		
Cu-Cu				396		530	565		
32d+35a=FD4	H	-7.9	7.3- 8.5	380	504	542	570	625	20
Mg-H_2				389	508	548	590	620	
Co-Co				380		510	552		
Cu-Cu				381		528	568		
Cu-H_2				380	500	537	563	626	
Cu-Fe				380		534	568	650	
36c+35a=SD4	H	-6.5	8.7- 9.9	385	506	541	570	626	15
Cu-Cu				385		532	568		
Co-Co				380		520	556		

* FD: Face-to-Face Dimer
SD: Slipped Dimer
FD5(3+1) was prepared by the coupling of dipropionic acid chloride and dimethylamine, FD5(2+2) was obtained by the coupling of diacetic acid chloride and diethylamine.

signal of dimer FD4 at room temperature is a evidence for its more rigid structure.

C. Electronic Spectroscopy

The visible spectra of the dimers provided convincing evidence of their conformations. All dimers showed a distinct blue shift (10-27 nm) of the intense Soret band and a weak red shift of the longer wavelength absorption [36,45]. The bands also appeared to be broadened. This strongly suggests the presence of exciton interaction. The shifts of the secondary amide linked dimers and tertiary amide linked dimers differed by about 10 nm; this may be due to the extent of slippage in the diporphyrins as the Soret band of the slipped dimer was less shifted than the corresponding face-to-face dimers. The shift of the Soret band and their quenched fluorescence were useful in characterization and identification of the diporphyrins during their preparations. It is evident from comparisons of the visible spectra of Mg-H_2 FD5, Mg-H_2 FD4 versus the mixture of H_2OEP and MgOEP that there are significant interactions of the porphyrin rings (Fig. 3-4).

D. Electron Spin Resonance Spectroscopy

The interplanar distances of the diporphyrins were determined by studying the dipolar interaction of two paramagnetic metal centers. Simple Cu(II) porphyrins have S=1/2 system with well-defined ESR characteristics [46]. If two copper porphyrins are close enough such that the spins interact, then the bimetallic system exhibit a triplet ESR spectrum.

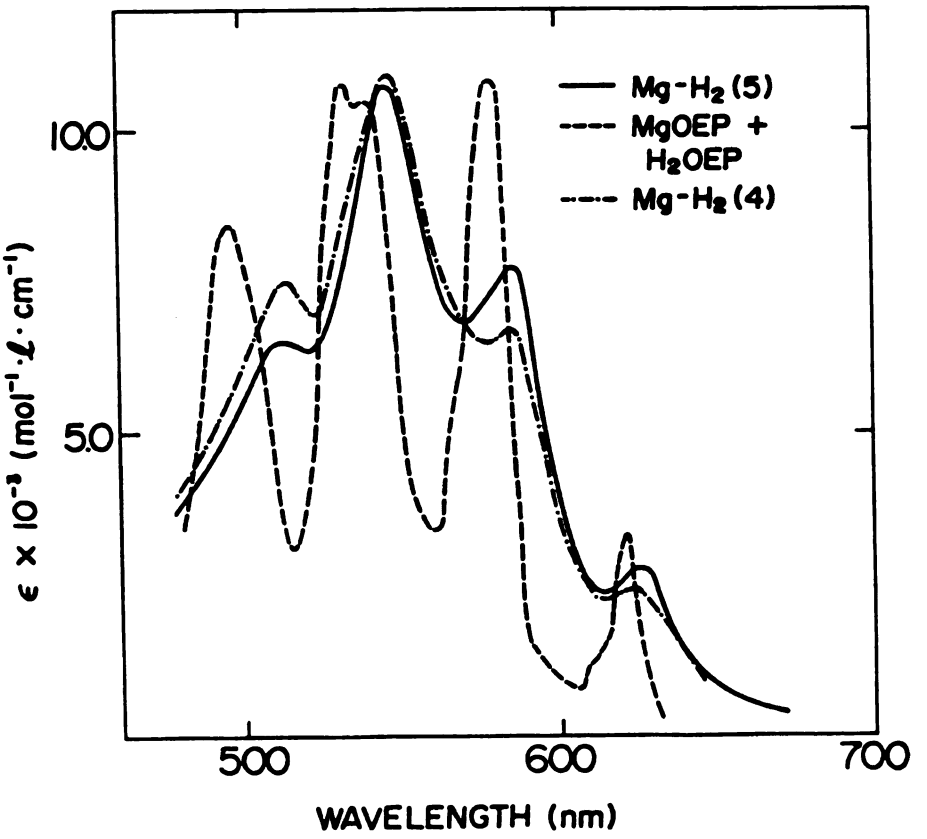


Fig. 3-4. Vis Spectra of Mg-H_2FD5, Mg-H_2FD4 and OEP/MgOEP

If the rate of electron exchange between these two metals is faster than the resonance frequency (10^{10}/sec), then the electron electron nuclear spin will equal to the total nuclear spin of the two metals (I=3 for Cu(II)). Thus the Cu-Cu dimer will exhibit 7 lines from the hyperfine interaction. At the same time the hyperfine splitting A is half that for a related monomer. The ESR transitions will be further split by the zero-field splitting [ZFS],D. D is half the distance between the centers of the parallel absorptions. A center is located as the midpoint of seven hyperfine lines (see Fig. 3-5).

The ZFS splitting parameter D (10^{-4} cm) has been used to estimate metal-metal spacing on the basis of eq.

$$D=0.65\ g_2^2/r^3.$$

$$g_2^2=g_{11}^2\ \mathrm{Cos}^2\theta + g_2^2\ \mathrm{Sin}^2\theta$$

where r ($\mathring{A}$) is the distance between the metal centers, is the angle between g_{11} axis and the Cu-Cu direction and Z is the interplane distance.

Several examples of ESR of di-copper porphyrins have appeared in the literature [36,37,41,42].

For dimer FD4, from the apparent zero-field splitting, the Cu-Cu distance 3.8 $\mathring{A}$ was obtained. The ESR spectrum of Cu-Cu slipped dimer SD5, showed weaker metal-metal interaction.

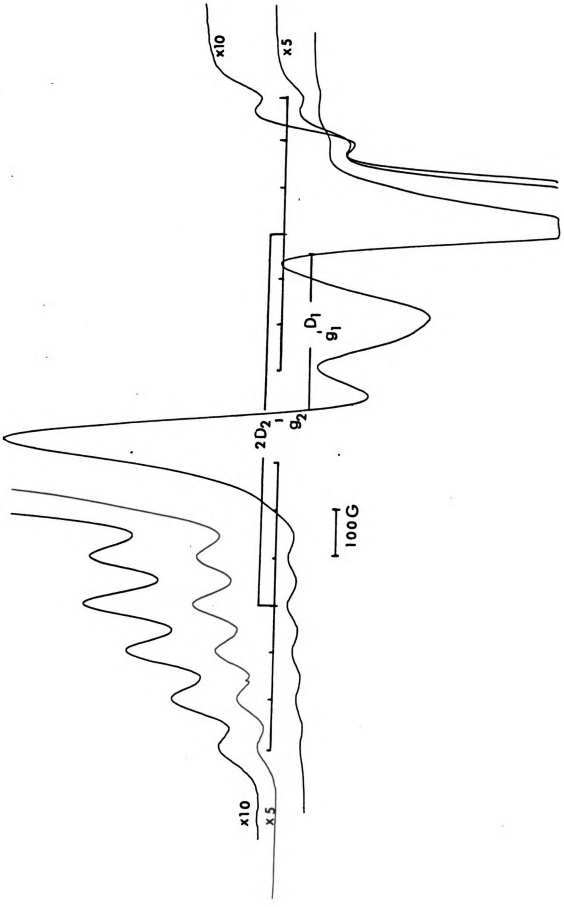


Fig. 3-5. ESR Spectrum of Cu-Cu FD4

E. Cyclic Voltammetry

From the cyclic voltammetry measurements, the redox potential of the metal and the effect of the metal-metal interaction can be obtained.

The Co(II)-Co(III) couple of Co-Co dimers were shifted to more positive potential than that in their monomer. For dimer FD4, the voltammetric wave was split into two waves (i.e. the second electron transfer is more difficult than the first). This is due to the interaction of two metals [41].

With the slipped dimer SD5, there is only one wave at 0.61 V, indicating a weak interaction between two cobalt metals (Table 3-2).

Table 3-2. Redox Potential of Cobalt porphyrins from C.V.

	Co(II)⇌Co(I)	Co(II)⇌Co(III)	Ring Reduction	Ring Oxidation
CoOEP	-1.05	0.30	-1.87	1.26, 1.06
Cofacial DM-4, Co-Co	-1.00,-1.20	0.55, 0.81	----	1.23, 1.05
Slipped DM-5, Co-Co	-0.97	0.61	----	1.25, 0.93

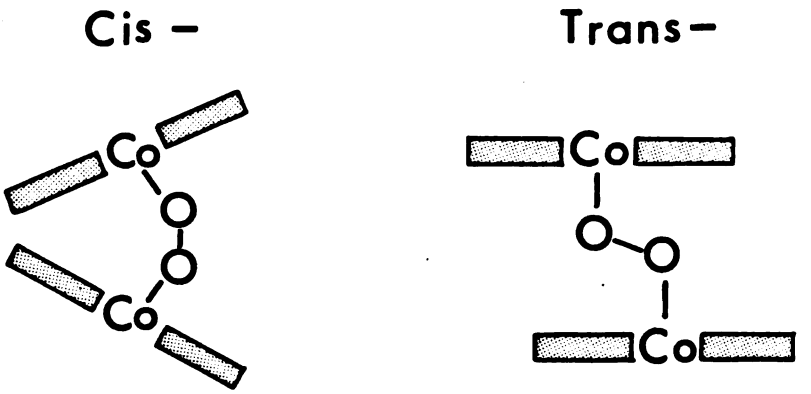
F. Oxygen Interaction with Dicobalt Porphyrins

When a bulky ligand, 1-tritylimidazole, was complexed with Co(III)-Co(II) diporphyrin-7 and exposed to oxygen, the visible, ESR spectra, and gasometric data all documented the

formation of a double 1:1 Co-O_2 compound. The oxygen affinity of this system was similar to those of monomeric Co(II) porphyrins. Complete oxygenation at 1 atm of O_2 could be achieved below -30° and the oxygen binding was completely reversible [36]. Co(II)-Co(II) diporphyrin-5, on the other hand, reacted quite differently with oxygen. Addition of O_2 to the [$\emptyset_3$ CIm-Co(II)] complex at room temperature instantaneously produced a species consistant with the formulation of $2Co/O_2$ (gasometry $Co:O_2$=1:0.55). This complex represented as [Co(III)-O_2-Co(III)], was diamagnetic and had no ESR signals. This μ-peroxo complex, however, can be oxidized readily to show a well-defined isotropic ESR spectrum consisting of 15 lines (Fig. 3-6A, g_{iso}= 2.024, $|A_{Co}|$=10 Gauss). This is interpreted as a u-superoxo [Co(III)-$\dot{O}$-Co(III)] complex in which the two equivalent Co-59 nuclei (I=7/2) would give a total of (2x2x7/2)+1=15 lines. This assignment has been substantiated by O-17 experiments [37].

Behavior of the Co(II)-Co(II) diporphyrin-4 was similar to the dimer-5, i.e. a μ-superoxo complex formed readily using the iodine oxidation method. A careful comparison of the 15-lines, μ-superoxo ESR spectra (Fig. 3-6B), however, indicates that the hyperfine lines of the dimer-4 have narrower line-width and consequently, the splittings are more symmetrical and better resolved, in comparison with the dimer-5. We believe that the spectral difference, albeit small, is indicative of the variation of the cobalt-oxygen

bonding in the diporphyrins. Recalling the extent of slippage of the diporphyrin structure, we suggest that the superoxo bridging ligand is bound in a trans-configuration in diporphyrin-5 but in a cis-geometry in diporphyrin-4.



There are two lines of evidence which seem to substantiate this proposal. First, many well-known cis-μ-superoxo binuclear cobalt complexes having an amido bridge, such as A, invariably exhibit symmetrical, sharply resolved hyperfine lines [47,48], very similar to the spectrum of diporphyrin-4. On the other hand, trans-μ-superoxo cobalt complexes, such as B, generally have a more diffused spectrum with larger line width for the hyperfine components. The difference has been attributed to the orientation of the lone-pair electrons on the oxygen yielding a local electric field perpendicular to the Co-Co axis [49].

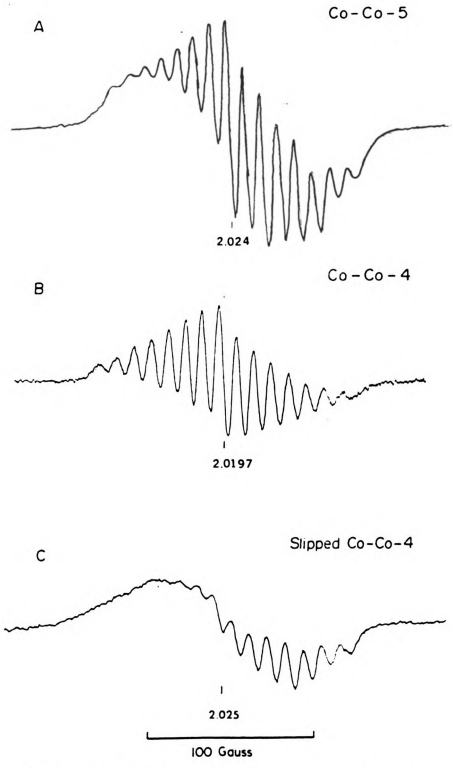
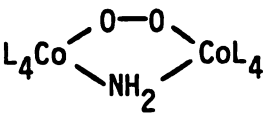
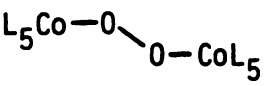


Fig. 3-6. ESR Spectra of μ-Superoxo Co-Co Diporphyrins
A. Diporphyrin-5 B. Diporphyrin-4
C. Slipped Diporphyrin-4



A



B

The slipped dimer-4 provided a further test of this proposal. In this molecule, the two rings are slipped by about 2.5 Å and the bridging oxygen ligand must bind in a trans-configuration. As shown by Fig. 3-6C, the μ-superoxo complex indeed exhibited the poorest resolved line shape.

Recently, binculear Co(II) and Fe(II) diporphyrins have been applied to the surface of graphite electrodes and tested for catalytic activity toward the electron reduction of dioxygen to water in aqueous electrolytes [42]. Most dimers tested exhibited some catalytic activity, but usually hydrogen peroxide rather than water was the major reaction product. However, Collman, Anson, and associates have reported [42] that a Co(II) Co(II) dimer FD4, similar to the one discussed above has produced a catalyzed reduction almost exclusively to water. Rotating ring-disk voltammetry was employed to diagnose the electrode reaction. It is unclear as why only the dimer-4, not the dimer-5, would give the activity since both dimers are capable of intercalating

molecular oxygen. Perhaps the cis-configuration of the diporphyrin-4, being more exposed to solvent, is more accessible to proton transfer and thus facilitates the cleavage of the stable peroxo bond. Similar consideration may be relevant to cytochrome oxidase activity since maintaining a flux of proton supply is as important as sustaining an electron flow at the oxygen reduction site.

G. Steric Effect in Oxygen and Carbon Monoxide Binding

X-ray structures of CO-hemoglobin and CO-myoglobin exhibit a bent or tilted configuration of the CO ligand with respect to the porphyrin ring [50], whereas in heme model compounds, the Fe-C-O bond is linear and perpendicular to the heme plane [51]. The origin of the different configuration is attributed primarily to nonbonding steric interactions of the axial ligand with residue at the distal side. This steric effect was postulated to decrease the affinity of CO in heme proteins [52]. An assumption is generally made that ligands such as O_2 and NO, which preferentially form bent complexes, should not suffer this steric effect [36,37]. Therefore, equilibrium and dynamic studies of O_2 and CO binding to the tightly spaced Fe-Cu diporphyrin should provide an excellent model to evaluate the steric effect on heme-ligand coordination.

The Fe-Cu dimer-4 was chosen for study because of its very short and rigid structure which could impose steric strain to the axial ligand(Fig. 3-7). Equilibrium constants of CO and O_2 binding to the ferrous heme were determined in

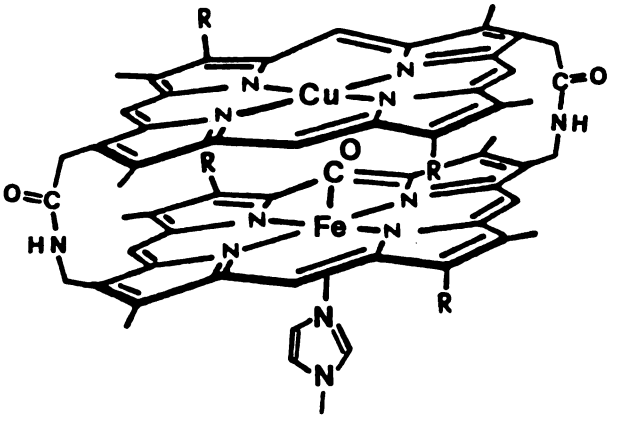


Fig. 3-7. Carbon Monoxide Binding to the Sterically Crowded Fe-Co Diporphyrin-4

benzene solution containing 0.2 M of N-methylimidazole. The nitrogen base can only coordinate only at the outside of the dimer to give a 5-coordinate heme. Kinetic rates were determined by a flash photolysis method [52] which permits direct measurements of CO and O_2 association rates as well as the the O_2 dissociation rate. The CO dissociation rate was calculated by $L_{CO} = \frac{l'on}{l\ off}$. The rate constants are tabulated in Table 3-3.

A comparison of the kinetic and equilibrium data of the Fe-Cu-dimer and those of a 5-coordinate mesoheme in nonpolar solvents clearly indicates that the effects of steric hindrance are mainly manifested in the ligand association rate constants. The CO association rate seems to be reduced more than the O_2 rate and the result is that both O_2 and CO affinities are reduced but not to the same extent. This can be seen by the smaller M value of the dimer. These findings are in good agreement with the prediction made earlier by Moffat et al. [50] on what effects steric hindrance have upon ligand hinding to heme proteins. It should be mentioned, however, that solvent effects can also play a major role in controlling equilibrium constants in small model compounds [52,55]. It is not clear from our data whether the relatively small variation in CO and O_2 off rates is due to steric effects or to local polarity effects. Further work is in progress to clarify this point. An important point contained in the Table 3-3 is that if steric effects only affect the ligand on rates then such effects are insignificant in R-state hemoglobins. Indeed, Traylor and coworkers [52,56]

Table 3-3. Kinetic and Equilibrium Constants For The Binding of CO and O_2 (20-22°C)

Compound	Solvent	k_1' M^{-1}	k_1' Sec^{-1}	k_1 Sec^{-1}	$P_{\frac{1}{2}}^{CO}$ torr	k_1' M^{-1}	k_1' Sec^{-1}	k_1 Sec^{-1}	$P_{\frac{1}{2}}^{O_2}$ torr	M	Ref
Chelated mesoheme	toluene	8	X 10^6	∿0.03	0.0004	5.3	X 10^7	1700	3.2	8 X 10^3	52 55
Fe-Cu dimer-4 N-MeIm	benzene	2.4	X 10^4	0.014	0.06	5.2	X 10^5	200	40	600	
Chelated protoheme	H_2O*	3.6	X 10^6	0.009	0.0018	2.6	X 10^7	47	1.0	560	55
Hb, isolated α^{SH}	H_2O	4	X 10^6	0.013	0.0024	5.0	X 10^7	28	0.3	130	33
Myoglobin	H_2O	3∿5	X 10^5	0.02∿0.04	0.014 ∿0.025	1∿2	X 10^7	10∿30	0.5∿1	20∿40	57
1-state Hb	H_2O	9	X 10^4	0.1	0.8	2.9	X 10^6	180	34	40	33

* Suspended in 2% CTAB

have shown the chelated protoheme model to bind both O_2 and CO in aqueous suspension with binding rates and thermodynamics almost identical to those of isolated hemoglobin chains. For the same reason, on the other hand, the steric effects may be very important in myoglobin and T-state Hb. It seems clear that one should keep in mind that there are many molecular processes that regulate the ligand affinity in hemoglobin [50]; different effects contribute differently at different stages of hemoglobin reactions for different ligands. This is an ideal case in which model studies could single out each molecular process, estimate the range and magnitude of individual effect and hopefully, inspire the direction for future elaborations.

H. Picosecond Measurement of the Electron Transfer in Slipped Mg-H_2 Dimer-SD5

In our previous work with Netzel et al. it has been shown that the cofacial Mg-H_2 dimer-5 yielded the charge transfer species with lifetime 380±40 ps in CH_2Cl_2 and 620±20 ps in CH_2Cl_2 with 0.1 M tetraethylammonium chloride following a 530 nm photoexcitation. In order to examine the effects of geometry, a slipped dimer-5 was synthesized. One of the macrocyclies is displaced slightly from the other resulting in a slipped diporphyrin and abbreviated as Mg-H_2 (5S) i.e. Mg and free base diporphyrin with two 5-atom bridges.

Fig. 3-8 shows the excited state spectra of Mg-H_2 (5S) in CH_2Cl_2. The spectrum at t=13 ps is similar to that of

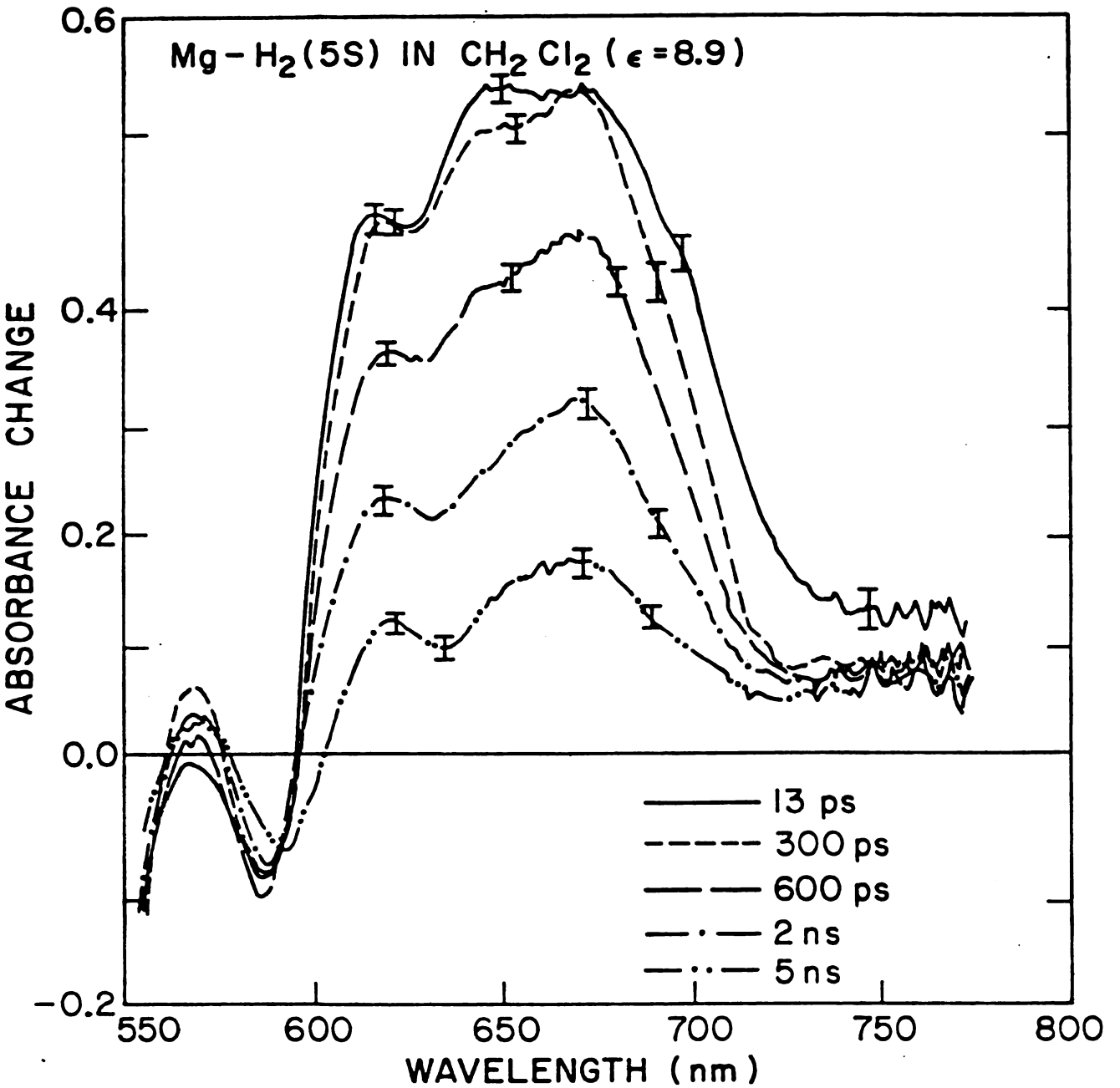


Fig. 3-8. Excited State Spectra of Slipped Dimer-5

Mg-H_2 (5) in CH_2Cl_2. The transient spectrum of 13 ps changes to the spectrum which is similar to that at 300 ps with estimated lifetime of 40 ps. The intensity longer than 680 nm decreases. This suggests the disappearance of the CT product. The spectrum at 300 ps looks like that of the singlet excited state. The transient between 100 ps to 300 ps changes little. Then the spectrum after 300 ps decays with a lifetime of about 2 ns (not single exponential). The pmr spectrum of slipped dimer-5 shows very complicated features which suggest multiple configurations of Mg-H_2 (5S) is considered to be dynamic instead of static. Probably the majority of the molecules have an open clam configuration which does not yield a CT species. Only a small number of molecules which have an overlap configuration yield CT product when excited. The overlap configuration also changes by thermal motion resulting in the ring opening or sliding. Based on the results of the cofacial dimer Mg-H_2 (5) and slipped dimer Mg-H_2 (5S), we can conclude that in order to stabilize charge transfer species the two porphyrin ring (donor and acceptor) are required to have parallel configuration.

Experimental

Most of the experiment materials and instruments were the same as described in Chapter 2.

Electron Spin Resonance Spectra

Spectra were collected on a Varian E-4 X-band spectrometer in a frozen glass (77^{o}K) of toluene and methylene chloride. The microwave frequency was measured by a cavity

wavemeter calibrated against the signal of diphenylpicryl-hydrazyl (DPPH) (g:2.0036).

Cyclic Voltammetry

Reagent: methylene chloride was distilled over CaH_2. Polarographic grade tetra-n-butylammonium perchlorate (TBAP) recrystallized three times from ethyl acetate/hexane before use as supporting electrolyte.

Apparatus: Cyclic voltammetry were carried out with a Model CV-1A instrument (Bioanalytical system Inc.). Current-voltage curves were recorded on an Moseley model 700 AM X-Y recorder. The reference electrode was an aqueous saturated calomel electrode (SCE). The working and counter electrodes were platinum.

Preparation of porphyrin amines

Reduction of diester porphyrin to diol 28

The diester porphyrin 27 (500 mg) was dissolved in 150 ml of THF. A suspension of $LiAlH_4$(1g) in 100 ml dry THF was added dropwise to the porphyrin solution with stirring. The reaction mixture was checked by TLC, until all ester was reduced to alcohol. The reaction was terminated by adding 1 ml ethyl acetate. The reaction mixture was passed through a silica gel pad, which was then elueted with 5% methanol/methylene chloride to give 28 in a 90% yield.

Mesylate porphyrin 29

The appropriate diol (400 mg) was dissolved in 1 ml triethylamine and 50 ml dry methylene chloride. The solution was cooled in an ice bath with stirring. Methanesulfonyl

chloride (0.5 ml) was added drop by drop and the reaction was monitored by TLC. After all diol was converted to mesylate, the solvent was removed, and the residue dried in vacuo. The mesylate was used without further purification.

N-Butyl amine porphyrins 30

The mesylate (300 mg) was dissolved in pure n-butylamine and refluxed overnight. After being checked by TLC to indicate the completion of conversion, the excess butylamine was removed on a rotary evaporator. The amine was precipitated by adding water and the solid (90%) was collected by filtration and washed thoroughly with water.

Preparation of primary amine porphyrin

Diacid porphyrin 31d

The methyl ester porphyrin 27e (500 mg) was dissolved in 30 ml 88% formic acid and 2 ml concentrated HCl, heated on an oil bath and refluxed for 1 hr. The solution was cooled and solvent was removed under reduced pressure. The residue was dried under vacuum to give the diacid porphyrin dihydrochloride 535 mg (100%). The other diacids were prepared in the same way.

Diacid chloride porphyrin 32d

Diacid 31d (535 mg) was dissolved in 2 ml $POCl_3$, after all solids were dissolved, 20 ml dry CH_2Cl_2 and 3 ml oxalyl chloride were added. The solution was refluxed for 1.5 hr, protected from moiture by $CaCl_2$. The solvent and unreacted oxalyl chloride were removed under reduced pressure and the residue dried under vacuum for 1 hr, a dark red solid 563 mg

(100%) was obtained. The other acid chloride was obtained by the same method without adding $POCl_3$.

Diacid azide porphyrin 33a

The acid chloride porphyrin 32d (300 mg) was dissolved in 25 ml dry methylene chloride. The mixture was cooled in ice bath and a solution of sodium azide (1 g) and tetra-n-butylammonium chloride (300 mg) in 10 ml water was added with vigorous stirring. After 10 min, the methylene chloride was removed under reduced pressure and a black solid was formed in water solution. The solid was collected, washed with water and dried under vacuum. The crude product was dissolved in 10 ml dry methylene chloride and passed through a silica gel pad. The pad was washed with more methylene chloride (100 ml) and the methylene chloride solution was concentrated under reduced pressure to give di(acid azide) 33a (250 mg, 91%).

IR: 1710; 2135 cm^{-1}.

PMR: 0.93 (poorly resolved triplet, 6H, $-(CH_2)_4\underline{CH_3}$), 1.30-1.80 (broad, 8H, $-(CH_2)_2-(\underline{CH_2})_2-CH_3$), 1.80-2.40 (broad, 4H, $-CH_2-\underline{CH_2}-C_3H_7$), 3.37 (s, 6H, $-CH_3$), 3.43 (s, 6H, $-CH_3$), 3.86 (t, J = 7.0 Hz, 4H, $-\underline{CH_2}-C_4H_9$), 4.47 (s, 4H, $-\underline{CH_2}-COOCH_3$), 9.67 (broad singlet, 4H, meso protons), -4.13 (broad, 2H, -NH).

Dipropionyl azide 33b was obtained in 98%

IR: 1690, 2140 cm^{-1}.

Dimethylisocyanate porphyrin 34a

Di(acid azide) porphyrin 34a (250 mg) was heated under reflux in dry benzene (100 ml) for 1 hr. The solution was removed under reduced pressure, the residue was dissolved in

methylene chloride and passed through a silica gel pad. The pad was washed with methylene chloride until no more product was obtained, the solution was concentrated on an evaporator, diisocyanate porphyrin 34a (207 mg, 90%) was obtained.

IR: 2250 cm^{-1}.

Diethylisocyanate porphyrin 34b

IR: 2260 cm^{-1}.

PMR: 1.00 (broad, 6H, $-(CH_2)_4-\underline{CH_3}$), 1.60 (broad, 8H, $-CH_2-CH_2-(\underline{CH_2})_2-CH_3$), 2.10 (broad, 4H, $-CH_2-\underline{CH_2}-C_3H_7$), 3.60 (s, 6H, $-CH_3$), 3.63 (broad, 12H, $-\underline{CH_2}-\underline{CH_2}-NCO$, $-\underline{CH_2}-C_4H_9$), 9.83 (s, 2H, meso protons), 10.0 (s, 2H, meso protons).

Dimethylamine porphyrin 35a

Diisocyanate porphyrin 34a (200 mg) was refluxed in 300 ml benzene and 200 ml 6N HCl for 1 hr. The mixture was cooled and the benzene layer was discarded. 500 ml of 9:1:0.5 chloroform:methanol:triethylamine was added into the acid solution and this mixture was cooled in an ice bath. 50% NaOH was added to the acid solution until it was neutralized. The organic layer was washed with water and passed through a silica gel pad. The solution was concentrated on an evaporator, 145 mg of 35a was obtained (79%); no further purification was necessary.

Diethylamine porphyrin 35b

This compound was prepared from 34b following the same procedure as 35a in 70% yield.

IR: 1600, 3350 cm^{-1}.

PMR: 1.00 (broad, 6H, $-CH_2)_4-\underline{CH_3}$), 1.67 (broad, 8H,

-($\underline{CH_2}$)$_2$-CH_3), 2.25 (broad, 4H, -$\underline{CH_2}$-C_3H_7), 3.63 (s, 6H, -CH_3), 3.70 (s, 6H, -CH_3), 4.00 (broad, 12H, -$\underline{CH_2}$-C_4H_9, -$\underline{CH_2}$-$\underline{CH_2}$-NH_2), 4.70 (broad, 4H, -NH_2).

General procedure for the diamide-linked diporphyrin preparation

Bis(acid chloride) porphyrin was dissolved in 60 ml dry methylene chloride and transfered to a 100 ml syringe under nitrogen gas. Diamino porphyrin was dissolved in 1 ml dry triethylamine and diluted with 60 ml dry methylene chloride, the solution was transfered to a 100 ml syringe under nitrogen gas. These two syringes were mounted on a motor-diver syringe pump (Sage Instruments Co. Model 352). The solution in syringes were injected at the same rate through stainless needles into 500 ml dry methylene chloride in a three-neck 1000 ml flask equipped with rubber septa and drying tube. When the addition was complete (1 hr), the solution was stirred for another hour. The mixture was evaporated under reduced pressure, the residue was dissolved in 50 ml methylene chloride and passed through a silica gel pad. The pad was washed with methylene chloride until no more product were eluted. The solution was concentrated to 5 ml, and charged on preparative TLC plates. A solvent mixture (CH_2Cl_2: MeOH, 95:5) was used as the developing solvent to isolate the diporphyrins. The diporphyrins prepared by this route may give two isomers "syn" and "anti". Attempts to separate them on TLC plate was unsuccessful. The diporphyrin bands were collected from the TLC plates and extracted by 5% MeOH

in CH_2Cl_2. The solution was reduced to 1 ml and diluted with methanol until precipitate formed. The solid was collected by filtration. The visible spectrum and PMR chemical shifts were listed on Table 3-1.

General method for copper insertion into porphyrins and diporphyrins

Porphyrins and diporphyrins were dissolved in dry methylene chloride (20 ml) and treated with excess copper acetate monohydrate dissolved in methanol. The mixture was refluxed for about 10 min. After the reaction was completed (monitor by visible spectra), the solution was concentrated to 1/10 volume and the precipitate was collected by filtration and washed with methanol.

General method for the preparation of Mg-Mg and Mg-H_2 diporphyrin

60 mg of magnesium metal and 1 ml iodomethane were added to 10 ml dry ether and refluxed until all metal was dissolved (about 30 min). 100 mg of 2,6-di-t-butylphenol was added to the Grignard solution, a yellowish solution was obtained. Diporphyrin was dissolved in 50 ml dry methylene chloride and the magnesium reagent was added. After swirling, a cherry-color solution was obtained. The solvent was reduced under reduced pressure to 1 ml, 20 ml methanol was added and the precipitate was collected by filtration. The Mg-Mg diporphyrin was obtained quantatively. The Mg-Mg diporphyrin was dissolved in 2 ml methylene chloride and charged on a TLC plate. After development by methylene

chloride, two pink color bands were obtained. The first band is Mg-Mg diporphyrin and the second band is Mg-H_2 diporphyrin. The products were collected by washing the silica gel bands with methylene chloride.

Cu-Fe dimer 4 [42]

I. Copper was introduced into the diacid porphyrin 31d by the copper acetate method and visible spectra confirmed the absence of free base porphyrin. The copper porphyrin (150 mg) was dissolved in 100 ml dry pyridine and 300 mg of p-nitrophenyl trifluoroacetate was added. The mixture was stirred overnight at room temperature under dark. The nitrophenyl ester gradually separated as brick-red microcrystals; 100 ml hexane was added and the mixture was cooled in an ice bath. The product was collected by filtration and washed with hexane to give 140 mg (73%) of nitrophenyl ester. The copper nitrophenyl ester porphyrin (140 mg) was dissolved in 100 ml dry pyridine, 90 mg of diamino porphyrin 35a in 30 ml warm dry pyridine was added, and the mixture was stirred at 70°C for 7 hr, light being excluded. The reaction was monitored by TLC to ascertain that all phenyl ester reacted. The solution was concentrated on an evaporator and dried under vacuum. The residue was dissolved in methylene chloride and washed with 10 ml 10% NaOH solution, then water. The organic layer was passed through a silica gel pad to remove the polymers and unreacted diamine. The dimer fraction was concentrated to 1 ml and diluted with methanol to form crystalline. Cu-H_2 dimer-4; 50 mg was obtained (yield 27%). Iron was

inserted into the Cu-H_2 dimer using the ferrous sulfate method.

Cu-Fe Dimer-4 and Dimer-5

II. Copper was introduced into the diacid porphyrins 31c and 31d by the acetate method. The acids were converted to acid chloride by reaction with oxalyl chloride. The respective acid chloride was coupled with amine 35a to obtain the Cu-H_2 dimer-5 and 4. Cu-Fe dimers were obtained by inserting iron to the Cu-H_2 dimer. No further purification was necessary.

CHAPTER 4

SYNTHESIS OF PORPHYRIN- AND CHLORIN-QUINONE DONOR-ACCEPTOR PAIR

Introduction

In photosynthesis, the functional unit is composed of several hundred chlorophyll (chl) moelcules in a protein matrix, a special pair of chl molecules which is the site of primary photoact, and a series of primary and secondary electron donors and acceptors. The primary photochemical process in algal and green-plant photosynthesis is known to be an one-electron transfer reaction from a chlorophyll donor to a plastoquinone acceptor. A similar process takes place in bacterial photosynthesis where the acceptor is a ubiquinone. The positive change left on the chlorophyll donor is ultimately linked to the oxidation of water.

One way to learn the primary events in photosynthesis is to synthesize a model system that would mimic some of the properties of photosynthetic apparatus.

In order to mimic the electron transferred process there are several approaches to be taken. One is to work with artificial membrane or micelles. Using detergents, one can prepare micelles, or artificial membranes absorbed with these chlorophyll or artificial pigment molecules. Electron donors and acceptors can be added to each side of the membrane. Upon illumination of this system, if proper components are

present, one can observe light promoted oxidation-reduction reactions.

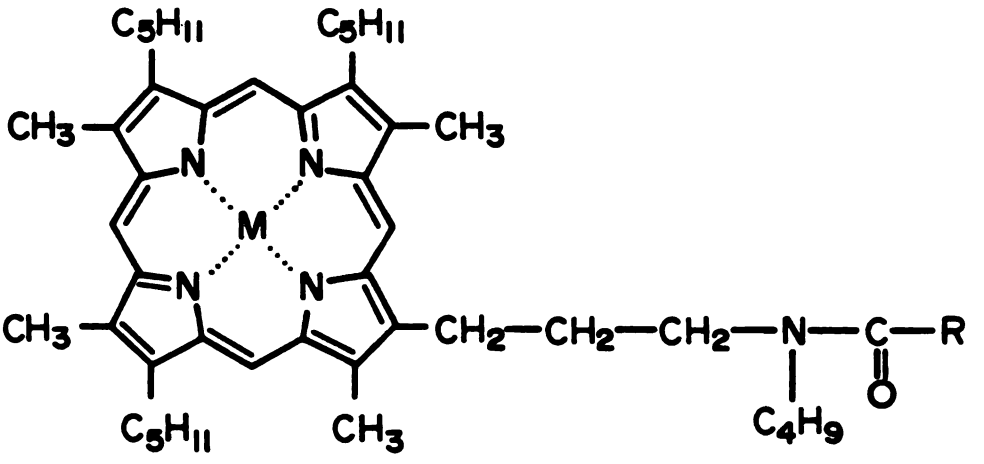
The bilayer lipid membrane (BLM) has been widely used as a light active model membrane since the photoelectric effects of BLMs were discovered in 1968 [58]. Several quinone-porphyrin compounds have been synthesized as the electron-transfer carrier. Tabushi et al. [59] have attached a benzoquinone to a TPP. Loach and King [60] have synthesized a similar compound with different chain length between quinone and TPP. Sanders [61] reported a quinone capped metalloporphyrins. On the other hand, because of the instability of chlorins, there was no chlorin-quinone compound reported. Chang [62] has recently synthesized a stable methylated chlorin from OEP; it should be possible to link a quinone to this chlorin to form a quinone-chlorin complex. In this study several quinone-porphyrin compounds were also prepared from the mono-propionate porphyrin 13.

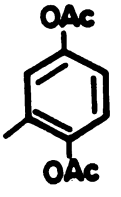
Results and Discussion

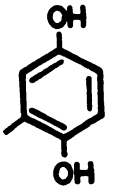
The monoketone chlorin was converted to ethyl acetate by lithio ethylacetate and then reduced by HI [63]. The monoester of porphyrin 13 and chlorin 37 were converted to butylamine 38 and 39 following the same procedure as Chapter 2. The synthesis of the quinone-porphyrin and -chlorin were shown in Scheme 4-1,2.

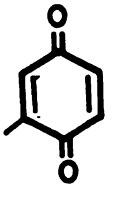
In order to overcome the instability of the hydroquinone during the linking process, the hydroxy groups was blocked by converting them into the acetate 40. The acid group was

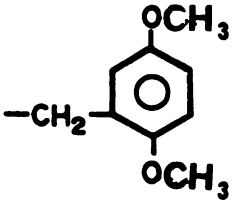
Scheme 4-1.

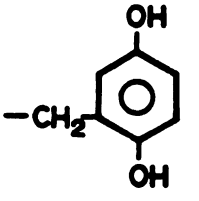


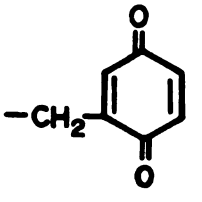
43 R = 

44 R = 

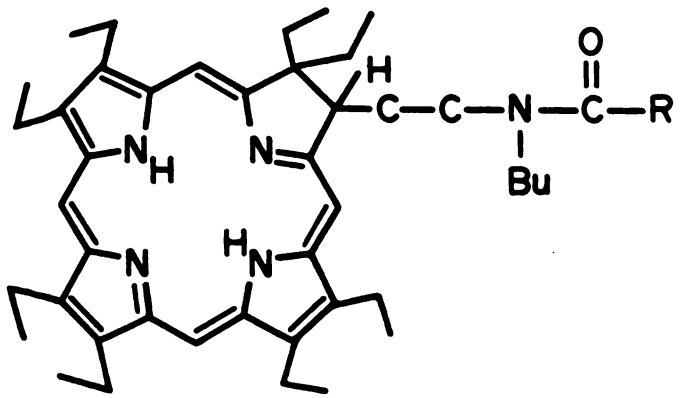
45 R = 

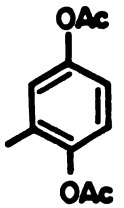
46 R = 

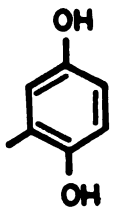
47 R = 

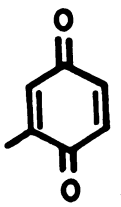
48 R = 

Scheme 4-2.



49 R = 

50 R = 

51 R = 

activated with thionyl chloride to get the acid chloride 41 and 42 and then condensed with the amines 38 and 39. In order to obtain the hydroquinoneyl functionality, 43 and 49 were hydrolyzed by methanolic hydrochloric acid. Compound 46 was demethylated using boron tribromide. The hydroquinone 44, 47 and 50 were converted into quinone by the oxidation of silver oxide. The quinone compounds were highly photolabile; it is important that extreme care must be taken to exclude light during their synthesis as well as during subsequent manipulations. Because of the thermodecomposition of those quinone compounds, there are no molecular ions in mass spectra.

The photovoltaic effect of these quinone compounds were obtained on a bilayer lipid membrane. The photovoltage of 45, 48 and 51 was 230 mv, 140 mv and 139 mv respectively. The photovoltage of zinc complex of 48 was increased to 180 mv. The photovoltage of chloroplast extract was only about 90 mv [64]. Bolton et al. [65] studied the electron transfer effect in monolayer assemblies, chlorophyll as an electron donor, various quinones as acceptor. With acceptor containing saturated side chain, the open circuit photovoltage was lower than that with unsaturated side chain. In compound 45 there has a carbonyl group to conjugate with quinone, on compound 48 the conjugation was interupted by a methylene group, and the photovoltage was dropped from 223 to 140 mv. The inserting of the zinc metal into compound 48 decreased the redox potential of porphyrin ring, make it is more easy for

electron transfer, the photovoltage increased to 177 mv.

Experimental

The purification of solvents and instruments were the same as chapter 2.

The basic photoinactive membrane forming solution for experiments is a 1 : 1.7 : 3.1 : 1.1 mixture of phosphatidylserine/phosphatidylcholine/phosphatidylethanolamine/cholesterol in n-octane to a final concentration of less than 1% (W/W). Sodium ascorbate acts as donor and ferric chloride acts as acceptor.

The technique used in the measurement of photovoltage is essentially the same as that described previously. BLMs solution were formed in a 1-mm aperture of a Teflon cup separation two aqueous bathing solutions. The cup was placed in a pyrex glass chamber with an optical glass window. Electrical contact between the two aqueous solutions was made by a pair of calomel electrodes with internal salt bridges. The photopotentials and photocurrents were measured with a high impedance electrometer (Keithley Model 610), with high input to the inside BLM chamber, and connected to ground. The membranes were formed in 0.1 M sodium acetate buffer at PH 5. After the membrane had thinned to the black state and its dark resistance has reached a steady value of approximately $10^8\Omega$, the electron donor 100 µl was added to the outside of the membrane (facing the light source), while the electron acceptor 100 µl was added to the opposite side of the membrane. Then the membrane was irradiated with white tungsten light

(200mW/cm^2) to obtain the photopotentials.

2,5-Diacetyl benzoic acid 40

2,5-Dihydroxy benzoic acid 3 (500 mg) and 500 mg anhydrous sodium acetate were dissolved in 2 ml acetic anhydride. The mixture was refluxed for 3 hr and then poured into 50 ml water, the pH value of the solution was adjusted to 7, and twice extracted with ether. The ether was removed under reduced pressure to give 700 mg of diacetate benzoic acid (91%). p.m.r. 2.27 (s, 6H, -CH_3), 7.00 (d, J = 8.0 Hz, 1H, Ha), 7.13 (d,d, J = 8.0, 2.0 Hz, 1H, Hb), 7.63 (d, J = 2.0 Hz, 1H, Hc). MS: M^+ = 238.

(2,5-Diacetyl)benzyl chloride 41

2,5-Diacetyl benzoic acid (500 mg) was dissolved in 20 ml dry benzene, 20 ml dry ether and 1 ml thionyl chloride. The mixture was refluxed for 5 hr and then allowed to stand overnight at room temperature. After removal of the solvent, a white crystal was obtained. No further purification was necessary. MS: M^+ = 256.

(2,5-Dimethoxy) phenylacetyl chloride 42

The acetyl chloride was obtained using the same procedure as 41. MS: M^+ = 204.

Preparation of secondary amine of porphyrins and chlorin

The secondary amine of porphyrins and chlorin was prepared using the same procedure as Chapter 3.

Porphyrin amine 38

MS: 632 (M^+-Bu).

Chlorin amine 39

MS: M^+ = 635.

General preparation of 45, 48, 51

The amine 50 mg was dissolved in 50 ml dry methylene chloride and 1 ml dry triethylamine, the methylene chloride solution of acid chloride was added in excess. The reaction mixture was stirred for 20 min. The solution was washed with water and passed through a silica gel short pad to remove the unreacted acid and amine. The filtrate then concentrated and purification on preparative TLC plate with a solvent of methylene chloride. The amide products 45, 58 and 51 were obtained in 60%.

Diacetyl benzene porphyrin 43

MS = 852 (M^+-Bu), p.m.r. 3.50 (s, OAc, 6H), 6.70 (1H). VIS: 398, 496, 536, 566, 620 nm.

Dimethoxy benzene porphyrin 46

MS: M^+ = 867. p.m.r. 3.5 (s, OCH, 6H), 6.0-6.9 (aromatic H). VIS: 397, 496, 530, 566, 619 nm.

Diacetyl benzene chlorin 49

MS: M^+ = 855. p.m.r. 0.80 (complex, $CH_2\underline{CH_3}$, unsaturated), 0.95 (t, $-(CH_2)_3-\underline{CH_3}$), 1.30 ($-CH_2\underline{CH_3}$, unsaturated), 1.50 ($-CH_2\underline{CH_3}$, unsaturated), 1.80 ($CO\underline{CH_3}$, $\underline{CH_2}CH_3$, saturated), 3.9-4.0 ($\underline{CH_2}CH_3$, unsaturated), 4.5 (broad, $\underline{CHCC}$), 6.7-7.2 (aromatic H).

Hydroquinone porphyrin 44

50 mg of 43 was dissolved in 10 ml dry methylene chloride and mixed with 10 ml of HCl saturated methanol. The mixture was heated on a steam bath for 20 min. The solvent was removed on a rotary evaporator and the residue dried in vacuo;

35 mg of dihydroxybenzene porphyrin was obtained. VIS: 398, 496, 530, 565, 620 nm.

Hydroquinone porphyrin 47

100 mg of porphyrin 46 was dissolved in 50 ml dry methylene chloride with stirring in a dry ice acetone bath. 2 g boron tribromide in 10 ml methylene chloride were added dropwise. The reaction mixture was stirred at -78°C for 5 hr and then warmed up to room temperature. It was kept stirring for another 2 hr before 10 ml water was added over a 10 min period to terminate the reaction. The organic layer was passed through a silica gel pad; the front fraction was discarded. The pad was then washed with 10% methanol/methylene chloride solution to collect the dihydroxy benzene porphyrin (yield 60%). MS = 631. VIS: 393, 496, 532, 564, 616. p.m.r. 6.1 (complex, aromatic H).

Hydroquinone chlorin 50

This compound was obtained as 44. VIS: 395, 495, 590, 644. MS: M^+ = 772. p.m.r. 6.8 (broad, aromatic H).

General procedure for the preparation of quinone porphyrins 45, 48, 51

The dihydroxybenzene porphyrin (20 mg) was dissolved in 20 ml dry THF. Anhydrous magnesium sulfate 1 g and 0.5 g silver oxide were added to the solution. The mixture was stirred in dark for 30-40 min. The reaction mixture was then passed through a silica gel pad to remove the solid and unreacted dihydroxy benzene porphyrin. The quinone porphyrin 45, 48 or 51 was obtained with about 85% yield.

Quinone porphyrin 45

VIS: 398, 498, 524, 556, 620 nm. IR: 1640, 1660 cm^{-1}. MS: decomposed.

Quinone porphyrin 48

VIS: 397, 496, 532, 563, 616 nm. IR: 1600, 1630, 1660 cm^{-1}. MS: Mz = 631. p.m.r. 4.87 (s, 2H, methylene H), 6.0 (complex, 2H), 6.5 (complex, 1H).

Quinone chlorin 51

VIS: 392, 488, 496, 522, 590, 644 nm. IR: 1615, 1670 cm^{-1}. MS: decomposed. p.m.r. 6.6-7.2 (aromatic H).

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