SYNTHESIS OF 2,2',12,12'-BISDECAMETHYLENEDI-(7,17-DIETHYL-3,8,13,18-TETRAMETHYLPORPHINE)

by

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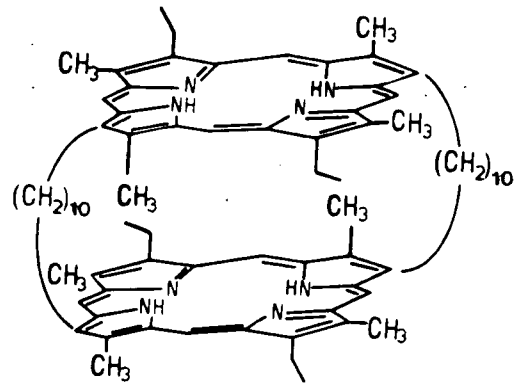
ABSTRACT

The interactions between porphyrins and related tetrapyrrolic macrocycles play many varied and important biological functions. In many of these systems the tetrapyrrolic macrocycles, whilst not covalently linked, are closely associated and the proximity and relative orientations are of critical importance.

This thesis describes the synthesis of a covalently bislinked dimeric porphyrin. Our approach consists of



constructing a single link first, and building a porphyrin onto either end, simultaneously, in symmetrical fashion via an a,c-biladiene. A variety of methenes were produced to enable the synthesis of porphyrins with reactive side-chains diagonally opposed to the first link. Singly linked porphyrins with C_6,C_8 and C_{10} chains were produced.

The porphyrin side chains were then modified to produce a terminal acetylene diagonally opposed to the first link. The second link was then achieved by an oxidative coupling

and catalytic hydrogenation to yield a bislinked porphyrin dimer with two hydrocarbon chains.

A model reaction is also described in which a monomeric porphyrin was dimerised to assess the feasibility of the side chain modification and the final oxidative coupling reaction to produce the singly linked dimer.

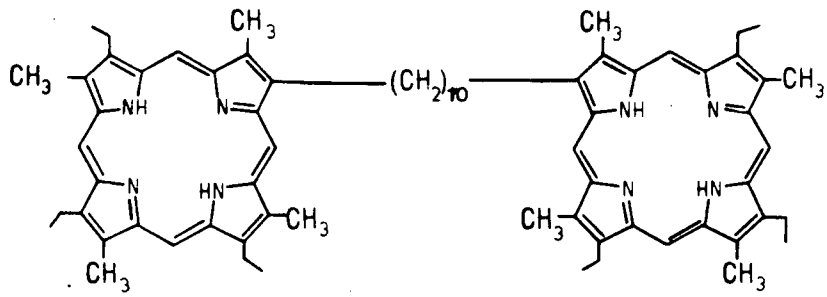


TABLE OF CONTENTS

Page

LIST OF FIGURES

ABBREVIATIONS

^{1}H NMR	=	proton nuclear magnetic resonance
^{13}C NMR	=	carbon-13 nuclear magnetic resonance
C_{6-6} etc	=	bis linkages of $(CH_2)_6$
Bz	=	benzyl
Et	=	ethyl
Me	=	methyl
EDA	=	ethylene diamine
DMSO	=	dimethylsulfoxide
σ-DCB	=	1,2-dichlorobenzene
Pyr	=	pyridine
TMEDA	=	tetramethylethylenediamine

Abbreviations in NMR Assignments

s	=	singlet	m	=	multiplets
d	=	doublet	bs	=	broad singlet
t	=	triplet	bd	=	broad doublet
q	=	quartet	pyr	=	pyrrole
			ppm	=	parts per million

ACKNOWLEDGEMENTS

I would like to thank Professor David Dolphin for his encouragement and guidance during the course of this work. It has been an enjoyable and rewarding experience.

My thanks to the members of the Dolphin Group, past and present, for their help and friendship.

My thanks also to all the Chemistry Department services, the help afforded to me by Peter Borda, the NMR and Mass Spectroscopy departments is gratefully acknowledged.

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To

Phillip, Paul and Annette

For Their

Love and Understanding

CHAPTER 1

INTRODUCTION

1. INTRODUCTION[1]

1.1 General Review of Bisporphyrins

Nature having once discovered a useful system has no reticence in exploiting it to the fullest. One such system is the porphyrin macrocycle and its dihydro and tetrahydro compounds, chlorin and bacteriochlorin. A diverse array of hemes are employed in nature, probably the best known being hemoglobin, the tetrameric heme protein responsible for oxygen transport in mammals. Myoglobin, its monomeric analog is used for oxygen storage in mammal tissue.

The cytochromes[2] are a series of heme proteins whose principal biological function is electron and/or hydrogen transport by virtue of a reversible valency change of their heme iron. The cytochromes are classified into four groups depending upon their heme groups. Cytochrome a contains a formyl side chain, cytochrome b has protoheme as the prosthetic group, cytochrome c has covalently linked proteins and cytochrome d has a chlorin prosthetic group.

Cytochrome oxidase is responsible for the terminal step in the four electron reduction of oxygen in the respiratory system, and contains two heme groups and two copper ions. The heme groups have been shown to differ and have been labelled cytochromes a, a_3;[3] the copper ions have also been shown by EPR to be different, one as cupric the

other of unknown valence.[4] An overall picture of the oxygen reduction is the addition of one electron from each of the two iron and the two copper ions. The short half lives of intermediates postulated by Greenwood and Gibson[5] suggest that the active site must contain all four metal ions in close proximity. The electrons for the oxidation are transported to cytochrome oxidase via a series of cytochromes. The electron transfer between heme groups would indicate the close proximity of these hemes during the transfer.

Catalase and peroxidase, heme proteins which bring about reductions of superoxide and peroxide, also exhibit electron transfer. Cytochrome P-450 a type b cytochrome exhibits oxygen binding and electron transfer in a variety of biological hydroxylations. NADPH is believed to enter the reduction twice, once as reductant of ferric P-450 and again transforming the initial oxygen adduct of ferrous P-450 into an active hydroperoxo-complex which then oxidises the bound substrate molecule after transformation into a ferryl form.

Chlorophyll, a dihydroporphyrin, and bacteriochlorophyll, a tetrahydroporphyrin, also have a variety of functions. In the photosynthetic process chlorophyll aggregates act as antenna to absorb light energy.[6] The electronic energy produced is then transferred along the chlorophyll chains

to the so called "special pair".[7] The "special pair" or P-700 (P870 in bacteria), so labelled because of their characteristic absorptions, is believed to be two chlorophyll molecules in close proximity which act as a primary electron donor. The radical formed by the expulsion of an electron is stabilized by the delocalisation over the pair of macrocycles. The P-700 radical has a characteristic Gaussian (ESR) signal with a g-value of 2.0025 and signal width 7 gauss which has been shown to be $1/\sqrt{2}$ that of the monomeric chlorophyll radical.[8] Theory predicts the signal should be $1/\sqrt{N}$ when the radical is spread over N chlorophyll molecules.

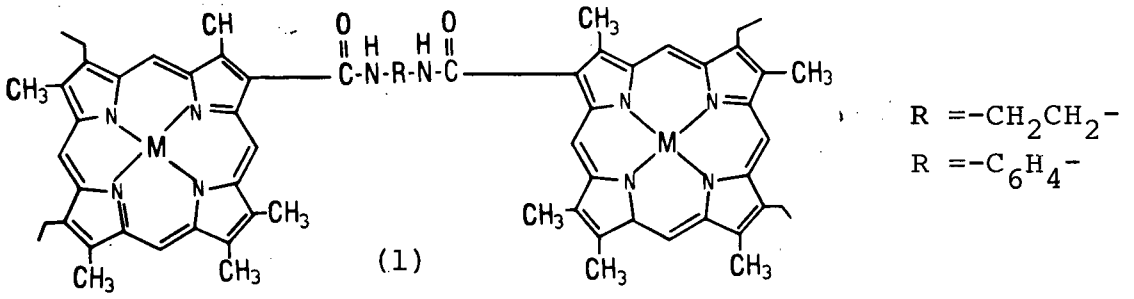
While in none of the above systems are the tetra-pyrrolic macrocycles covalently linked, their proximity and relative orientations are of critical importance. In nature this spacing is in general achieved by orientation in membranes. As yet the bioorganic chemist is not sufficiently skilled to mimic these membranes. Instead the relative disposition of dimeric porphyrins have been controlled by linking them covalently. We describe here the synthetic approaches towards such systems and some properties exhibited by dimeric porphyrins.

1.1.1 Synthesis

The initial approach was to take two porphyrins and covalently link them with amide, ester or ether linkages.

Here follows a chronological review of these syntheses.

In 1972 Schwartz et al.[9] reported the synthesis of a covalently linked bisporphyrin (1). The authors



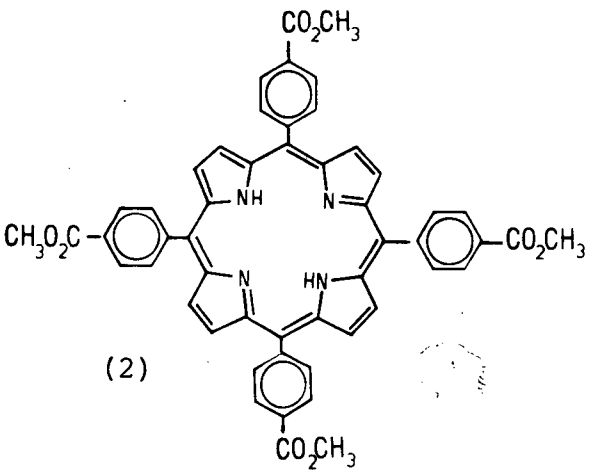
(1)

reacted 2-carboxyl-7,12-diethyl-3,8,13,17,18 penta-methylporphyrin with oxalyl chloride to give the acid chloride; this was treated with an excess of ethylene diamine or phenylene diamine to give 2-(p-amino-ethylaminocarboxyl) or 2-(p-amino-phenylaminocarboxyl) porphyrins. These were metallated with copper or cobalt and reacted with more of the acid chloride porphyrin to give a series of singly metallated bisporphyrins. Treatment with zinc acetate afforded the mixed metal bisporphyrins.

While this method of covalent linkage is almost trivially easy, and despite the fact that others (vide infra) have followed the same path, the amide linkages (and esters or ethers also employed) present two major problems. Porphyrins and metalloporphyrins are inherently of low solubility and dimeric porphyrins even more so; and the incorporation of an amide linkage additionally decreases the solubility. Secondly, the amide linkage is a reasonably reactive functional group, and although amide linkages maintain their integrity

under physiological conditions this is not necessarily the case in the laboratory. It has been found that such covalently linked dimeric porphyrins readily cleave to monomeric species. The only advantage other than convenience to such linkages is that mixed-metal dimers are most readily prepared by coupling of pre-metallated monomers.

In 1976 Anton et al.[10] transesterified 5,10,15,20-tetra(4-carbomethoxyphenyl)porphyrin (2) with an equimolar quantity of ethylene glycol. The resultant six component



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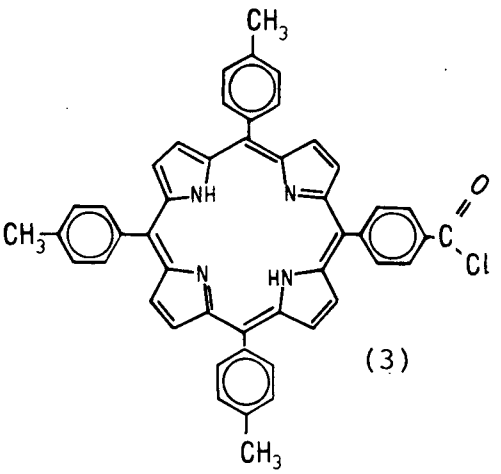
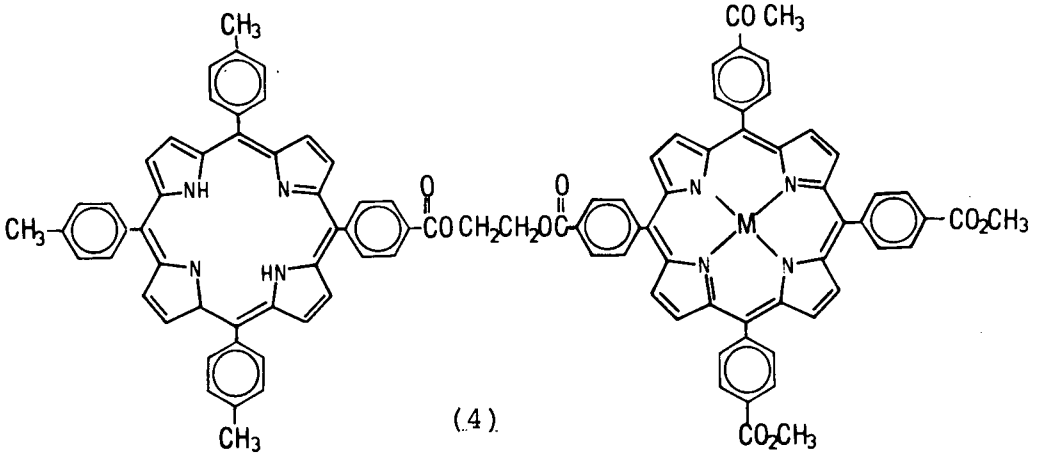


(3)

mixture was separated by chromatography to give starting material monotransesterified, two ditransesterified, tri-transesterified and the fully transesterified products. The mono and ditransesterified products were metallated and reacted with the acid chloride of 5-carboxyphenyl-10,15,20-tritolyporphyrin (3) (prepared by a mixed-aldehyde synthesis) to give the bisporphyrin (4) and two trisporphyrins one of which is shown (5).



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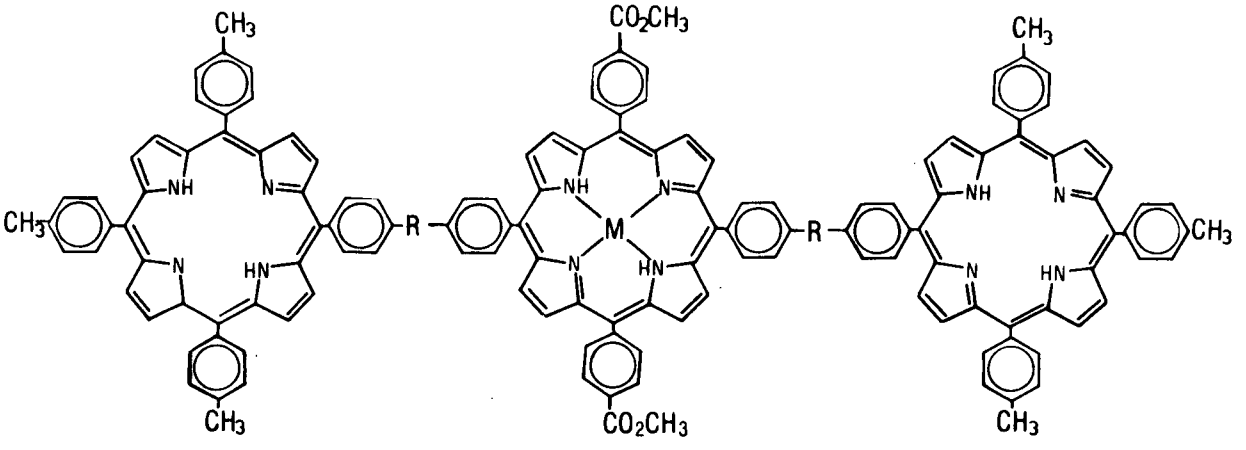
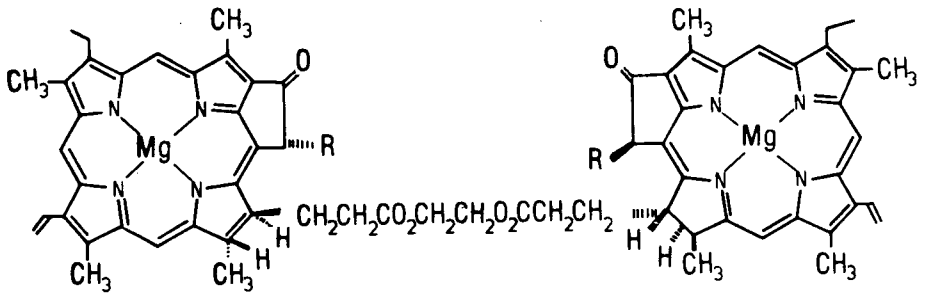


(5) R =-$CO_2CH_2CH_2O_2C$-

Boxer and Closs,[11] working on P-700 models, in the hope of mimicking the chlorophyll "special pair", transesterified methyl pyropheophorbide a with ethylene glycol to afford the monoester. Treatment with pyropheophorbide a activated by 1,1'-carbonyldiimidazole resulted in the di-ester which was metallated with magnesium by the Eschenmoser method[12] to give (6).



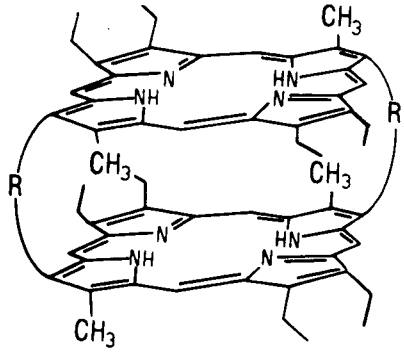
(6) R = H

(7) R =$-CO_2CH_3$

Wasielewski et al.[13] working in the same field treated pheophorbide a at room temperature in tetrahydrofuran/pyridine with methyl chloroformate and esterified the anhydride with excess ethylene glycol to give the monoester of pheophorbide a. Coupling was carried out in pyridine at 0° with a 2:1 molar ratio of the monoester to pheophorbide a using the mild acylating agent phosgene to give the dimer (7).

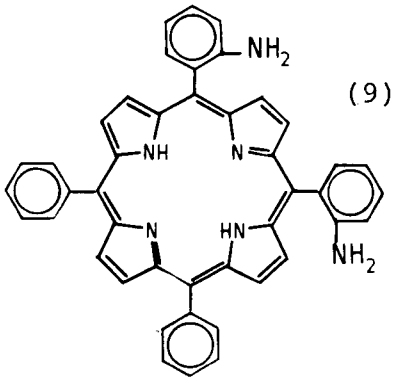
While a single covalent link ensures the two porphyrins are held within a specified distance of each other there is no guarantee of metal-metal interactions; one would thus like to have better control over the relative disposition of the two macrocycles. In an attempt to meet this criterion the synthesis of doubly linked porphyrins was undertaken.

In 1977 Ogoshi et al.[14] reacted 7,17-bis-(2-carboxyethyl)2,3,12,13-tetraethyl-8,18-dimethylporphyrin with isobutyl chloroformate in tetrahydrofuran, this was highly diluted and added dropwise to a tetrahydrofuran solution of 7,17-bis-(3-hydroxypropyl)-2,3,12,13 tetraethyl-8,18-dimethylporphyrin to give the doubly linked bisporphyrin (8).



(8) R $=-CH_2CH_2CO_2CH_2CH_2CH_2-$

Collman et al.[15] condensed pyrrole (2 eq) with benzaldehyde (1 eq) and 2-nitrobenzaldehyde (1 eq) in acetic acid to give a mixture of tetraphenylporphyrin and mono, di, tri and tetranitrophenylporphyrins. Chromatographic separation gave the diphenyldinitrophenylporphyrins. These were reduced with $SnCl_2/HCl$ to give the α, α-trans (9) and α, α-cis diaminophenyl-diphenylporphyrins (10). The α, α-trans diaminophenyl-diphenylporphyrin



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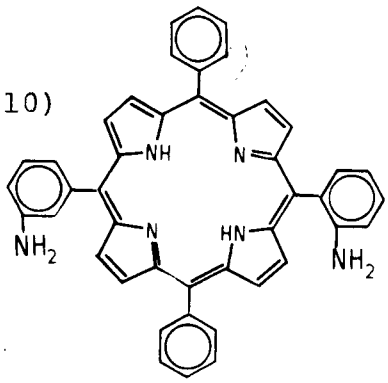
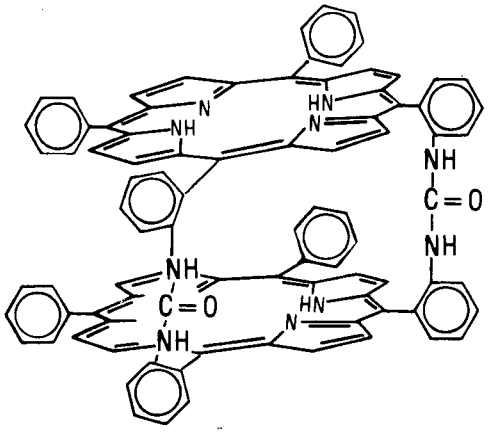


was treated with excess phosgene followed by a second equivalent of itself to give bisporphyrin (11). The same procedure using the α,α cis-diaminophenyl-diphenylporphyrin resulted in the two bis porphyrins (12) and (13). Reaction of α,α-cis diaminophenylporphyrin with mesoporphyrin IX diacidchloride resulted in the bisporphyrin (14).



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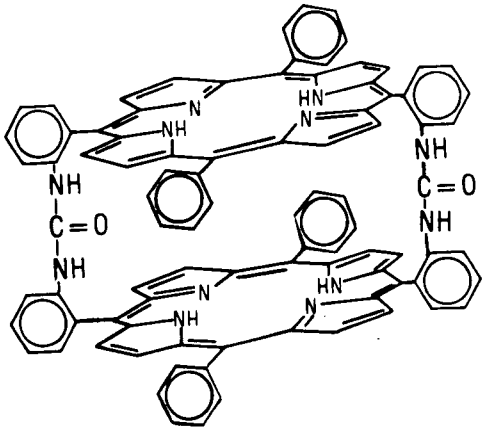

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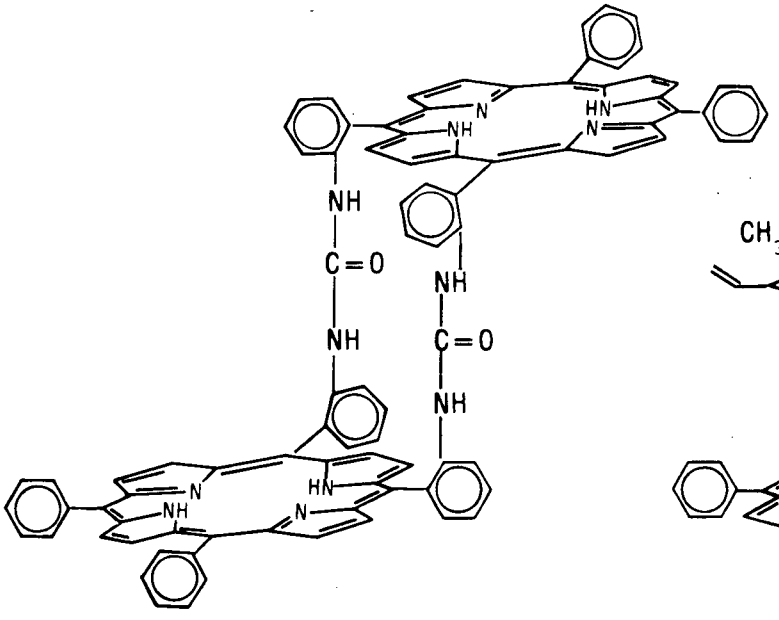

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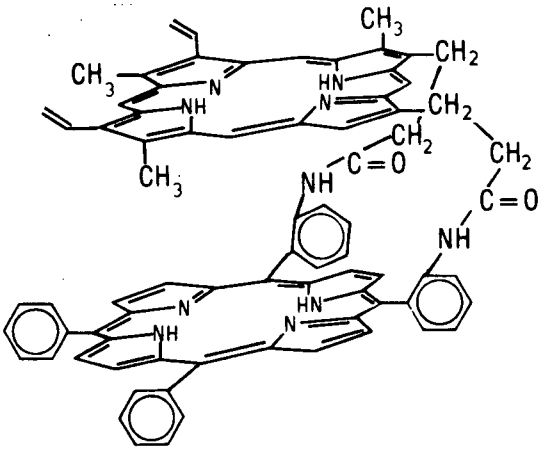
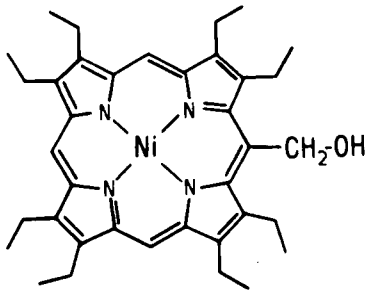


(14)

Arnold et al,[16] whilst working on the reactions of meso-hydroxymethylporphyrin,found that octaethyl-meso-hydroxymethyl porphinatonickel (15) refluxed in dimethylformamide in the presence of sulfuric acid gave 50% yields of meso, meso'-ethylenebisoctaethylporphinato nickel (16). This was the first reported dimer linked solely through carbon. The synthesis, of course, is not amenable to linkages other than two-carbons long.



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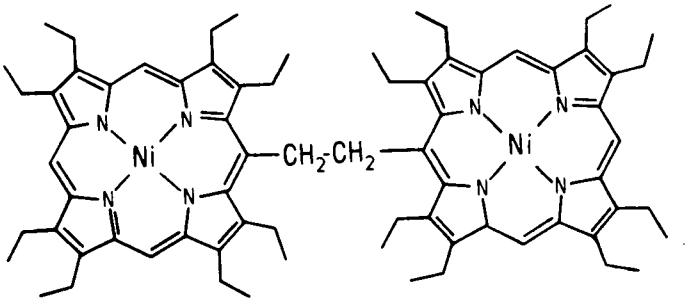
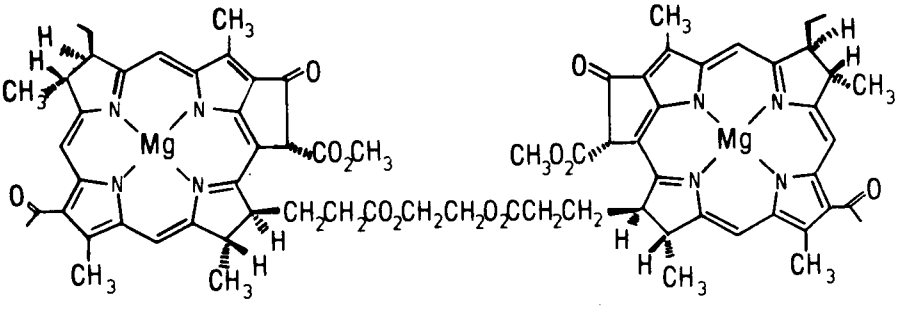


(16)

Wasielewski et al.[17] produced the bacteriochlorophyll dimer (17) by the esterification of bacteriopheophorbide a with ethylene glycol using benzotriazole N-methanesulfonate and triethylamine in tetrahydrofuran to give the mono ester.



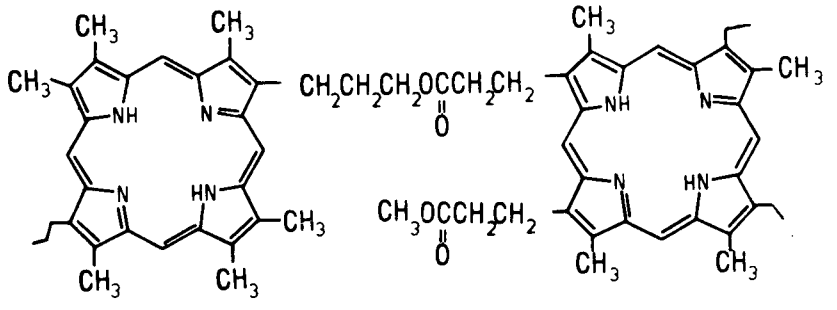
(17)

This was coupled with a second bacteriopheophorbide by the same method, except 4-dimethylaminopyridine was used as the base and methylene chloride as solvent.

Whereas earlier work had used synthetic porphyrins it was found to be convenient to use mixtures of monoesters available from the unselective mono-saponification of the diester (or mono-esterification of the diacid) of the readily available naturally derived porphyrins such as protoporphyrin.

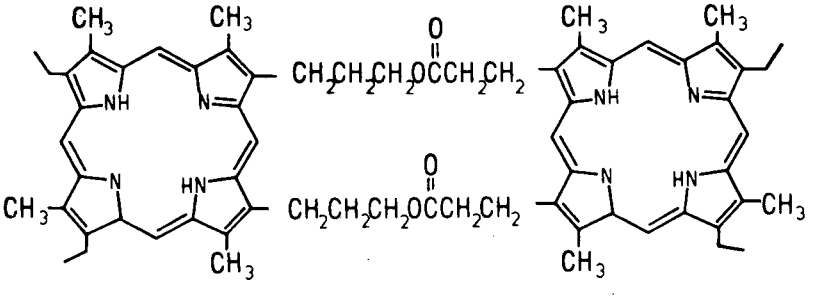
Owing to the lability of the vinyl groups to photo-oxidise, they are usually hydrogenated to ethyls (mesoporphyrin) or cleaved off (deuteroporphyrin) before being applied to dimer work.

Ichimura[18] prepared a mixture of singly-linked porphyrins (one of which is shown as (18) by reacting the acid chloride of the mixture of monomethyl esters of mesoporphyrin IX (derived from a partial saponification of the diester)



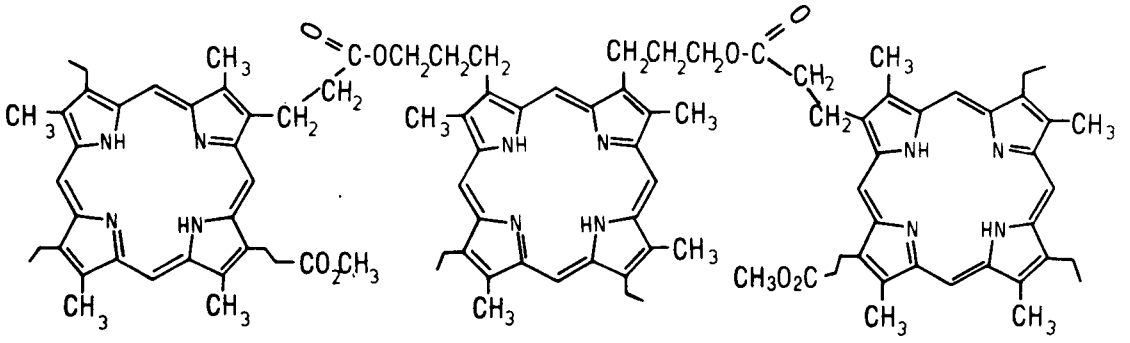
(18)

with 2-(3-hydroxypropyl)-3,7,8,13,17,18-hexamethyl-12-propylporphyrin. Reaction of the diacid chloride of mesoporphyrin IX with 3,7-bis(3-hydroxypropyl)-2,8,13,18-tetramethyl-12,17-diethylporphyrin gave the doubly linked bisporphyrin (19) as an isomeric mixture. Reaction of the



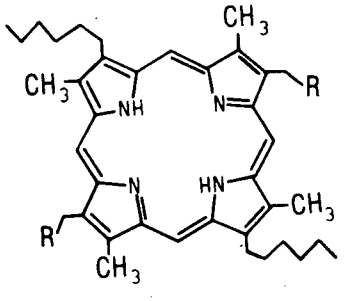
(19)

same bis(3-hydroxypropyl) porphyrin with 2 equivalents of the acid chloride of the monomethyl ester of mesoporphyrin IX gave a mixture of trimers (such as 20).



(20)

Chang et al.[19] synthesised the porphyrin (21) R=COOH or R=CH_2COOH, and manipulated the side chains to give R=$CH_2NR'H$ or R=$CH_2CH_2NR'H$. High dilution coupling of pairs of these porphyrins gave a series of cofacial dimers (22).



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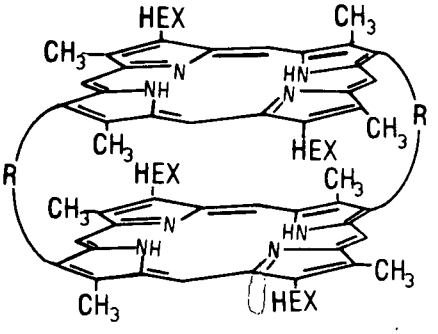


R= $(CH_2)_2CONR(CH_2)_2$

R= $(CH_2)_2CONR(CH_2)_3$

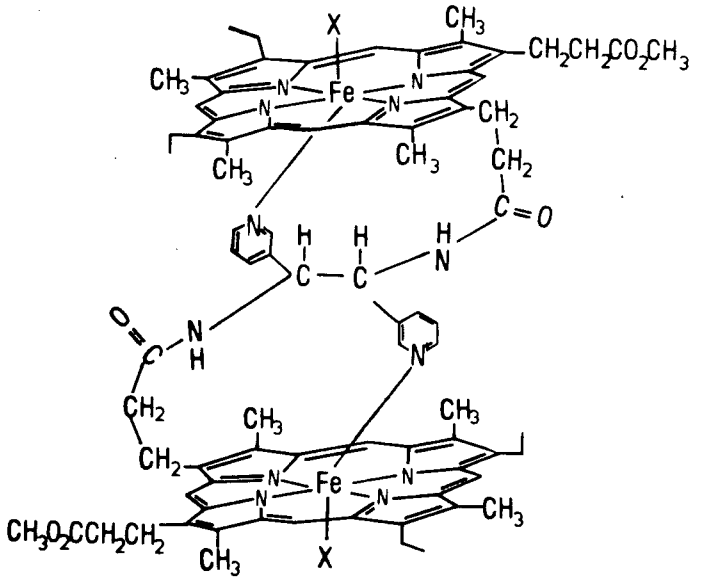
R=$CH_2CONR(CH_2)_2$

R=$CH_2CONR(CH_2)_3$

(22)

Various metal ions were incorporated at the monomer stage to give mixed metal systems. In order to relieve the low solubility discussed above, hexyl side chains were used to enhance the solubility in organic solvents.

Traylor et al.[20] coupled meso-1,2-di(3-pyridyl)-ethylenediamine with mesoporphyrin IX monomethyl ester through the pivaloyl anhydride to give the bisporphyrin. Insertion of iron gave the bisporphyrin (23).

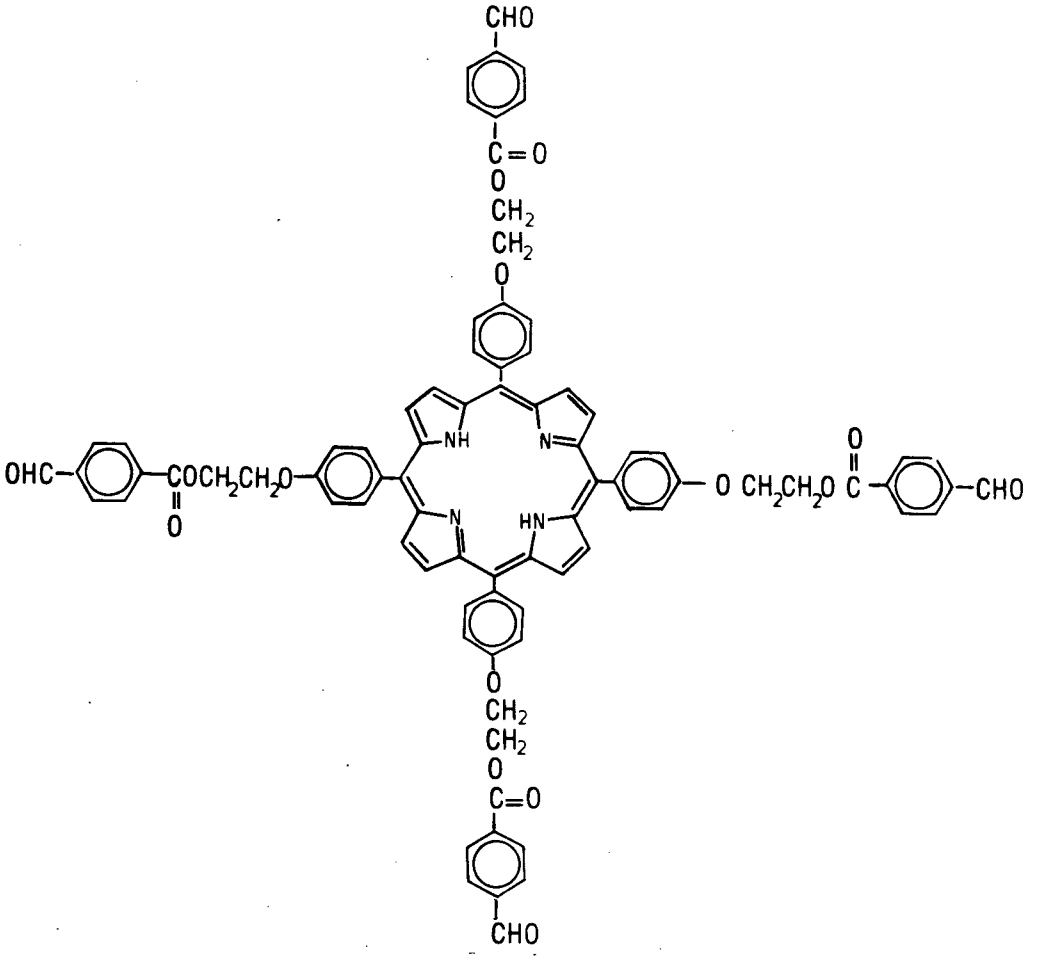


(23)

Porphyrin dimers linked <u>four</u> times have been prepared as well. If applied to β-octaalkyl porphyrin dimers, four links would remove the ambiguity of orientation inherent with dimers linked only twice (through diametrically opposite beta-positions), and result in a single, well defined substance. Such a synthesis has yet to be reported.

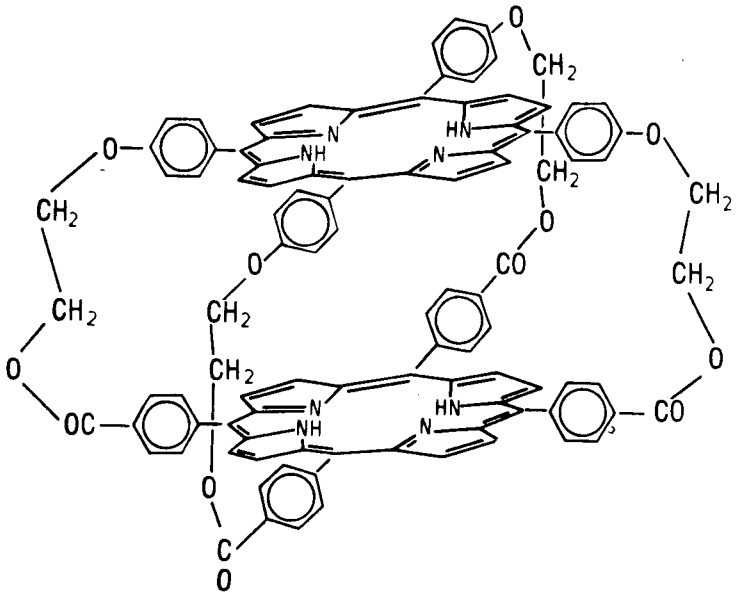
In the context of meso-tetraaryl porphyrin chemistry, even two linkages (through opposite meso-positions) will result in but a single isomer. The two additional linkages were added more to discourage slippage or tilting of the two porphyrin units with respect to each other, and to provide a more rigidly defined geometry thereby. The only example reported so far is by Kagan. The enormous problems of producing four covalent links between two porphyrins was overcome by the synthesis of

the second porphyrin in situ at the ends of the four links in a similar manner to that used by Almog et al.[21] in the synthesis of capped porphyrins. Kagan et al,[22] took p-2-hydroxyethoxybenzaldehyde and reacted it with pyrrole in refluxing acidified xylene, followed by esterification with the aid of p-carboxybenzaldehyde to give (24). Reaction



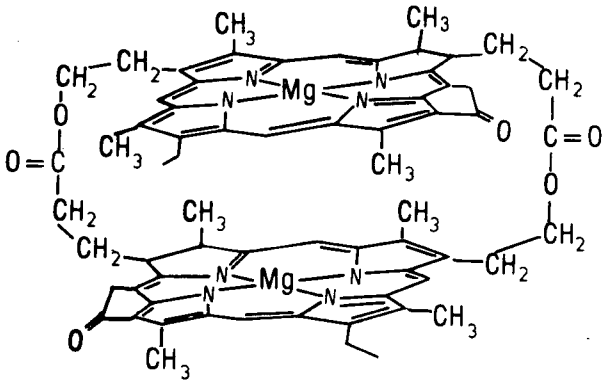
(24)

of (24) with pyrrole (4 eq) in refluxing propionic acid/ethylbenzene gave the tetra linked bisporphyrin (25).



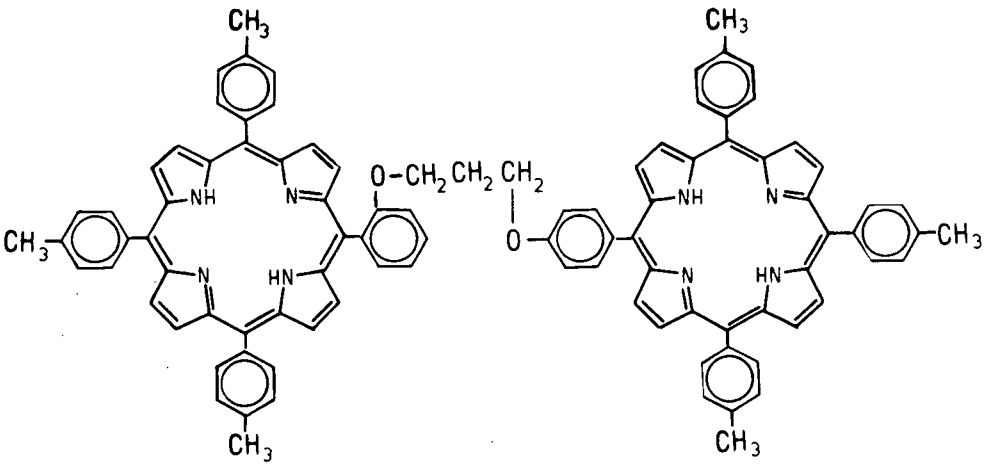
(25)

Chlorophyll derivatives have also been doubly linked to form the "sandwich" dimers. In 1978 Wasielewski et al.[23] converted pheophytin a to methylpyropheophorbide a and effected an indirect anti-Markownikoff hydration of the vinyl group by means of the thallium(III) nitrate oxidation to the aldehyde acetal, followed by hydrolysis and cyanoborohydride reduction. The methyl ester was hydrolysed in HCl to yield the hydroxy-acid which was self-coupled with 2-chloro-N-methylpyridinium iodide in the presence of triethylamine and 4-dimethylaminopyridine in refluxing butyronitrile. Magnesium was inserted with iodomagnesium-2,6-di-tert-butyl-4-methylphenolate in refluxing dichloromethane to give the chlorophyll dimer (26).



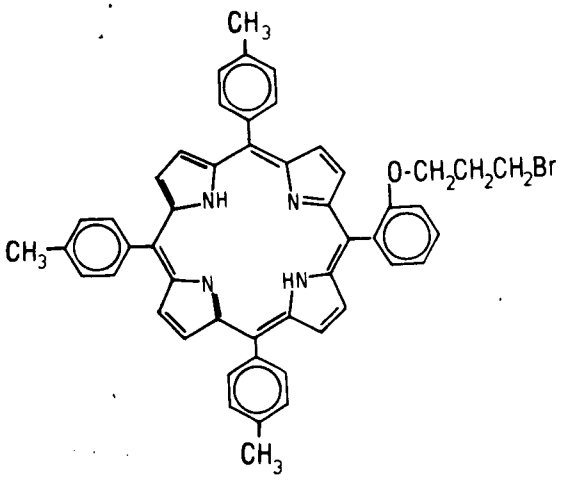
(26)

Little,[24] extending his work on oxygen binding models, employed a simple high yield ether linkage for the synthesis of the bisporphyrin (27). 5-(2-Hydroxyphenyl)-10,15,20-tritolylporphyrin was reacted with a greater than 10 fold excess of



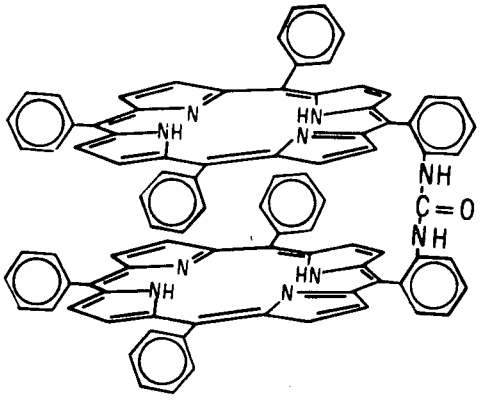
(27)

1,3-dibromopropane in refluxing dimethyl formamide in the presence of potassium carbonate for 24 hours to yield the ω-bromoalkylporphyrin (28). This was reacted with two fold excess of 5-(4-hydroxyphenyl)-10,15,20-tritolylporphyrin to give, after gel permeation chromatography, the bisporphyrin (27).



(28)

Landrum et al.[25] adopted the previously reported synthesis of Collman et al.[26] to give a singly linked bisporphyrin (29). This was then treated with $FeBr_2$ or $MnBr_2$ to give the metallo-bisporphyrin and subsequently treated with tetrabutyl ammonium imidazolate in dry tetrahydrofuran to give the imidazolate bridged bisporphyrin (30).



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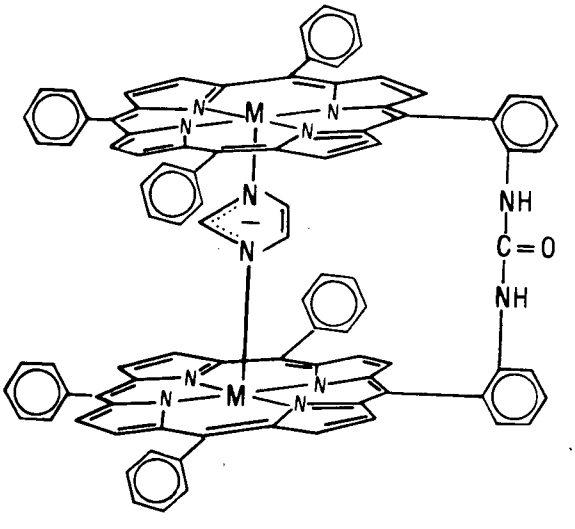
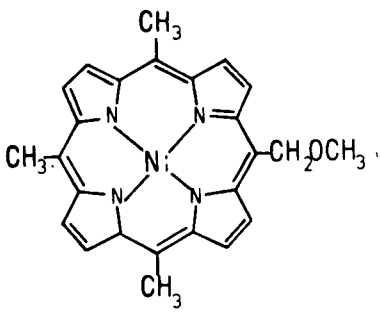


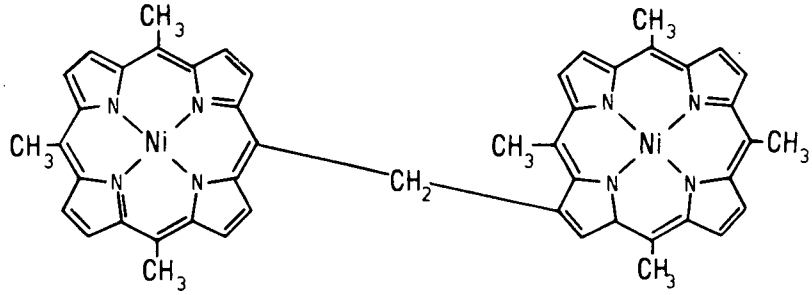
(30)

In a singular departure from the more usual work in the field, Maltzan[27] reacted meso-tetramethylporphyrin with N-bromosuccinimide to obtain the bromomethyl and the β-bromo

substituted products which were then reacted to form polymers. The bromomethyl compound was converted to the methoxymethyl (31) with sodium methoxide/methanol. Subsequent reaction with



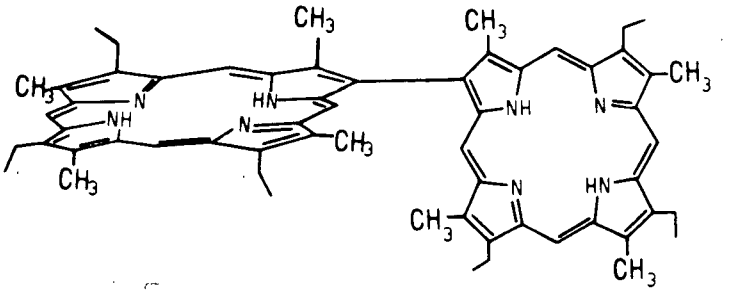
(31)



(32)

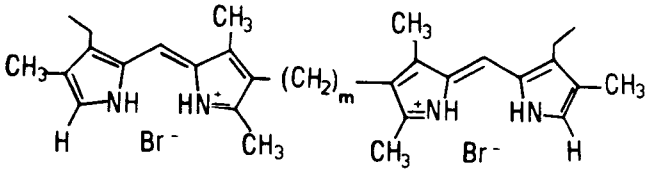
meso-tetramethylporphyrin in chloroform and bubbling HCl gas gave the bisporphyrin (32) in 70% yield. The Ni-Ni and Ni-Pd dimers were produced by appropriate metallation of the monomers with subsequent coupling. This was the first reported example of meso-beta' dimer (also linked solely through carbon) but is clearly not capable of much generalization.

The use of amide or ester linkages had caused a decrease in solubility in these systems (which already had low solubility), thus in our own laboratories we took a different approach to the linking of octaalkyl porphyrins. Dolphin and Paine[28] covalently linked bisporphyrins by an unbroken chain of carbon atoms (of variable length), accomplished by constructing the link first and subsequently building a porphyrin at each end. This has the advantage of allowing very short chains, i.e. β, β'-biporphyrin (33), and results in a greater stability of the link, i.e. no hydrolysis as in esters and amides. The porphyrins were formed from the



(33)

linked bisdipyrromethenes (34) under the conditions of the Johnson porphyrin synthesis[29] (stannic chloride in dichloromethane followed by dimethyl sulfoxide, pyridine) to give the bisporphyrins (35).



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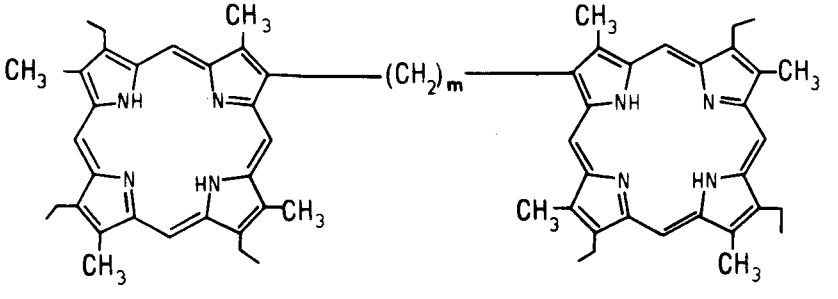
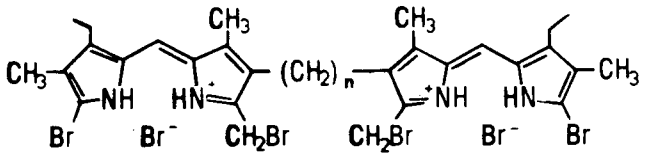


(35)

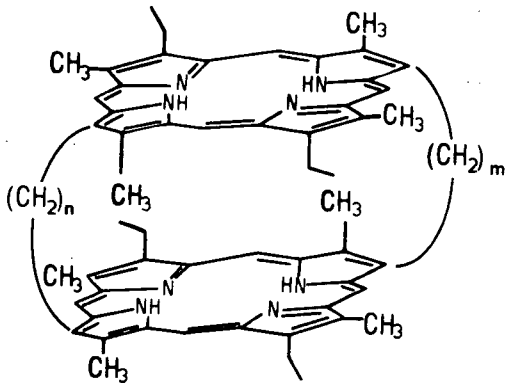
This synthesis is amenable to branched chains, even functionalized ones, as well as linear. The β, β'-biporphyrin was the first reported example of <u>directly</u> linked porphyrin dimers; Paine[30] has since managed to synthesize a meso-β'-biporphyrin in low yield from an α, β'-dipyrrylmethane but

to date, similar approaches to a meso, meso'- biporphyrin (from a 1,2-bis-2-pyrrolyethane) have proved fruitless. (The linkage is cleaved during the oxidation process).

To avoid the usual difficulties with long-term stability, Dolphin and Paine sought to prepare strati-bis-porphyrins linked solely through carbon-carbon bonds, as their singly-linked dimers had been. The obvious route entailed a head-to-tail coupling of the dimeric pyrromethenes (34) used in their earlier work. To minimize polymerization, the reaction had to be effected under conditions of high dilution, and hence only Johnson's stepwise porphyrin synthesis would serve. Tetrabromination of the dimeric pyrromethenes (34), for which a new procedure had to be devised to ensure maximal yield and purity, afforded dimeric pyrromethene (36), which was reacted with its alphafree precursor (or analog) under high dilution

(36) 

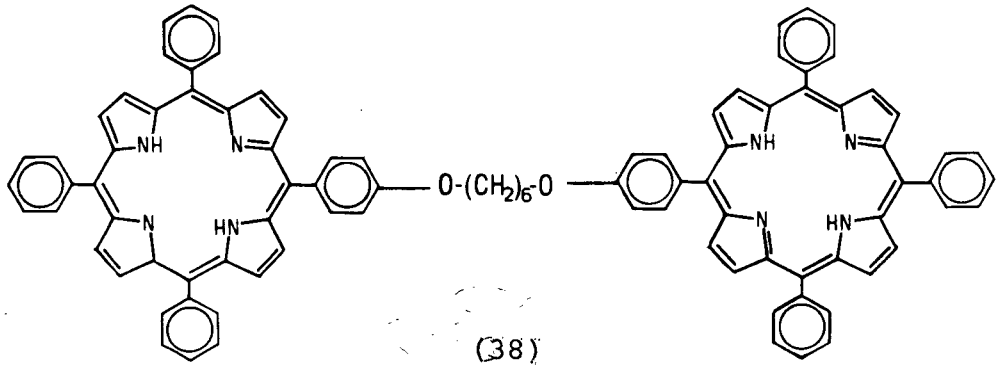
(stannic chloride - dichloromethane) to give a doubly linked bis-biladiene, whose cyclization under the usual conditions gave the bisporphyrin (37) in moderate yield. As the synthesis



(37)

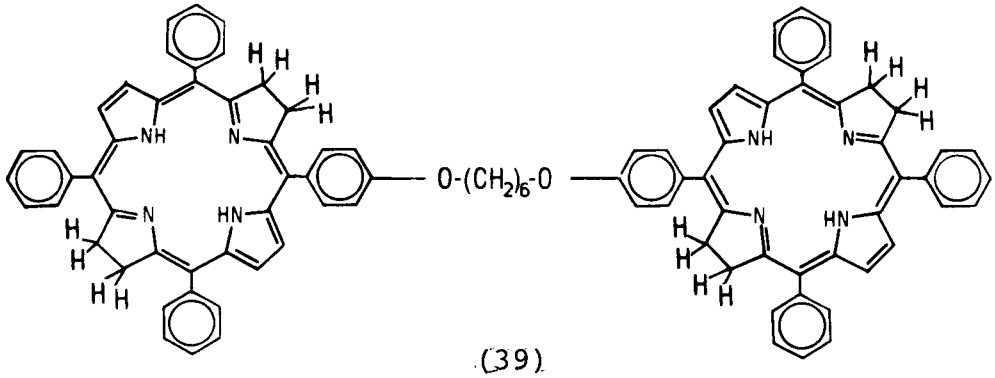
was stepwise, the two linkages needed not be of the same length, enabling a synthesis of unsymmetrical, "tilted" strati-bis-porphyrins, as well as symmetrical ones.

Work was also carried out on tetraphenylporphine dimers. Zingoni[31] treated 5-(p-hydroxyphenyl)-10,15,20-triphenylporphine with 1,6-ditosyloxyhexane and anhydrous potassium carbonate in DMF for 24 hours at room temperature. Purification by chromatography on an alumina column with dichloromethane solvent produced the TPP dimer (38) in 77% yield. This was then reduced with p-toluenesulfonylhydrazine in pyridine in the presence of anhydrous potassium carbonate at 105° to yield the bacterio-



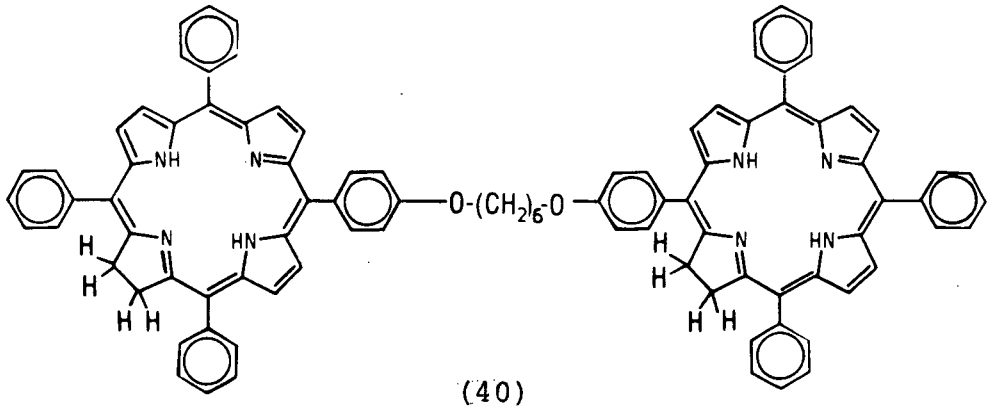
(38)

chlorin dimer (39). Partial oxidation of the bacteriochlorin dimer with equimolar DDQ in benzene produced the chlorin dimer



(39)

(40) as a mixture.



(40)

In 1980 Wasielewski and Svec[32] published the full details of their earlier syntheses of dimeric chlorophyll a, Pyrochlorophyll a, chlorophyll b and Bacteriochlorophyll b, where the phytol tails had been replaced by an ethylene glycol linkage.

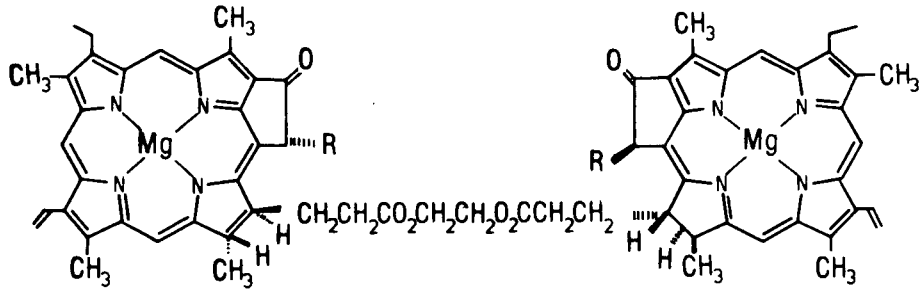
1.1.2 Spectral Properties

The presence of two close and interacting chlorophyll molecules in P-700 has been suggested by NMR and ESR.[33] Chlorophyll a adducts with ethanol or water have been prepared which mimic the optical and ESR properties of P-700.[34] Several structures for P-700 have been put forward,[35] the major structural facet being the hydrogen bonding of a polar molecule between the magnesium of one chlorophyll and the ring V keto carbonyl of the second chlorophyll. The adduct formation showed a highly unfavorable entropy factor indicated by high

chlorophyll concentration at low temperatures (77K). This can be removed by the expedient of covalently bonding the two chlorophylls together to prevent diffusion of the reactive sites.

Any P-700 models thus formed should mimic certain characteristics of P-700. They should have a red shifted absorption compared to the monomer from 677nm to 700nm (780nm to 870nm for bacteriochlorophyll), should exhibit similar ESR and NMR spectra and should undergo photobleaching reactions.

The magnesium free diester (41) of Boxer and Closs[11] had visible absorption and fluorescence spectra indistinguishable from the monomer, showing no chromophore interaction. The bispyrochlorophyllide a (42) also showed no differences in dry benzene but in wet benzene a red shift was observed in the absorption spectra of 666nm to 696nm, and to 717nm in emission.



(41) Free base R = H

(42) R = H

(43) R = CO_2CH_3

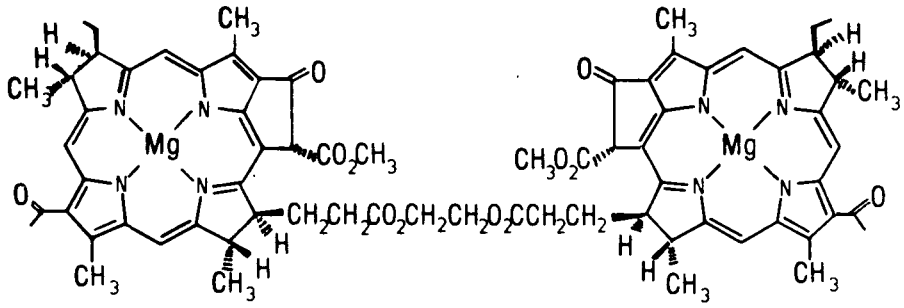
The ^1H NMR resonances were broad in dry benzene but sharpened on the addition of water. The addition of pyridine-d_5 caused further chemical shift differences attributable to a strong coordination to the magnesium ion thus preventing close association of the chromophores. ^1H NMR also showed the maximum overlap in rings III and V.

The bischlorophyll a (43) of Wasielewski[13] again showed a dependence on the addition of polar molecules to produce the red shift from 677nm to 697nm; water, ethanol, methanol and primary alkanethiols were all used. The ability of non-aqueous hydrogen bonding ligands to induce the red shift opens up the possibility that amino acid residues in the protein may be responsible for the P-700 formation. Several nonpolar solvents were also used suggesting a hydrophobic environment around the special pair as in the hemoglobin system. The ^1H NMR closely resembled the monomer with broadened peaks, this being due to the equilibrium of stereoisomers at C-10 established in polar solvents giving a 3 : 1 mixture of a-a and a-a' diastereomers. The system was shown to undergo photobleaching with I_2, the 697nm absorption being bleached in 10 minutes in the dark and 30 seconds in red light. The ESR signal from the bleached system corresponded to that expected from an electron delocalised over both chlorophyll a molecules and compared with that observed with P-700 in *chlorella vulgaris*.

It was observed that some absorption remained at 677nm even with polar solvent and after photobleaching. This was

attributed to the 25% a-a' dimer which would not fold to give the hydrogen bonded dimer due to steric interactions of one carbomethoxy group between the macrocycles.

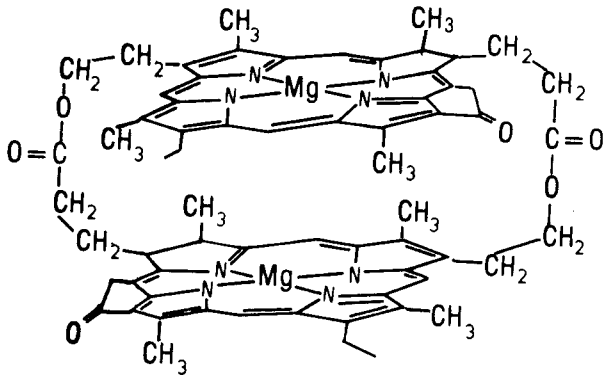
The bisbacteriochlorophyll a[17] (44) was analogous to the bischlorophyll a, the absorption being red shifted from 780nm to 803nm but not sufficiently to account for the 865nm of bacteriochlorophyll a special pair. The ^{1}H NMR was consistent



(44)

with the dimer structure as in the chlorophyll a model. Thus the C-2 acetyl takes no part in the hydrogen bonding of the model system but could possibly in vivo. The system did undergo photobleaching and exhibited an absorption at 1150nm as opposed to the 1250nm absorption of the special pair cation radical.

The bis(chlorophyll)cyclophane[23] (45) showed no solvent dependence in its absorption and ^{1}H NMR spectra, these being unchanged from the monomer. No 700nm absorption could be produced and the photo oxidation product showed a line width in the esr indicative of the electron delocalized over the



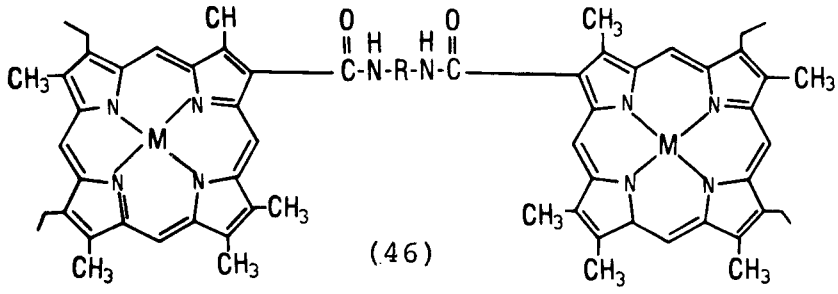
(45)

two macrocycles. The ^{1}H NMR indicated that the stacking is central as opposed to the maximum overlap of rings III and V in the singly linked bischlorophyll a.

The chlorophyll special pair models could be judged to be successful if they mimic the properties in the in vivo system. The bisporphyrins on the other hand have no obvious criteria to meet.

The bisporphyrins are thus synthesised and their properties observed, the interactions between macrocycles and metal-metal interactions being a possible measure of their usefulness. To determine these interactions the absorption, emission, fluorescence and phosphorescence spectra are often compared to the monomer.

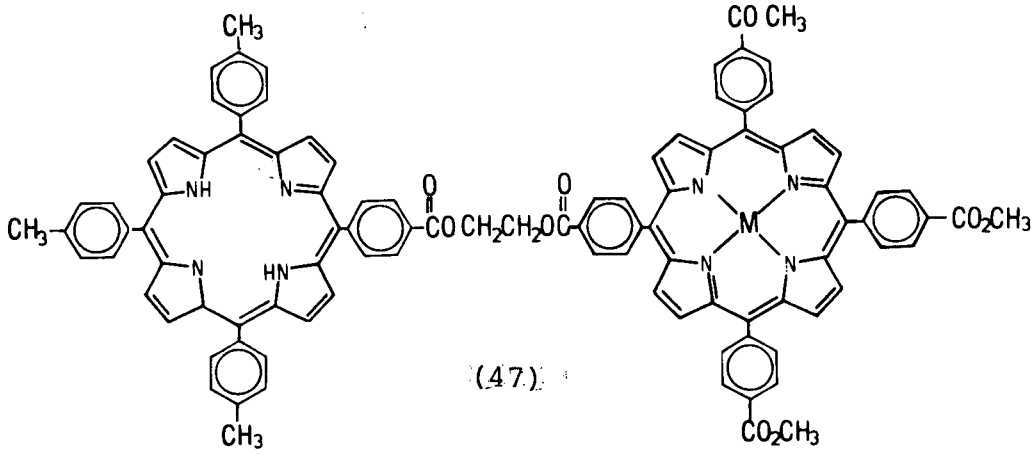
Schwartz et al.[9] found no difference in the absorption spectra of their singly linked bisporphyrin (46) but emission spectra at 77K showed triplet-triplet interaction for the ethylene bridged system, manifested as a shortening of zinc porphyrin triplet state lifetime and quenching of the zinc porphyrin phosphorescence.



(46)

R =$-CH_2CH_2-$ or $-C_6H_4-$ M = Cu, Zn

Anton et al.[36] found no difference in the absorption spectra of their dimer (47) or trimers (48) with respect to their monomers (49) and (50). The ^1H NMR spectra were also the sum of the monomer spectra plus resonances for the 8 protons of the ethylene links which appeared at 4.93ppm.



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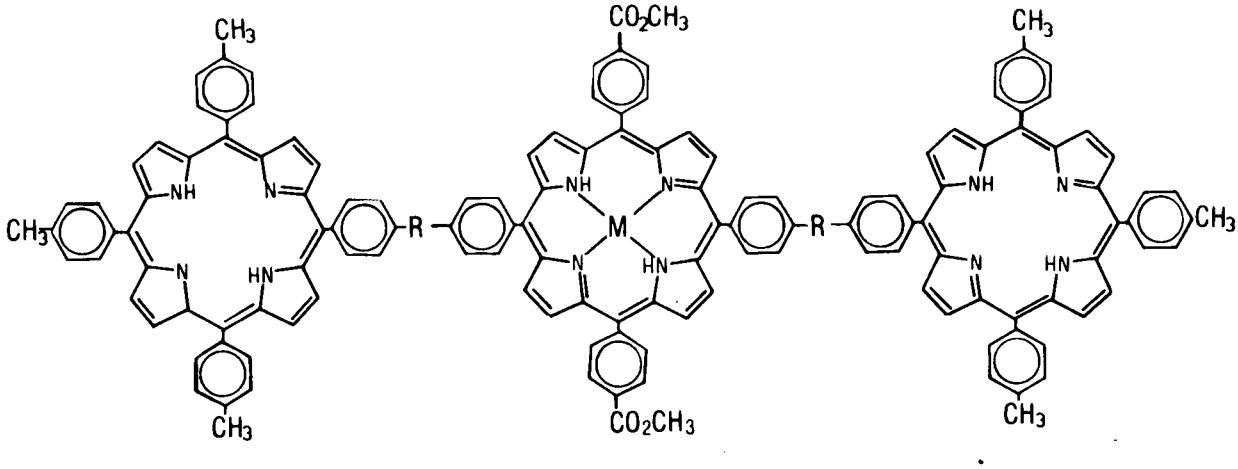
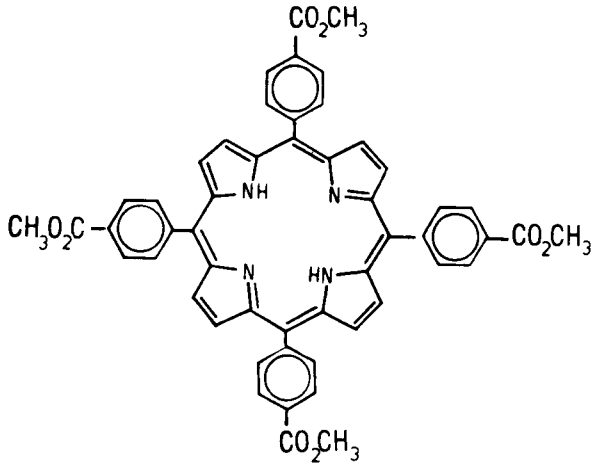


(48) R =$-CO_2CH_2CH_2O_2C-$



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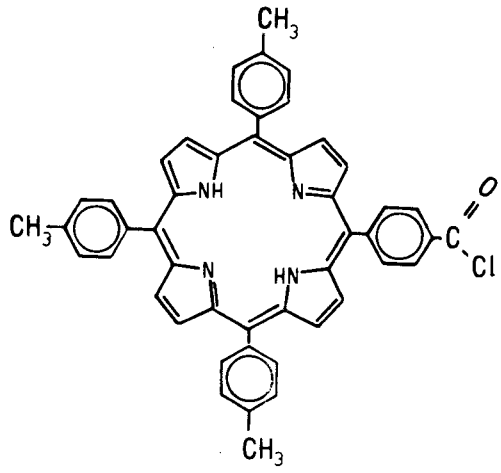
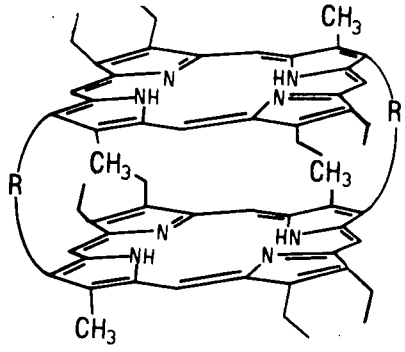


(49)

Ogoshi et al[14] also noticed no shifts in the absorption spectra of the di-zinc complex of their bisporphyrin (51) but did observe incomplete incorporation of zinc on treatment with

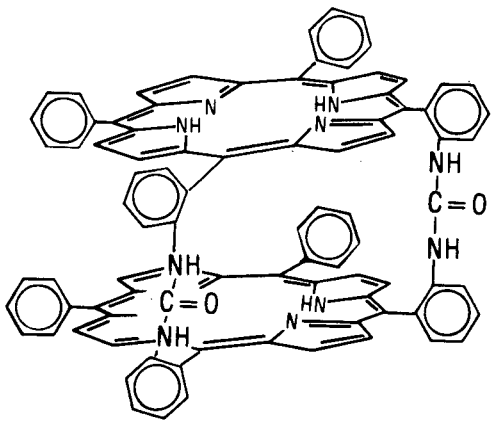


(51)

zinc acetate/methanol. The proton NMR spectra exhibited 9 signals for the 8 meso protons between 9-10ppm attributed by the author to an equal mixture of the syn and anti stereoisomers. In the zinc complex the meso protons are centered about 10ppm

in a narrower band of 0.2ppm which the author saw as indicative of a more face to face configuration than with the free base, which had a parallel displacement resulting in higher magnetic field shifts, due to the ring currents of the porphyrins. A similar trend was observed with the methyl resonances as would be expected.

Collman et al.[15] found no spectral changes for their porphyrins which were not cofacial (52) and (53) but in contrast to Ogoshi found that Soret bands of (54) and (55) had been blue shifted by approximately 15nm in the free base porphyrins and 4-5nm for the cobalt and copper complexes. ESR spectra of the cobalt and copper complexes of (54) and (55) show hyperfine splitting consistent with metal-metal separation of approximately 6.5Å.



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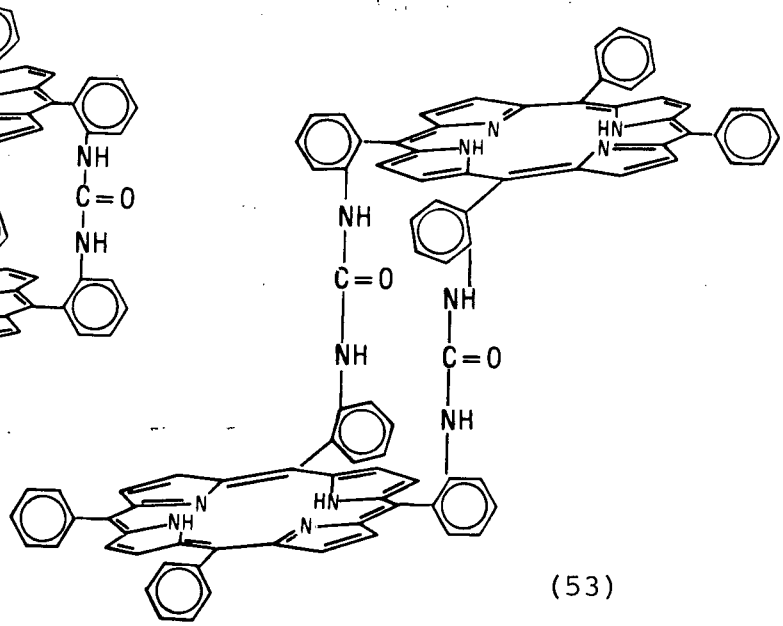

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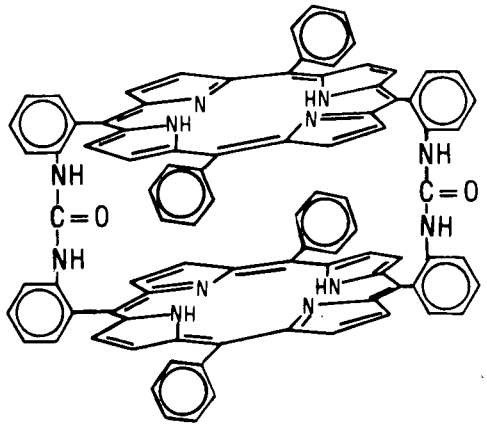

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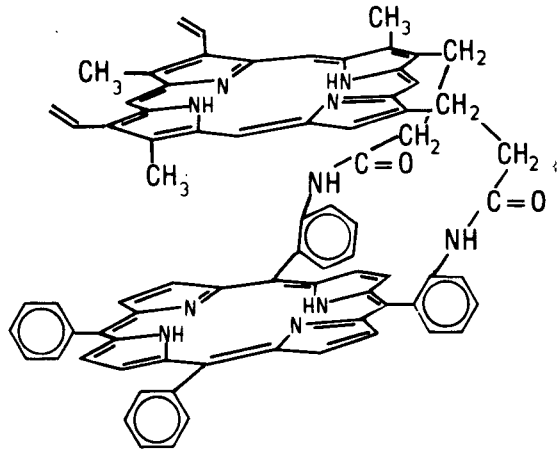
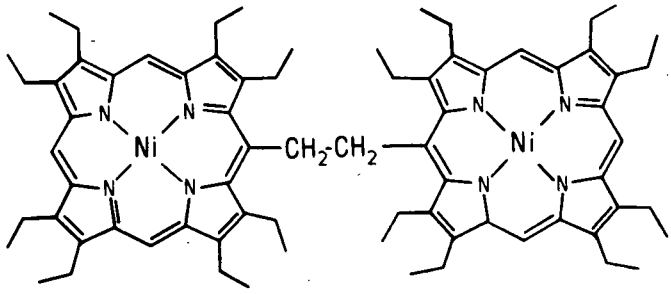


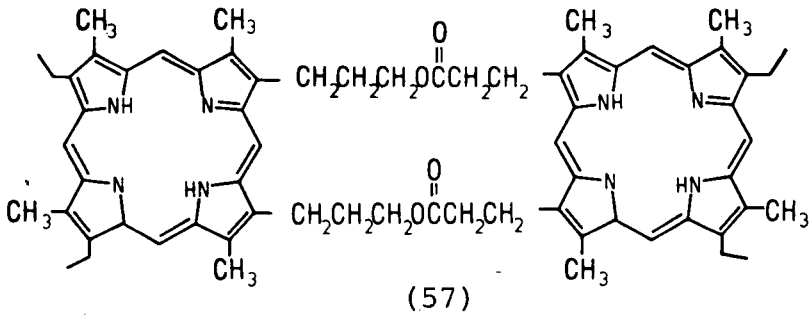
(55)

Unlike the previous singly linked bisporphyrins whose synthesis had been deliberate, Arnold et al.[16] had produced a nickel porphyrin whose broadened Soret band, red shifted by 11nm and visible bands 3nm red shifted, had led them to identify the product as a bisporphyrin (56), and whose identification was confirmed by mass spectrometry.



(56)

Ichimura[18] observed a blue shift of 8nm in the Soret of (57) and greater than 10nm for the zinc and copper dimers with small red shifts in the visible bands. The trimer (58) showed a split Soret, one band blue shifted with small red shifts in the visible bands. The zinc complexes showed considerable



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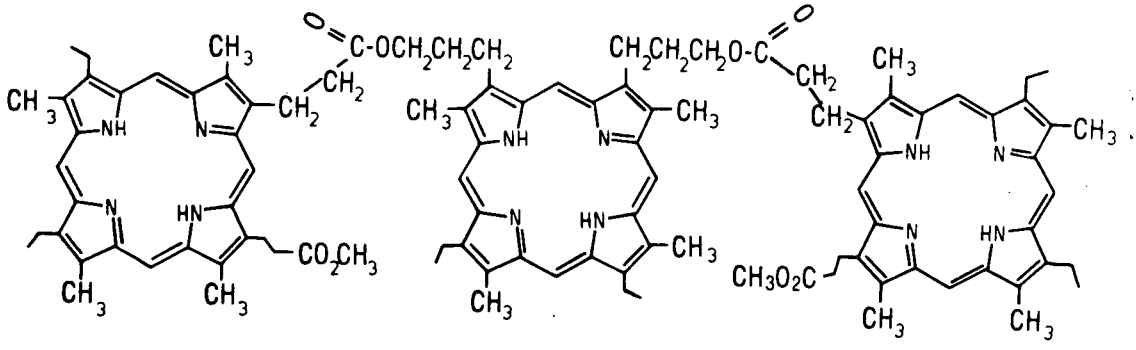
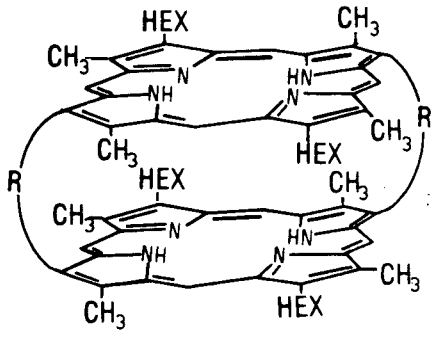


(58)

self quenching of fluorescence, whereas the magnesium complexes exhibited only slight decrease in fluorescence intensity.

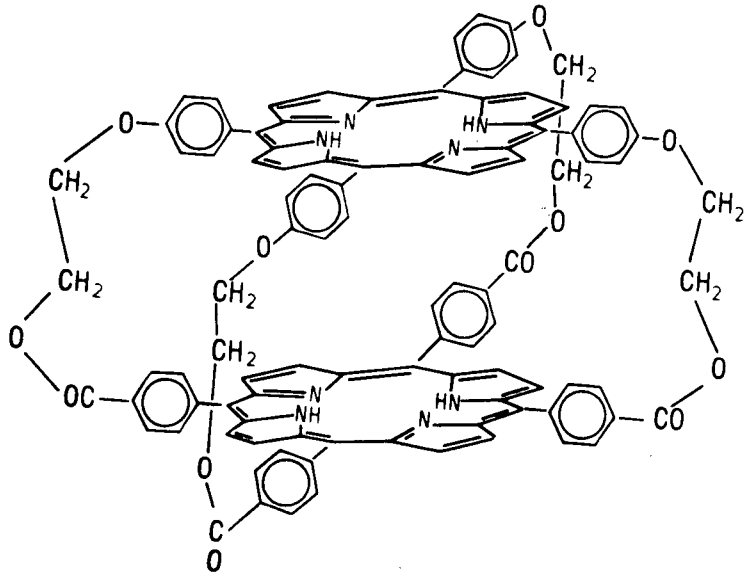
Chang[37] found blue shifts of 14-16nm in the Soret with red tails for his bisporphyrins (59) with small red shifts in the visible region. In the copper, zinc and magnesium complexes the Sorets were blue shifted. These results were explained in terms of exciton coupling between two parallel transition dipoles. The shifts would depend on two components, a solvent parameter representing the difference in the effect of solvation of the ground and excited states, and the nature of the exciton coupling which would depend on the geometry of the dimer.



(59)

If the dimer geometry was of ideal D_{4h} symmetry, the result would be a blue shift to the Soret band, tempered by a red shift due to the solvent parameter. However, tilting or sliding of the porphyrin planes would cause fluctuation of higher exciton levels and develop the lower exciton levels which was a possible explanationfor the red tail in the 450nm region. In the visible region the solvent parameter and inhomogeneous solvent broadening were considered comparable in magnitude to the exciton coupling parameter resulting in the small red shifts. The model predicted fluorescence quenching but not to the magnitude shown by the dimers and this was believed to be a manifestation of the red tail in the Soret enhancing self-quenching.

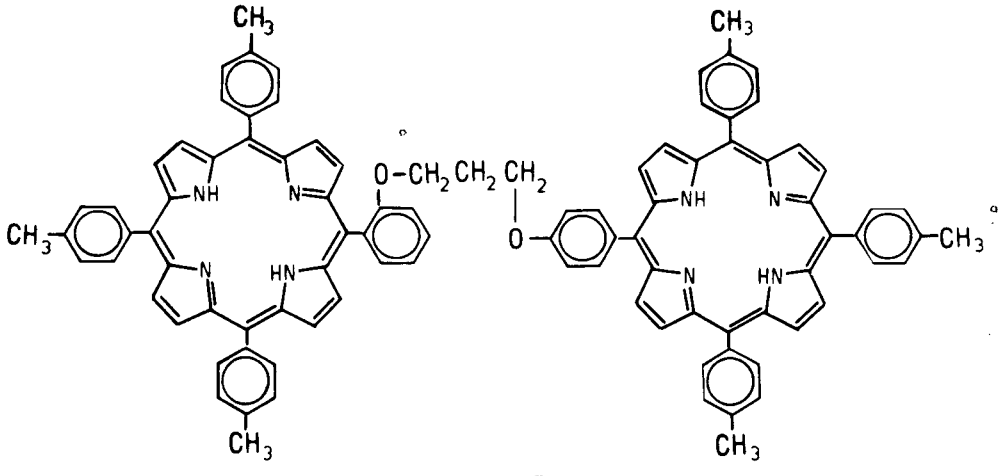
Kagan et al.[22] found absorption and emission spectra of their tetra linked bisporphyrin (60) to be broadened and red shifted in the free base. The zinc complex had a broadened but unshifted Soret band while the visible band and emission spectra were both red shifted and broadened. Quenching was also observed in the emission spectrum. The proton



(60)

NMR showed A_2B_2 degeneracy of the phenoxy and benzoyl ring protons of the monomer split into AA'BB' quadruplets as the interior and exterior facing protons are not distinguishable. The alkyl protons appeared as AA'BB' multiplet due to the restricted rotation of the O-C-C-O bonds.

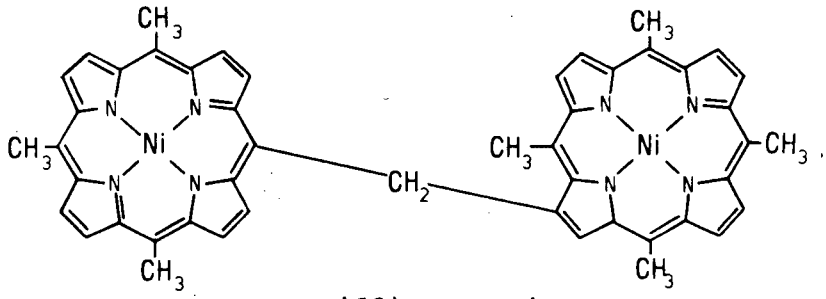
Little [24] found no positional shift in the absorption spectra of (61) but found the intensity of the Soret was only



(61)

70% of that expected, apparently the result of a splitting of the Soret observed as a distinct shoulder to the red. Identical spectra were obtained in different solvents ruling out the possiblity of two species, folded and unfolded, being present. The ESR spectrum was the sum of the simple monomers and no-metal-metal interaction could be observed.

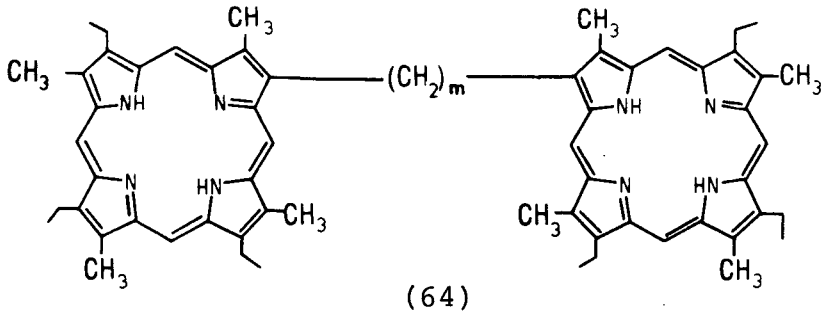
Maltzan[27] observed a split Soret red shifted 7-15nm for his Ni-Ni (62) and Ni-Pd (63) dimers. The visible band in the Ni-Ni dimer was also slightly red shifted which he



(62) M = Ni
(63) M = Pd

attributed to meso substitution effects. Variable temperature ^{1}H NMR was used to assign the configuration and confirm that rotation about the methylene linkage was restricted.

Paine et al.[28] in the series of porphyrins (64) m = 0-8 found no difference in the spectra of m = 8 and the monomer, aetioporphyrin I, but when m = 1 and 0 the Soret was broadened

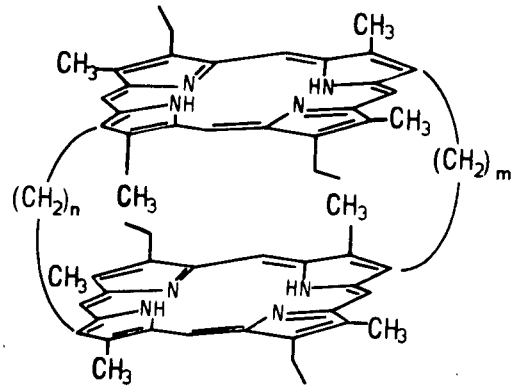


(64)

and red shifted in the free base. The protonated porphyrin gave a red shifted split Soret the visible bands also being red shifted. The well resolved dication doublet was explained by considering that the Soret of the dication monomers arise from doubly degenerate excited states. They can be considered to interact in pairs resulting in four dimer excited states. For m = 0 the transition dipoles would be expected to be parallel to the vector between centers resulting in a red shifted low energy state and perpendicular to the vector between centers resulting in an unshifted or blue shifted state. The ^{13}C CMR for m = 3 showed the porphyrin nuclei to be pseudosymmetrical, the meso carbons giving a single broad band. For m = 0 or 1, the meso carbons were resolved into four well defined peaks. For m = 2 the meso carbons appeared as a 6:2 doublet.

The doubly linked dimers of Paine[38] showed shifts in the absorption spectra apparently dependent upon the length of the links and the orientation of the two porphyrin links. The shorter the links the larger the shift assuming both links are shortened equally. Shortening one link appears to reduce the interaction, presumably by tilting the macrocycles and the C_{8-6} has less shift than the C_{8-8}.

The dimer (65) m = n = 8 had a blue-shifted Soret of 8nm in the Zn-Zn complex, 3nm for the protonated species and 9nm for the free base compared to OEP.



(65)

Dimer (65) m = 8, n = 6 had smaller shifts than the C_{8-8}, the Zn-Zn complex had 3nm shifted Soret, the protonated species 2nm and the free base 7nm.

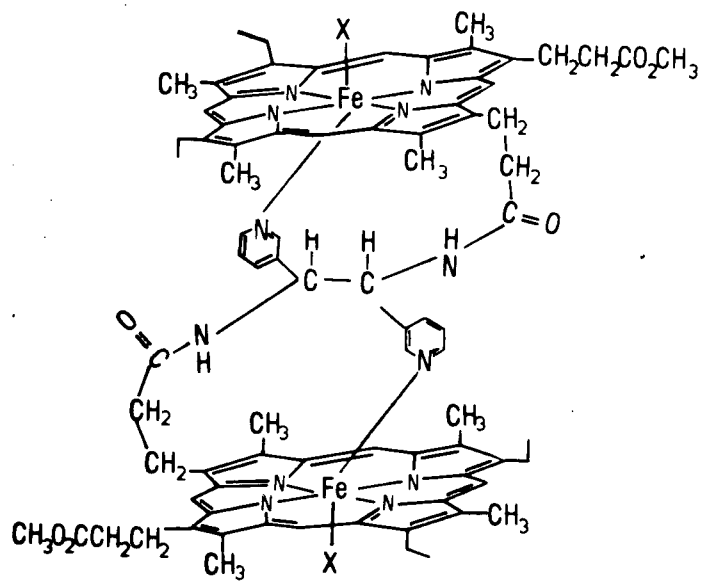
The C_{5-5} dimer (65) (m = n = 5) had the largest Soret shifts, the Zn-Zn complex 14nm, the protonated species 14nm and the free base 13nm. The visible bands had smaller shifts in the C_{8-8} free base. The protonated species' visible bands were not changed.

1.1.3 Applications

The chlorophyll model systems have developed our understanding of the photosynthetic process. The determination of the mechanism by which photo-energy is converted to chemical energy is a major goal in the efficient harnessing of this energy resource. The chlorophyll dimers of Boxer and Closs[11] and Wasielewski et al.[13] proved to be good models for the P-700 photocenter. The bacteriochlorophyll dimer[17] did not

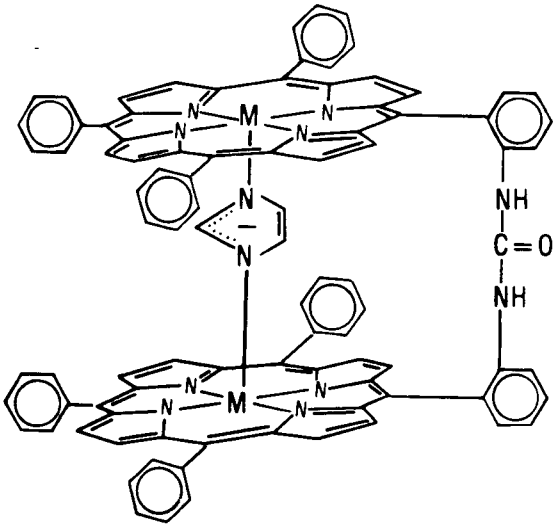
however mimic the P-870 and other factors must be considered in this case.

Traylor's[20] bisporphyrin (66) is a model system for heme



(66)

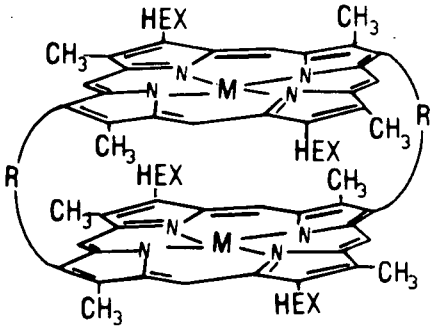
oxygen binding. The dimer was found to bind oxygen reversibly, a characteristic shown by other monoheme models,[39] but unlike other models it reacted with carbon monoxide with two different rate constants, displaying a cooperativity effect, an effect shown by hemoglobin. The double rate constant was explained by considering that the strain imposed by the short link caused base elimination of one of the heme groups giving a partially 4-coordinate form. This fast reacting form binds CO rapidly and closes to a 6-coordinate state, the second heme then proceeds to bind CO slowly without base elimination. Half oxidation of (66) resulted in the disappearance of the fast rate which would be expected as the faster reacting form would oxidise first.



(67)

Landrum's[25] imidazolate bridged bisporphyrin (67), an attempted cytochrome oxidase model, showed significant antiferromagnetic coupling, thus there is heme-heme interaction, but the J values did not compare to those of cytochrome oxidase. The authors considered the metal-metal distances too large and other ligands might possibly bring them into closer proximity.

Chang[40] carried out partial electrolytic reduction of (70c) Mg-Mg and obtained a violet solution (λ_{max} 670nm) which was believed to be the monocation radical. EPR measurements showed a single line, g = 2.003, with a peak separation of

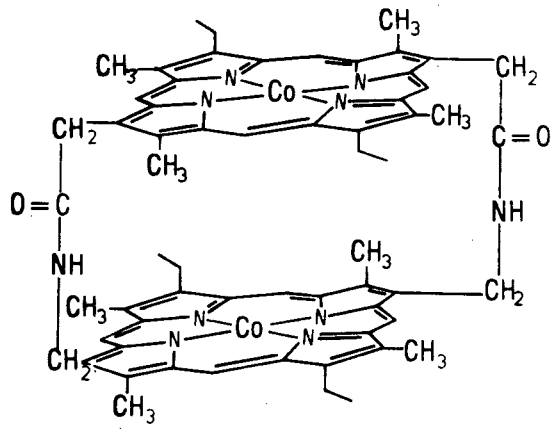


(68) R $=-CH_2CH_2CON(nBu)CH_2CH_2-$
(69) R $=-CH_2CON(nBu)CH_2CH_2-$
(70) R $=-CH_2CON(nBu)CH_2-$
a M = Zn
b M = Co
c M = Cu

1.05 Gauss, less than half that of $MgOEP^+$ radicals under the same conditions. The narrowing of line width indicates extensive electron exchange between the macrocycles similar to that observed in P-700 and P-870.

Chang[41] also investigated the possibility of multi-electron reduction of oxygen by these dimers. Oxygenation of 5-coordinate imidazole complexes of (68b, 69b, 70b) showed two different behaviors. The large metal-metal separation dimers (68b, 69b) formed reversible 1 : 1 $Co-O_2$ adducts with adsorption spectra showing 395nm Soret with only a small shoulder at 417nm. The shorter metal-metal separation of (70b) showed a 2:1 $Co-O_2$ adduct which was not reversible on evacuation and showed an absorption spectrum with the major absorption at 417nm. Unfortunately Co(III)-X, oxygenated $Co-O_2$ and binuclear $Co-O_2-Co$ all have near identical absorption bands so only the rate and difference of reaction of (70b) can be observed. The oxygen adduct of (70b) was believed to be the μ-peroxo dicobalt complex ($Co-O_2-Co$) which is diamagnetic and shows no EPR signal. However, treatment with I_2 should yield a 15 line EPR spectrum if it becomes oxidised to the μ-superoxo dicobalt complex, this indeed was observed. The iron bisporphyrins showed similar behaviour, however, addition of oxygen to (70a) resulted in spontaneous oxidation of the heme even at $-45^{o}C$. The rate of reaction was rapid due to the favorable position of the two hemes for the formation of the μ-peroxo complex, the rate determining step in monohemes.

Collman et al.[42] carried out a series of experiments with a range of porphyrin dimers. As in Chang's earlier work a short M-M distance dimer (71) showed considerable catalytic activity



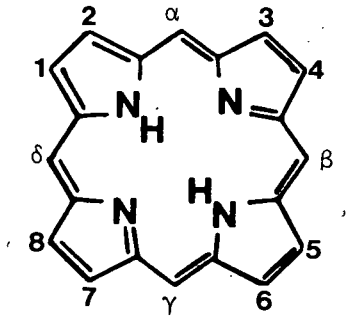
(71)

to the reduction of oxygen without the production of significant hydrogen peroxide. The bisporphyrin was introduced onto a pyrolytic graphite disk by adsorption from dilute dichloromethane solution. Rotating disk experiments were carried out with the graphite disk and a platinum ring in 0.5M perchloric acid or 0.5M trifluoroacetic acid with oxygen at atmospheric pressure. For longer linked bisporphyrins and Co-Pd (71) considerable hydrogen peroxide was formed. However no hydrogen peroxide was formed with (71), a hydrogen peroxide containing solution without oxygen was tested to show that it did not reduce or disproportionate hydrogen peroxide. The ability of (71) to reduce oxygen was found to be dependent on the availability of protons; unbuffered solutions tend to produce hydrogen peroxide when the supply of protons is exhausted. The x-ray crystal structure[43] of (71) shows a syn form as drawn with a M-M separation of 6.332 Å .

1.2 Nomenclature

The widespread use of trivial names adopted by Fischer[44] and others has led to a haphazard nomenclature in porphyrin chemistry. The adoption of a systematic nomenclature for porphyrins will require a system flexible enough to embrace the Fischer system yet informative enough to differentiate a vast number of natural and synthetic analogues.

The Fischer system is based on the numbering system shown (72). The peripheral positions are numbered 1 to 8 and the methine positions, termed meso, are designated α, β, γ and δ. The system also includes a large number of trivial



(72)

names based on the type of substituents and an isomer numbering system based on their peripheral arrangements. Thus "Uroporphyrin III" has two different substituents, acetic (A) and propionic (P), one of each per ring, these are arranged in the sequence A, P, A, P, A, P, P, A. The full series of Uroporphyrins is shown in Figure 1. The systematic name of this compound would be 2, 7, 12, 18-tetracarboxymethyl-3, 8, 13, 17-tetracarboxyethyl-

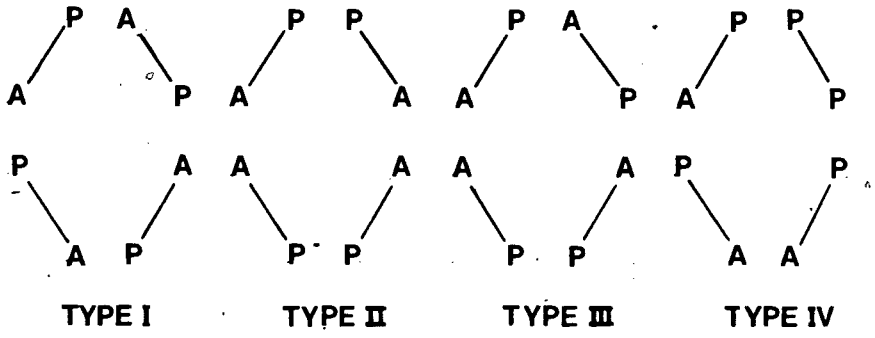


FIGURE 1: Schematic of Uroporphyrin series

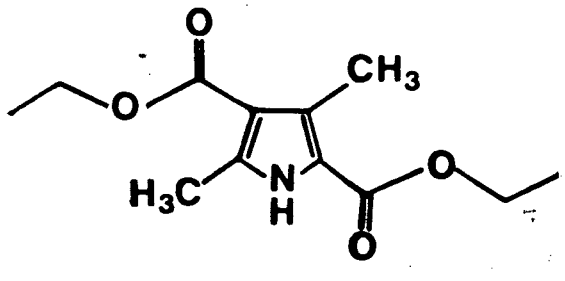
porphyrin, a much too complex name for the conversational Uroporphyrin III.

In a recent review Bonnett[45] outlined a semisystematic approach which retained the more important of the Fischer names but systemised and rationalised the less important trivial names.

The nomenclature used in the following work will be consistent with the following guidelines, trivial names are given in brackets.

1.2.1 Pyrroles

The nitrogen is numbered 1 and the substituents to give the lowest number to the first alphabetically as in (73).

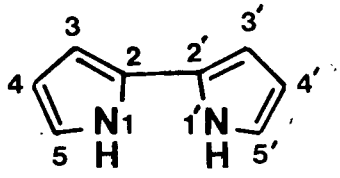


(73)

2,4-Diethyloxycarbonyl-3,5 dimethylpyrrole
(Knorr's pyrrole)

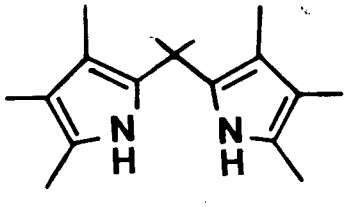
1.2.2 Dipyrroles

Compounds containing two pyrrole rings are numbered to give the smallest numbers to the dipyrrolic link as in (74).

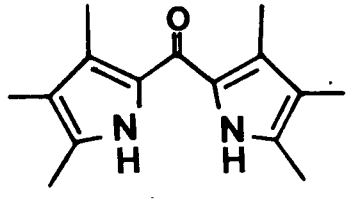


(74)
2,2'-Bipyrrole

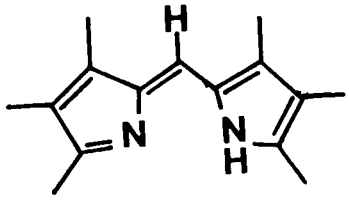
or with an intermediate carbon atom (75), (76) and (77).



(75)
2,2'-Dipyrrolylmethane



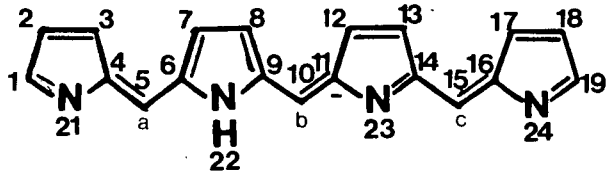
(76)
2,2'-Dipyrrolylketone



(77)
2-(2H-Pyrrol-2-ylidenemethyl)pyrrole (Dipyrromethene)

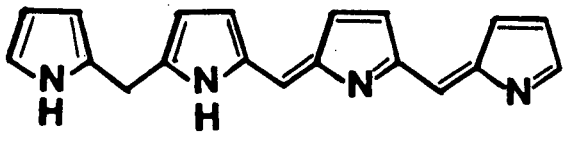
1.2.3 Tetrapyrroles

The nomenclature of the linear tetra pyrroles is based on Bilin (78).

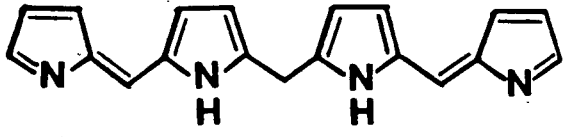


(78)
Bilin : 22H Tautomer

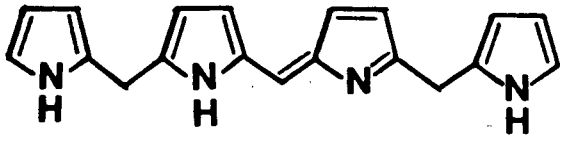
The number 20 is omitted to give the corresponding numbers in the porphyrin (also used in corrin system). The reduced systems are as in (79), (80) and (81).



(79)
5,21-Dihydrobilin (b,c-Biladiene)

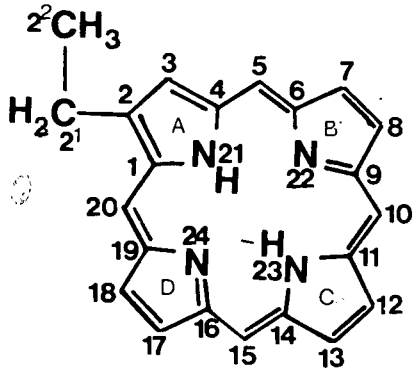


(80)
10,23-Dihydrobilin (a,c-Biladiene)



(81)
5,15,21,24-Tetrahydrobilin (b-Bilene)

Porphyrin nomenclature is based on the parent porphin and is numbered as in (82).



(82)

The rings are lettered A to D and side-chains positions can be numbered as shown when necessary.

Where metal complexes are formed the macrocycle becomes porphinato metal complex.

CHAPTER 2

RESULTS AND DISCUSSION

2.1 Synthetic Objective

Once the singly linked bisporphyrin of Paine and Dolphin[28] had been prepared it seemed logical to continue and produce the doubly linked bisporphyrin with two unbroken carbon chains. Thus any destabilising effect from the polar links of previous bisporphyrins upon the metalloporphyrin adducts would be removed. Two methods seemed to have synthetic possibilities, the first a modification of Paine's single link synthesis, whereby the linked methene was reacted with a linked tetrabrominated methene to give the doubly linked porphyrin. This reaction would have to be carried out at high dilution to reduce the possibility of polymerisation. However, at this time the methods for bromination of the α-methyl-α-unsubstituted methenes did not give pure products and due to the instability of the bromomethyl group recrystallisation is out of the question. Thus until a better method for brominating these compounds was found the second possibility seemed favourable.

This scheme was a continuation of the single link synthesis, the first link should be formed with side chains containing reactive sites diagonally opposed to the link. These could be modified and then joined to give the doubly linked bisporphyrin.

The initial scheme (Figure 2) was the synthesis of a C_6 linked dimer with haloethyl sidechains which were to be linked with a C_2 unit. This was quickly discarded once the problems associated with the high dilution reaction in the final step had been envisaged.

The second scheme (Figure 3) seemed to have all the prerequisites of a feasibly synthetic route to doubly linked bisporphyrins. The final link was unimolecular and had been accomplished by many other researchers on comparably sized systems. It was therefore decided to produce the C_8-C_8 doubly linked bisporphyrin.

After many attempts to produce the C_8-C_8 dimer, the synthesis of the butyne side chain was found to be unattainable. This is due to the instability of 2-haloethyl substituents towards elimination of hydrogen halide under the conditions required for the formation of the alkyne. It was thus decided that the C_{10}-C_{10} dimer would be synthesised as it was available from the more stable bromopropyl side chain. (Figure 4)

The feasibility of these reactions was tested by the synthesis of a singly linked bisporphyrin (Figure 5). The product of this synthesis was compared to a sample produced by the method of Paine and Dolphin and shown to be identical. The synthesis of the doubly linked dimer was thus considered practicable by this route and the synthesis attempted.

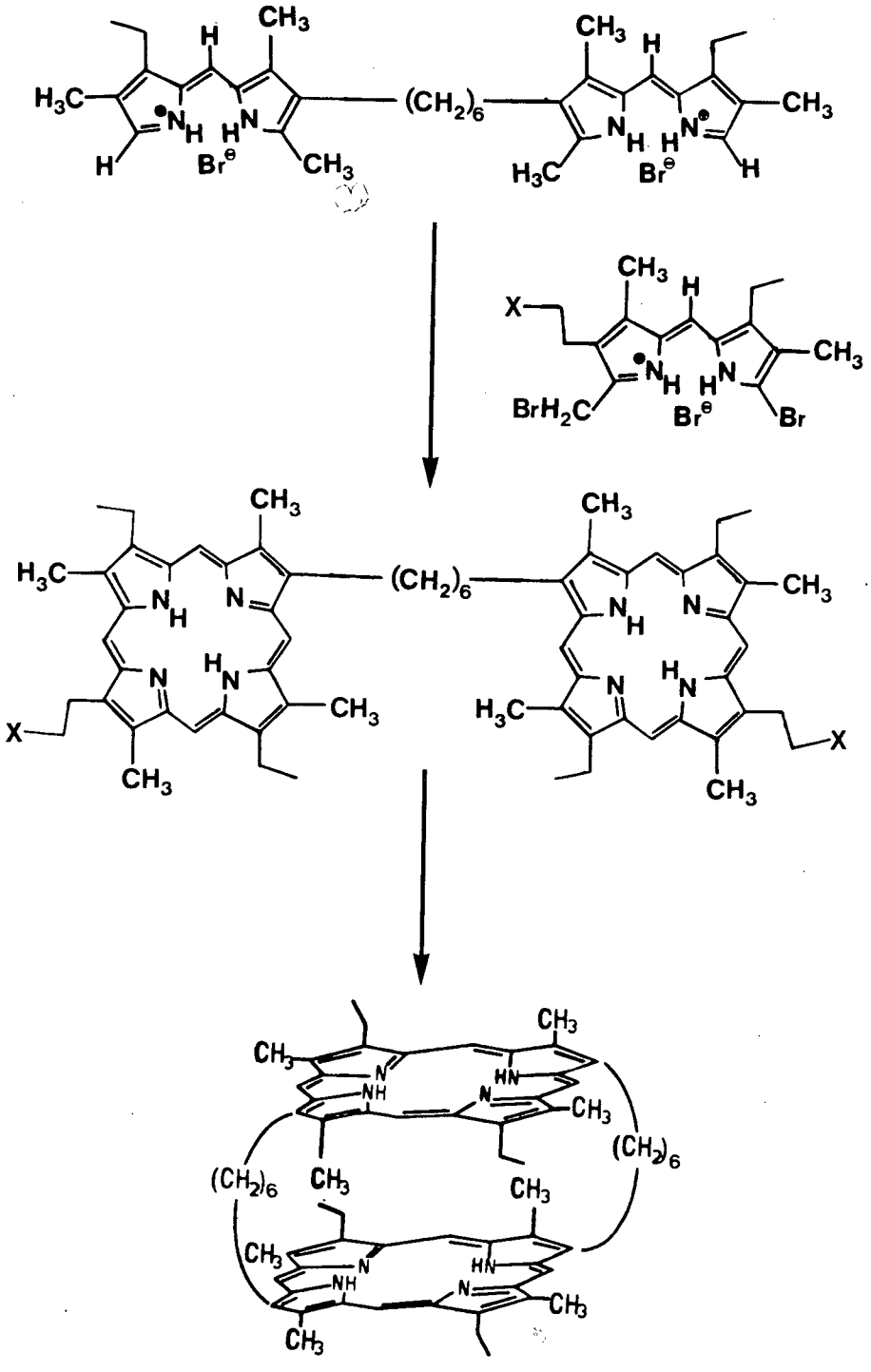


FIGURE 2: Proposed Route to C_{6-6} Dimer

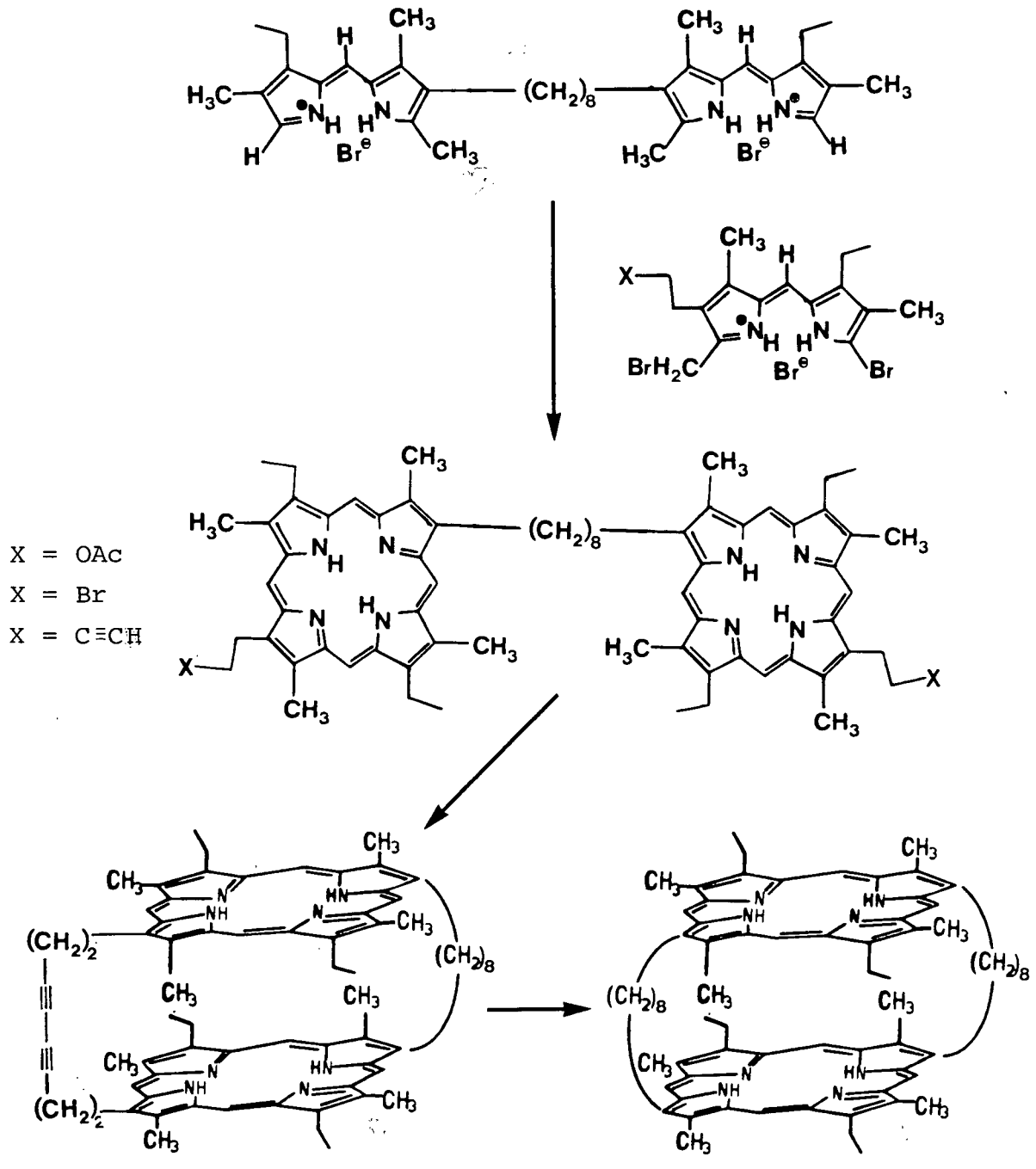


FIGURE 3: Proposed Route to C_{8-8} Dimer

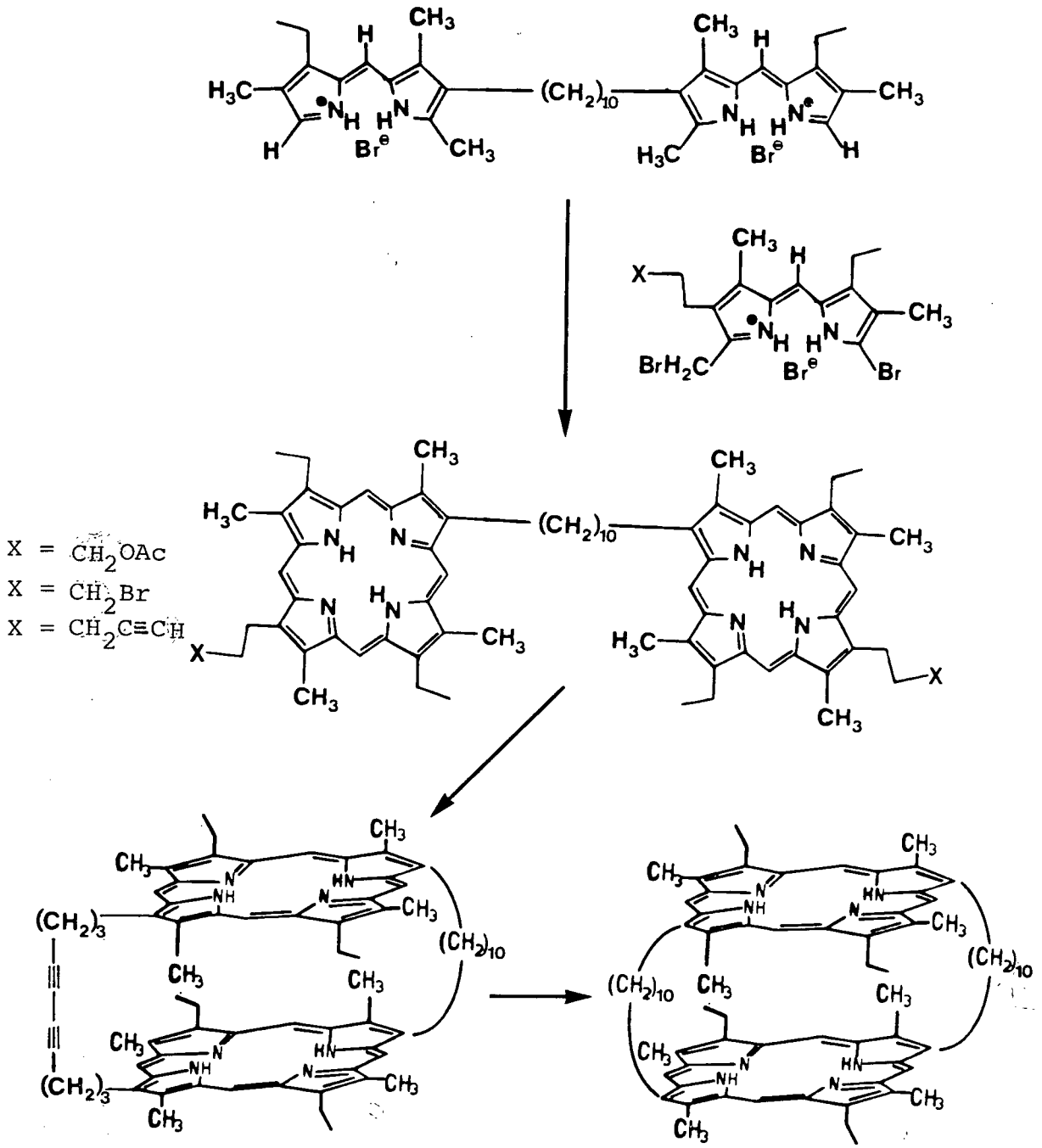


FIGURE 4: Proposed Route to C_{10-10} Dimer

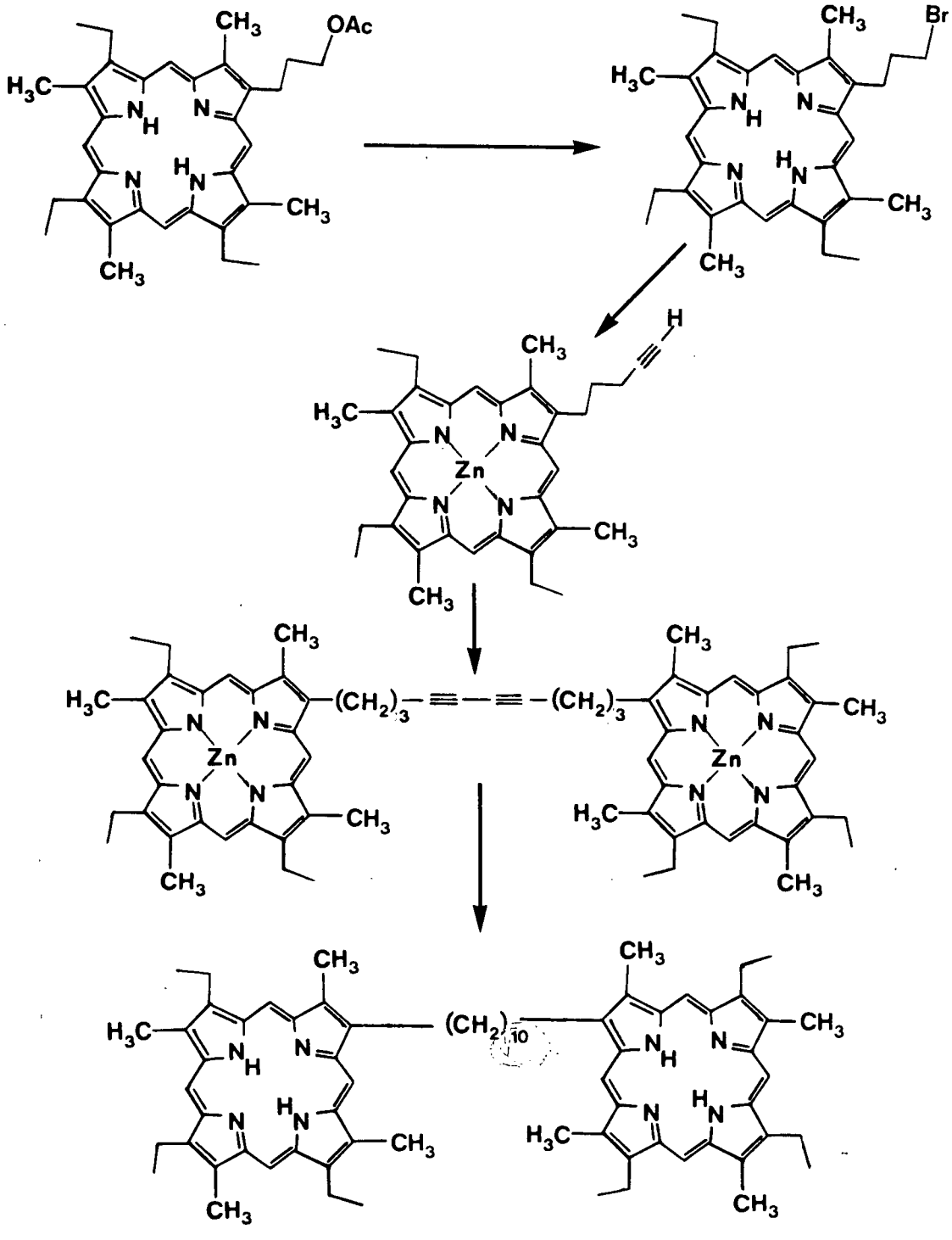


FIGURE 5: Proposed Route to Model C_{10} Dimer

2.2 Pyrroles

The synthesis of porphyrins in this work is based on four pyrroles which were synthesised in large quantities by a modified Knorr[46] synthesis. The Knorr synthesis is a low yield reaction (30-50%) but uses inexpensive starting materials and can be carried out on large batches (10-12 moles). The limiting factors are seemingly the quantity of hoodspace and large volume glassware. In the classical Knorr reaction, (Figure 6), ethyl acetoacetate (83) is reacted with ½ mole aqueous sodium nitrite to give an equimolar mixture of ethylacetoacetate and ethyl oximino acetoacetate (84). The oxime (84) is then reduced with zinc/acetic acid to give the α-amino ketone (85); this reacts with (83) to form the Schiff's base (86) which cyclises forming the pyrrole (87) on loss of water. The α-aminoketone unfortunately self condenses to give a mixture of Schiff's bases and these lead to undesirable side products.

Modification of the Knorr synthesis is possible by variation both of the oxime and of the β-diketone. Isolation of the oxime and its dropwise addition to a reducing mixture containing excess β-diketone also reduces the possibility of self condensation to give the wrong Schiff's base. Consideration of these modifications and future synthetic requirements dictated the starting pyrroles. Where possible one would prefer to use benzyl esters as opposed to ethyl esters,

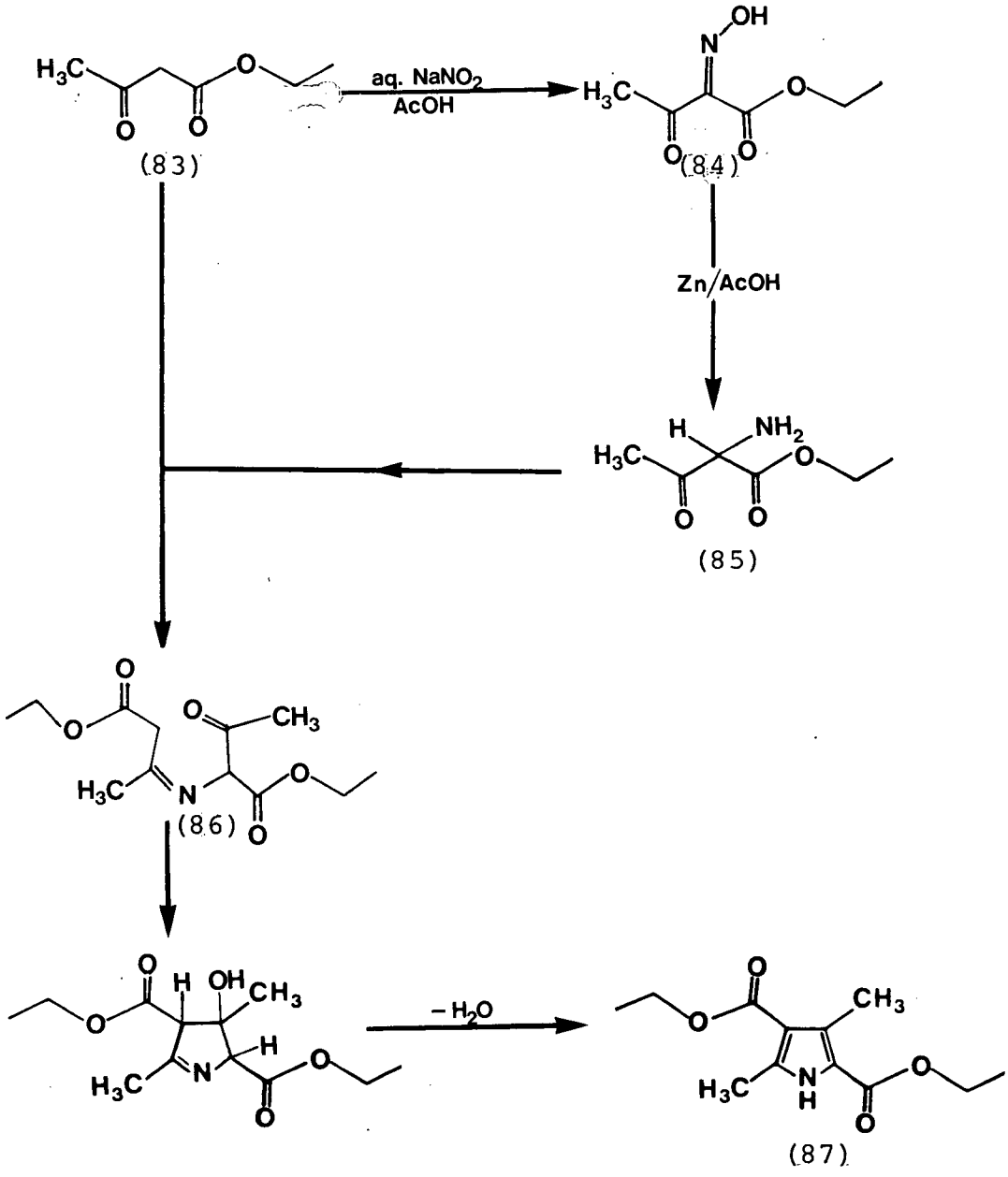


FIGURE 6: Synthesis of Knorr's Pyrrole

due to the ease of removal by catalytic hydrogenolysis, thus benzyl acetoacetate was substituted for ethylacetoacetate wherever possible. Pyrroles with reactive β-sidechains (the reactive sidechain required for the second link in the porphyrin) were produced by using meso-substituted β-diketones.

2.2.1 Monopyrroles

The β-free pyrrole (88) (Figure 7) was required in the synthesis of the first link and thus had to undergo Friedel Crafts acylation with $SnCl_4$. Benzyl esters are cleaved under these conditions thus an ethyl ester was necessary. Kleinspehn[47] deduced that ethyl oximinomalonate (89) with 2,4-pentanedione would lead to the β-free pyrrole. The

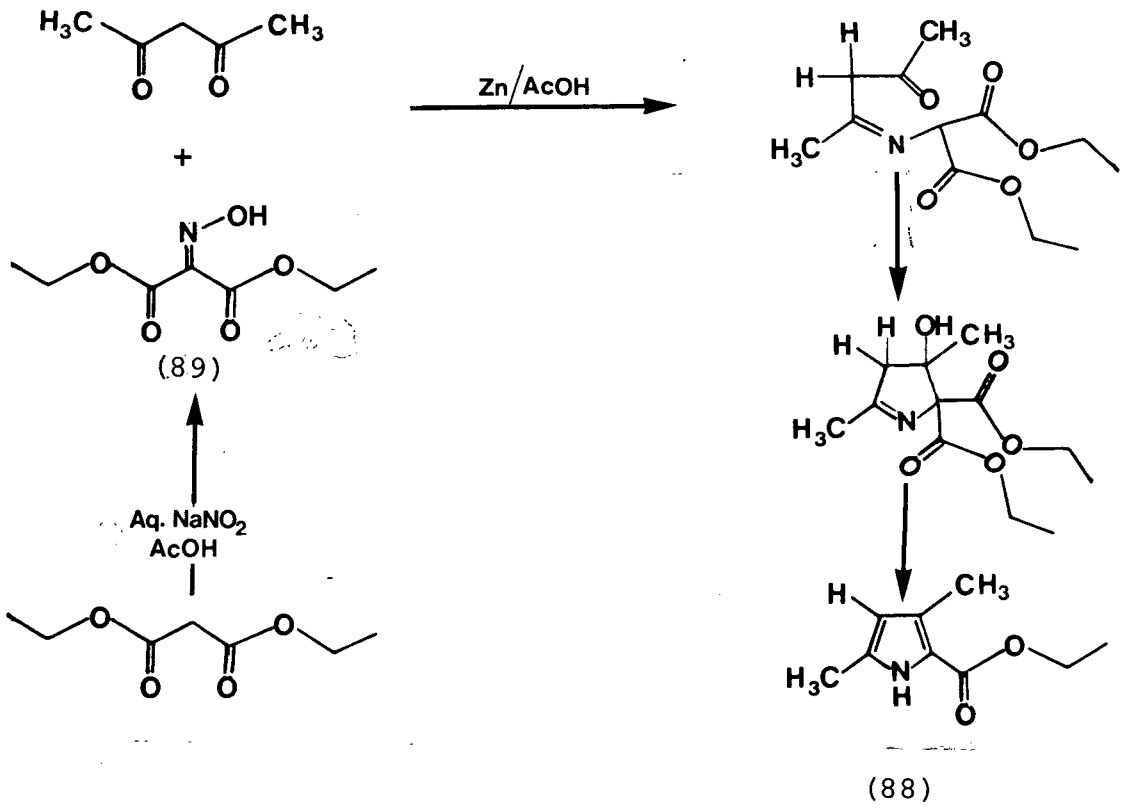


FIGURE 7: Synthesis of β-free Pyrrole (88).

nitrosation was found to be less efficient and thus 3 moles of aqueous sodium nitrite are required to produce the oxime.

The use of benzyl acetoacetate (90) (Figure 8) and 2,4-pentanedione led to the synthetically useful 4-acetyl-2-benzyloxycarbonyl-3,5-dimethylpyrrole (91). After reduction of the acetyl group to ethyl this pyrrole was manipulated to produce several other pyrroles.

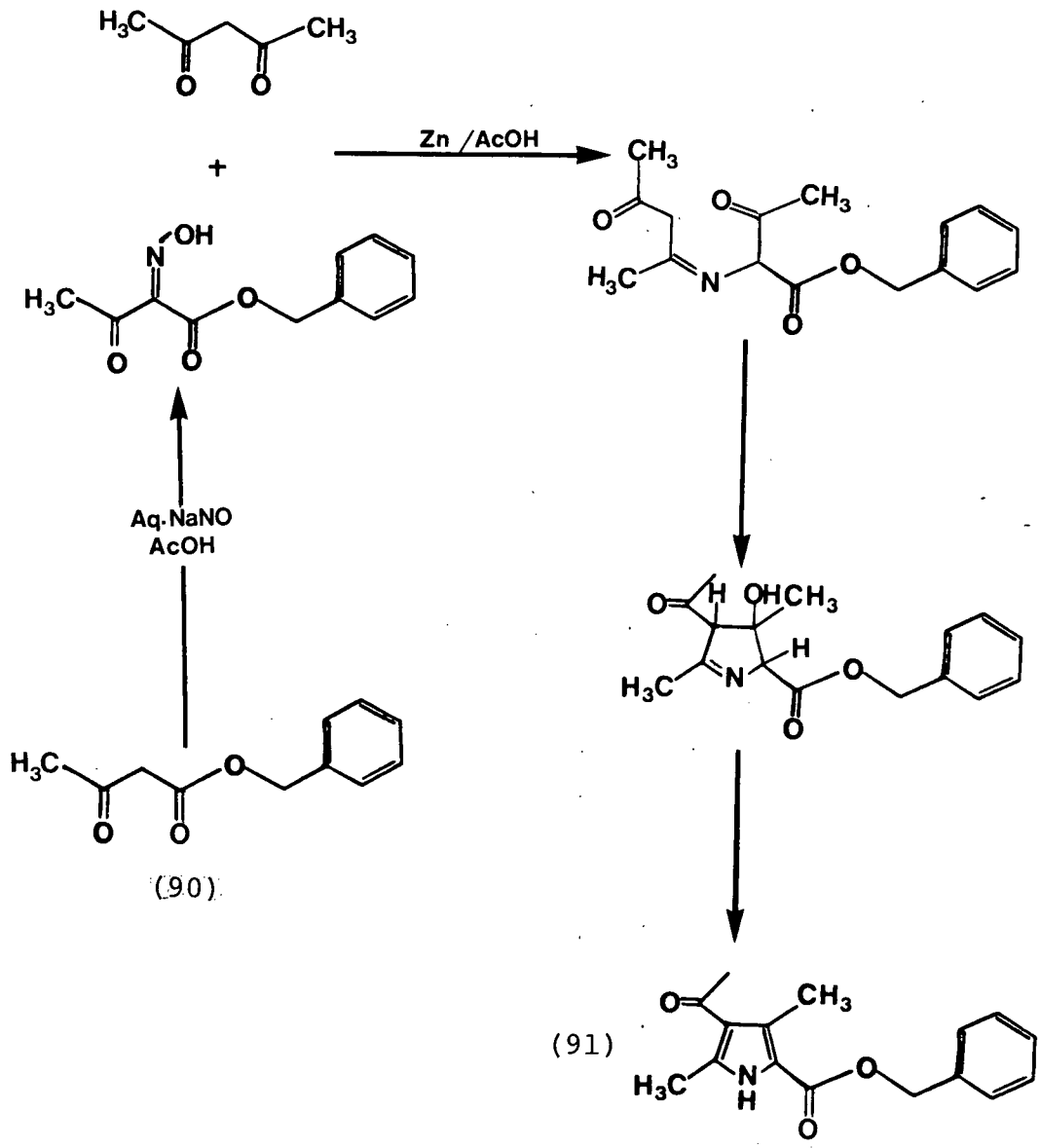
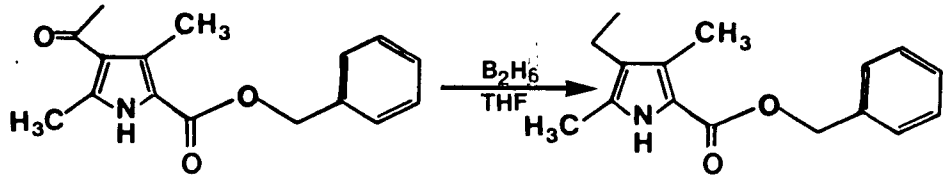


FIGURE 8: Synthesis of pyrrole (91)

The synthesis of pyrroles with reactive β-sidechains was accomplished using the Johnson[29] variation of the Knorr synthesis where 3-alkyl-2,4-pentanedione was substituted for 2,4-pentanedione. Reaction of benzyl oximinoacetoacetate with methyl-3-acetyl-4-oxopenanoate (92) (R = $CH_2CO_2CH_3$) (Figure 9) under the usual conditions led to the substituted pyrrole (93) (R = $CH_2CO_2CH_3$). Reduction of the ester group with diborane/tetrahydrofuran gave the hydroxyethyl pyrrole (94) which could later be manipulated to the desired functionalised ethyl side chain.

The use of methyl-4-acetyl-5-oxohexanoate (95) (R = $CH_2CH_2CO_2CH_3$) under the above conditions yielded pyrrole (96) (R = $CH_2CH_2CO_2CH_3$) which was the starting pyrrole for the propyl side chain porphyrins.

2.2.2 Synthetically useful pyrroles from 4-acetyl-2-benzyloxycarbonyl-3, 5-dimethylpyrrole (91)



(91) (97)

All porphyrin rings with ethyl and methyl groups are synthesised from this pyrrole. The initial step is the diborane reduction of the acetyl group, reported by Whitlock

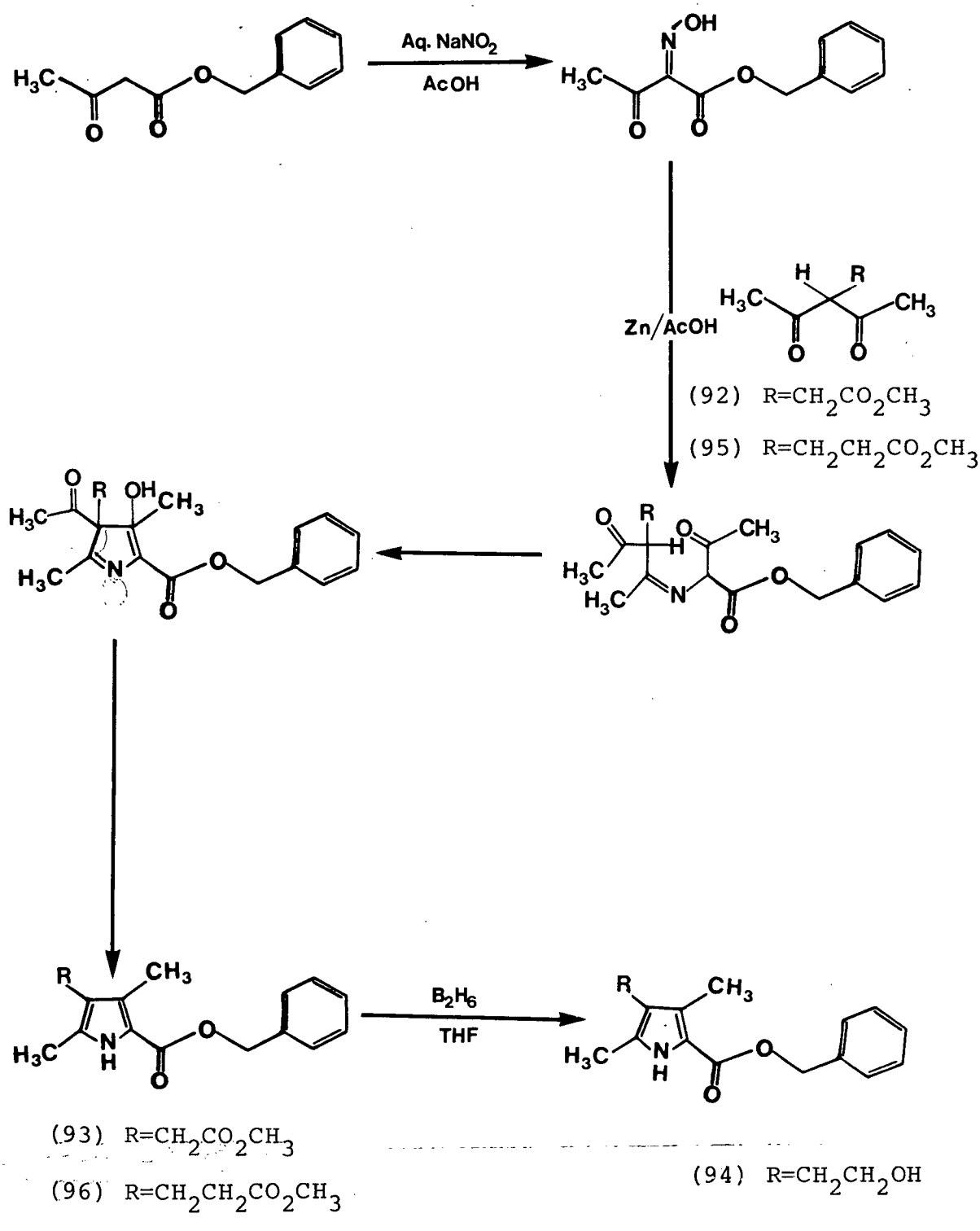


FIGURE 9: Synthesis of β-Side Chain Pyrroles

and Hanauer,[48] to produce the 2-benzyloxycarbonyl-4-ethyl-3,5-dimethylpyrrole (97).

Throughout the following work diborane reductions are commonly used, they are reasonably efficient (usually greater than 80% yields being obtained), easily carried out and the major side product boric acid is easily removed.

The method used varied only slightly for all the reductions carried out i.e. ethyl acetate composed 25% of the solvent in reactions where an ester was present in the molecule that was not required to be reduced.

The diborane was generated in situ by the dropwise addition of boron trifluoride etherate to a cooled stirred suspension of sodium borohydride, and the material to be reduced, in tetrahydrofuran.

$$4BF_3 + 3NaBH_4 \longrightarrow 2B_2H_6 + 3NaBF_4$$

The diborane is complexed by solution in tetrahydrofuran to give the stable adduct $BH_3 \cdot THF$.

The progress of the reactions was observed by tlc and on completion they were quenched by the addition of glacial acetic acid followed by addition of water. The addition of acetic acid to quench the reaction reduces the over vigorous reaction on quenching found when water alone is used.

The diborane reductions of the "benzylic" ketones it should be noted, do not stop at the secondary alcohol

but proceed further to the methylene group. This can be considered due to the stabilisation of the carbonium ion produced (Figure 10) by C-O bond cleavage followed by abstrac-

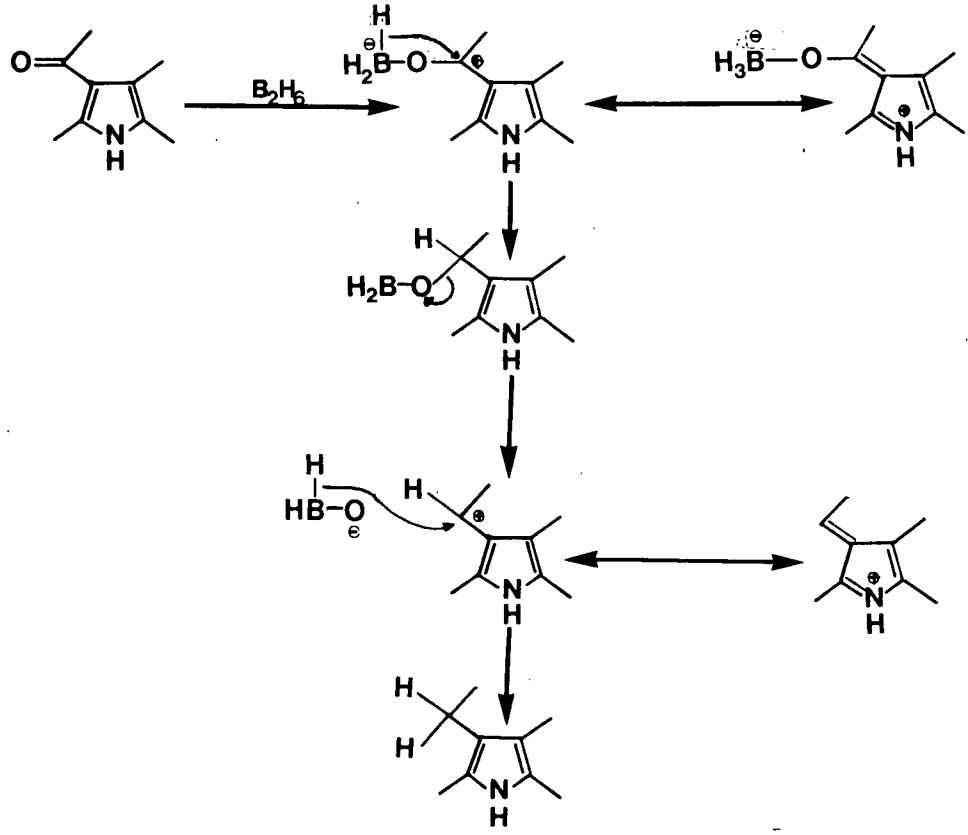


FIGURE 10: Borohydride reduction of acetyl.

tion of a hydride ion to give the fully reduced methylene.

To produce synthetically useful pyrroles the α positions of (97) must be modified. The greater reactivity of the α-substituent over the β-substituent of pyrroles is employed to modify the α-methyl without changing the β-methyl group. The first step in activating the methyl group is the dichlorination by sulfuryl chloride to give the dichloromethylpyrrole (98) (Figure 11) followed by hydrolysis to the

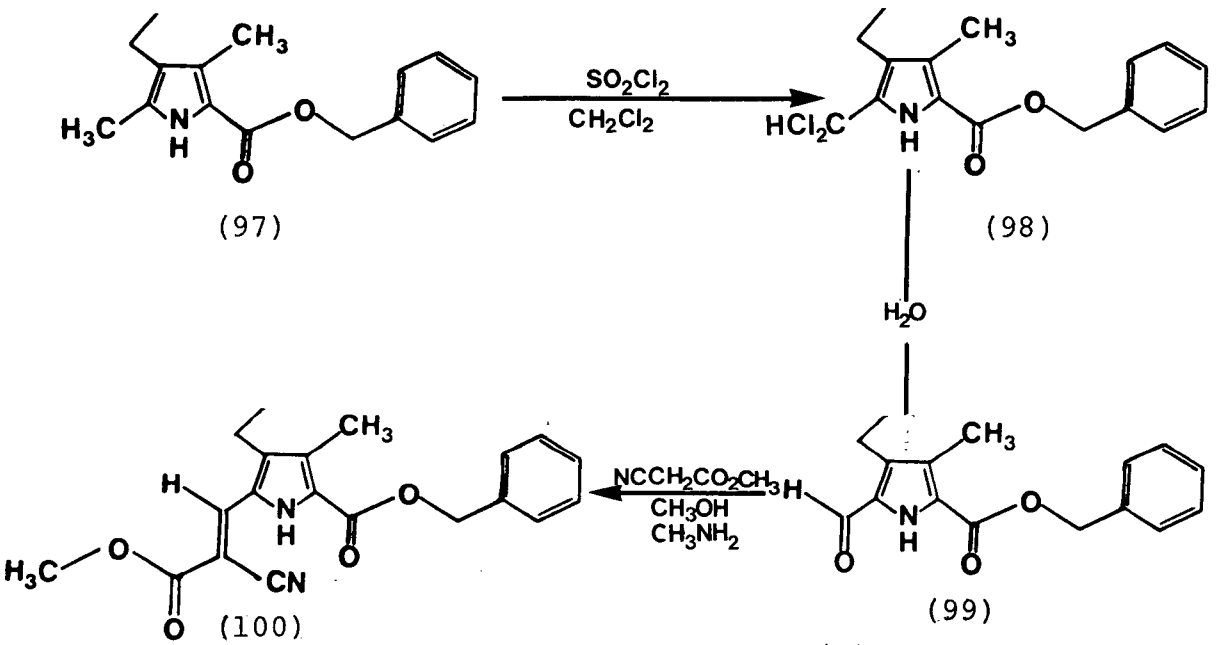


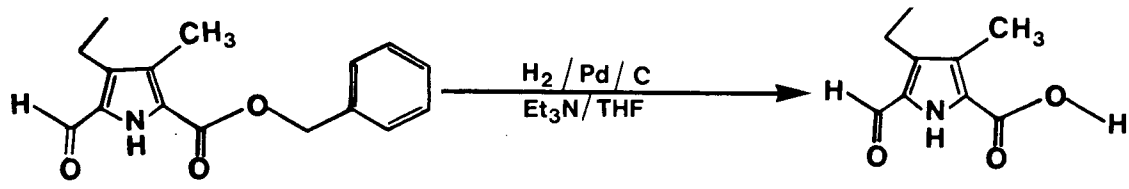
FIGURE 11: Oxidation of α-methyl to aldehyde.

α-formyl pyrrole (99). This was carried out in ice cold dichloromethane to reduce the possibility of trichlorination which would lead to the carboxyl pyrrole on hydrolysis. It had also been shown that trichlorination was less effective in dichloromethane alone than other solvents.[49]

Hydrolysis was carried out by stirring the mixture with water overnight, the organic layer was separated and the solvent removed under vacuum. The resulting oil was extracted with hot 1:1 water/ethanol, the product crystallising when cool. The remaining mother liquor was extracted by the expedient of converting the formyl group to the methyl cyanoacrylate group (100), by reaction in methanol with methyl cyanoacetate and methylamine. This reaction

was also carried out on pure (99) in the same manner, in 98% yield. The bright yellow analytically pure solid crystallises out on cooling; this is an excellent purification method for the formyl pyrrole as the impurities are left in the methanol solution.

The 2-carboxyl-4-ethyl-5-formyl-3-methylpyrrole (101) was produced by hydrogenolysis of (99) in triethylamine/ tetrahydrofuran with 10% palladium/charcoal. The solution was filtered into acetic acid and the solvent removed under reduced pressure. The product crystallised with difficulty from methanol with water.



(99) (101)

The benzyl ester (100) was cleaved by hydrogenolysis with palladium/charcoal in tetrahydrofuran to give the carboxypyrrole (102) (Figure 12) which upon removal of tetrahydrofuran, crystallised from methanol in greater than 98% yield. The carboxypyrrole (102) can then be decarboxylated to give the α-free pyrrole (103) by an indirect proceedure via the iodination product (104) which gives better yields than the bromination product (105).

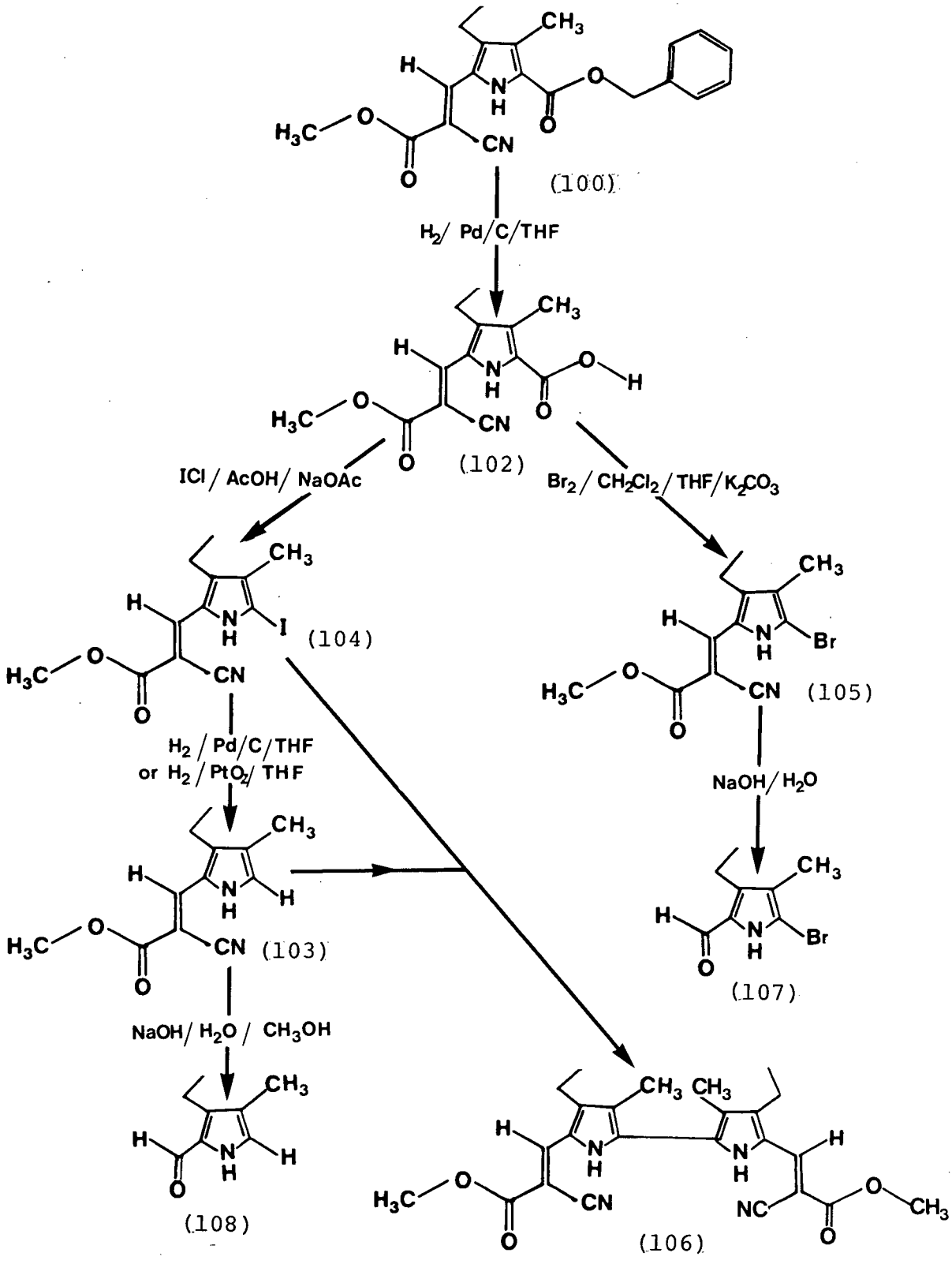


FIGURE 12: Preparation of Synthetically Useful Pyrroles via Transformations of α -Substituents of (100)

The α-iodopyrrole (104) was produced from (102) by the dropwise addition of iodine monochloride to the pyrrole suspended in glacial acetic acid, acetic anhydride in the presence of excess sodium acetate as buffer. Excess iodine was removed by hypophosphorous acid and crystallisation induced by addition of water. The product was recrystallised from methanol/water to give bright yellow needles in 82% yield.

The reduction of the iodopyrrole (104) was attempted by hydrogenolysis using 10% palladium/charcoal in tetrahydrofuran. The α-free product (103) was found to be orange due to contamination from the 2,2'-bipyrrole (106) produced by condensation of (103) and (104). This is a photoinduced reaction and can be reduced greatly by the exclusion of light during the hydrogenolysis.

It was found that 99% yield could be obtained from this reaction using platinum oxide as catalyst in the dark over a three day period. During one reaction a quantity of barrier solution (copper sulphate solution) was sucked into the reaction vessel. This resulted in the precipitation of a large quantity of the 2,2'-bipyrrole (106) in an analytically pure form, a reaction comparable to the Ullmann[50] coupling.

The α-free pyrrole (103) was deprotected by dissolving in the minimum volume of methanol and adding 5-6N sodium hydroxide solution. The solution was boiled to remove the

methanol and then refluxed for 2-3 hours under nitrogen. The solution was allowed to cool and the pale brown solid (108) filtered and washed. The compound was used in this form to produce all methenes. An analytical sample was recrystallised from water/methanol to give white needles. Yields varied slightly between 80-85% due to some loss by steam distillation of the product which could be detected by the presence of white needles in the condenser.

The carboxypyrrole (102) was also converted to the α-bromo-pyrrole (105) by the reaction of bromine in dichloromethane added dropwise to a stirred suspension of (102) and anhydrous potassium carbonate in tetrahydrofuran. The addition was carried out in the dark and followed by tlc, at the first sign of bipyrrole the reaction was quenched by pouring into water. Recrystallisation of the product from methanol/water gave an 80% yield of the product.

It had been found necessary during the synthesis of some methenes to produce the bromo-formylpyrrole (107) in quantity. Previous synthesis had been difficult and the products unreliable, deprotection of (105) by the usual method (103) - (108) had produced intractable tars. Necessity being the mother of invention it was decided that a method for this deprotection had to be found.

The deprotection was carried out in the normal manner and the reaction observed by visible spectroscopy. During the initial stages where the methanol was boiled off no changes in the spectrum was observed. During the following

3-4 hours loss of the 320 nm peak occurred. On work up the yield of (107) was less than 20%. As no change in the visible spectrum had occurred before the methanol was removed and the pyrrole remained in solution after the methanol was removed it was decided to use very small quantities of methanol in the reaction. The visible spectra showed no changes except that the reaction reached completion in only 2½ hours. Upon work up the yield had unexpectedly risen to approximately 45%. It was thus decided that the absolute minimum of methanol would be used. To determine this the pyrrole would be heated to boiling in aqueous sodium hydroxide and once boiling any remaining pyrrole would be dissolved by the dropwise addition of methanol. Just below the boiling point of the solution all of the pyrrole dissolved. At the same time a change in the visible spectrum greater than any seen before in similar times was observed. The reaction went to completion as determined by the loss of the 320 nm band in less than 1½ hours and on work up the product was isolated in 80% yield as tan needles Mpt 104.5 - 105.5^{o}. Later experiments increased the yield to 88%; recrystallisation from methanol/water gave pale tan needles which were analytically pure although this compound was usually used without recrystallisation as is (108). This deprotection method was attempted by others on various pyrroles with results varying from disastrous to moderately unsuccessful, although this work did point the way to the subsequent use of a higher boiling point alcohol (n-propanol) for some deprotections.[51]

2.2.3 Modification of β-substituted pyrroles

The initial synthesis schemes were based on the chloroethyl side chain, thus (94) (Figure 13) was converted to the β-chloro-ethylpyrrole (109). This was carried out by the dropwise addition of thionyl chloride to a refluxing mixture of (94) and anhydrous potassium carbonate in dichloromethane. The product crystallised as white fluffy needles in 92% yield from methanol on removal of dichloromethane by reduced pressure distillation.

It was discovered in the cyclisation of the porphyrin that the chloroethyl sidechain was partially converted to the bromoethyl. It was therefore necessary to produce other side chains with protecting groups stable to the cyclisation conditions. The first of these was the bromoethylpyrrole (110) which was synthesised similarly to the chloroethyl, thionyl bromide substituting for thionyl chloride. The other possibility was to protect the alcohol until after the cyclisation and then produce the halide after cyclisation. To try this route two esters were used, benzoate (111) and the acetate (112). The benzoate (111) was produced by the action of benzoyl chloride on (94) in pyridine/tetrahydrofuran and gave white needles in 90% yield recrystallised from methanol. The acetate (112) was produced from (94) by treating with pyridine/acetic anhydride overnight in the

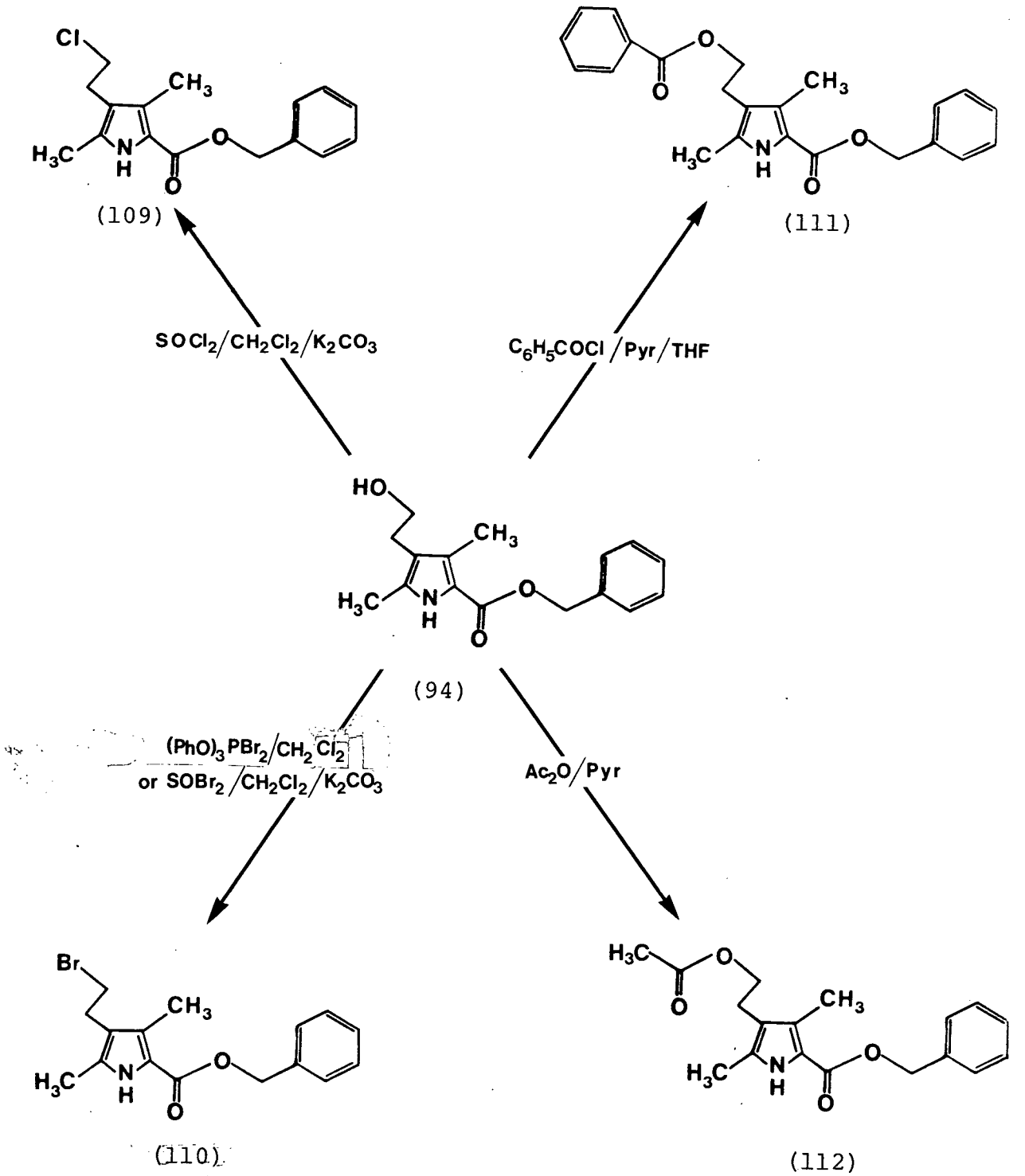
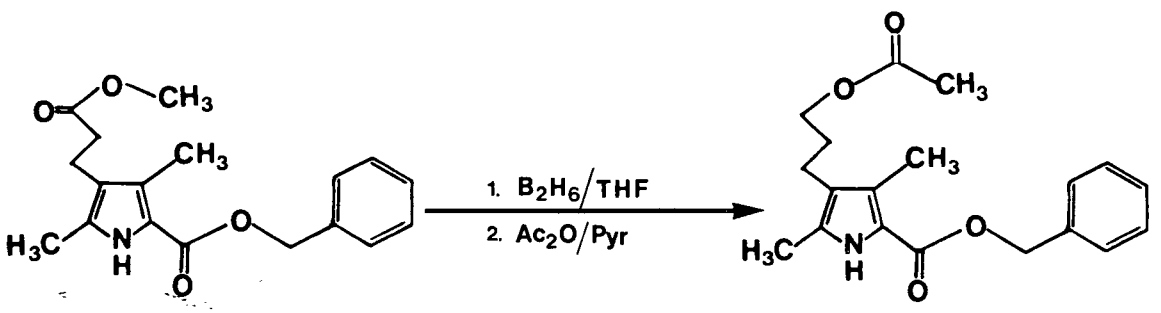


FIGURE 13: Preparation of Protected Hydroxyethyl Pyrroles from (94)

dark. The mixture was then poured into ice water, filtered, and the product recrystallised from methanol as white needles in 92%.

From the results obtained from these protected alcohols it was found that the acetate protecting group was the most satisfactory for our purposes and thus only the acetate was subsequently used.



(96) (113)

The acetoxypropylpyrrole (113) was produced from the methoxycarbonylethylpyrrole (96) directly without isolation of the hydroxypropylpyrrole. The product of the diborane reduction was dissolved in pyridine/acetic anhydride and the above procedure followed. The acetoxypropylpyrrole was isolated in an overall 96% yield for the two reactions.

2.3 The First Link

The first link was carried out in the manner described by Paine.[28] The diacid chlorides (114, 115, 116) (Figure 14) were produced by heating the diacids (117, 118, 119) on a steambath with thionyl chloride for 1 hour; excess thionyl

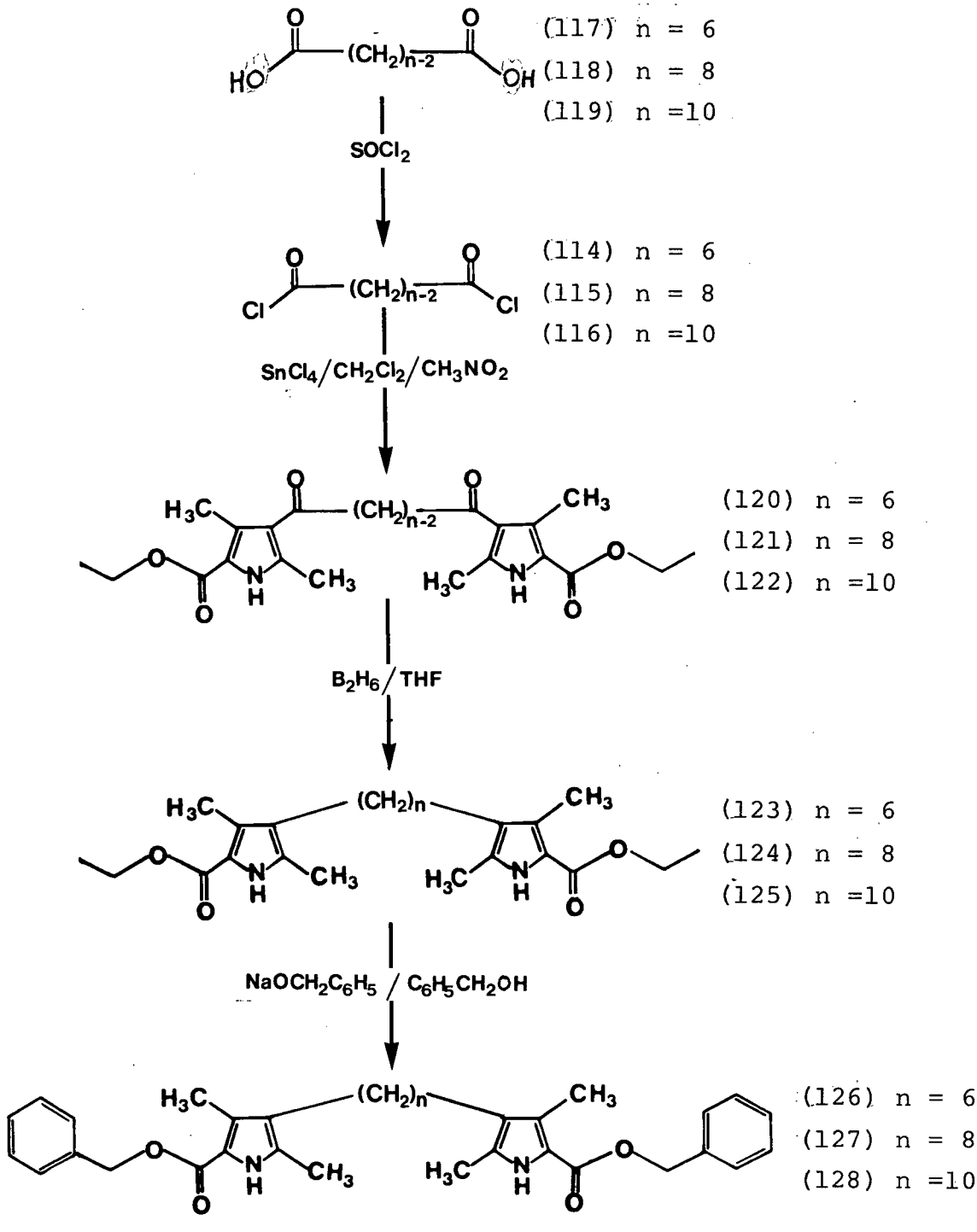


FIGURE 14: Synthesis of Chain Linked Bis Pyrrolic Intermediates

chloride was then removed under reduced pressure. Any last traces were removed by adding carbon tetrachloride and removing under reduced pressure. The crude diacidchloride was added to an excess of β-free pyrrole (88) in 1:1 dichloromethane-nitromethane and $SnCl_4$ added dropwise. The conditions varied for the different chain lengths; during the period between synthesising the C_8 link and the C_{10} link it had been discovered that lower concentrations of $SnCl_4$ could be used; the reaction could be run at room temperature as opposed to 0^oC and the addition time could be reduced from 1 hour to ½ hour without loss of yield or purity. The bisacylation products (120, 121, 122) were obtained in 80-85% yield, they were extremely insoluble, but recrystallisation from hot acetone produced analytically pure compounds.

The reduction of the two ketone functionalities to methylenes was carried out with diborane in tetrahydrofuran and monitored by tlc. The alkane linked bispyrroles (123, 124, 125) were obtained in 83, 82, 89% yields respectively. The higher yield of (125) was the result of carrying out the reaction at room temperature as opposed to the 0° used in the previous experiments; this was again a modification which hadoccurred during the work on C_8 and C_{10} linked dimers.

Due to the ease of removal of benzyl esters it was decided to transesterify the ethyl to the benzyl esters. The transbenzylation was affected by a

modification of Kenner's [52] procedure. The alkane bispyrroles (123, 124, 125) were dissolved under nitrogen in boiling benzyl alcohol (previously distilled from anhydrous potassium carbonate), and a solution of sodium benzyloxide catalyst (freshly prepared from sodium and benzyl alcohol) was added in 1 mL portions. Vigorous evolution of ethanol was observed and the 1 mL portions repeated till ethanol was no longer evolved. The solution was then allowed to cool slightly and poured into methanol containing acetic acid to remove the catalyst. The solution was diluted with water to induce crystallisation; the yields of the benzyl esters (126, 127, 128) were greater than 90%.

2.4 2-(2H-Pyrrol-2-ylidenemethyl)pyrroles (Methenes)

All the methenes produced in this work were synthesised by reaction of a α-carboxypyrrole (129) (Figure 15) with α-formylpyrrole (130). This is a minor modification of the general aldehyde synthesis of methenes which makes use of the α-free pyrrole (131) reacting with the α-formylpyrrole. The α-free is formed in situ by acidic decarboxylation on the addition of hydrobromic acid. The protonated α-formylpyrrole is also formed; this is in effect a pyrrolhydroxycarbinyl cation (132) which reacts with the α-free pyrrole to give the transient meso-hydroxydipyrromethane (133). Water is lost instantly to give the methene (134). The free base methenes are not stable and are thus produced and used as the hydrobromide salts.

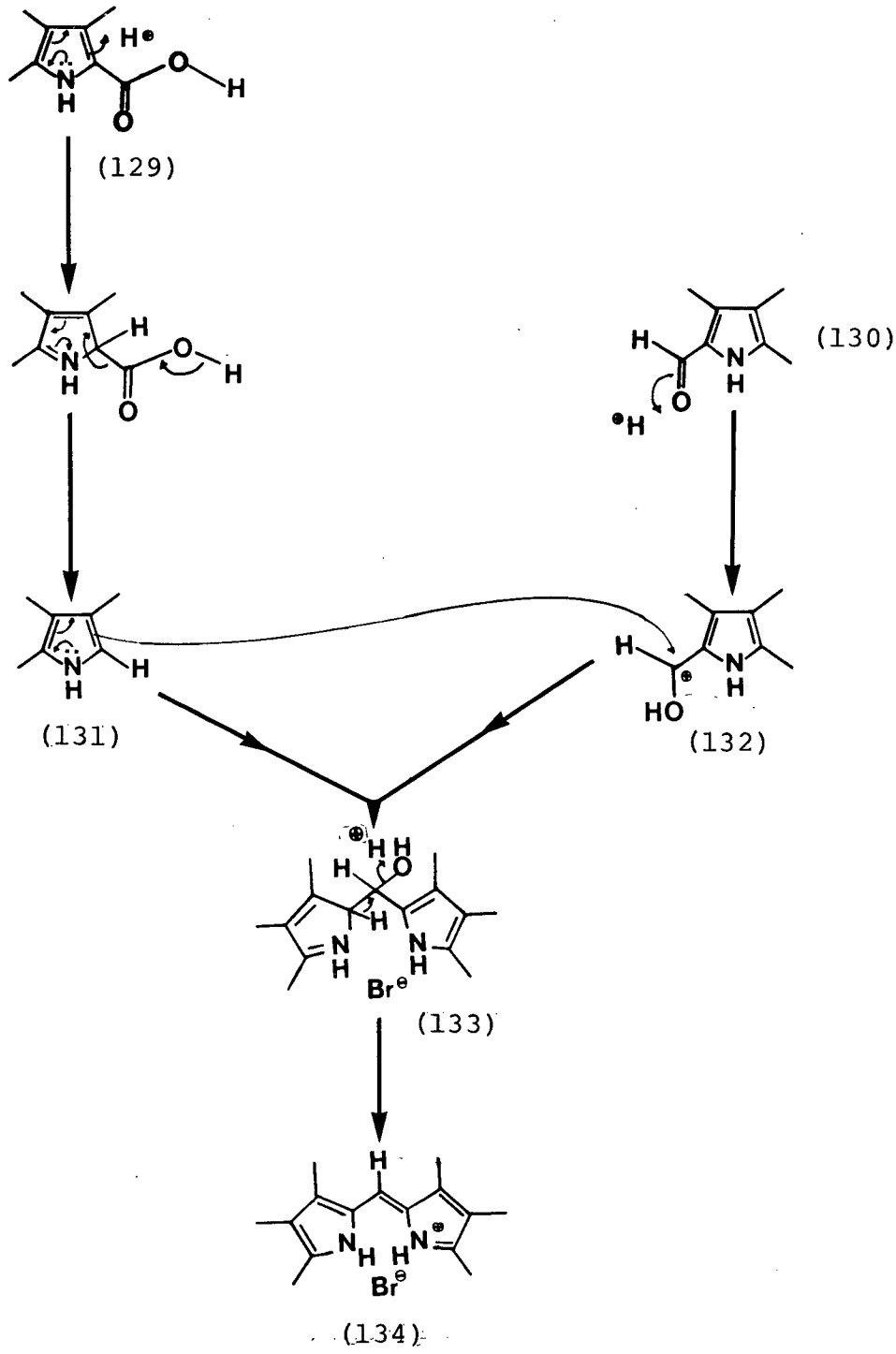


FIGURE 15: Synthesis of Pyrromethene from α-Carboxy and α-Formyl Pyrroles

2.4.1 Linked Methenes

With the synthesis of (126, 127, 128) (Figure 16,) we have the first ring of the porphyrin linked by an alkyl chain. The porphyrin can now be simultaneously and symmetrically built at the ends of the link. The first step in the synthesis of the porphyrin ring is the formation of the linked bismethenes.

The benzyl esters of (126, 127, 128) were cleaved by catalytic hydrogenolysis with palladium/charcoal in tetrahydrofuran to produce the α-carboxypyrroles (135, 136, 137). To the solution of α-carboxypyrrole was added 2.1 moles of (108), the solution was then filtered to remove the hydrogenation catalyst and hydrobromic acid was added; instantly there was a darkening in the color of the solution to a dark yellow. The solution was diluted with methanol and tetrahydrofuran removed by reduced pressure distillation. The solvent was reduced in volume until solid (138, 139, 140) appeared in the solution at which point it was cooled in ice. The solid was filtered and washed with ethyl acetate. These solids crystallised analytically pure in approximately 90-95% yields. In one preparation of (140) the analysis was found to be marginally outside the acceptable limits and re-crystallisation from methanol/hydrobromic acid yielded the analytically pure compound.

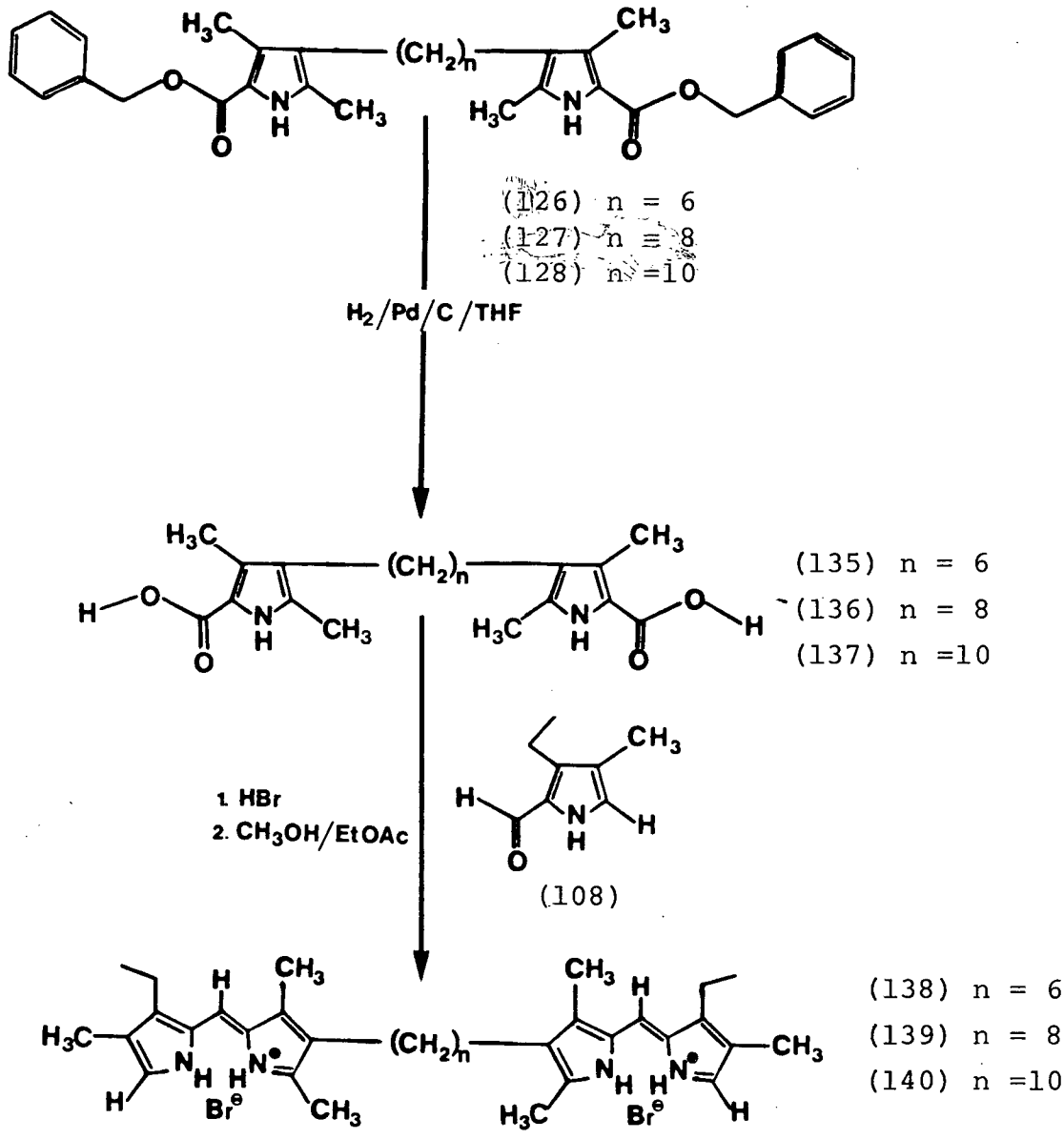


FIGURE 16: Synthesis of Chain Linked Bismethenes

2.4.2 The Reactive Side Chain Methenes

All the porphyrins were synthesised from two methenes, the first the linked bismethene and a second methene containing the reactive side chain which could be cyclised via the Johnson[29] synthesis. This second methene had two requirements, one the reactive side chain on the position diagonally opposite the first link, secondly it must be capable of only one cyclization reaction with the linked methene.

It thus required a reactive sidechain adjacent to an α-methyl and the other α-position to contain a group capable of conversion to the α-bromo. The simplest way to achieve these requirements was considered to be the methene (141) obtained from the β-chloroethyl-α-carboxypyrrole (142) (Figure 17), obtained from (109) by catalytic hydrogenolysis, with the α-formyl-α'-carboxypyrrole (101).

This did not yield the required methene but gave intractible tars when carried out in acetic acid, as in the Fischer method, even after several modifications to the method. It was thus decided that other β-substituted pyrroles should be tried, the hydroxyethylpyrrole (143) gave the same results as did the benzyl ester (144).

The α-carboxypyrrole was therefore abandoned and the more roundabout route to the α-free-α'formylpyrrole was followed. Reaction of (142) (Figure 18), with (108) also

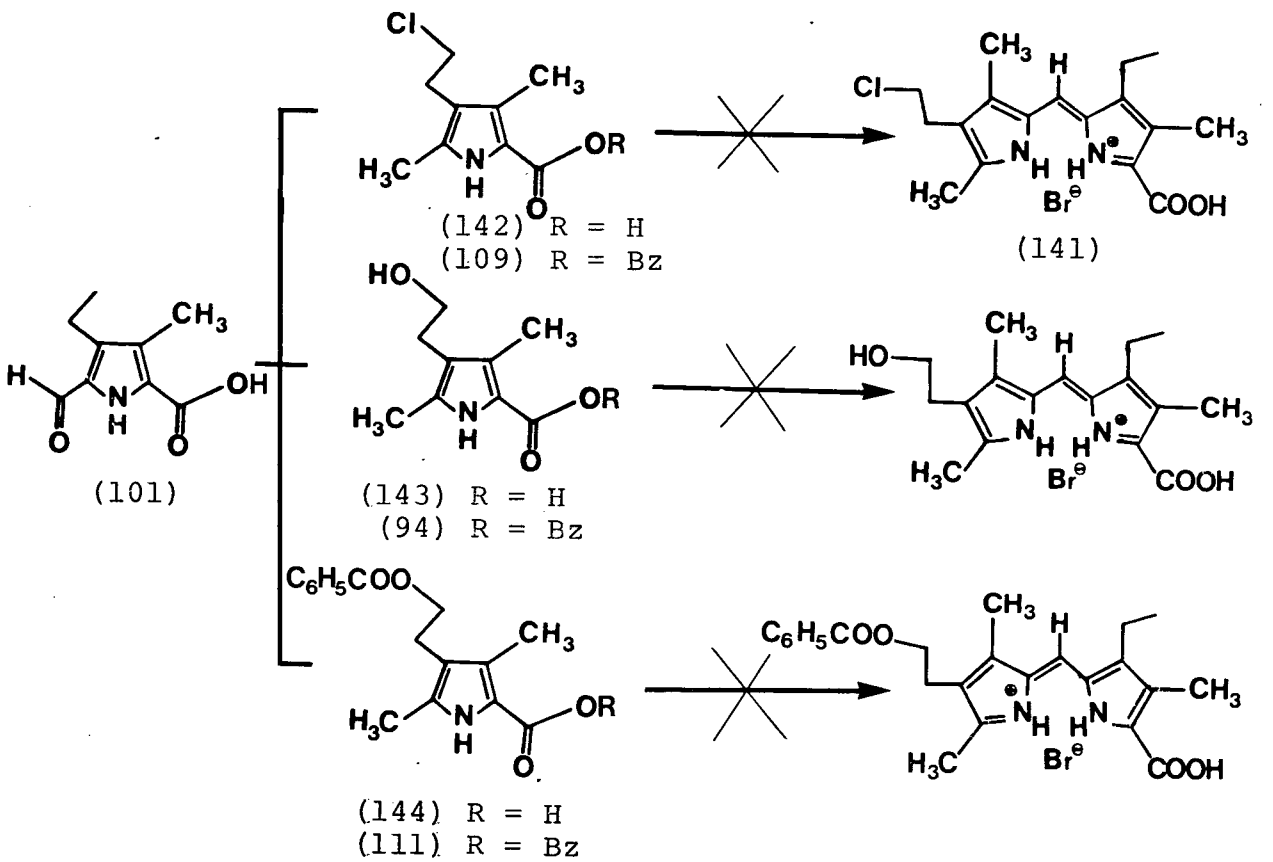


FIGURE 17: Proposed Synthesis of Substituted Side Chain Methenes

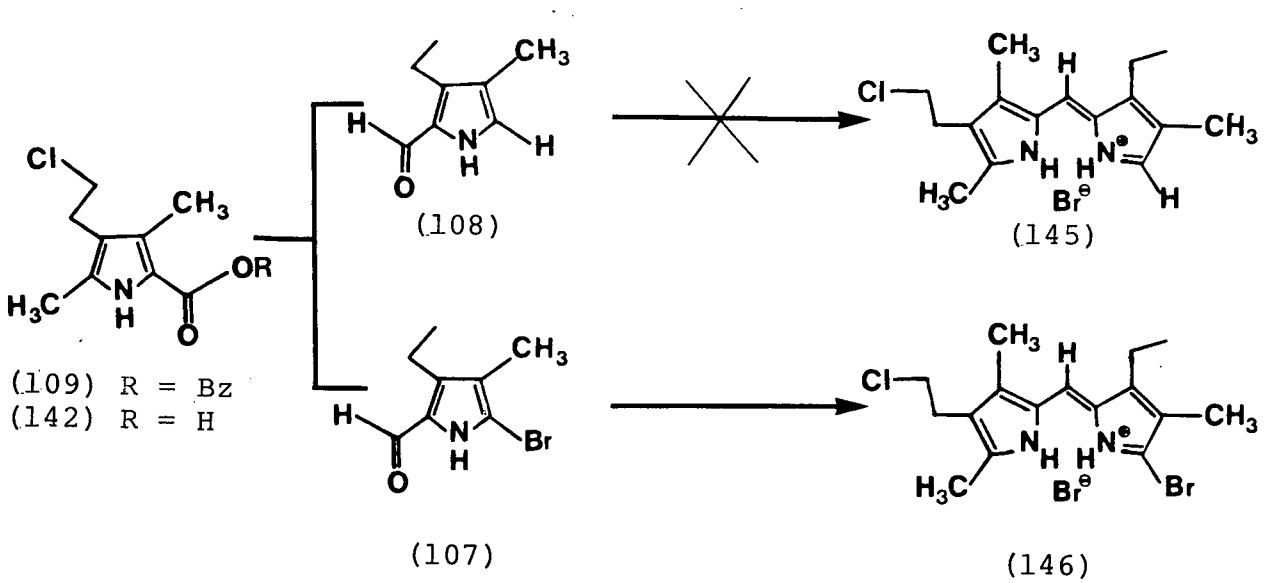


FIGURE 18: Synthesis of Chloroethyl Methenes

unexpectedly did not yield the methene (145), this was a great blow as it had been expected to be a facile reaction. It was at this point that the decision to produce the α-bromo-α-formylpyrrole (107) was made. When (107) was reacted with (142) the required methene (146) was obtained in over 90% yield.

On reaction of this methene after bromination with the linked methene it was observed that a partial substitution of the chloroethyl side chain occurred thus rendering the whole sequence inoperable; a new reactive sidechain had to be produced which would undergo the cyclisation reaction. With this in mind several other methenes were produced.

It was now considered unnecessary to use (107) as other workers[64] had used (108) for similar methenes. Thus (108) (Figure 19) was reacted with (147, 148 and 149) to give the methenes (150, 151 and 152) in approximately 90% yields with only one modification to the usual methene method. The methanol was added before or with the hydrobromic acid and the methanol volume never allowed to reduce excessively during the concentration because the esters could be cleaved, giving oils rather than the crystalline products.

For the C_{10} linked dimer the propyl group was synthesised, by this time it was known that the acetate was the most useful protecting group and so the acetoxypropyl methene (153) was produced by reacting (108) with (154) in the normal manner.

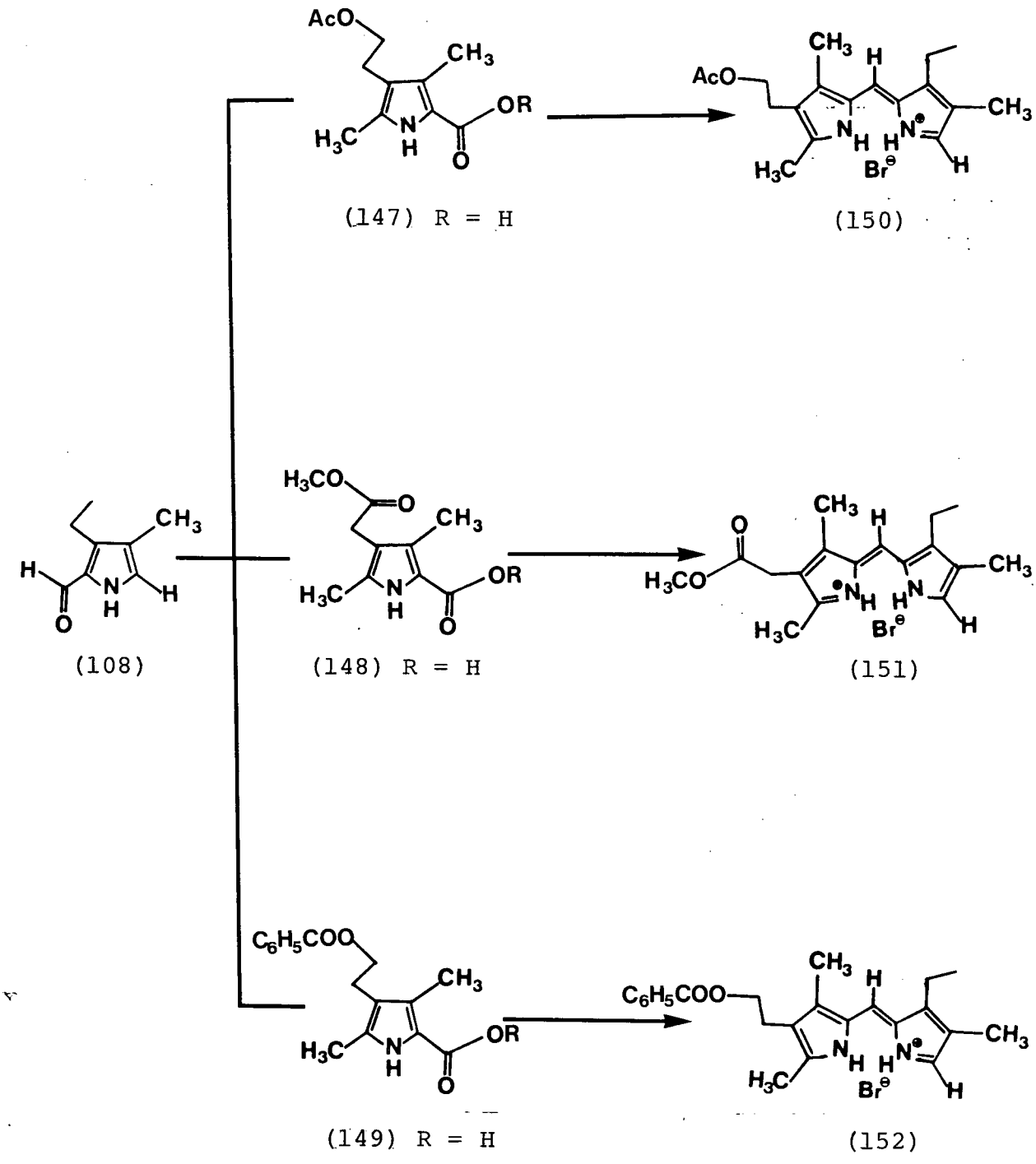
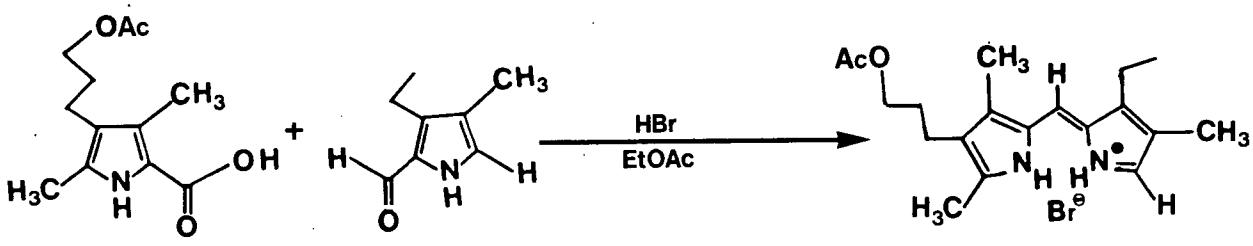


FIGURE 19: Synthesis of Protected Hydroxyethyl Methenes



(154) (108) (153)

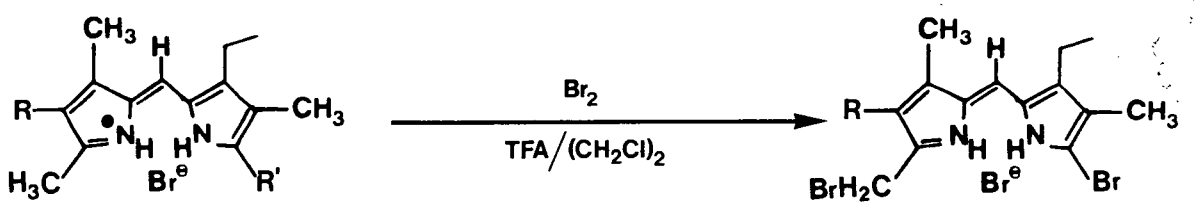
2.4.3 Bromination of Methenes

As mentioned earlier (Section 2.1) a good method for the conversion of methenes to bromo-bromomethylmethenes was not available in the early work. The methene had to be refluxed with the requisite quantity of bromine in small volumes of glacial acetic acid until bromine could no longer be observed in the vapours. The reaction was then quenched by cooling rapidly and filtering the crystallised solid. The reaction could then be checked by NMR to determine the purity of the product. This often had to be repeated before the reaction went to completion; excess bromine could not be used, even though vapour was always lost, due to the tendency to form the dibromomethyl analogs.

Fortunately a reliable method for the bromination of methenes was developed which gave pure products in good yield (usually 90%) without the tendency to over brominate.

The bromination was carried out in 1:3 trifluoracetic acid/ 1,1-dichloroethane with excess bromine at room temperature over 4-5 days (some reacted in 3 days but were not adversely affected if left even 7 days).

The methenes (146, 150, 151, 153) (Figure 20), were all treated with bromine in trifluoracetic acid/ 1,1-dichloroethane;



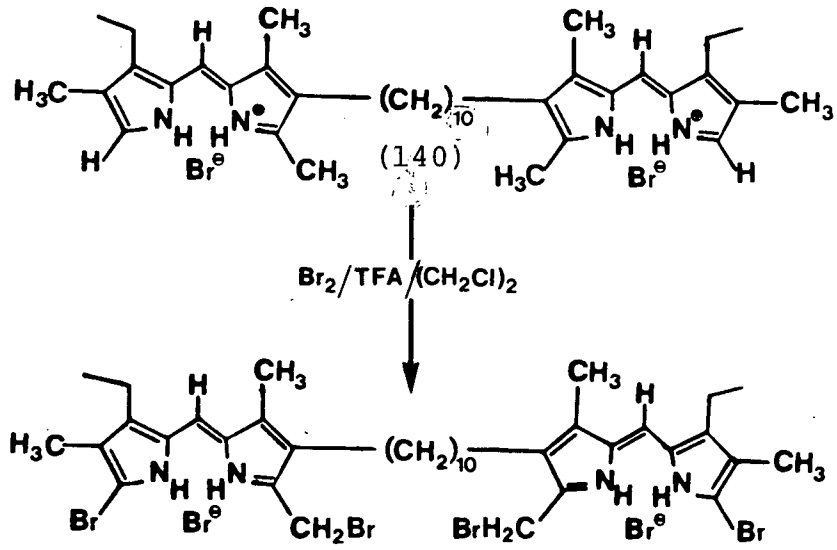
	R	R'		R
(146)	CH_2CH_2Cl	Br	(155)	CH_2CH_2Cl
(150)	$CH_2CH_2O_2CCH_3$	H	(156)	$CH_2CH_2O_2CCH_3$
(151)	$CH_2CO_2CH_3$	H	(157)	$CH_2CO_2CH_3$
(153)	$CH_2CH_2CH_2O_2CCH_3$	H	(158)	$CH_2CH_2CH_2O_2CCH_3$

FIGURE 20: Bromination of Methenes

the dibrominated methenes (155, 156, 157, 158) were obtained by evacuating excess bromine and evaporating to dryness. The solid (in some cases oil) was redissolved in 1,1-dichloroethane and crystallised by the addition of ethyl ether and petroleum 30-60° to the ice cold solution. Any perbromide could be destroyed at the crystallisation stage by addition of cyclohexene or by dissolving in dichloromethene treating with cyclohexene and then evaporating to dryness before use.

The C_{10}-C_{10} bismethene (14) was tetrabrominated to give (159) by the above method to enable the $C_{10}C_{10}$ dilinked

bisporphyrin to be synthesised by Paine's method to give a material for comparison purposes.



2.5 Porphyrin Synthesis

Synthesis of porphyrins based on the condensation of two dipyrrolic intermediates (2 + 2 synthesis) have been widely used. In the early work of Fischer mixtures of products were frequently obtained, resulting in tedious separations of isomeric porphyrins. The condensation of components in a succinic acid melt often removed or altered β and meso substituents and minuscule yields were common.

The dipyrromethane synthesis developed by MacDonald[53] was

thus a great improvement having notable successes e.g. Woodward's[65] synthesis of chlorophyll a. Unfortunately there were limitations and symmetrical pyrromethenes are required; electronegative stabilising groups are required to prevent cleavage of the dipyrromethane bridge with subsequent recombination and isomer formation. The Johnson porphyrin synthesis via ac-biladienes eliminated these problems and produced unambiguous porphyrins.

2.5.1 The Johnson Porphyrin Synthesis

The initial condensation of ac-biladienes with copper acetate had similar symmetry restrictions to the previous methene syntheses thus other cyclisation methods were sought.

Bromination of 5-unsubstituted-5'-methyldipyrromethene hydrobromide (160) (Figure 21) to give 5-bromo-5'-bromomethyldipyrromethene hydrobromide (161) enabled the synthesis of 1-alkyl-19-bromo-1,19-dideoxybiladiene-ac (162) by condensation with a 5-unsubstituted-5'-alkydipyrromethene (163) in the presence of $SnCl_4$. The tin complexes were not isolated but converted to the dihydrobromide in good yield. The salts were then cyclised by refluxing in σ-dichlorobenzene to give high yields of the required porphyrin (164). The reaction was modified by the use of dimethyl sulfoxide and pyridine in the dark at room temperature which gave excellent yields of octaalkylporphyrins via the porphodimethene (165).

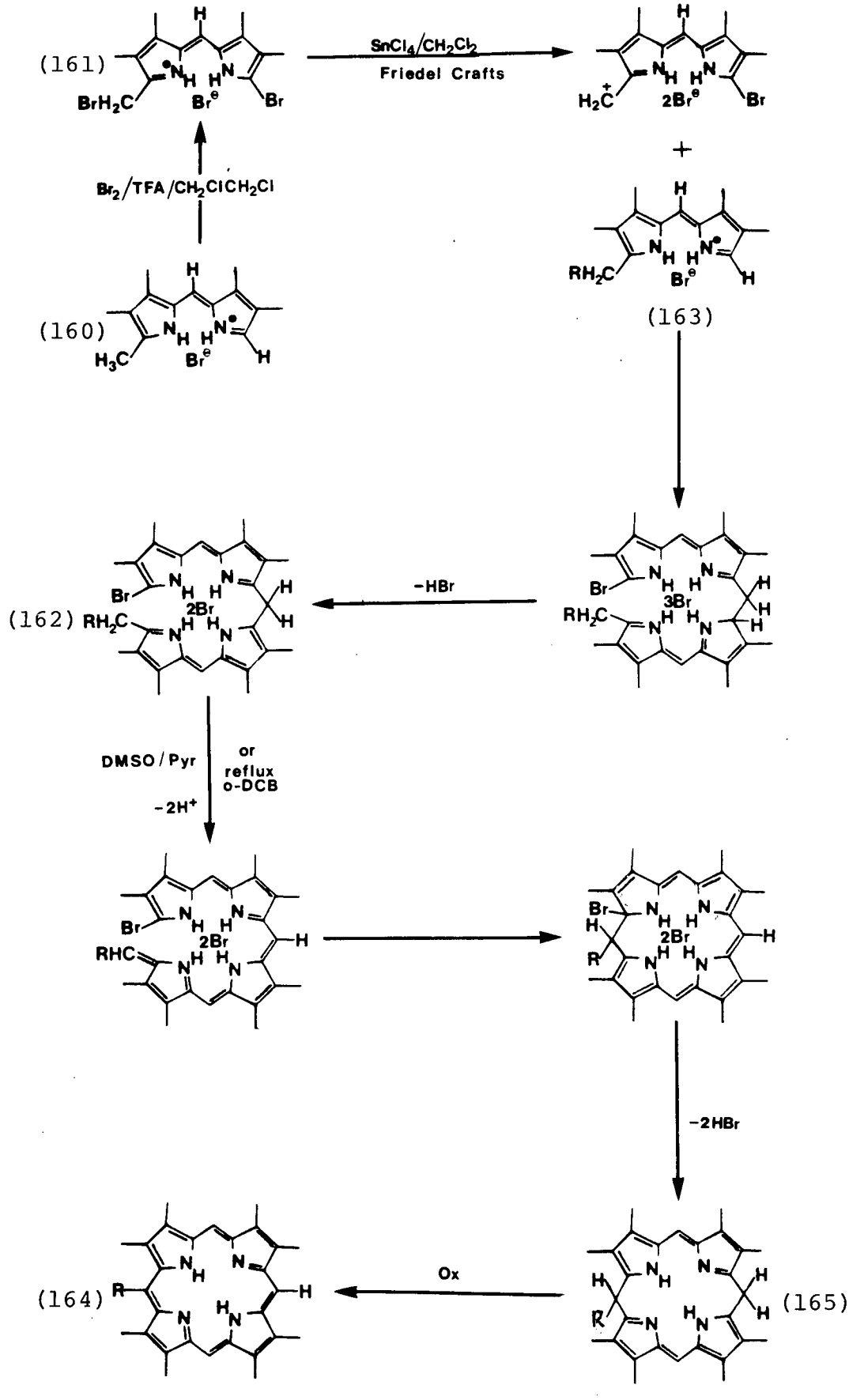


FIGURE 21: Mechanism of Porphyrin Cyclisation

Both cyclisation methods for the biladienes were used, although the DMSO/pyridine method was preferred for the protected hydroxyalkylporphyrins, as this gave better yields and cleaner products.

The method varied somewhat during the porphyrin syntheses in the method of isolation or in some cases the non isolation of the biladiene dihydrobromide.

Equivalent quantities of 5-bromo-5-bromomethyldipyrromethene hydrobromide and 5-unsubstituted-5'-methyldipyrromethene hydrobromide were dissolved in dry dichloromethane, and $SnCl_4$ added, the mixture was then left for 1½ hours and quenched with 48% hydrobromic acid/water. The organic phase was separated and washed with water to remove the tin. Methanol (or ethyl acetate) and hydrobromic acid was added and the dichloromethene removed under reduced pressure at 25°. The dihydrobromide salt was filtered, washed with ethyl ether or ethyl acetate and dried under vacuum.

The cyclisation was then accomplished by refluxing the solid in o-dichlorobenzene for up to 1 hour or dissolving it in dimethyl sulfoxide/pyridine and allowing to stand in the dark for several days. The porphyrin formed as a scum on the surface of the solution, and was filtered, washed with methanol and dried.

2.5.2 Singly Linked Porphyrins

Although the C_6-C_6 (166) dimer was eliminated as a possible route to doubly linked dimers early in its synthesis it was decided to carry through the reactions to determine their feasibility whilst concurrently synthesising the C_8 linked bismethene (139). Thus the synthesis of a bis-(chloroethylporphyrin) hexane (167) was attempted. The biladiene was synthesised in the normal manner from (146) (Figure 22) and (138) and cyclised by both the DMSO/pyridine

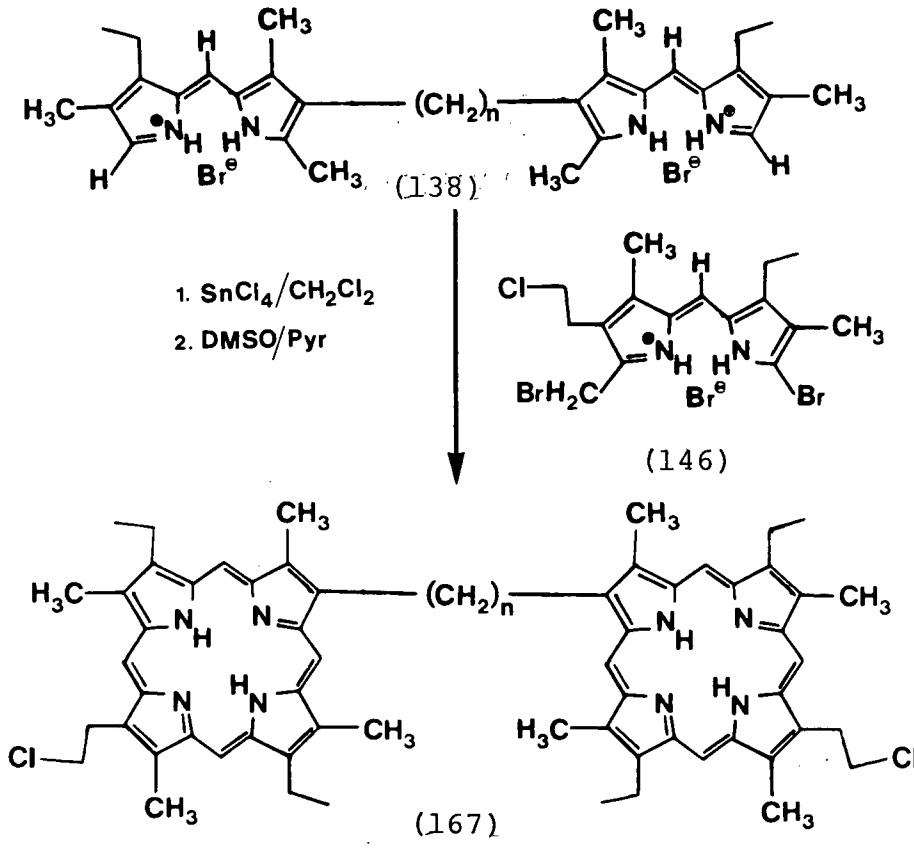


FIGURE 22: Synthesis of Chloroethyl porphyrin

and o-dichlorobenzene methods in 45 and 39% yields. Synthesis of the bis-(chloroethylporphyrinyl) octane (168) was attempted by the o-dichlorobenzene method, but ^{1}H and ^{13}C NMR showed (167) and (168) to be mixtures of chloroethyl and bromoethylporphyrins. It was thus necessary to protect the haloethyl functionality during the porphyrin synthesis.

The use of the acetate-protected hydroxyethyl was decided upon as this had been previously used to produce haloethyl sidechains by other workers.[54] The cyclisation of (139) (figure 23) with two moles of (156) yielded the porphyrin (169) in 61.8% yield. For the synthesis of the bisporphyrin the next step was the bromination of the hydroxyethyl side-chain. The obvious methods for bromination of the hydroxyl functionality, hydrobromic acid, triphenylphosphine/carbon-tetrabromide etc. did not produce the bromoethylporphyrin and usually led to dark green solutions. Bromination of the hydroxyl group via the mesylate and tosylate were attempted and these methods again gave green solutions. The green solutions were observed to have a strong absorption indicative of chlorins thus it was postulated that the bromoethylporphyrins were eliminating hydrogen bromide to yield vinyl porphyrins, which were then able to undergo a photoproto type reaction to yield a chlorin. Thus a mild brominating agent was required which was not strongly acidic or basic and did not attack the porphyrin ring.

The method finally attempted was the use of triphenyl-phosphite dibromide in dichloromethane. This was produced

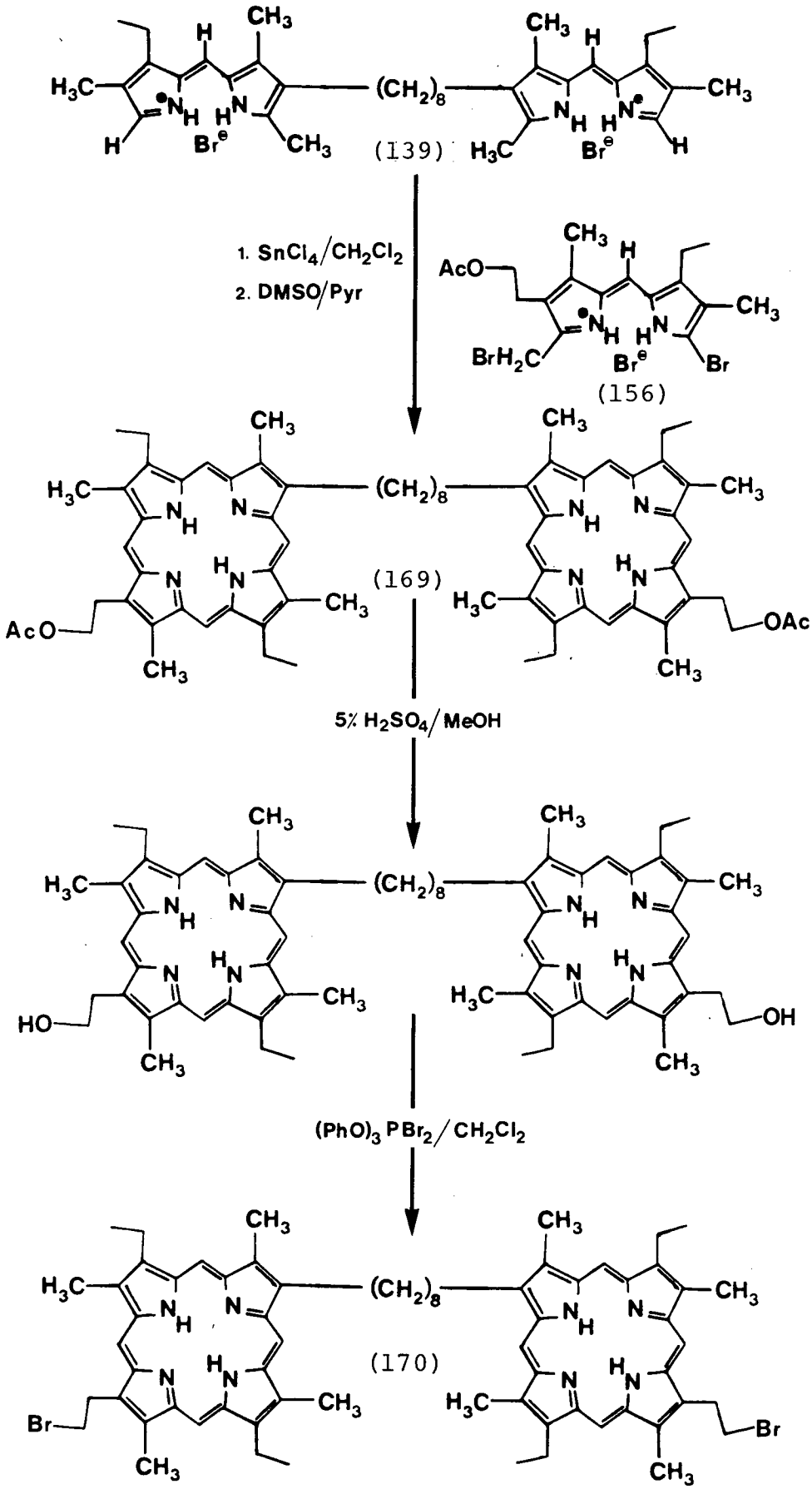


FIGURE 23: Synthesis of C_8 Bis(bromoethyl porphyrin).

by adding bromine dissolved in dichloromethane to an ice cold solution of triphenyl phosphite in dichloromethane. The hydroxyethylporphyrin was added as a solid which dissolved in a few minutes to give a purple solution. A tlc was taken as a reference for further samples and surprisingly it showed a large fast-running red band. The reaction was observed over the next two hours but showed little change. The reaction was quenched with water and upon workup was found to yield the bromoethylporphyrin (170) in 65%.

The mass spectrum of (170) exhibited a M^+-2HBr rather than M^+ peak; large peaks at m/e = 79,81 and 80,82 in 1:1 ratios showed evidence for the loss of HBr; analysis and NMR were corroborative of the structure assigned to (170).

The synthesis of the butyne sidechain was attempted with lithium acetylide ethylenediamine complex in DMSO but upon reaction the solution turned green even in the absence of sunlight and oxygen. Various attempts were made with different solvents, under varying conditions but to no avail as all attempts to react the bromoethylporphyrin led to elimination.

It was decided at this time to produce the C_{10}-C_{10} dimer as this would be produced from the bromopropylporphyrin (171) which should not be subject to the elimination reaction encountered with the bromoethylporphyrin, there being no conjugation with the ring as in vinyl porphyrins.

To ensure that the butyne functionality was feasible by

the proposed route, the model compound 2,12,17-triethyl-3,8,13,18-tetramethyl-7-(penty-4-yne) porphine (171) (Figure 24) was produced.

Synthesis of the acetoxypropylporphine (172) from the methenes (173) and (153) was accomplished in 56.6% yield by the DMSO/pyridine method. Bromination of the hydroxypropylporphine (174) was carried out in 48% hydrobromic acid/sulfuric acid and also with triphenylphosphite dibromide in 77 and 85% yields. Treatment of the bromopropylporphine (175) with a large excess of lithium acetylide ethylenediamine complex in DMSO at 45°C yielded a porphyrin with mass spectra, and analysis which agreed with that expected although the 80MHz ^{1}H NMR was inconclusive due to overlapping bands. Attempted dimerisation of the porphyrin failed to yield any dimeric porphyrin. A 400MHz ^{1}H NMR spectra obtained at this point indicated the presence of a methyl group $\delta = 1.77$ppm with a small coupling J2Hz. This is indicative of an internal acetylene and further interpretation of the spectra enabled its structure to be assigned as the but-3-yneporphine (176).

This seemed to be a mortal blow as this procedure had been used successfully to produce terminal acetylenes by many workers.[55] It seemed possible that the rearrangement of the acetylene was due to the conditions of the reaction (strong bases are known to rearrange acetylenes), thus the synthesis was attempted using 1:1.2 molar ratio of reagents, unfortunately this had no effect upon the product. It was

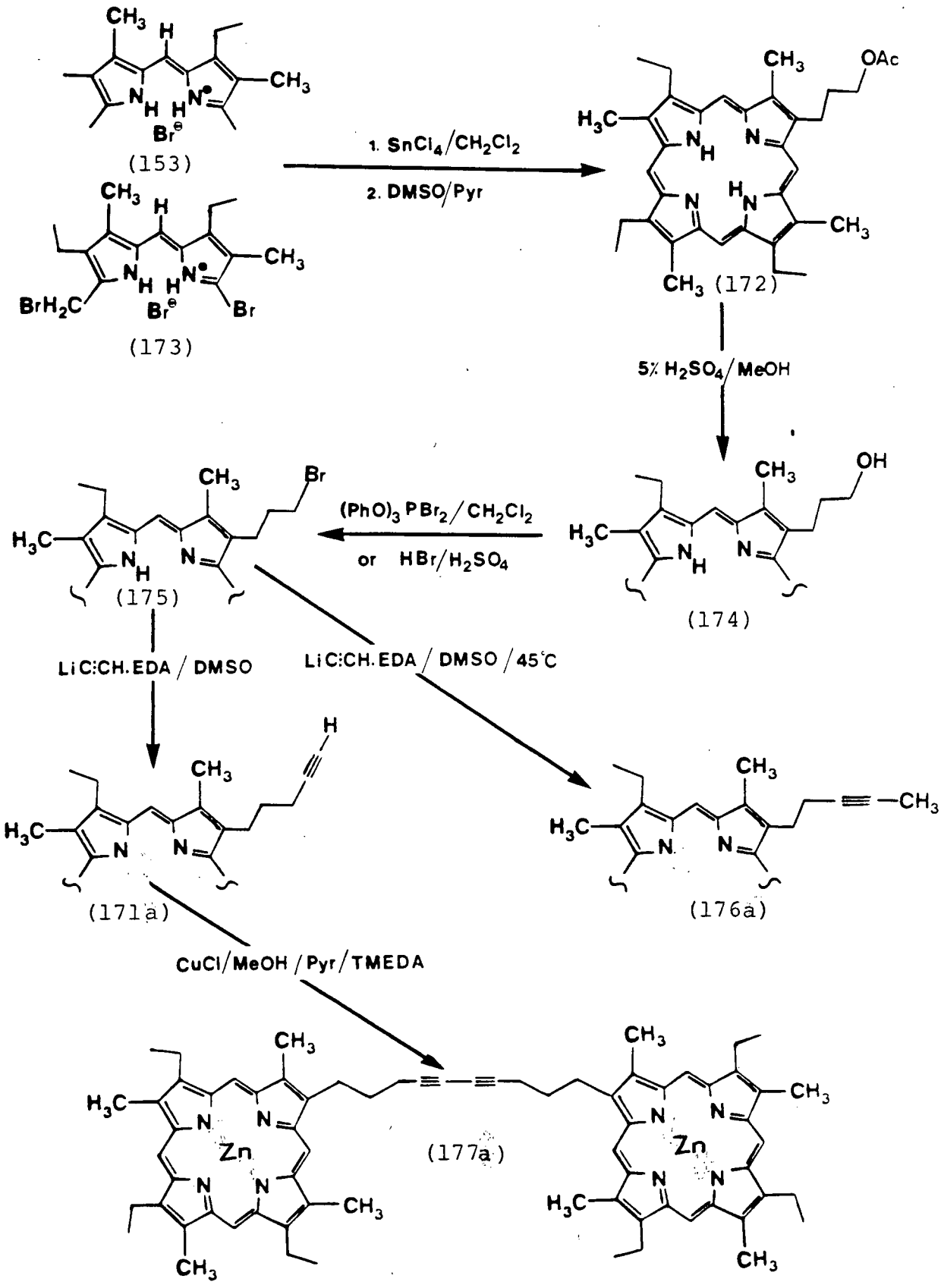


FIGURE 24: Synthesis of Model Diyne Bisporphyrin.

then decided to run the reaction at lower temperatures. Although in DMSO it is not possible to use temperatures below 20°C it was decided to remain with DMSO as solvent and try the reaction at ambient temperature and a shorter reaction time of 2 hours. The product from this reaction proved to be the required but-4-yneporphine (171), shown by the absence of a methyl signal in the 400MHz NMR, the analysis and mass spectra remaining correct.

Dimerisation of the zinc complex was accomplished by treatment of (171a) with cuprous chloride in methanol/pyridine/TMEDA under an oxygen atmosphere at 45°C. It had already been ascertained that zinc would not be replaced by copper under these conditions. The reaction was monitored for 24 hours there apparently being no further change after 18 hours. The product (177) was obtained in 56.5% yield, readily shown to be the dimer by high molecular weight fragments in the mass spectra. The mass spectrum showed an isotope distribution at 1154 - 1164 identical to that expected for (177a).

Catalytic hydrogenation with palladium oxide/formic acid[56] reduced the bisdiyne to the bisporphinyldecane (178) (figure 25) which was shown to be identical to an authentic sample produced by the method of Paine.

With this encouraging series of results it was concluded that the dimeric porphyrin should follow a similar pattern and produce a dimeric bislinked porphyrin. Unlike the monomeric porphyrins the dimers are extremely insoluble and thus reactions had to be carried out in dichloromethane

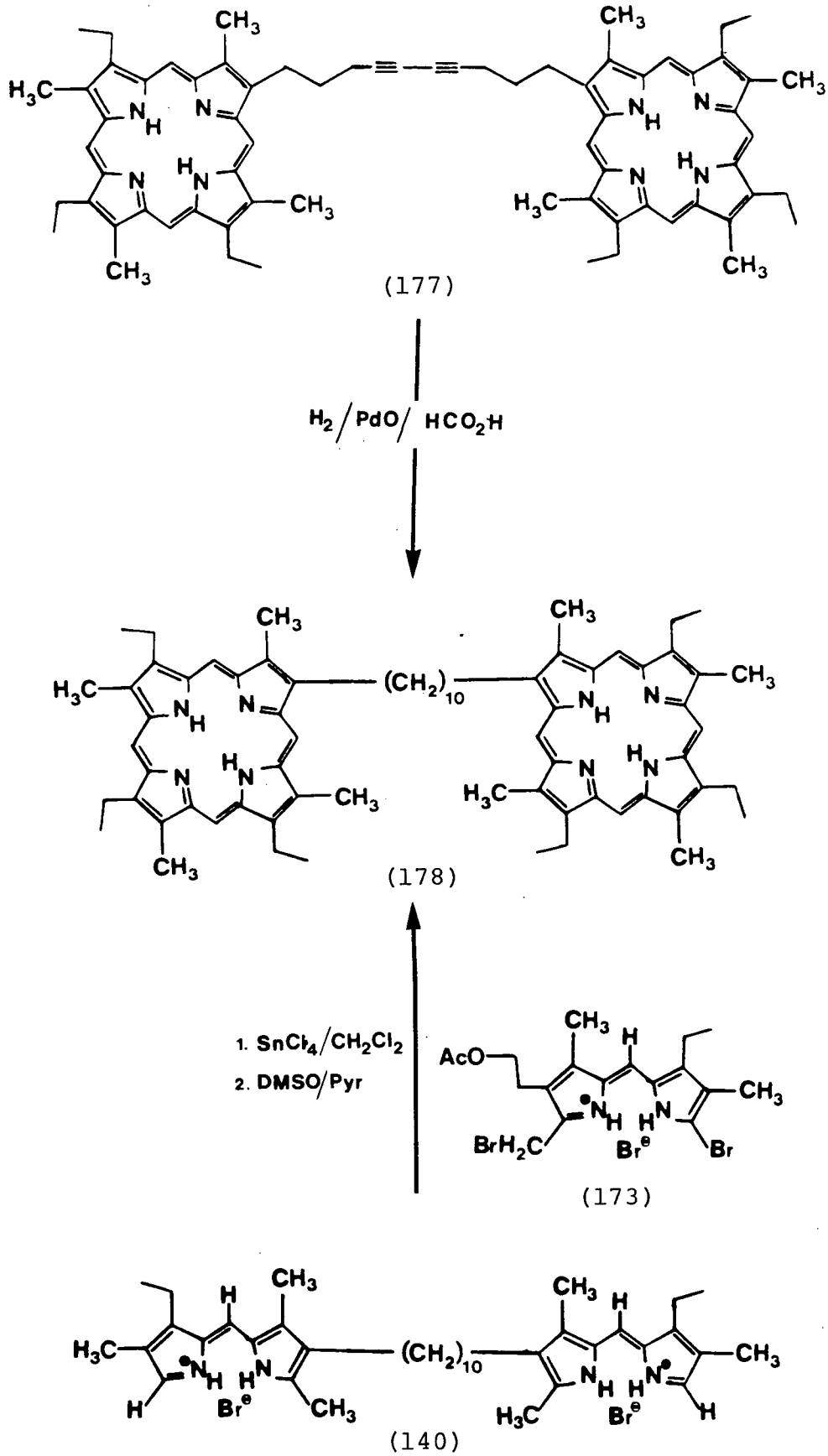


FIGURE 25: Synthesis of C_{10} Bisporphyrin.

or with acid present to solubilise the porphyrins.

The bis(acetoxypropylporphinyl)decane (179) was synthesised in a manner similar to that used for the C_8 analogue (169) (Figure 26). Deprotection of the acetate in 5% sulfuric acid/methanol was trivial but recrystallisation of the product proved extremely difficult due to its low solubility. Once the tetracation was neutralised the bis(hydroxypropylporphinyl)decane (180) precipitated from solution as a dark brown solid which could not be produced analytically pure but its ^1H NMR showed loss of acetoxyprotons at δ = 2.0ppm and was consistent with that of (180).

As bromination of the hydroxypropylporphyrin (174) had been found to occur in hydrobromic acid/sulfuric acid it was reasonable to assume that this should be true for the dimer. Unfortunately the dimer (180) did not dissolve readily even when the sulfuric acid concentration was increased to a 1:1 ratio. Upon workup it was found that a considerable portion of the dimer had been destroyed and the yield of C_{10} bisbromopropylporphine (181) was minor. The triphenylphosphite dibromide method was attempted and although the dimer took considerably longer to dissolve in the reagent (up to 2 hours in some cases) it did yield (181) in up to 65% yields; some mono-bromination occurred and was variable in quantity in different runs. The workup was considerably aided by virtue of converting (181) to its dizinc salt (181a) which was soluble in THF. Thus the column chromatography of

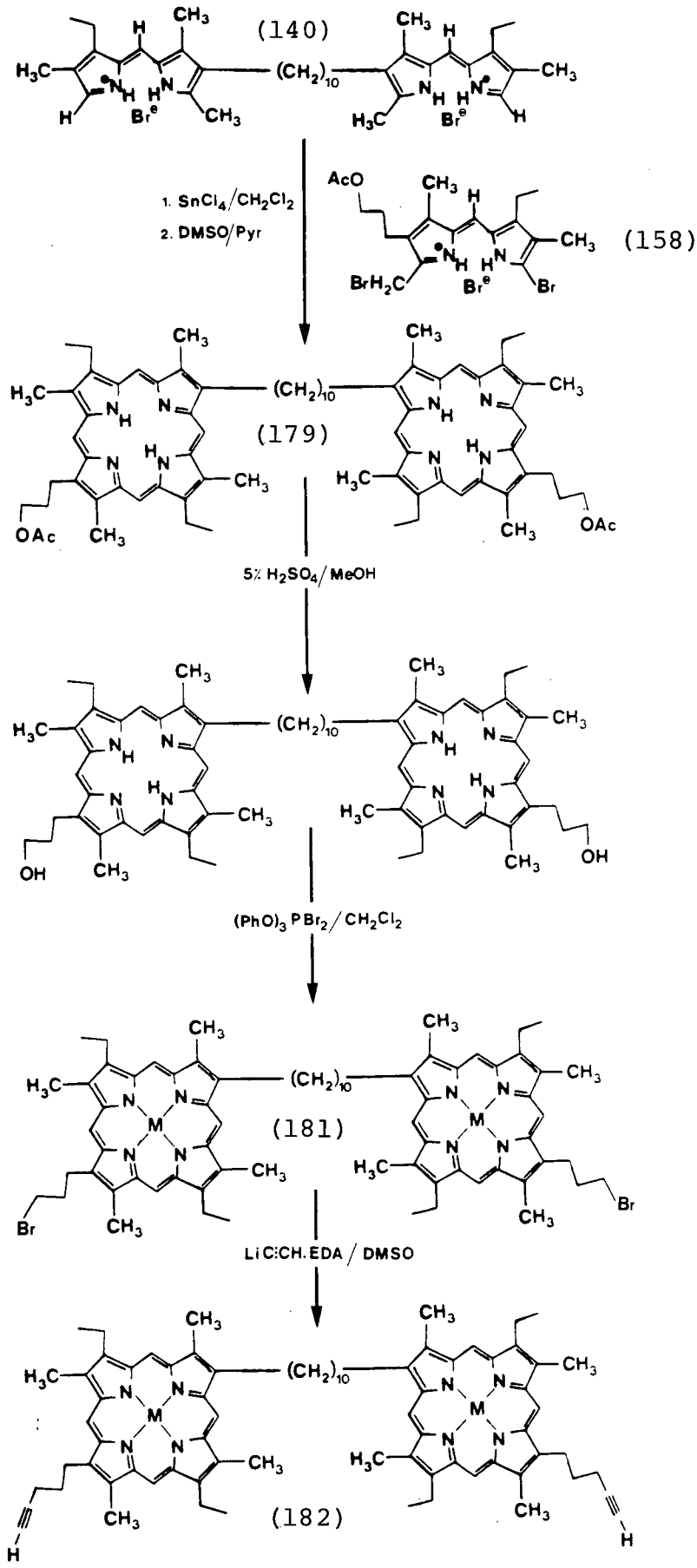


FIGURE 26: Synthesis of C_{10} Bis(pent-4-yne porphyrin).

the dimers was found to be considerably easier. The compounds could be dissolved in the minimum of THF diluted with dichloromethane, adsorbed onto the column and dichloromethane then used to elute the bands. The dizinc porphyrins ran very quickly (R_f 0.95 by tlc) with dichloromethane as eluent and the monozinc dimers could be eluted with 2% methanol/dichloromethane.

The dizinc dimers were also necessary to prevent formation of the copper salts and to increase the solubility of the dimers in DMSO the favoured solvent for reactions of lithium acetylide EDA. The non metallated dimer has only minimal solubility in DMSO, whereas its dizinc complex is very soluble and reacts readily to give the C_{10} bispentyne porphine (184) in 70% yield. The analysis agreed well with the expected results and mass spectra gave the expected isotope ratio. However the ^{13}C NMR appeared to give a mixture of alkynes, indicated by the alkyne carbon signals at δ = 70.160 and 83.993 and δ = 77.659 and 78.654. This could be due to running the sample overnight in 5% TFA/$CDCl_3$ solution (the ^{1}H NMR after ^{13}C NMR was considerably more complex).

2.5.3 The Final Link

Cyclisation of (182a) (figure 27) was carried out by a high dilution oxidative coupling reaction. The dimer

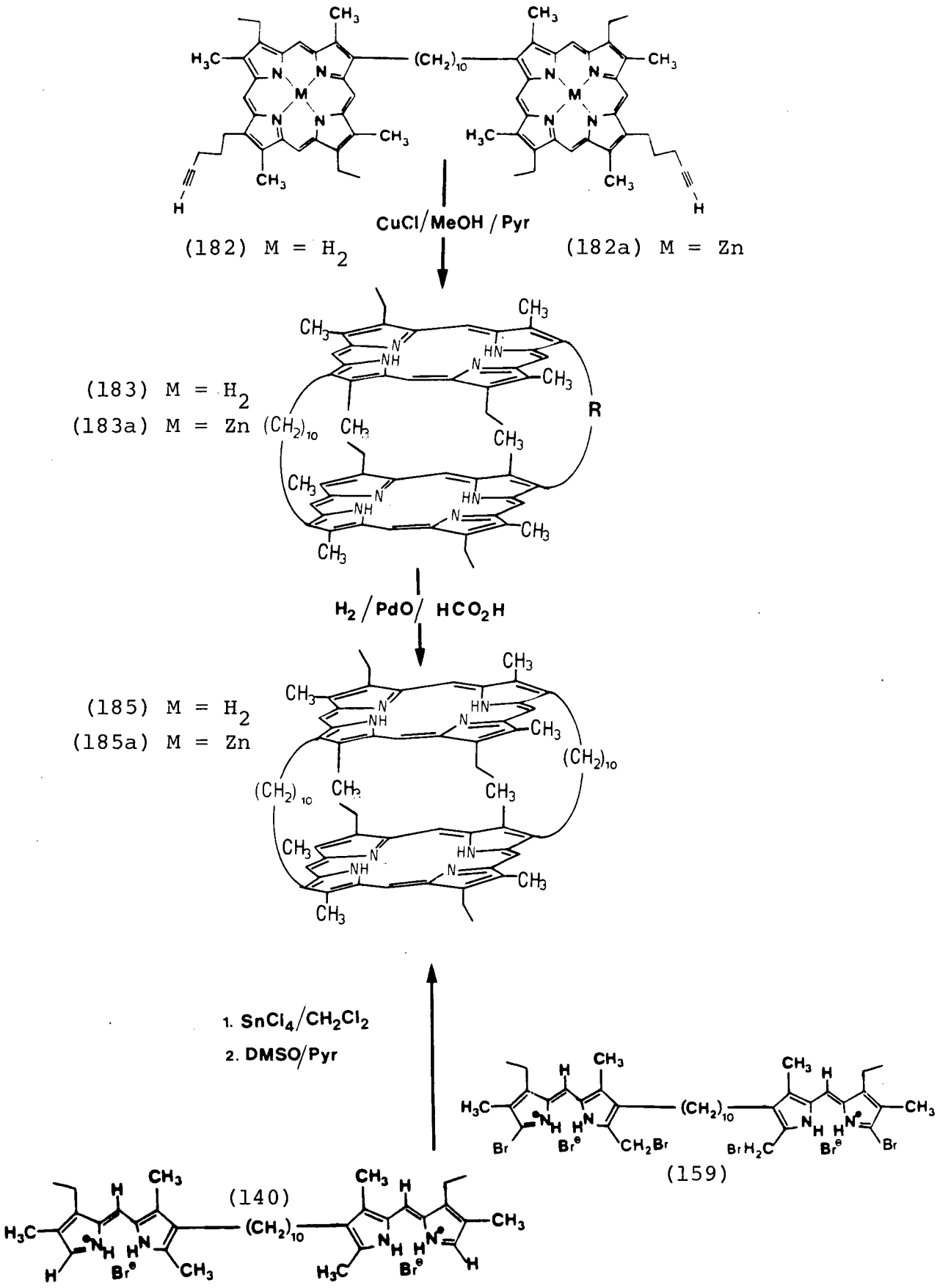


FIGURE 27: Synthesis of C_{10}-C_{10} Doubly Linked Dimer.

(182a) was dissolved in THF/dichloromethane and added, using a syringe pump, over a seven hour period to a solution of cuprous chloride in methanol/pyridine into which was bubbled oxygen. Workup consisted of washing with water, evacuating to dryness under reduced pressure and the usual chromatographic system. A very fast moving band was obtained which proved to be similar to starting material, on elution with dichloromethane/2% methanol a slower band was obtained. Even with such a mild workup it was found that the product could be obtained with only one zinc and that remetallating to give the dizinc dimer was extremely slow (observed by visible spectrum); this is a phenomenon noticed by other workers[14] with cofacial dizinc dimers, and had not been observed with the singly linked diyneporphine (177). The yield of dimer (183a) for this reaction was found to be extremely low (only 4%), recovery of starting material was 50%. The recovered (182a) was recycled through the reaction but although some product was obtained the yield was even less than that previously obtained. Although this failure could possibly be attributed to a mixture of (182a) and (184a) at the starting material stage, rearrangement under the basic conditions of the reaction is possible.

The fact that some cyclised product could be obtained from the recyclised material would tend to suggest that the major problem might not lie in the rearrangement but in that the conformation required for cyclisation could be extremely unfavourable.

Catalytic hydrogenation of the diyne was attempted with PdO/formic acid but difficulty was found in maintaining the dimer (183a) in solution. THF was added and this overcame the solubility problems but reduced the activity of the catalyst as compared to the singly linked dimer (177). The C_{10}-C_{10} dimer (185) produced was compared, using tlc, mass spectroscopy and ^{1}H NMR, and found to be identical to a sample produced by the method of Paine. The yield once again was extremely low (~5%) it seemingly being easier to reduce the porphyrin than the diyne system. The normal method of regenerating the porphyrin after reduction by bubbling air into the solution was found to regenerate porphyrin only once and then to only a minor degree.

Thus we had produced the same compound via two distinct routes. The stepwise synthesis discussed in this thesis whilst not viable for producing quantities of dilinked bisporphyrins does prove the structure of the single step cyclisation product of Paine, which can of course be used to produce a variety of chain lengths and thus various metal-metal distances.

CHAPTER 3

EXPERIMENTAL

3.1 GENERAL METHODS

Melting Point Determinations

Melting points were obtained with a Thomas-Hoover Unimelt, a capillary/oil immersion apparatus; the results are presented uncorrected.

Elemental Analysis

Elemental analyses were performed by Mr. P. Borda of the Microanalytical Laboratory, U.B.C.

Nuclear Magnetic Resonance Spectroscopy

Unless otherwise stated, proton NMR spectra were obtained at 100 MHz with a Varian XL-100 spectometer. 80 MHz spectra were recorded on a Bruker WP-80 spectrometer, 270 MHz spectra on a UBC NMR Centre modified Nicolet-Oxford H-270 spectrometer. 400 MHz and ^{13}C NMR were recorded with a Bruker WH-400 spectrometer. Some ^{13}C NMR were also recorded with a Varian CFT-20. All spectra were recorded with TMS as internal standard $\delta = 0$. Chemical shifts are recorded in the δ(ppm) scale.

Mass Spectrometry

Mass spectra were recorded on a Varian MAT CH 4-B spectrometer or a Kratos/AEI MS-902 spectrometer. High molecular weight porphyrin spectra were obtained on a Kratos/AEI MS-50 spectrometer.

Electronic Spectroscopy

A Cary recording spectrometer (Model 17) was used to obtain uv and visible spectra.

Chromatography

Column chromatography was performed using silica gel obtained from ICN Pharmaceuticals (Woelm, 70-150 mesh, activity I). Thin Layer Chromatography (tlc) was performed using precoated silica gel plates (Analtech-Uniplate, 250) and the compounds were detected by uv light (254 nm and 366nm).

Starting Materials

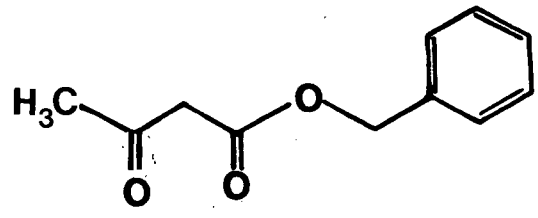
As none of the pyrroles required for this work was commercially available at a reasonable price, all of the pyrrolic starting materials had to be synthesized. Although most of these compounds have appeared previously in the literature, their syntheses have been included here for completeness, and the convenience of any who might wish to make use of the information contained herein. In some cases, useful modifications have been made.

Reagents and Solvents

All chemicals and solvents were reagent grade unless otherwise indicated. The dry dichloromethane used during this work was distilled from calcium hydride.

3.2 Synthesis of Acyclic Precursers

Benzyl acetoacetate (90)

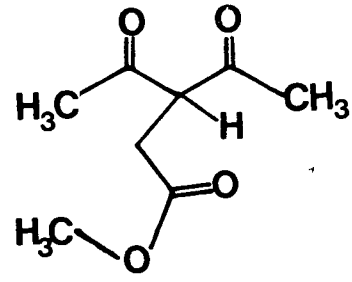


Ethyl acetoacetate (1400 mL, 11 mole) and benzyl alcohol (1042 mL, 10 mole) were mixed and left overnight. The mixture was heated to reflux and ethanol (560 mL, calc. 500) distilled over. The resulting mixture was distilled under reduced pressure and the product (1444.6g, 78%) had BP. 140-145°C/10 Torr (lit. 152-157°C/11 Torr). n_D^{20} = 1.4734.

Anal: Calc. for $C_{11}H_{12}O_3$: C,68.73; H,6.29; Found: C,68.38; H,6.44%.

^{1}H NMR: (δ, CCl_4); a) keto form; 2.00 (s, -C$\underline{H}_3$); 3.24 (s, -CO-C$\underline{H}_2$-CO); 4.98 (s, 2H, -C$\underline{H}_2C_6H_5$); 7.18 (s, 5H, -$C_6\underline{H}_5$); b) enol form (ca.15%); 1.80 (s, C$\underline{H}_3$).

Methyl-3-acetyl-4 oxopentanoate (92)

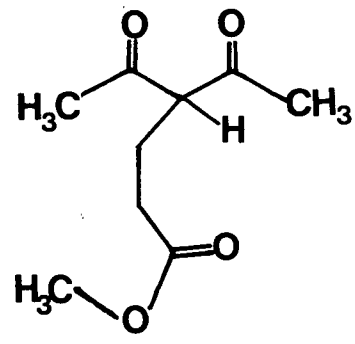


Methyl chloracetate (548 mL, 6 mole) was added dropwise to a stirred mixture of 2,4-pentanedione (616 mL, 6 mole) anhydrous potassium carbonate (830g, 6 mole), potassium iodide (180g, 1.08 mole) and 2-butanone (3000 mL). When the mixture had ceased to reflux, it was heated on a steam bath for a further 1 hour. The mixture was filtered when cool, and the solvent removed under pressure. The residual oil was distilled under reduced pressure, the product (610.7g) had BP. 105-110°C/6 Torr (lit.[57] 130-132°C/21 Torr) n_D^{20} = 1.4566 (lit. 1.4555).

Anal. Calc. for $C_8H_{12}O_4$: C,55.80; H,7.03: Found: C,55.50; H,7.07%.

^{1}H NMR: (δ, CCl_4); a) keto form; 2.15 (s,-CH_3); 2.75 (d, J7Hz,-$C\underline{H}_2CO$-); 3.56 (s, -$OC\underline{H}_3$); 4.06 (t, -H); b) enol form (ca.30%); 2.06 (s, -CH_3); 3.20 (s, -$C\underline{H}_2$-CO-).

Methyl-4-acetyl-5-oxohexanoate (95)



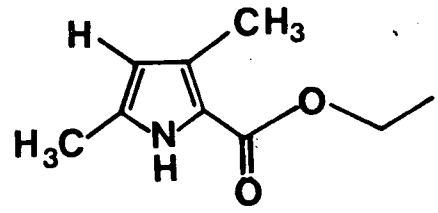
Methyl acrylate (200 mL, 2.22 mole) was added dropwise over 2 hours to a solution of 2,4-pentanedione (250 mL, 2.43 mole) and anhydrous potassium carbonate (10g, 70 mmole) in 2-butanone (175 mL). The mixture maintained reflux during the addition, when complete the reaction was heated for 20 min. and then filtered to remove the catalyst. The solvent was removed under reduced pressure and the fraction between 144-150°C/12 Torr collected (294g, 72%). (lit[59] 148° 14/Torr).

Anal: Calc. for $C_9H_{14}O_4$: C, 58.05; H, 7.58: Found: C, 58.48; H, 7.80%

^{1}H NMR (400 MHz): (δ, $CDCl_3$); a) keto; 2.36 (m, J8Hz, 2H, $-C\underline{H}_2CH_2CO$); 2.44 (s, 6H, $C\underline{H}_3CO$); 2.55 (t, J8Hz, 2H, $-CH_2C\underline{H}_2CO$); 3.90 (s, 3H, $-OC\underline{H}_3$); 3.98 (t, J8Hz, 1H, $-C\underline{H}-$). b) enol (ca. 22%); 1.39 (s, 6H, $C\underline{H}_3CO$); 1.64 (t, J10Hz, 2H, $-C\underline{H}_2CH_2CO$); 1.83 (t, J10Hz, 2H, $-CH_2C\underline{H}_2CO$); 1.91 (s, 3H, $OC\underline{H}_3$).

3.3 Synthesis of Monopyrroles

2-Ethyloxycarbonyl-3,5-dimethylpyrrole (88)

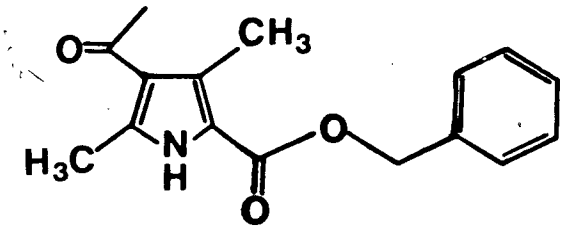


A solution of sodium nitrite (2070g, 30 mole) in water (3000 mL) was slowly added to a stirred solution of diethyl malonate (1600g, 10 mole) in glacial acetic acid (1800 mL). The oxime separated out as a yellow oil which was added slowly to a solution of 2,4-pentanedione (1000g, 10 mole) in glacial acetic acid (2,400 mL), zinc (1308g, 20 mole) was added in portions always maintaining an excess of zinc. The solution was maintained between 50-60°C during the addition of oxime then heated on a steambath for 1 hour. The mixture was poured into water when cool and filtered, extracted with methylene chloride and the water separated. The solvent was replaced by methanol under reduced pressure, recrystallisation gave product (661g, 39.5%) as small pale tan crystals MP. 120-121°C (lit[60] 116-118°).

Anal: Calc. for $C_9H_{13}NO_2$: C, 64.65; H, 7.84; N, 8.38: Found: C, 64.35; H, 7.90; N, 8.28%.

^{1}H NMR: (δ, $CDCl_3$); 1.36 (t, J7.5Hz, 3H, $-OCH_2C\underline{H}_3$); 2.26 (s, 3H, $-C\underline{H}_3$); 2.32 (s, 3H, $-C\underline{H}_3$); 4.38 (q, J7.5Hz, 2H, $-OC\underline{H}_2CH_3$); 5.82 (d, J3Hz, 1H, pyr-$\underline{H}$); 9.57 (bs, 1H, N$\underline{H}$).

2-Benzyloxycarbonyl -4-acetyl-3,5-dimethylpyrrole (91)

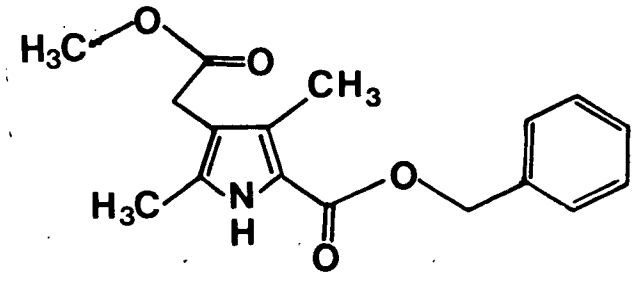


A solution of sodium nitrite (414g, 6 mole) in water (800 mL) was slowly added to a stirred solution of benzyl acetoacetate (90) (1152g, 6 mole) in glacial acetic acid (1250 mL) the temperature being maintained below 10°C. This was then added to a solution of 2,4-pentanedione (600g, 6 mole) in glacial acetic acid (2,200 mL), a mixture of zinc (780g, 12 mole) and anhydrous sodium acetate (985g, 12 mole) was added in portions throughout the addition maintaining an excess of zinc at all times. When the addition was complete, the mixture was heated on a steam bath for one hour and then poured into water. The solid was filtered off, the product extracted with methylene chloride and the water removed. The solvent was replaced under reduced pressure by methanol, crystallisation from methanol gave product (738g, 45.4%) as white needles MP.133-134°C

Anal: Calc. for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16; Found: C, 70.76; H, 6.44; N, 5.19%.

^{1}H NMR: (δ, $CDCl_3$); 2.44 (s, 3H, $-C\underline{H}_3$); 2.51 (s, 3H, $-C\underline{H}_3$); 2.61 (s, 3H, $-COC\underline{H}_3$); 5.35 (s, 2H, $-C\underline{H}_2C_6H_5$); 7.40 (bs, 5H, $-C_6\underline{H}_5$); 9.65 (bs, 1H, N$\underline{H}$).

2-Benzyloxycarbonyl-4-methoxycarbonylmethyl-3,5-dimethylpyrrole (93)

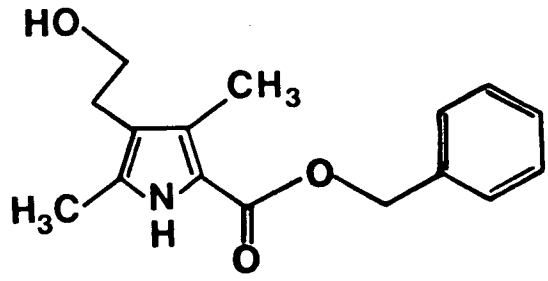


A solution of sodium nitrite (100g, 1.45 mole) in water (350 mL) was slowly added to a stirred solution of benzyl acetoacetate (90) (260g, 1.35 mole) in glacial acetic acid (450 mL) the temperature being maintained below 10°. After being left in the refrigerator overnight the solution was slowly added to a solution of methyl-3-acetyl-4-oxopentanoate (92) (220g, 1.28 mole) in glacial acetic acid (260 mL), a mixture of zinc dust (260g, 4 mole) and anhydrous sodium acetate (260g, 3.17 mole) was added in portions throughout the addition maintaining an excess of zinc at all times. When the addition was complete the reaction mixture was further heated on a steam bath for 1 hour and then poured into water. The solid was filtered off, and the product extracted with methylene chloride and the water removed. The solvent was then replaced by methanol under reduced pressure, crystallisation from methanol gave fine needles of the product (127g, 33%) MP. 104-105.5°C (lit.[58] 93-94°C).

Anal: Calc. for $C_{17}H_{19}NO_4$: C, 67.76; H, 6.36; N, 4.65; Found: C, 68.01; H, 6.36; N, 4.73%.

<u>^{1}H NMR</u>: (δ, $CDCl_3$); 2.21 (s, 3H, $-C\underline{H}_3$); 2.31 (s, 3H, $-C\underline{H}_3$); 3.40 (s, 2H, $-C\underline{H}_2CO-$); 3.67 (s, 3H, $-OC\underline{H}_3$); 5.32 (s, 2H, $-C\underline{H}_2C_6H_5$); 7.39 (m, 5H, $-C_6\underline{H}_5$); 9.18 (bs, 1H, $N\underline{H}$).

2-Benzyloxycarbonyl-4-(2-hydroxyethyl-3,5-dimethylpyrrole (94)

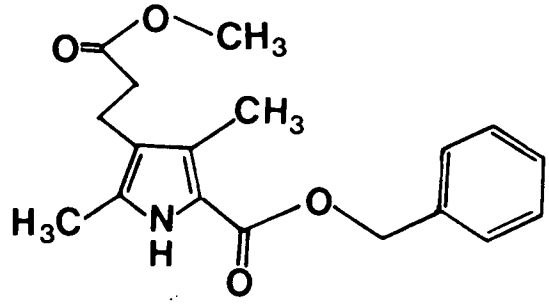


Borontrifluoride etherate (38 mL, 0.30 mole) was added dropwise to an ice cold stirred mixture of 2-benzyloxycarbonyl-4-methoxycarbonylmethyl-3,5-dimethylpyrrole (93) (20g, 66 mmole), sodium borohydride (8g, 0.22 mole) in THF (150 mL) under nitrogen. When the addition of boron trifluoride was complete the reaction was checked for complete conversion by tlc and then quenched by dropwise addition of glacial acetic acid (50 mL), followed by water (50 mL). The product was extracted into methylene chloride (100 mL) and the solvent replaced under reduced pressure with methanol, recrystallised from methanol/water to give the product (16.9g, 93.2%) as white needles. MP. 117-118°C (lit[58] 120-121.5^{o}C)

Anal: Calc. for $C_{16}H_{19}NO_3$: C, 70.13; H, 7.01; N, 5.13: Found: C, 70.41; H, 7.22; N, 5.21%.

^{1}H NMR: (δ, $CDCl_3$); 1.58 (s, 1H, -O$\underline{H}$); 2.21 (s, 3H, -C$\underline{H}_3$); 2.30 (s, 3H, -C$\underline{H}_3$); 2.65 (t, J7Hz, 2H, -C$\underline{H}_2$CH$_2$OH); 3.66 (t, J7Hz, 2H, -CH$_2$C$\underline{H}_2$OH); 5.30 (s, 2H, -C$\underline{H}_2$C$_6$H$_5$); 7.38 (bs, 5H, -C$_6\underline{H}_5$); 8.84 (bs, 1H, N$\underline{H}$).

2-Benzyloxycarbonyl-4-(2-methoxycarbonylethyl)-3,5-dimethylpyrrole (96)

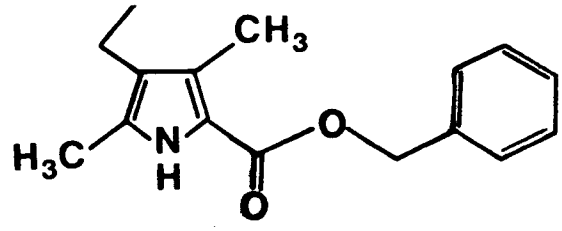


To a stirred, ice cold solution of benzylacetoacetate (90) (280g, 1.5 mole) in glacial acetic acid (300 mL), was added a solution of sodium nitrite (145g, 2.1 mole) in water (200 mL) over a 30 min. period. The mixture was stirred for a further 10 min. and the oxime separated from the aqueous layer. This was added dropwise over a period of 2 hours to a cooled suspension of methyl-4-acetyl-5-oxohexanoate (95) (275g, 1.49 mole), zinc (360g, 5.66 mole) in glacial acetic acid (1500 mL). The solution was refluxed for 30 min. and then poured into water (4000 mL). The resulting solid was filtered, redissolved in dichloromethane (535 mL) and crystallised from methanol by removal of the dichloromethane under reduced pressure to yield product (190.5g, 40.3%) MP. 98.5-99°C (lit[59] 99-100°C).

<u>Anal</u>: Calc. for $C_{18}H_{21}NO_4$: C, 68.55; H, 6.71; N, 4.44: Found: C, 68.69; H, 6.56; N, 4.44%.

<u>^{1}H NMR</u>: (δ, $CDCl_3$) 2.28 (s, 3H, $C\underline{H}_3$); 2.38 (s, 3H, $C\underline{H}_3$); 2.52 (m, 2H, $C\underline{H}_2CH_2CO_2CH_3$); 2.82 (m, 2H, $CH_2C\underline{H}_2CO_2CH_3$); 3.75 (s, 3H, $CO_2C\underline{H}_3$); 5.41 (s, 2H, $C\underline{H}_2C_6H_5$); 7.49 (bs, 5H, $CH_2C_6\underline{H}_5$); 9.12 (bs, 1H, $N\underline{H}$).

2-Benzyloxycarbonyl-4-ethyl-3,5-dimethylpyrrole (97)

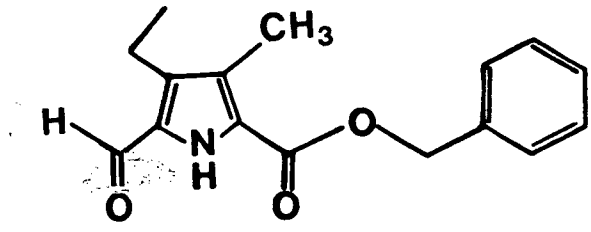


Boron trifluoride etherate (336 mL, 2.67 mole) was added dropwise to a stirred, ice cooled mixture of 2-benzyloxycarbonyl-4-acetyl-3,5-dimethylpyrrole (91) (308g, 1.14 mole), sodium borohydride (76g, 2 mole) in THF (1000 mL) and ethyl acetate (350 mL). When addition was complete the reaction mixture was checked for complete reaction by tlc and quenched by dropwise addition of glacial acetic acid (500 mL). The product was extracted with methylene chloride and the solvent replaced by ethanol under reduced pressure, crystallisation from 3:1 ethanol/water mixture gave product (234.3g, 80.2%) as white needles MP. 102-103°C (lit.[61] 104-105°C).

Anal: Calc. for $C_{16}H_{19}NO_2$: C, 74.68: H, 7.44; N, 5.44: Found: C, 74.50; H, 7.51; N, 5.43%.

^{1}H NMR: (δ, $CDCl_3$); 1.15 (t, J8Hz, 3H, $-CH_2C\underline{H}_3$); 2.24 (s, 3H, $-C\underline{H}_3$); 2.42 (s, 3H, $-C\underline{H}_3$); 2.50 (q, J8Hz, 2H, $-C\underline{H}_2CH_3$); 5.44 (s, 2H, $-C\underline{H}_2C_6H_5$); 7.52 (m, 5H, $-C_6\underline{H}_5$); 9.36 (bs, 1H, N$\underline{H}$).

2-Benzyloxycarbonyl-4-ethyl-5-formyl-3-methylpyrrole (99)

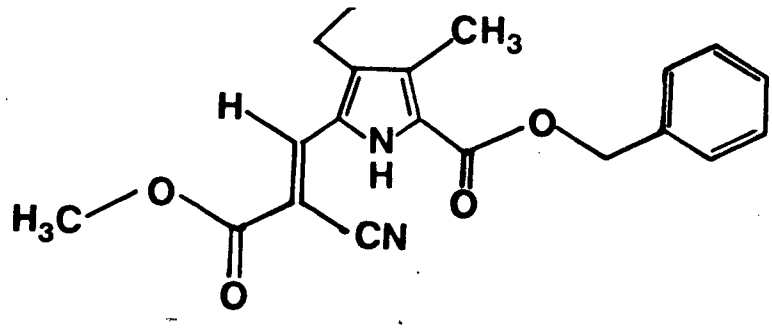


Sulfuryl chloride (66.2 mL, 0.81 mole) in methylene chloride (1000 mL) was added dropwise to an ice cold, stirred solution of 2-benzyloxycarbonyl-4-ethyl-3,5-dimethylpyrrole (97) (102.8g, 0.4 mole) in methylene chloride (200 mL) under nitrogen. When the addition was complete the mixture was heated on a steam bath for 1 hour. Water (500 mL) was added and the solution left to stir overnight. The organic phase was separated and the solvent removed under reduced pressure. The oil obtained was extracted with hot water/ethanol 1:1 and on cooling product (92g, 84.9%) crystallised as a white solid 86-87°C (lit.[62] 86-87°C).

Anal: Calc. for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16; Found: C, 70.81; H, 6.25; N, 5.16%.

^{1}H NMR: (δ, $CDCl_3$); 1.20 (t, J8Hz, 3H, $-CH_2C\underline{H}_3$); 2.32 (s, 3H, $-C\underline{H}_3$); 2.76 (q, J8Hz, 2H, $-C\underline{H}_2CH_3$); 5.37 (s, 2H $-C\underline{H}_2C_6H_5$); 7.42 (s, 5H, $-C_6\underline{H}_5$); 9.60 (bs, 1H, N$\underline{H}$); 9.79 (s, 1H, -C$\underline{H}$O).

2-Benzyloxycarbonyl-5-(2-cyano-2-methoxycarbonylvinyl)-4-ethyl-3-methylpyrrole (100)

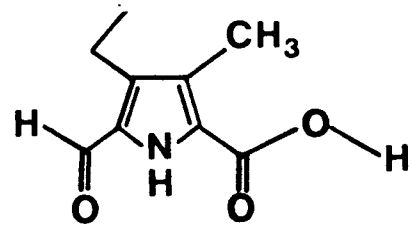


2-Benzyloxycarbonyl-4-ethyl-5-formyl-3-methylpyrrole (99) (35.8g, 0.13 mole) was dissolved in boiling methanol (50 mL) to this solution was added methyl cyanoacetate (25g, 0.17 mole) and methylamine (1 mL) the solution was allowed to boil for 5 minutes and then cooled. The product (45.7g, 98%) crystallised out as yellow prisms MP. 122-123°C

Anal: Calc. for $C_{20}H_{20}N_2O_4$: C, 68.17; H, 5.72; N, 7.94: Found: C, 68.13; H, 5.64; N, 7.94%.

^{1}H NMR: (δ, $CDCl_3$); 1.14 (t, J8Hz, 3H, $-CH_2C\underline{H}_3$); 2.33 (s, 3H, $-C\underline{H}_3$); 2.65 (q, J8Hz, 2H, $-C\underline{H}_2CH_3$); 3.92 (s, 3H, $OC\underline{H}_3$); 5.41 (s, 2H, $-C\underline{H}_2C_6H_5$); 7.45 (m, 5H, $-C_6\underline{H}_5$); 8.06 (s, 1H, $-\underline{H}$); 10.28 (bs, 1H, $N\underline{H}$).

2-Carboxyl-4-ethyl-5-formyl-3-methylpyrrole (101)

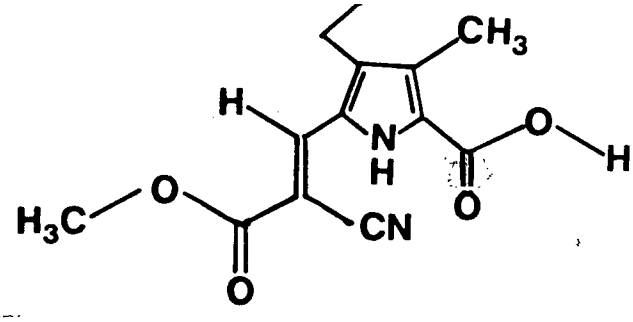


2-Benzyloxycarbonyl-4-ethyl-5-formyl-3-methylpyrrole (99) (5.42g, 20 mmole), 30% palladium on charcoal (0.35g) in THF (150 mL) and triethylamine (3 mL) was hydrogenated until hydrogen uptake ceased (500 mL). The solution was filtered into glacial acetic acid (10 mL) and the volume of solvent reduced; methanol (50 mL) and water (50 mL) was added and the solvent removed under reduced pressure, the product (3g, 82.9%) crystallised as metallic copper colored crystals MP. 190°C(d)

Anal: Calc. for $C_9H_{11}NO_3$: C, 59.66; H, 6.12; N, 7.73; Found: C, 59.57; H, 6.16; N, 7.56%.

^{1}H NMR: (δ, $CDCl_3$/TFA); 1.26 (t, J7.5Hz, 3H, $-CH_2C\underline{H}_3$); 2.37 (s, 3H, $-C\underline{H}_3$); 2.84 (q, J7.5Hz, 2H, $-C\underline{H}_2CH_3$); 9.78 (s, 1H, C$\underline{H}$O); 10.09 (bs, 1H, N$\underline{H}$).

5-(2-Cyano-2-methoxycarbonylvinyl)-4-ethyl-3-methylpyrrole -2-carboxylic acid (102)

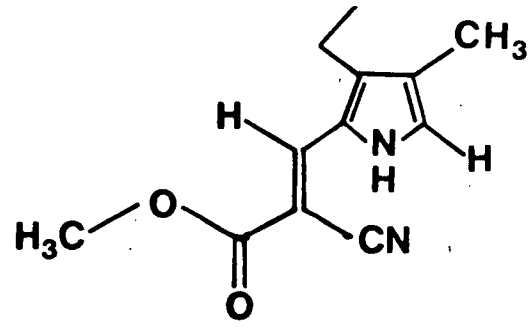


A suspension of 2-benzyloxycarbonyl-5-(2-cyano-2-methoxycarbonylvinyl)-4-ethyl-3-methylpyrrole (100) (23.5g, 67 mmole), 10% palladium on charcoal (2g) in THF (250 mL) and triethylamine (1 drop) was hydrogenated until uptake of hydrogen ceased (1700 mL). The solution was filtered and the solvent replaced by methanol under reduced pressure, the product (17.25g, 98.6%) was obtained as a pale yellow powder MP. 200°C(d).

Anal: Calc. for $C_{13}H_{14}N_2O_4$: C, 59.53; H, 5.38; N, 10.68: Found: C, 59.55; H, 5.52; N, 10.47%.

^{1}H NMR: (δ, $CDCl_3$/TFA); 1.17 (t, J7.5Hz, 3H, $-CH_2C\underline{H}_3$); 2.36 (s, 3H, $-C\underline{H}_3$); 2.70 (q, J7.5Hz, 2H, $-C\underline{H}_2CH_3$); 3.01 (s, 3H, $-OC\underline{H}_3$); 8.19 (s, 1H, -H); 10.16 (bs, 1H, N$\underline{H}$).

2-(2-Cyano-2-methoxycarbonylvinyl)-3-ethyl-4-methylpyrrole (103)

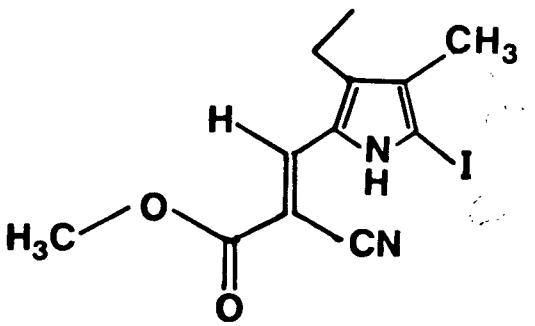


A stirred suspension of 5-(2-cyano-2-methoxycarbonyl-vinyl)-4-ethyl-2-iodo-3-methylpyrrole (104) (10g, 30 mmole), platinum oxide (0.2g) in THF (150 mL) was hydrogenated in the dark over 3 days until uptake ceased (730 mL). The suspension was filtered and the solvent replaced under reduced pressure with methanol. The product (6.3g, 99%) was obtained as pale yellow microcrystals MP. 141-142°C

Anal: Calc. for $C_{13}H_{14}N_2O_2$: C, 66.03; H, 6.47; N, 12.84; Found: C, 65.98; H, 6.45; N, 12.74%.

^{1}H NMR: (δ, $CDCl_3$); 1.10 (t, J8Hz, 3H, $-CH_2C\underline{H}_3$); 2.02 (s, 3H, $-C\underline{H}_3$); 2.58 (q, J8Hz, 2H, $-C\underline{H}_2CH_3$); 3.81 (s, 3H, $-OC\underline{H}_3$); 6.98 (d, J4Hz, 1H, pyr-$\underline{H}$); 7.95 (s, 1H, -C$\underline{H}$=C-); 9.70 (bs, 1H, N$\underline{H}$).

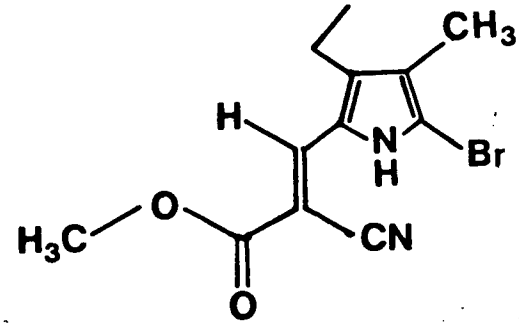
2-(2-Cyano-2-methyoxycarbonylvinyl)-3-ethyl-5-iodo-4-methylpyrrole. (104)



Iodine monochloride (9g, 55 mmole) in glacial acetic acid (50 mL) was added dropwise to a stirred suspension of 5-(2-cyano-2-methoxycarbonylvinyl)-4-ethyl-3-methylpyrrole -2-carboxylic acid (102) (13g, 50 mmole), anhydrous sodium acetate (15g, 0.18 mole), acetic anhydride (10 mL) and glacial acetic acid (200 mL) which had been gently heated to 80°C. When addition was complete the solution was cooled and water (300 mL) added, excess iodine removed with hypophosphorus acid, the solid filtered, washed with water and dried. Recrystallisation from methanol/water gave product (14g, 82%) as yellow needles MP. 163-164°C

Anal: Calc. for $C_{12}H_{13}N_2O_2I$: C, 41.88; H, 3.81; N, 8.14; I, 36.66: Found: C, 41.92; H, 3.75; N, 8.00; I, 36.66%.
^{1}H NMR: (δ, $CDCl_3$); 1.23 (t, J7.5Hz, 3H, $-CH_2C\underline{H}_3$); 2.02 (s, 3H, $-C\underline{H}_3$); 2.64 (q, J7.5Hz, 2H, $-C\underline{H}_2CH_3$); 3.88 (s, 3H, $-OC\underline{H}_3$); 7.86 (s, 1H, $-\underline{H}$), 9.65 (bs, 1H, N$\underline{H}$).

2-Bromo-5-(2-cyano-2-methoxycarbonylvinyl)-4-ethyl-3-methyl-pyrrole (105)

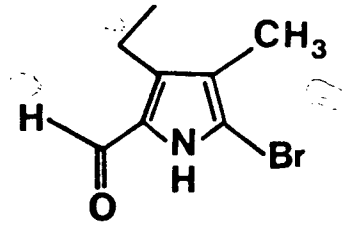


Bromine (2.3g, 14.4 mmole) in methylene chloride (30 mL) was added dropwise to a stirred solution of 2-(2-cyano-2-methoxycarbonylvinyl)-3-ethyl-4 methylpyrrol-2-carboxylic acid (102) (3g, 11.5 mmole), anhydrous potassium carbonate (2g, 20 mmole) in THF (60 mL). The reaction was carried out in the absence of light and followed by tlc; at the first signs of the orange bipyrrole, addition of bromine was ceased and the solution poured into water (100 mL). The product was extracted with methylene chloride and the solvent replaced by methanol under reduced pressure. Crystallisation from methanol/water gave bright yellow crystals of product (2.7g, 80%) MP. 140-141°C

Anal: Calc. for $C_{12}H_{13}N_2O_2Br$: C, 48.50; H, 4.41; N, 9.43; Br, 26.89: Found: C, 48.52; H, 4.31; N, 9.32; Br, 26.66%.

^{1}H NMR: (δ, $CDCl_3$); 1.15 (t, J8Hz, 3H, $-CH_2C\underline{H}_3$); 2.04 (s, 3H, $-C\underline{H}_3$); 2.66 (q, J8Hz, 2H, $-C\underline{H}_2CH_3$); 3.91 (s, 3H, $-OC\underline{H}_3$); 7.94 (s, 1H, $-\underline{H}$); 9.65 (bs, 1H, N$\underline{H}$).

2-Bromo-4-ethyl-5-formyl-3-methylpyrrole (107)



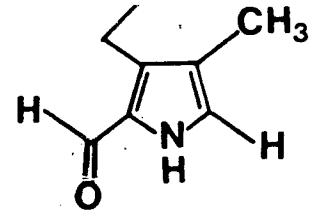
A mixture of 2-bromo-5-(2-cyano-2-methoxycarbonylvinyl)-4-ethyl-3-methylpyrrole (105) (4g, 13.5 mmole), water (40 mL) and potassium hydroxide (10g, 0.1 mmole) was refluxed under nitrogen for 1½ hours and the reaction observed by visible spectroscopy. The solution was allowed to cool and the pale brown solid filtered. Crystallisation from methanol/water gave the product (2.55g, 88%) as pale tan needles.

MP. 104.5-105.5°C

Anal: Calc. for $C_8H_{10}NOBr$: C, 44.44; H, 4.63; N, 6.48; Br, 37.04: Found: C, 44.37; H, 4.53; N, 6.64; Br, 37.00%.

^{1}H NMR: (δ, $CDCl_3$); 1.17 (t, J7.5Hz, 3H, $-CH_2C\underline{H}_3$); 1.94 (s, 3H, $-C\underline{H}_3$); 2.70 (q, J7.5Hz, 2H, $-C\underline{H}_2CH_3$); 9.46 (s, 1H, $-C\underline{H}O$); 10.38 (bs, 1H, $N\underline{H}$).

3-Ethyl-2-formyl-4-methylpyrrole (108)

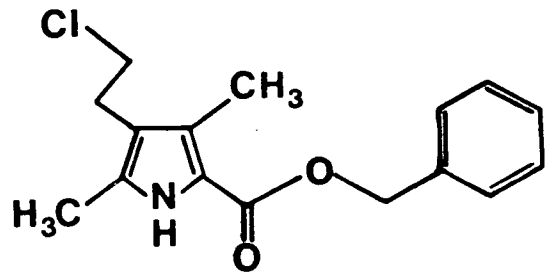


A mixture of 2-(2-cyano-2-methoxycarbonylvinyl)-3-ethyl-4-methylpyrrole (103) (4.4g, 20 mmole), water (100 mL) and potassium hydroxide (8g, 0.14 mole) was refluxed under nitrogen for 3 hours and the reaction observed by visible spectroscopy. The solution was then left to cool and the product filtered as brown solidified oil (2.3g, 83%), reactions were carried out with the compound in this crude form. Recrystallisation from water/methanol gave an analytical sample. MP. 74-75°C

Anal: Calc. for $C_8H_{11}NO$: C, 70.04; H, 8.08; N, 10.21; Found: C, 70.13; H, 8.15; N, 10.17%.

^{1}H NMR: (δ, $CDCl_3$/TFA); 1.22 (t, J8Hz, 3H, $-CH_2C\underline{H}_3$); 2.06 (s, 3H, $-C\underline{H}_3$); 2.75 (q, J8Hz, 2H, $-C\underline{H}_2CH_3$); 6.87 (d, J5Hz, 1H, pyr-$\underline{H}$); 9.62 (s, 1H, $-C\underline{H}O$).

2-Benzyloxycarbonyl-4-(2-chloroethyl)-3,5-dimethylpyrrole (109)

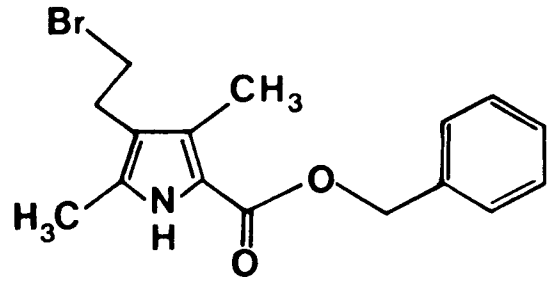


Thionyl chloride (8 mL, 0.11 mole) was added dropwise to a stirred, refluxing mixture of 2-benzyloxycarbonyl-4-(2-hydroxyethyl)-3,5-dimethylpyrrole (94) (10g, 36.6 mmole), anhydrous potassium carbonate (20g, 0.14 mole) in methylene chloride (500 mL). The mixture was stirred and refluxed for 2 hours then filtered when cool. The solvent was replaced by methanol under reduced pressure, crystallisation from methanol gave product (9.8g, 91.8%), as fluffy white needles MP. 118-118.5°C (lit.[63] 121°C)

Anal: Calc. for $C_{16}H_{18}NClO_2$: C, 65.86; H, 6.22; N, 4.80; Cl, 12.15: Found: C, 66.11; H, 6.00; N, 4.72; Cl, 11.95%.

^{1}H NMR: (δ, $CDCl_3$); 2.26 (s, 3H, $-C\underline{H}_3$); 2.34 (s, 3H, $-C\underline{H}_3$); 2.88 (t, J8Hz, 2H, $-C\underline{H}_2CH_2Cl$); 3.56 (t, J8Hz, 2H, $-CH_2C\underline{H}_2Cl$); 5.35 (s, 2H, $-C\underline{H}_2C_6H_5$); 7.44 (bs, 5H, $-C_6\underline{H}_5$); 8.76 (bs, 1H, N$\underline{H}$).

2-Benzyloxycarbonyl-4-(2-bromoethyl)-3,5-dimethylpyrrole (110)

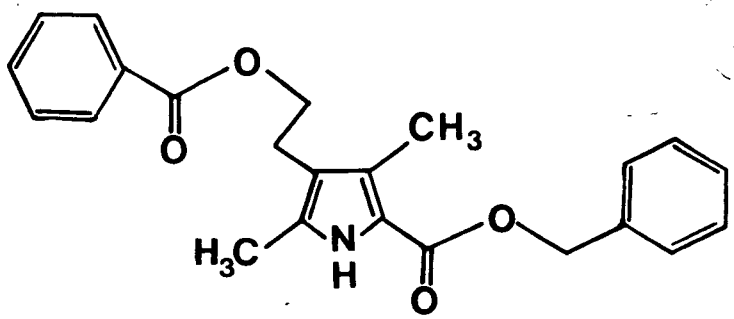


Thionyl bromide (3g, 15 mmole) was added dropwise to a stirred, refluxing mixture of 2-benzyloxycarbonyl-4-(2-hydroxyethyl)-3,5-dimethylpyrrole (94) (3.3g, 12 mmole), anhydrous potassium carbonate (10g, 70 mmole) in dichloromethane (50 mL). The mixture was stirred and refluxed for 2 hours then filtered when cool. The solvent was replaced by methanol under reduced pressure; crystallisation from methanol gave product (2.58g, 65.5%), as off white needles MP. 124-125°C.

Anal: Calc. for $C_{16}H_{18}NBrO_2$: C, 57.15; H, 5.40; N, 4.09; Br, 23.77. Found: C, 56.92; H, 5.38; N, 4.09; Br, 23.84%.

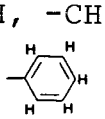
^{1}H NMR:(δ, $CDCl_3$) 2.22 (s, 3H, $C\underline{H}_3$); 2.30 (s, 3H, $C\underline{H}_3$); 2.94 (t, J7Hz, 2H, $C\underline{H}_2CH_2Br$); 3.77 (t, J7Hz, 2H, $CH_2C\underline{H}_2Br$); 5.32 (s, 2H, $C\underline{H}_2C_6H_5$); 7.39 (s, 5H, $CH_2C_6\underline{H}_5$); 9.04 (bs, 1H, N$\underline{H}$).

2-Benzyloxycarbonyl-4-(2-benzoxyethyl)-3,5-dimethylpyrrole (111)

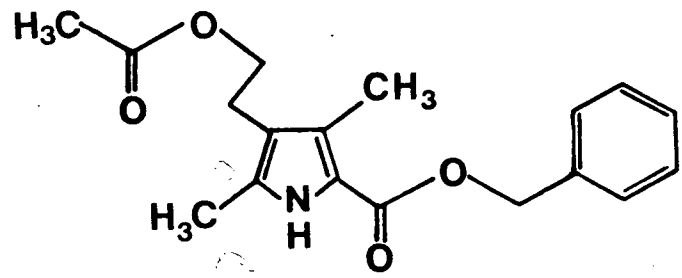


Benzoyl chloride (20 mL, 0.17 mole) was added to a solution of 2-benzyloxycarbonyl-4-(2-hydroxyethyl)-3,5-dimethylpyrrole (94) (25.5g, 93 mmole), pyridine (30 mL) in THF (200 mL) the mixture was stirred for 40 minutes and then poured into water (200 mL). The aqueous phase was extracted with ether, the organic phase was evaporated to dryness and the solid, suspended in sodium bicarbonate solution overnight. The suspension was then extracted with methylene chloride; the organic phase was separated and the solvent replaced by methanol under reduced pressure, crystallisation from methanol gave white needles (31.5g, 89.7%) MP. 109-110°C

Anal: Calc. for $C_{23}H_{23}NO_4$: C, 73.19; H, 6.14; N, 3.71; Found: C, 73.11; H, 6.15; N, 3.81%.

^{1}H NMR: (δ, $CDCl_3$); 2.19 (s, 3H, $-C\underline{H}_3$); 2.30 (s, 3H, $-C\underline{H}_3$); 2.81 (t, J7Hz, 2H, $-C\underline{H}_2CH_2O-$); 4.28 (t, J7Hz, 2H, $-CH_2C\underline{H}_2O-$); 5.25 (s, 2H, $-C\underline{H}_2C_6H_5$); 7.34 (m, 5H, $-CH_2C_6\underline{H}_5$); 7.45 (m, 3H, -CO ); 8.01 (dd, J6Hz, 2H, ); 8.85 (bs, 1H, N$\underline{H}$).

2-Benzyloxycarbonyl-4-(2-acetoxyethyl)-3,5-dimethylpyrrole (112)

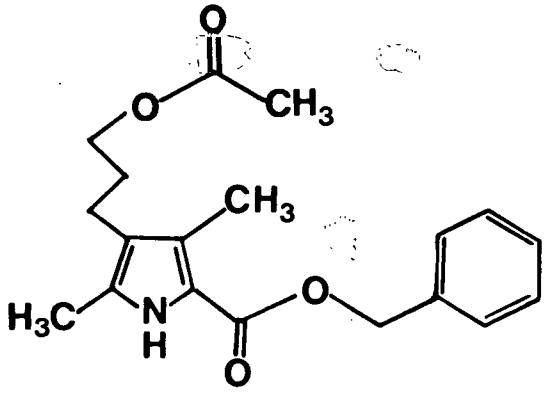


Acetic anhydride (20 mL, 0.21 mole) was added to a solution of 2-benzyloxycarbonyl-4-(2-hydroxyethyl)-3,5,-dimethylpyrrole (94) (10g, 36.5 mmole) in pyridine (30 mL, 0.37 mole) and the mixture stirred for 2 hours at room temperature. The solution was then poured slowly into ice water (2000 mL) and the precipitated solid filtered off. Crystallisation from methanol gave the product (10.6g, 91.9%) as white needles MP. 73-74°C (lit.[58] 73.5-74.5°C)

Anal: Calc. for $C_{23}H_{23}NO_4$: C, 68.55; H, 6.71; N, 4.44: Found: C, 68.35; H, 6.75; N, 4.50%.

^{1}H NMR: (δ, $CDCl_3$); 2.04 (s, 3H, $-C\underline{H}_3$); 2.21 (s, 3H, $-C\underline{H}_3$); 2.32 (s, 3H, $-COC\underline{H}_3$); 2.71 (t, J7Hz, 2H, $-C\underline{H}_2-CH_2O-$); 4.08 (t, J7Hz, 2H, $-CH_2C\underline{H}_2O-$); 5.32 (s, 2H, $-C\underline{H}_2C_6H_5$); 7.39 (m, 5H, $-C_6\underline{H}_5$); 9.18 (bs, 1H, N$\underline{H}$).

2-Benzyloxycarbonyl-4-(3 acetoxypropyl)-3,5-dimethylpyrrole (113)



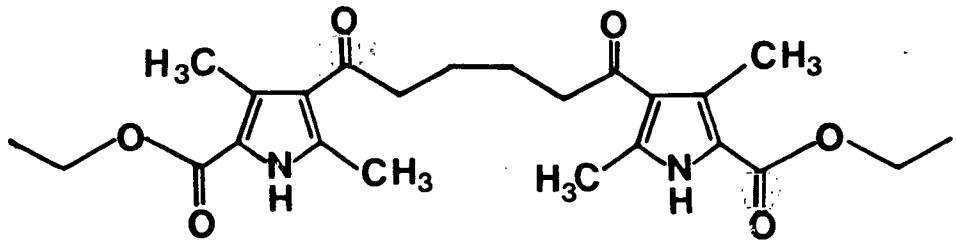
Boron trifluoride etherate (100 mL, 0.79 mole) was added dropwise to a stirred ice cold suspension of 2-benzyloxycarbonyl-4-methoxycarbonylethyl)-3,5-dimethylpyrrole (96) (63g, 0.2 mole), sodium borohydride (20g, 0.53 mole) in THF (300 mL) under nitrogen. The reaction was followed by tlc and when complete was quenched by the addition of glacial acetic acid (100 mL) followed by water (200 mL); the mixture was extracted into methylene chloride and evaporated to dryness. The solid was dissolved in pyridine (60 mL), and treated with acetic anhydride (90 mL); the solution was left to stir overnight, poured into ice water (2L) and the precipitate filtered. Crystallisation from methanol/water gave product (63.3g, 96%) as fine white needles MP.76-77°C

Anal: Calc. for $C_{19}H_{23}NO_4$: C, 69.28; H, 7.04; N, 4.25: Found: C, 68.99; H, 7.00; N, 4.36%.

^{1}H NMR: (δ, $CDCl_3$); 1.75 (m, J7Hz, 2H, $-CH_2\underline{CH_2}CH_2O-$); 2.03 (s, 3H, $-C\underline{H_3}$); 2.16 (s, 3H, $-C\underline{H_3}$); 2.29 (s, 3H, $-OC\underline{H_3}$); 2.46 (t, J7Hz, 2H, $-C\underline{H_2}CH_2CH_2O-$); 4.05 (t, J7Hz, 2H, $-CH_2CH_2\underline{CH_2}O-$); 5.32 (s, 2H, $-C\underline{H_2}C_6H_5$); 7.39 (m, 5H, $-C_6\underline{H_5}$); 9.31 (bs, 1H, $N\underline{H}$).

3.4 Synthesis of Chain Linked Pyrroles

1,6-Bis (5-ethyloxycarbonyl-4,2-dimethylpyrrol-3-yl)-1,6-hexanedione (120)

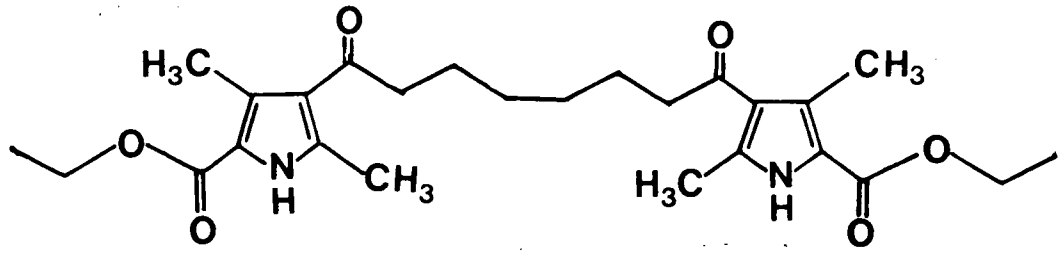


A mixture of adipic acid (21.9g, 0.15 mole) and thionyl chloride (35 mL, 0.49 mole) was heated on a steam bath until dissolved. Carbon tetrachloride (25 mL) was added and the solvent removed under reduced pressure to remove the excess thionyl chloride. The resulting liquid was added to a solution of 2-ethoxycarbonyl-3,5-dimethylpyrrole (50.1g, 0.30 mole) in methylene chloride (250 mL) and nitromethane (250 mL). The mixture was stirred under nitrogen and cooled in ice, stannic chloride (75 mL, 0.64 mole) was added dropwise over 1 hour and the solution stirred for a further hour. The solution was poured into dilute hydrochloric acid (1000 mL), the organic layer separated and washed with water. The solvent was replaced with methanol under reduced pressure; crystallisation from methanol gave product (56g, 84.1%) as a white powder. An analytical sample was recrystallised from $CDCl_3$/TFA/THF washed with dichloromethane MP. 254°C(d).

Anal: Calc. for $C_{24}H_{32}N_2O_6$: C, 64.84; H, 7.26; N, 6.30: Found: C, 64.19; H, 7.26; N, 6.08%.

^{1}H NMR: (δ, $CDCl_3$/TFA); 1.45 (t, J7Hz, 6H, $-CH_2C\underline{H}_3$); 1.99 (bm, 4H, $-COCH_2C\underline{H}_2$); 2.65 (s, 12H, $-CH_3$); 3.07 (bt, 4H, $COC\underline{H}_2$); 4.49 (q, J7Hz, 4H, $-C\underline{H}_2CH_3$); 10.43 (bs, 2H, N$\underline{H}$).

1,8-Bis(5-ethyloxycarbonyl-2,4-dimethylpyrrol-3-yl)-1,8-octanedione. (121)

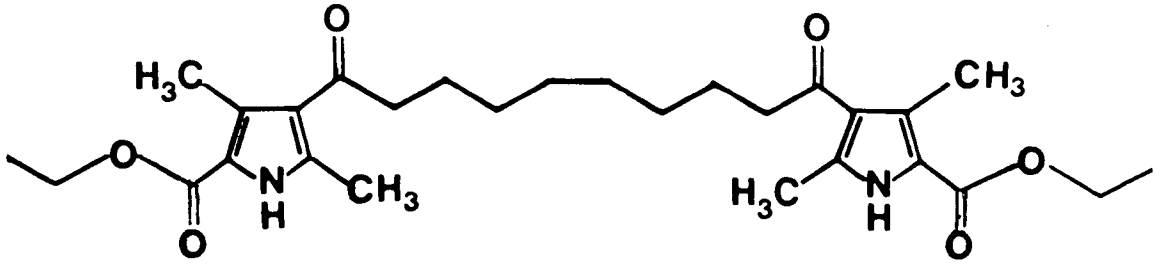


A mixture of octanedioc acid (26.1g, 0.15 mole) and thionyl chloride (35 mL, 0.49 mole) was heated on a steambath until dissolved. Carbon tetrachloride (25 mL) was added and the solvent removed under reduced pressure to remove excess thionyl chloride. The resulting liquid was added to a solution of 2-ethyloxycarbonyl-3,5-dimethylpyrrol (50.1g, 0.30 mole) in methylene chloride (250 mL) and nitromethane (250 mL). The mixture was stirred under nitrogen and cooled in ice, stannic chloride (75 mL) added dropwise over 1 hour and the solution stirred for a further hour. The solution was poured into dilute hydrochloric acid (1000 mL), the organic layer separated and washed with water. The solvent was replaced with methanol under reduced pressure; crystallisation from methanol gave product (59.9g, 84.6%) as a white powder MP 178°C(d)

Anal: Calc. for $C_{26}H_{36}N_2O_6$: C, 66.08; H, 7.68; N, 5.93: Found: C, 66.35; H, 7.47; N, 5.64%.

^{1}H NMR: (δ, $CDCl_3$/TFA); 1.42 (t, J7Hz, 6H, $-OCH_2C\underline{H}_3$); 1.79 (bs, 8H, $-COCH_2(C\underline{H}_2)_4CH_2CO-$); 1.56 (s, 6H, $-C\underline{H}_3$); 1.58 (s, 6H, $-C\underline{H}_3$); 2.85 (t, J8Hz, 4H, $-COC\underline{H}_2(CH_2)_4C\underline{H}_2CO-$); 4.44 (q, J7Hz, 4H, $-OC\underline{H}_2CH_3$).

1,10-Bis(5-ethyloxycarbonyl-4,2-dimethyl-3-yl)-1,10-decanedione (122).



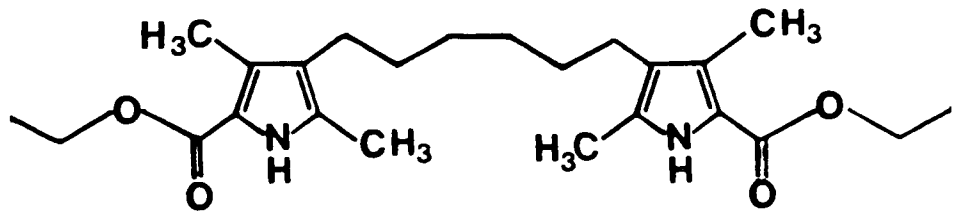
A mixture of sebacic acid (30.3g, 0.15 mole) and thionylchloride (35 mL, 0.49 mole) was heated on a steam bath until dissolved. Carbon tetrachloride (25 mL) was added and solvent removed under reduced pressure to remove the excess thionylchloride. The resulting liquid was added to a solution of 2-ethoxycarbonyl-3,5-dimethylpyrrole (50.1g, 0.30 mole) in methylene chloride (250 mL). The mixture was stirred under nitrogen and $SnCl_4$ (75 mL, 0.64 mole) was added dropwise in ½ hour during which time the product crystallised out. The suspension was washed with dilute hydrochloric acid, the pink solid filtered and recrystallised from hot acetone to give product (64g, 85.1%) as a white powder.

MP. 171-172°C.

Anal: Calc. for $C_{28}H_{40}N_2O_6$: C, 67.17; H, 8.05; N, 5.60: Found: C, 66.80; H, 8.04; N, 5.40%.

^{1}H NMR: (δ, $CDCl_3$/TFA); 1.38 (bs, 4H, $-COCH_2CH_2(C\underline{H}_2)_2$); 1.45 (t, J7Hz, 6H, $-CH_2C\underline{H}_3$); 1.70 (bm, 4H, $-COCH_2C\underline{H}_2$); 2.61 (s, 6H, $-C\underline{H}_3$); 2.63 (s, 6H, $-C\underline{H}_3$); 2.93 (t, J8Hz, 4H, $COC\underline{H}_2$); 4.47 (q, J7Hz, 4H, $-C\underline{H}_2CH_3$); 11.30 (bs, 2H, N$\underline{H}$).

1,6-Bis(5-ethyloxycarbonyl-2,4-dimethylpyrrole-3-yl)-hexane. (123)

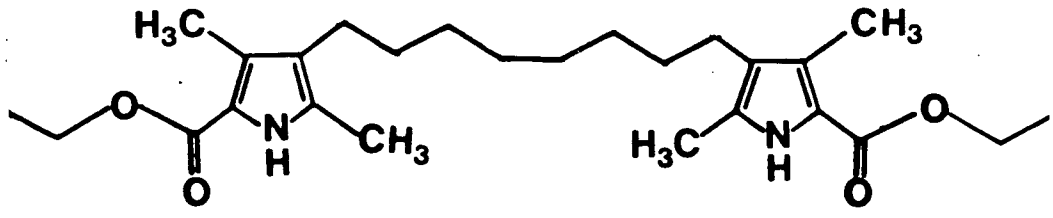


Borontrifluoride etherate (70 mL, 0.56 mole) was added dropwise to an ice cold stirred suspension of 1,6-bis(5-ethyloxycarbonyl-2,4-dimethylpyrrol-3-yl)-1,6-hexanedione (120) (55g, 0.11 mmole), sodium borohydride (16g, 0.42 mole) in THF (500 mL) under nitrogen. The reaction was checked by tlc for completion and quenched by the dropwise addition of glacial acetic acid (200 mL). On the addition of water (150 mL) the product precipitated out, this was filtered, redissolved in hot THF and recrystallised to give product (42.8g, 83.1%) as a white powder MP. 181-183°C.

Anal: Calc. for $C_{24}H_{36}N_2O_4$: C, 69.20; H, 8.71: N, 6.73: Found: C, 68.92; H, 8.70; N, 6.70%.

^{1}H NMR: (δ, $CDCl_3$/TFA); 1.35 (bs, 8H, $-CH_2(CH_2)_4CH_2-$); 1.38 (t, J7.5Hz, 6H, $-CH_2C\underline{H}_3$); 2.24 (s, 6H, CH_3); 2.28 (s, 6H, CH_3); 3.36 (bs, 4H, $-C\underline{H}_2(CH_2)_4C\underline{H}_2-$); 4.36 (q, J7.5Hz, 4H, $C\underline{H}_2CH_3$); 9.35 (bs, 2H, N$\underline{H}$).

1,8-Bis(5-ethyloxycarbonyl-2,4-dimethylpyrrole-3-yl)-octane (124)

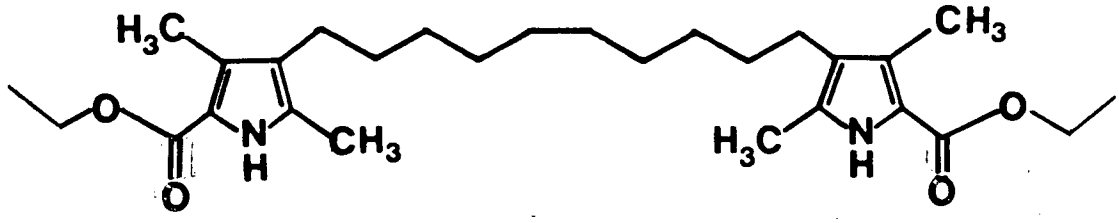


Borontrifluoride etherate (70 mL, 0.56 mole) was added dropwise to an ice cold stirred suspension of 1,8-bis(5-ethyloxycarbonyl-2,4-dimethylpyrrol-3-yl)-1,8-octanedione (121) (40g, 85 mmole),sodium borohydride (16g, 0.42 mole) in THF (500 mL) under nitrogen. The reaction was quenched by the dropwise addition of glacial acetic acid (100 mL) and water (500 mL) and extracted with methylene chloride (500 mL). The solution was evacuated to dryness and the solid recrystallised from THF to give product (29.9g, 79.5%) as white powder MP. 155-157°C.

Anal: Calc. for $C_{26}H_{40}N_2O_4$: C, 70.23; H, 9.07; N, 6.30: Found: C, 70.09; H, 9.15; N, 6.28%.

^{1}H NMR: (δ, $CDCl_3$/TFA); 1.28 (bm, 12H, $-CH_2(C\underline{H}_2)_6CH_2-$); 1.33 (t, J7Hz, 6H, $-OCH_2C\underline{H}_3$); 2.16 (s, 6H, $-C\underline{H}_3$); 2.21 (s, 6H, $-C\underline{H}_3$); 2.32 (t, J6Hz, $-C\underline{H}_2(-CH_2)_6C\underline{H}_2$); 4.29 (q, J7Hz, 4H, $-OC\underline{H}_2CH_3$); 9.25 (bs, 2H, N$\underline{H}$).

1,10-Bis(5-ethyloxycarbonyl-2,4-dimethylpyrrol-3-yl)-decane (125)

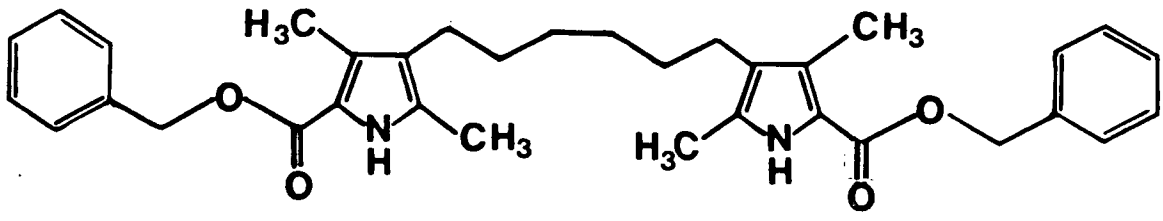


Boron trifluoride etherate (70 mL, 0.56 mole) was added dropwise to a room temperature, stirred suspension of 1,10-bis(5-ethyloxycarbonyl-2,4-dimethylpyrrol-3-yl)-1, 10-decanedione (122) (35g, 70 mmole), sodium borohydride (16g, 0.42 mole), in THF (500 mL) under nitrogen. The reaction was checked for completion by tlc and quenched by the drop-wise addition of glacial acetic acid (100 mL) and water (200 mL). The precipitated solid was filtered, washed with water and dried. The solid was dissolved in dichloromethene and the solvent replaced by methanol under reduced pressure to give product (29.5g, 89%) as white powder MP.143-144°C

Anal: Calc. for $C_{28}H_{44}N_2O_4$: C, 71.15; H, 9.38; N, 5.93: Found: C, 70.89; H, 9.41; N, 5.70%

^{1}H NMR: (δ, $CDCl_3$/TFA); 1.28 (bm, 16H, $-CH_2(C\underline{H}_2)_8CH_2-$); 1.30 (t, J7Hz, 4H, $OCH_2C\underline{H}_3$); 2.14 (s, 12H,$-C\underline{H}_3$); 2.34 (t, 4H, $-C\underline{H}_2(CH_2)_8C\underline{H}_2-$); 4.26 (q, J7Hz, 4H, $-C\underline{H}_2CH_3$); 8.81 (bs, 2H, N$\underline{H}$).

1,6-Bis(5-benzyloxycarbonyl-2,4-dimethylpyrrol-3-yl)-hexane. (126)

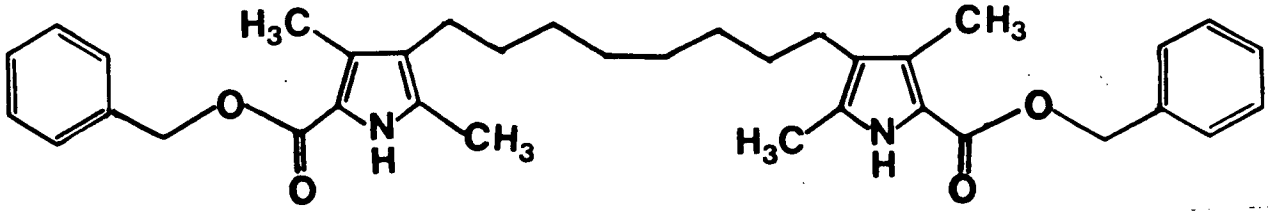


1,6-Bis(2-ethyloxycarbonyl-3,5-dimethylpyrrol-4-yl)-hexane (123) (18.7g, 45 mmole) was dissolved in dry benzyl alcohol (30 mL, 0.29 mole) and heated to reflux under nitrogen. To this solution was added 1 mL portions of freshly prepared sodium benzyloxide in benzyl alcohol until ethanol evolution ceased. The hot solution was then poured into a stirred solution of methanol (400 mL), water (250 mL) and glacial acetic acid (10 mL). The precipitated solid was filtered, washed and recrystallised from methanol to give product (22.1g, 91%) as a pink powder MP. 174-176.5^{o}C.

Anal: Calc. for $C_{34}H_{40}N_2O_4$: C, 75.52; H, 7.46; N, 5.18: Found: C, 75.77; H, 7.51; N, 5.20%

^{1}H NMR: (δ, $CDCl_3$/TFA); 1.33 (bs, 8H, $-CH_2(C\underline{H}_2)_4CH_2-$); 2.20 (s, 6H, $-C\underline{H}_3$); 2.25 (s, 6H, $-C\underline{H}_3$); 2.35 (t, overlap, 4H, $-C\underline{H}_2(CH_2)_4C\underline{H}_2-$); 5.34 (s, 4H, $-C\underline{H}_2C_6H_5$); 7.40 (bs, 10H, $-C_6\underline{H}_5$); 9.40 (bs, 2H, N$\underline{H}$).

1,8-Bis(5-benzyloxycarbonyl-2,4-dimethylpyrrol-3-yl)-octane (127)

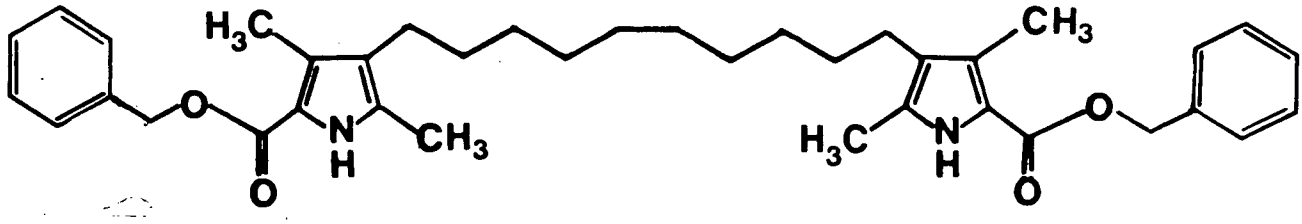


1,8-Bis(5-ethyloxycarbonyl-2,4-dimethylpyrrol-3-yl)-octane (124) (17g, 38 mmole) was dissolved in dry benzyl alcohol (50 mL, 0.5 mole) and heated to reflux under nitrogen. To this solution was added 1 mL portions of freshly prepared sodium benzyloxide in benzyl alcohol until ethanol evolution ceased. The hot solution was then poured into a stirred solution of methanol (300 mL), water (100 mL) and acetic acid (20 mL). The precipitated solid was filtered washed and recrystallised from methylene chloride/methanol to give product (19.5g, 89.7%) as off white powder MP. 133.5-135°C.

Anal: Calc.for $C_{36}H_{44}N_2O_4$: C, 76.02; H, 7.80; N, 4.93: Found: C, 75.96; H, 7.70; N, 4.90%.

^{1}H NMR: (δ, $CDCl_3$) 1.25 (bs, 12H, $-CH_2-(C\underline{H}_2)_6-CH_2$); 2.08 (s, 6H, $-C\underline{H}_3$); 2.20 (s, 6H, $-C\underline{H}_3$); 2.30 (t, overlap, 4H, $-C\underline{H}_2(CH_2)_6C\underline{H}_2-$); 5.22 (s, 4H, $-C\underline{H}_2C_6H_5$); 7.30 (m, 10H, $C_6\underline{H}_5$); 8.99 (bs, 2H, N$\underline{H}$).

1,10-Bis(5-benzyoxycarbonyl-2,4-dimethylpyrrol-3-yl)-decane (128)



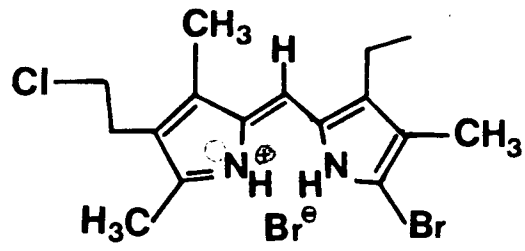
1,10-Bis(5-ethyloxycarbonyl-2,4-dimethylpyrrol-3-yl)-decane (125) (18g, 38 mmole) in dry benzyl alcohol (75 mL, 0.75 mole) and heated to reflux under nitrogen. To this solution was added 1 mL portions of freshly prepared sodium benzyloxide in benzyl alcohol until ethanol evolution ceased. The hot solution was poured into stirred methanol (500 mL) containing acetic acid (25 mL) and when cool, water (200 mL) was added. The solid was filtered, dried and recrystallised from methanol to give product (21.8g, 95.9%) as white powder MP. 142.5-144°C.

Anal: Calc. for $C_{38}H_{48}N_2O_4$: C, 76.47; H, 8.11; N, 4.69: Found: C, 76.59; H, 8.30; N, 4.60%.

^{1}H NMR: (δ, $CDCl_3$/TFA); 1.29 (bs, 16H, $-CH_2-(C\underline{H}_2)_8-CH_2-$) 2.23 (s, 6H, $-C\underline{H}_3$); 2.27 (s, 6H, $-C\underline{H}_3$); 2.36 (t, overlap, 4H, $-C\underline{H}_2(CH_2)_8C\underline{H}_2-$); 5.36 (s, 4H, $-C\underline{H}_2C_6H_5$); 7.41 (s, 10H, $C_6\underline{H}_5$); 9.47 (bs, 2H, N$\underline{H}$).

3.5 Synthesis of Methenes

5'-Bromo-4-(2-chloroethyl)-3'-ethyl-3,4',5-trimethyl-2-(2H-pyrrol-2'-ylidenemethyl)pyrrole hydrobromide (146)

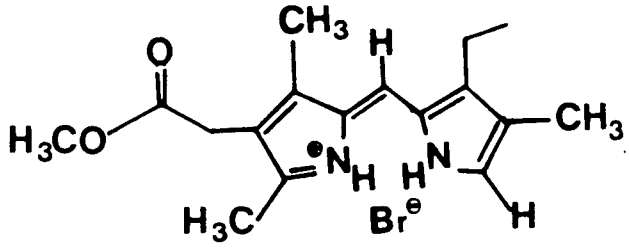


2-Benzyloxycarbonyl-4-(2-chloroethyl)-3,5-dimethylpyrrole (109) (3g, 10.3 mmole), 10% palladium on charcoal (1.3g) was hydrogenated in tetrahydrofuran until uptake of hydrogen ceased (240 mL). 2-Bromo-4-ethyl-5-formyl-3-methylpyrrole (107) (2.3g, 10.6 mmole) was added, the solution filtered and 48% hydrobromic acid (10 mL) was added followed by methanol (50 mL). The solution was concentrated under reduced pressure and the product (3.3g, 73.5%) obtained as orange/red crystals MP. 200°C(d). The remaining solution was placed in the refrigerator overnight and product (1g, 22.3%) obtained as deep purple crystals. The two were shown to be identical by analysis and nmr.

Anal: Calc. for $C_{16}H_{21}N_2Br_2Cl$: C,44.01; H, 4.85; N, 6.42; Br, 36.61; Cl, 8.12: Found: C, 44.57; 44.62; H, 4.93, 4.95; N, 6.38, 6.40; Br, 36.16; Cl. 8.26%.

^{1}H NMR: (δ, $CDCl_3$); 1.22 (t, J8Hz, 3H, $-CH_2C\underline{H}_3$); 2.06 (s, 3H, $-C\underline{H}_3$); 2.38 (s, 3H, $-C\underline{H}_3$); 2.69 (s, overlap, $-C\underline{H}_3$); 2.70 (q, overlap, $-C\underline{H}_2CH_3$); 2.93 (t, J7Hz, 2H, $-C\underline{H}_2CH_2Cl$); 3.64 (t, J7Hz, 2H, $-CH_2C\underline{H}_2Cl$); 7.19 (s, 1H, $-C\underline{H}=$); 12.29 (bd, 2H, $N\underline{H}$).

4-(2-Acetoxyethyl)-3'-ethyl-3,4',5-trimethyl-2-(2H-pyrrol-2'-ylidenemethyl) pyrrole hydrobromide (150)

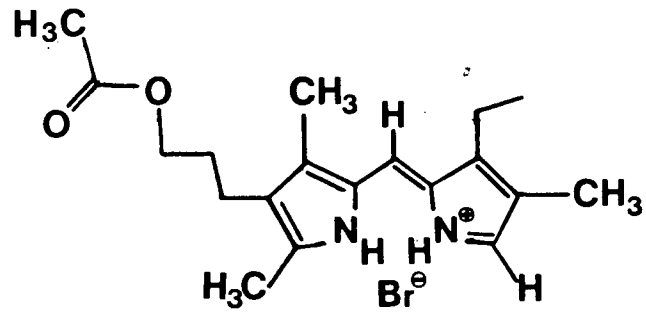


A suspension of 2-benzyloxycarbonyl-4-(2-acetoxyethyl)-3,5-dimethylpyrrole (112) (4.5g, 14.3 mmole), 10% palladium on charcoal (0.4g), triethylamine (2 drops) in THF (200 mL) was hydrogenated until uptake of hydrogen ceased (360 mL). To this mixture was added 4-ethyl-5-formyl-3-methylpyrrole (108) (2.74g, 20 mmole) and the solution filtered under vacuum; the resulting solution was treated with 48% hydrobromic acid (5 mL), the solution turned a dark yellow almost immediately. The solvent was then replaced with methanol under reduced pressure, crystallisation gave product (4.4g, 80.9%) as red orange crystals MP. 148-149(d)^{o}C.

Anal: Calc. for $C_{18}H_{25}N_2O_2Br$: C, 56.69; H, 6.61; N, 7.35; Br, 20.96: Found: C, 56.76; H, 6.57; N, 7.10; Br, 21.00%.

^{1}H NMR: (δ, $CDCl_3$/TFA); 1.17 (t, J7.5Hz, 3H, $-CH_2C\underline{H}_3$); 1.98 (s, 3H, $-C\underline{H}_3$); 2.03 (s, 3H, $-C\underline{H}_3$); 2.36 (s, 3H, $OOC\underline{H}_3$); 2.63 (s, 3H, $-C\underline{H}_3$); 2.75 (m, overlap, 4H, $-C\underline{H}_2CH_3$ and $-C\underline{H}_2CH_2O-$); 4.10 (t, J6.5Hz, 2H, $-CH_2C\underline{H}_2O-$); 6.81 (s, 1H, $-C\underline{H}=$); 7.44 (d, J3Hz, pyr-$\underline{H}$); 12.83 (bs, 1H, N$\underline{H}$); 13.00 (bs, 1H, N$\underline{H}$).

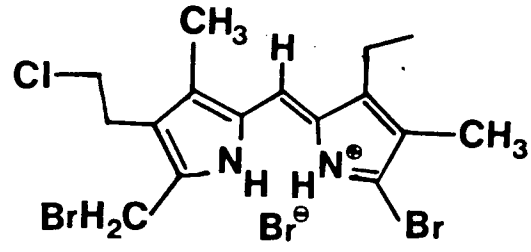
4-(3-Acetoxypropyl)-3'-ethyl-3,4',5-trimethyl-2-(2H-pyrrol-2'-ylidenemethyl)pyrrole hydrobromide (153)



2-Benzyloxycarbonyl-4-(3-acetoxypropyl)-3,5-dimethyl-2-(2H-pyrrol-2'-ylidenemethyl)pyrrole hydrobromide (113) (3.29g, 10 mmole), 10% palladium on charcoal (0.33g) in THF (200 mL) was hydrogenated until hydrogen uptake ceased (500 mL). 4-Ethyl-5-formyl-3-methylpyrrole (108) (1.4g, 10.2 mmole) was added, the solution filtered and 48% hydrobromic acid (2 mL) added. Ethyl acetate (30 mL) was added and the solution concentrated under reduced pressure; the product (3.48g, 88%) crystallised as bright orange crystals MP.148°C(d)

Anal: Calc. for $C_{19}H_{27}N_2BrO_2$: C, 57.22; H, 6.88; N, 7.09; Br, 20.21: Found: C, 57.68; H, 6.85; N, 7.05; Br, 20.11%.
^{1}H NMR: (δ, $CDCl_3$); 1.16 (t, J8Hz, 3H, $-CH_2C\underline{H}_3$); 1.76 (m, J7.5Hz, 2H, $-CH_2C\underline{H}_2CH_2O$); 2.04 (s, 6H, $-C\underline{H}_3$ and $-COC\underline{H}_3$); 2.28 (s, 3H, $-C\underline{H}_3$); 2.50 (t, J7.5Hz, 2H, $-C\underline{H}_2CH_2CH_2O$); 2.67 (q, J8Hz, 2H, $-C\underline{H}_2CH_3$); 2.68 (s, 3H, $-C\underline{H}_3$); 4.05 (t, J7.5Hz, 2H, $-CH_2CH_2C\underline{H}_2O$); 7.15 (s, 1H, $-C\underline{H}=$); 7.54 (d, J4Hz, 1H, pyr-$\underline{H}$); 13.02 (bs, 1H, N$\underline{H}$); 13.20 (bs, 1H, N$\underline{H}$).

5'-Bromo-5-bromomethyl-3'-(2-chloroethyl)-3,4'-dimethyl-2-(2H-pyrrol-2'-ylidenemethyl)pyrrole hydrobromide (155)

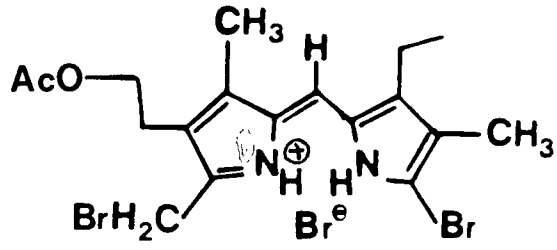


2-Benzyloxycarbonyl-4-(2-chloroethyl)-3,5-dimethylpyrrole (109) (2.63g, 9 mmole), 10% palladium on charcoal (0.25g) were hydrogenated in THF (200 mL) until hydrogen uptake ceased (460 mL). 2-Bromo-4-ethyl-5-formyl-3-methylpyrrole (107) (2g, 9.2 mmole) was added, the solution filtered and 48% hydrobromic acid (10 mL) added. Methanol (50 mL) was added and the solution concentrated under reduced pressure; the product (3.85g, 83.2%) crystallised as deep red crystals MP 150°C(d)

Anal: (calc. for $C_{16}H_{20}N_2Br_3Cl \cdot \frac{1}{2}HBr$: C, 34.56; H, 3.63; N, 5.04; Br, 50.31; Cl, 6.38: Found: C, 34.35; H, 3.56; N, 4.81; Br, 50.09; Cl, 6.44%.

^{1}H NMR: (δ, $CDCl_3$); 1.20 (t, J7.5Hz, 3H, $-CH_2C\underline{H}_3$); 2.04 (s, 3H, $-C\underline{H}_3$); 2.36 (s, 3H, $-C\underline{H}_3$); 2.75 (q, J7.5Hz, 2H, $-C\underline{H}_2CH_3$); 2.99 (t, J7Hz, 2H, $C\underline{H}_2CH_2Cl$); 3.67 (t, J7Hz, 2H, $CH_2C\underline{H}_2Cl$); 4.90 (s, 2H, CH_2Br); 7.18 (s, 1H, $-C\underline{H}=$); 7.48 (bs, 1H, $N\underline{H}$).

4-(2-Acetoxyethyl)-5'-bromo-5-bromomethyl-3'-ethyl-3,4'-dimethyl-2-(2H-pyrrol-2'-ylidenemethyl)pyrrole hydrobromide (156)



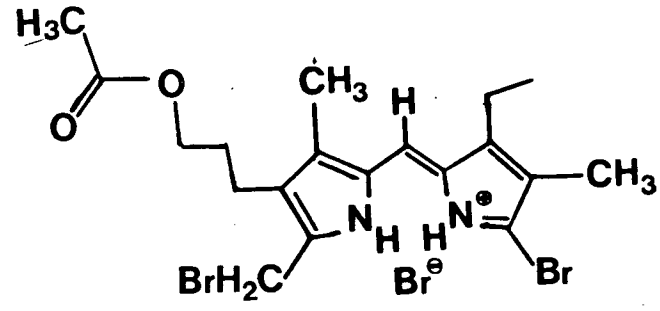
4-(2-Acetoxyethyl)-3'-ethyl-3,4',5-trimethyl-2-(2H-pyrrol-2'-ylidenemethyl)pyrrole hydrobromide (150) (1.5g, 4 mmole) was dissolved in 1,2 dichloroethane (12mL) and trifluoracetic acid (4 mL), bromine (2g, 11 mmole) was added and the mixture left protected from moisture for 5 days. The solvent and excess bromine was removed under vacuum, and the resulting solid dissolved in dichloroethane (20 mL). This solution was cooled in ice and ethyl ether (10 mL) added slowly with swirling; petroleum ether (10 mL) was then added slowly until crystallisation of the product (2.05g, 97%) as dark red/purple crystals occurred. The product was washed with ether and dried. MP. 177(d)^{o}C.

Anal: Calc. for $C_{18}H_{23}N_2Br_3O_2$: C, 40.10; H, 4.30; N, 5.20; Br, 44.47. Found: C, 39.20; H, 4.10; N, 4.92; Br, 44.80%.

^{1}H NMR: (δ, $CDCl_3$/TFA); 1.24 (t, J7.5Hz, 3H, $CH_2C\underline{H}_3$) 2.10 (s, 3H, $C\underline{H}_3$); 2.17 (s, 3H, $COC\underline{H}_3$); 2.39 (s, 3H, $C\underline{H}_3$);

2.82 (q, J7.5Hz, 2H, $C\underline{H}_2CH_3$); 2.95 (t, J7Hz, 2H, $C\underline{H}_2CH_2$-O); 4.33 (t, J7Hz, 2H, $CH_2C\underline{H}_2O$); 4.86 (s, 2H, $C\underline{H}_2Br$); 7.32 (s, 1H, =C$\underline{H}$-); 12.99 (bd, 2H, NH).

4-(3-Acetoxypropyl)-5'-bromo-5-bromomethyl-3,4-dimethyl-2-(2H-pyrrol-2'-ylidenemethyl)pyrrole hydrobromide (158)



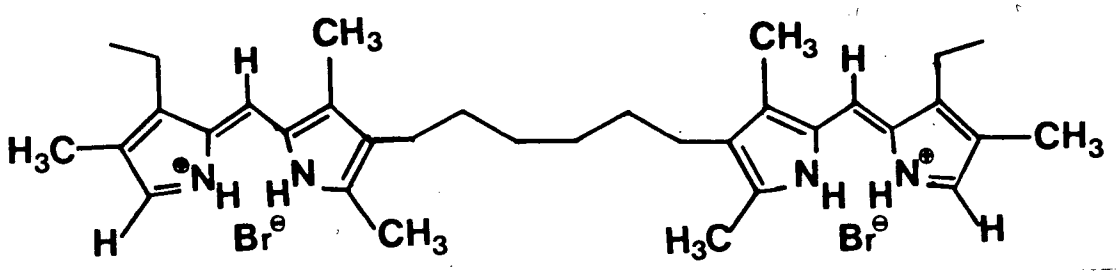
4-(3-Acetoxypropyl)-3'-ethyl-3,4',5-trimethyl-2-(2H-pyrrol-2'-ylidenemethyl)pyrrole hydrobromide (153) (2g, 5.1 mmole) was dissolved in 1,2-dichloroethane (14 mL) and trifluoracetic acid (7 mL); bromine (4g, 25 mmole) was added and the mixture left protected from moisture for 5 days. The solvent and excess bromine were removed under vacuum, and the resulting solid dissolved in 1,2-dichloroethane (15 mL); cyclohexene (5 mL) was added followed by ethyl ether (10 mL) and the solution cooled in ice. Petroleum ether (30 mL) was then added slowly with stirring, the product (2.49g, 89%) bing obtained as dark red crystals MP. 172(d)^{o}C.

Anal: Calc. for $C_{19}H_{25}N_2Br_3O_2$: C, 41.25; H, 4.56; N, 5.06; Br, 43.34: Found: C, 40.95; H, 4.41; N, 5.00; Br, 43.11%.

^{1}H NMR: (δ, $CDCl_3$/TFA); 1.16 (t, J8Hz, 3H, $-CH_2C\underline{H}_3$); 1.92 (m, 2H, $CH_2C\underline{H}_2CH_2O$); 2.04 (s, 3H, $-COC\underline{H}_3$); 2.08 (s, 3H, $-C\underline{H}_3$); 2.30 (s, 3H, $-C\underline{H}_3$); 2.60 (t, overlap, $-C\underline{H}_2CH_2CH_2O$); 2.75 (q, J8Hz, $-C\underline{H}_2CH_3$); 4.12 (t, J6Hz, $-CH_2CH_2C\underline{H}_2O$); 4.85 (s, 2H, $-CH_2Br$); 7.19 (s, 1H, -CH=); 13.42 (bs, 2H, N$\underline{H}$).

3.6 Synthesis of Chain Linked Methenes

1,6-Bis{3'-ethyl-3,4',5-trimethyl-2-(2H-pyrrol-2'-ylidenemethyl) pyrrol-4-yl}-hexane dihydrobromide (138)

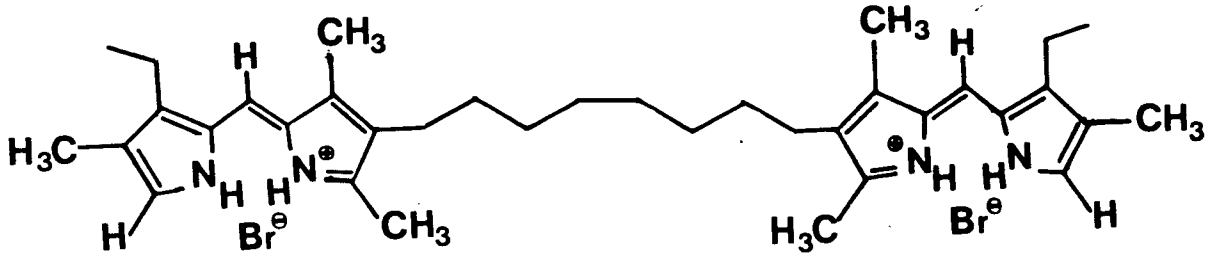


1,6-Bis(2-benzyloxycarbonyl-3,5-dimethylpyrrol-4-yl)-hexane (126) (2.7g, 5 mmole), 30% palladium on charcoal (0.1g) were hydrogenated in THF (250 mL) until hydrogen uptake ceased (250 mL). 4-Ethyl-5-formyl-3-methylpyrrole (108) (1.5g, 11 mmole) was added, the solution filtered and the solvent removed under reduced pressure. The solid was dissolved in methanol (50 mL) and 48% hydrobromic acid (4 mL) added. The solution was concentrated under reduced pressure; the precipitate formed was filtered and washed with 20% methanol/ethyl ether to yield (2.85g, 84.8%) red brown crystals MP. 189°C(d).

Anal: Calc. for $C_{34}H_{48}N_4Br_2$: C, 60.71; H, 7.19; N, 8.33; Br, 23.76: Found: C, 60.66; H, 7.16; N, 8.14; Br, 23.87%.

^{1}H NMR: (δ, $CDCl_3$/TFA); 1.20 (t, J8Hz, 6H, $-CH_2C\underline{H}_3$); 1.36 (bs, 8H, $-C\underline{H}_2(C\underline{H}_2)_4C\underline{H}_2-$; 2.09 (s, 6H, $-C\underline{H}_3$); 2.31 (s, 6H, $-C\underline{H}_3$); 2.44 (t, J7Hz, 4H, $-C\underline{H}_2(CH_2)_4C\underline{H}_2$); 2.67 (s, 6H, $-C\underline{H}_3$); 2.71 (q, J8Hz, 4H, $-C\underline{H}_2CH_3$); 7.20 (s, 2H, -C$\underline{H}$=); 7.56 (d, J3.5Hz, 2H, pyr-$\underline{H}$), 12.62 (bs, 2H, N$\underline{H}$); 12.78 (bs, 2H, N$\underline{H}$)

1,8-Bis{3'-ethyl-3,4',5-trimethyl-2-(2H-2'-ylidenemethyl) pyrrol-4-yl}-octane dihydrobromide (139)

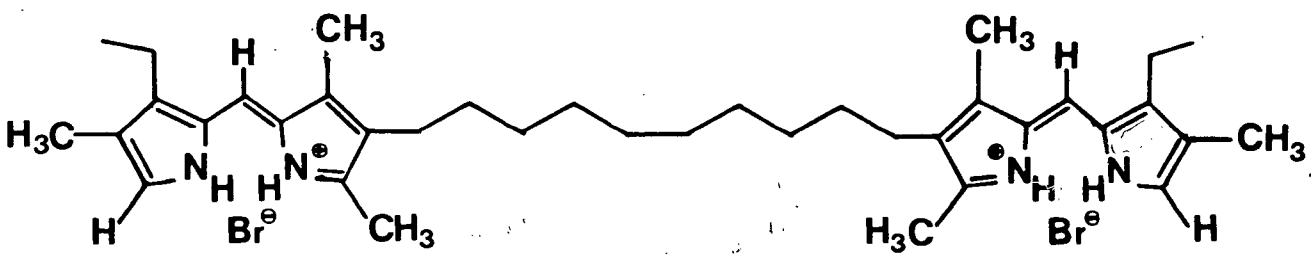


1,8-Bis(2-benzyloxycarbonyl-3,5-dimethylpyrrol-4-yl)-octane (127) (2g, 3.5 mmole), 10% palladium on charcoal (0.2g) was hydrogenated in THF (200 mL) until hydrogen uptake ceased (200 mL). 4-Ethyl-5-formyl-3-methylpyrrole (1.3g, 9.5 mmole) was added, the solution filtered, and 48% hydrobromic acid (5 mL) was added followed by methanol (50 mL). The solution was concentrated under reduced pressure and the product (2.4g, 95.3%), obtained as red brown crystals, was washed with 20% methanol/ethyl ether. MP. 200°C(d).

Anal: Calc. for $C_{36}H_{52}N_4Br_2$: C, 61.71: H, 7.48; N, 8.00; Br, 27.81: Found: C, 61.54; H, 7.47; N, 7.81; Br, 22.99%.

^{1}H NMR: (δ, $CDCl_3$): 1.20 (t, J8Hz, 6H, $-CH_2C\underline{H}_3$); 1.32 (bs, 12H, $-CH_2(C\underline{H}_2)_6CH_2-$); 2.09 (s, 6H, $-C\underline{H}_3$); 2.31 (s, 6H, $OC\underline{H}_3$); 2.44 (t, J7Hz, 4H, $-C\underline{H}_2(CH_2)_6C\underline{H}_2-$); 2.71 (s, 6H, $-C\underline{H}_3$); 2.72 (q, J8Hz, 4H, $-C\underline{H}_2CH_3$); 7.18 (s, 2H, $-C\underline{H}=$); 7.54 (d, J3.5Hz, 1H, pyr-$\underline{H}$); 12.97 (bs, 2H, $N\underline{H}$); 13.17 (bs, 1H, $N\underline{H}$).

1,10-Bis{3'-ethyl-3,4',5-trimethyl-2-(2H-pyrrol-2'-ylidenemethyl) pyrrol-4-yl}-decane dihydrobromide. (140)

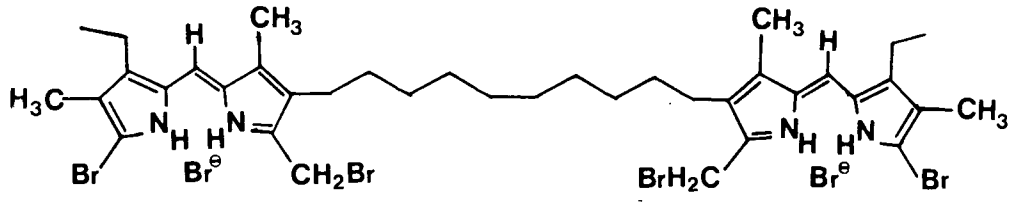


1,10-Bis (2-benzyloxycarbonyl-3,5-dimethylpyrrol-4-yl)-decane (128) (5.96g, 10 mmole), 10% palladium on charcoal (0.5g) was hydrogenated in THF (200 mL) until hydrogen uptake ceased (500 mL). 4-Ethyl-5-formyl-3-methylpyrrole (108) (2.9g, 21 mmole) was added and the solution filtered; 48% hydrobromic acid (5 mL) was added in methanol (5 mL) followed by ethylacetate (50 mL). The solution was concentrated under reduced pressure and the product (7g, 96%) obtained as a dark brown powder, washed with ethyl acetate MP. 179°C(d).

Anal: Calc. for $C_{38}H_{56}N_4Br_2$: C, 62.63; H, 7.75; N, 7.53; Br, 21.93; Found: C, 62.53; H, 7.65; N, 7.69; Br, 21.85%.

^{1}H NMR: (δ, $CDCl_3$); 1.20 (t, J8Hz, 6H, $-CH_2C\underline{H}_3$); 1.29 (bs, 16H, $-CH_2(C\underline{H}_2)_8CH_2-$); 2.09 (s, 6H, $-C\underline{H}_3$); 2.31 (s, 6H, $-C\underline{H}_3$); 2.43 (t, J7Hz, 4H, $-C\underline{H}_2(CH_2)_8C\underline{H}_2-$); 2.70 (s, 6H, $-C\underline{H}_3$); 2.71 (q, J8Hz, 4H, $-C\underline{H}_2CH_3$); 7.18 (s, 2H, $-C\underline{H}=$); 7.54 (d, J2Hz, pyr-$\underline{H}$); 13.00 (bs, 2H, $N\underline{H}$); 13.20 (bs, 2H, $N\underline{H}$).

1,10-Bis{5'-bromo-5-bromomethyl-3'-ethyl-3,4'-dimethyl-2-(2H-pyrrol-2'-ylidenemethyl)pyrrol-4-yl}decane dihydrobromide (159)



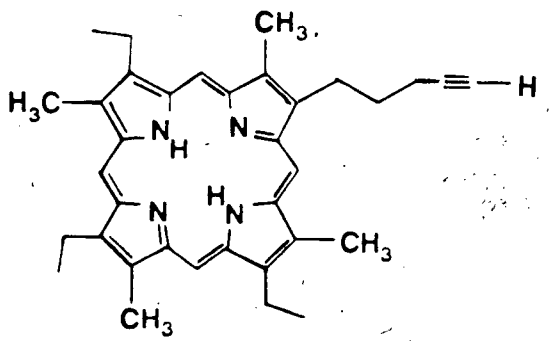
Bromine (1.0g, 6.3 mmole) was added to a solution of 1,10-bis(3'-ethyl-3,4',5-trimethyldipyrromethen-4-yl)-decane dihydrobromide (140) (1.0g, 1.4 mmole) in 30% TFA/1,2-dichloroethane (25 mL) and left for 4 days. To this solution was added, slowly with swirling, a mixture of cyclohexene (5 mL) and ethylether (15 mL). Dark red/purple crystals formed without cooling; pet. ether (10 mL) was added to ensure complete crystallisation. The product (1.41g, 98.4%) was filtered, washed with pet. ether and dried. MP. 190°C(d).

Anal: Calc. for $C_{38}H_{52}N_4Br_6$: C, 43.70; H, 5.02; N, 5.37; Br, 45.91. Found: C, 43.59; H, 5.16; N, 5.30; Br, 46.13%.

^{1}H NMR: (400 MHz) (δ, $CDCl_3$/TFA) 1.21 (t, J8Hz, 6H, $CH_2C\underline{H}_3$); 1.28, 1.32 (bd, 12H, $CH_2CH_2(C\underline{H}_2)_6CH_2CH_2$); 1.52 (bs, 4H, $CH_2C\underline{H}_2(CH_2)_6C\underline{H}_2CH_2$); 2.07 (s, 6H, CH_3); 2.29 (s, 6H, CH_3); 2.49 (t, J 7Hz, 4H, $C\underline{H}_2(CH_2)_8C\underline{H}_2$); 2.74 (q, J8Hz, 4H, $C\underline{H}_2CH_3$); 4.79 (s, 4H, $C\underline{H}_2Br$); 7.15 (s, 2H, =C$\underline{H}$-); 12.91, 12.96 (s, 4H, N$\underline{H}$).

3.7 Synthesis of Model Porphyrin

2,12,17-Triethyl-3,8,13,18-tetramethyl-7-(pent-4-yne)porphine (171)



3-Bromopropylporphine (175) (90mg, 0.16 mmole) was dissolved in DMSO (25 mL) and treated with excess lithium acetylide ethylenediamine under an inert atmosphere and stirred for 2 hours protected from moisture. The reaction was quenched by pouring into water and extracting with dichloromethane. The solution was evaporated to dryness, the solid redissolved in dichloromethane and column chromatographed on activity IV silica gel, using dichloromethane as eluent.

The product (55mg, 67.6%) was crystallised from dichloromethane/methanol.

Anal: Calc. for $C_{35}H_{40}N_4$: C, 81.35; H, 7.80; N, 10.84: Found: C, 81.56; H, 7.74; N, 10.84%.

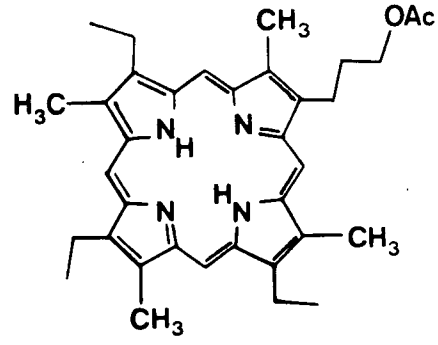
^{1}H NMR: (400 MHz) (δ, $CDCl_3$/TFA); 1.70 (t, J7.5Hz, 9H, $-CH_2C\underline{H}_3$); 2.38, 2.41 and 2.47 (overlap, 5H, $CH_2C\underline{H}_2C\underline{H}_2C{\equiv}C\underline{H}$);

3.80 and 3.81 (2s, 12H, $C\underline{H}_3$); 4.27 (q, J7.5Hz, 6H, $-C\underline{H}_2CH_3$); 4.43 (t, J7Hz, 2H, $C\underline{H}_2(CH_2)_2C{\equiv}CH$); 10.69 (s, 3H, meso H); 10.83 (s, 1H, meso H).

Visible Spectrum (CH_2Cl_2) :

λ_{max} (nm)	397	497	530	566	620
peak ratio	36.43	2.86	2.04	1.36	1.00

2-(3-Acetoxypropyl)-7,12,17-triethyl-3,8,13,18-tetramethylporphine (172)



Cyclohexene (2 mL) was added to a solution of 5'-bromo-5-bromomethyl-4,3'-diethyl-3,4'-dimethyldipyrromethene hydrobromide (173) (2.90g, 6.0 mmole) in dry dichloromethane (100 mL) and the solution evaporated to dryness under reduced pressure. The resulting solid and 4-(3-acetoxypropyl)-3'-ethyl-3,4',5-trimethyldipyrromethene hydrobromide (153) (1.97g, 5.0 mmole) were dissolved in dry dichloromethane (100 mL) and treated with stannic chloride (3 mL).

After standing for 1½ hours the bright orange/red solution was quenched with 48% hydrobromic acid (10 mL) in methanol (5 mL). The solution was washed with water (100 mL x 3) and treated with 48% hydrobromic acid (5 mL), ethyl acetate (50 mL) and methanol (50 mL). The dichloromethane was removed under reduced pressure and the dark red/brown precipitate (3.2g) formed, filtered, washed with ether/pet. ether and dried.

The biladiene was dissolved in pyridine (25 mL) and DMSO (100 mL) and left in the dark open to the atmosphere

for 5 days. The porphyrin (1.553g, 56.6%) was filtered, washed with methanol and dried. An analytical sample was prepared by column chromatography on activity IV silica gel using dichloromethane as solvent due to some deprotection of hydroxypropyl functionality.

Anal: Calc. for $C_{35}H_{42}N_4O_2$: C, 76.33; H, 7.69; N, 10.17: Found: C, 76.55; H, 7.69; N, 10.16%.

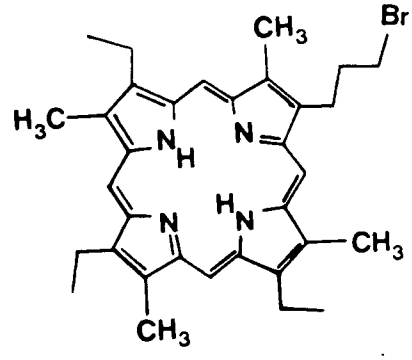
^{1}H NMR: (400 MHz) (δ, $CDCl_3$/TFA): 1.68 (t, J8Hz, 9H, $-CH_2C\underline{H}_3$); 2.15 (s, 3H, $-COC\underline{H}_3$); 2.41 (m, J7Hz, 2H, $-CH_2C\underline{H}_2CH_2-O-$); 3.58 (s, 12H, $-C\underline{H}_3$); 4.04 (q, J8Hz, 6H, $-C\underline{H}_2CH_3$); 4.12 (t, J7Hz, 2H, $-C\underline{H}_2CH_2CH_2-O-$); 4.30 (t, J7Hz, 2H, $-CH_2CH_2C\underline{H}_2-O$); 10.53, 10.54 (2s, 4H, -H).

^{13}C NMR: (δ, 5% TFA/$CDCl_3$): 171.34 (1C, -COO-); 143.62, 142,47, 142.03, 141.53, 140.42, 137.45, 136.91 (16C, - and - pyrrolic carbons); 98.21 (4C, meso-carbons 5-, 10-, 15- and 20-C); 63.66 (1C, $-CH_2CH_2\underline{C}H_2-O-$); 30.93 (1C, $-CH_2\underline{C}H_2-CH_2-O-$); 23.07 (1C, $-\underline{C}H_2CH_2CH_2-O-$); 20.94 (1C, $C\underline{H}_3$ CO); 20.08 (3C, $-\underline{C}H_2CH_3$); 16.42 (3C, $-CH_2\underline{C}H_3$); 11.74 (4C, B- CH_3).

Visible Spectrum (CH_2Cl_2) :

λ_{max} (nm)	397	497	530	516	619
peak ratio	31.2	2.66	1.93	1.3	1

2-(3-Bromopropyl)-7,12,17-triethyl-3,8,13,18-tetramethylporphine. (175)



Method A

3-Acetoxypropylporphine (172) (250mg, 0.45 mmole) was refluxed in 48% hydrobromic acid (15 mL) and sulfuric acid (2 mL) for 3 hours. The reaction was checked by tlc and found to be incomplete; further reflux did not appear to improve the yield and the reaction was thus quenched by washing with water (30 mL) and extracting with dichloromethane (30 mL). The extract was washed with water until neutral and the solvent removed under reduced pressure. The product (200mg, 77%) was chromatographed on activity IV silica gel with 2% methanol/dichloromethane as eluent. Increasing methanol content enabled the recovery of 3-hydroxypropylporphine (50mg, 21.6%).

Method B

The product was produced by the triphenylphosphite dibromide method used for compound (181) using 3-hydroxypropylporphine (174) (50mg, 98 mmole) and triphenyl phosphite

dibromide (150mg, 300 mmole), yielding 3-bromopropyl-porphinato zinc (175a) (53mg, 85%).

Anal: Calc. for $C_{33}H_{39}N_4Br \cdot H_2O$: C, 67.22; H, 7.01; N, 9.50; Br, 13.55. Found: C, 67.19; H, 6.79; N, 9.47; Br, 13.44%.

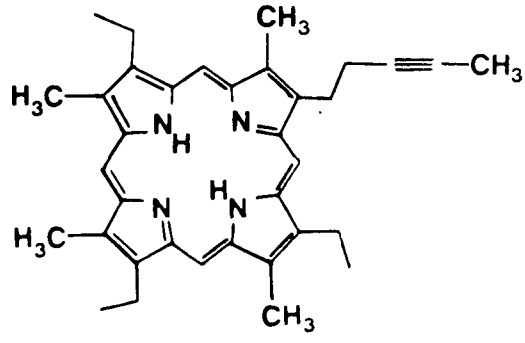
^{1}H NMR: (400 MHz) (δ, $CDCl_3$/TFA). 1.75 (t, J7.5Hz, 9H,$-CH_2C\underline{H}_3$); 2.48 (m, J7.5Hz, 2H, $-CH_2C\underline{H}_2CH_2Br$); 3.66 and 3.68 (2s, 12H, $-CH_3$); 4.15 (q, J7.5Hz, 6H, $-C\underline{H}_2CH_3$); 4.21 (t, J7.5Hz, 2H, $-CH_2CH_2C\underline{H}_2Br$); 4.38 (t, J7.5Hz, 2H, $-C\underline{H}_2CH_2CH_2Br$); 10.62 and 10.63 (2s, 4H, meso -H).

^{13}C NMR: (δ, 5% TFA/$CDCl_3$): 144.531, 144.482, 144.434, 142.698, 142.650, 142.516, 142.104, 141.922, 141.788, 141.606, 140.830, 138.415, 138.136, 137.736, 137.699 (16C, α- and β- carbons); 98.882, 98.518 (4C, meso carbons 5-, 10-, 15- and -20C); 34.461, 33.102 (2C, $-CH_2-CH_2\underline{C}H_2\underline{C}H_2Br$); 24.608 (1C, $-\underline{C}H_2CH_2CH_2Br$); 20.191 (3C, $-\underline{C}H_2CH_3$); 16.284 (3C, $-CH_2-\underline{C}H_3$); 11.989, 11.819, 11.746 (4C, β-CH_3).

Visible Spectrum (CH_2Cl_2):

λ_{max} (nm)	397	497	531	566	620
peak ratio	35.60	2.92	2.05	1.40	1.00

2,12,17-Triethyl-3,8,13,18-tetramethyl 7-(pent-3-yne)porphine (176)

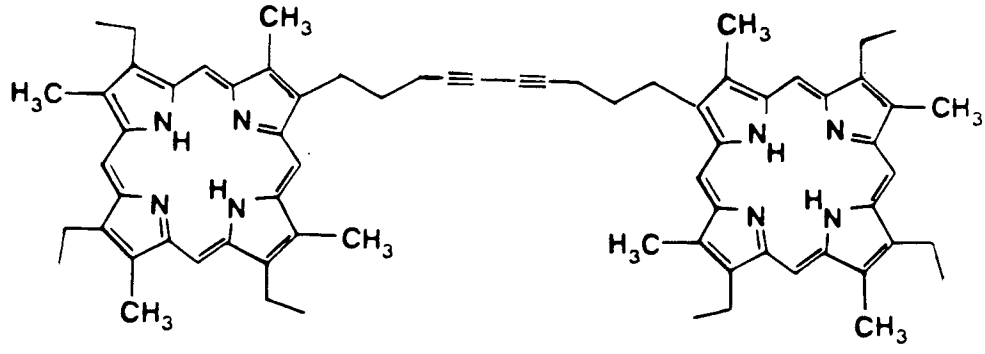


The reaction was carried out on (175) (50mg, 0.087 mmole) as for (171) but the reaction was heated to 50°C overnight. The product (42.5mg, 94.1%) was found to have identical analysis, visible spectra, and parent mass to the pent-4-yne porphine (171). Assignment was by ^{1}H NMR.

^{1}H NMR: (δ, $CDCl_3$) -3.81 (s, 2H, N$\underline{H}$), 1.77 (t, J2Hz, 3H, C CC$\underline{H}_3$); 1.85 (t, J7.5Hz, 9H, $CH_2C\underline{H}_3$); 3.05 (m, J2Hz, J7Hz, 2H, $CH_2C\underline{H}_2C{\equiv}CCH_3$); 3.61 and 3.63 (2s, 12H, C$\underline{H}_3$); 4.07 (q, J7.5Hz, 6H, -C$\underline{H}_2CH_3$); 4.24 (t, J7Hz, 2H, C$\underline{H}_2CH_2C{\equiv}$C-); 10.07 (s, 4H, meso H).

3.8 Synthesis of Singly Linked Porphyrins

Bis 1,10-(7,12,17-triethyl-3,8,13,18-tetramethylporphin-2-yl) deca-4,6-diyne (177)



To a solution of (171) (15mg, 0.03 mmole) in dichloromethane (10 mL) was added saturated solution of zinc acetate in methanol. The solution was washed with water (2 x 20 mL) and the solvent removed under reduced pressure. The solid was dissolved in pyridine (10 mL) and methanol (5 mL), cuprous chloride (20mg) and TMEDA (1 mL) were added and resultant solution bubbled with oxygen while stirring, the solution was heated to 45°C and left overnight.

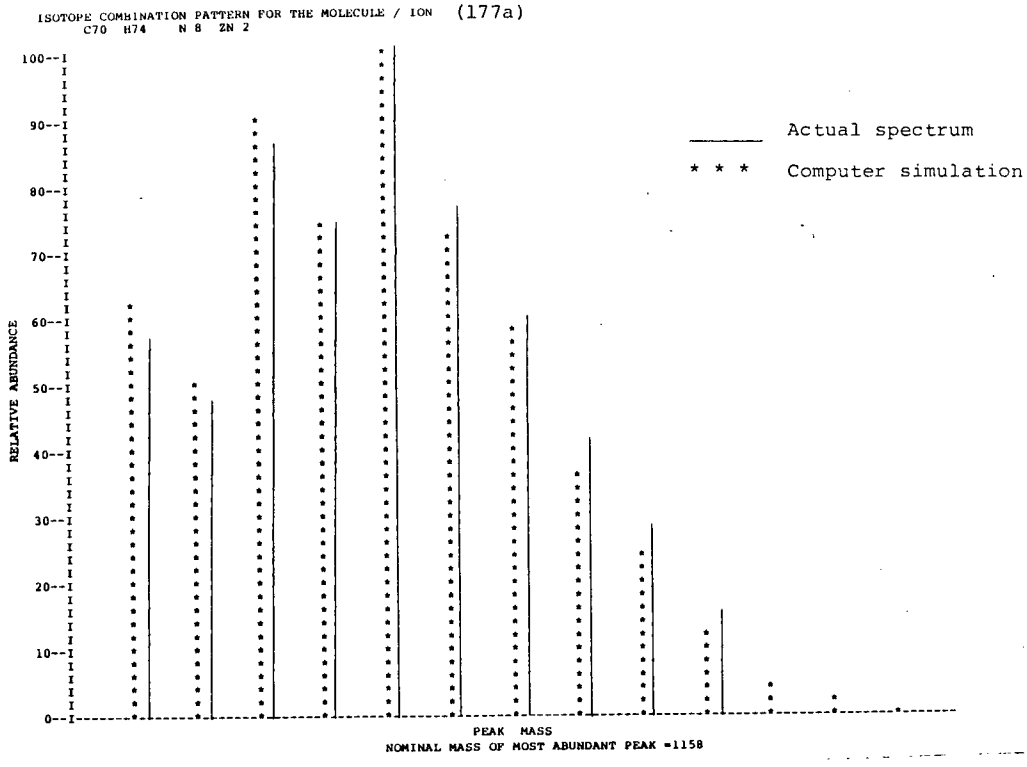
Tlc showed a fast running band of starting material with a slower running band which also fluoresced after 6 hours. After 18 hours the slower running band was stronger than the first but after 24 hours no further change seemed obvious thus the reaction was quenched with water (50 mL) and extracted with dichloromethane (50 mL). The organic phase was washed with water (2 x 30 mL) and sat. sodium chloride

solution (30 mL). The solvent was removed under reduced pressure and the product chromatographed on activity IV silica gel eluted with dichloromethane. The product (9.5mg, 56.5%) was crystallised from dichloromethane/pet. ether.

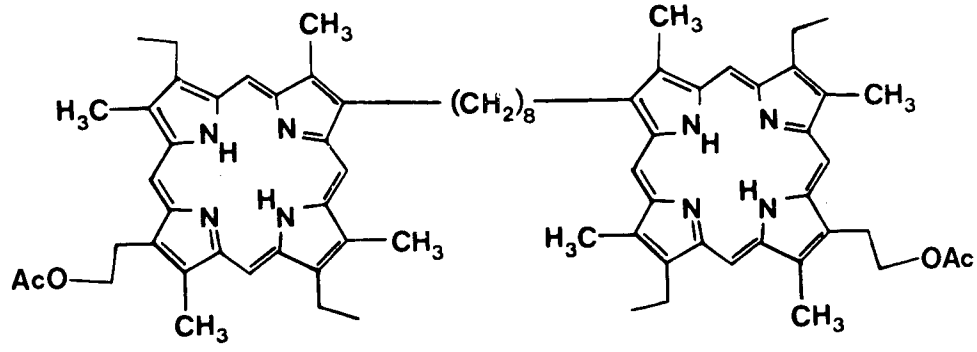
Visible Spectrum (CH_2Cl_2) :

λ_{max} (nm)	397	498	531	567	620
peak ratio	31.07	2.80	2.04	1.39	1.00

Mass Spectrum: (177a)



Bis 1,8{12-(2-acetoxyethyl)-7,17-diethyl-3,8,13,18-tetramethylporphin-2-yl} octane (169)



Cyclohexene (3 mL) was added to a solution of 4-(2-acetoxyethyl)-5'-bromo-5-bromomethyl-3'-ethyl-3,4'-dimethyldipyrromethene hydrobromide (156) (1.45g, 2.7 mmole) in dry dichloromethane (50 mL). The solution was evaporated to dryness under reduced pressure. The resultant solid and 1,8-bis(3'-ethyl-3,4'-5-trimethyldipyrromethene-4-yl)octane dihydrobromide (139) (0.9g, 1.3 mmole) were dissolved in dry dichloromethane (100 mL), treated with stannic chloride (3 mL) and left to stand, protected from moisture for 1½ hours.

The reaction was quenched by the addition of 48% hydrobromic acid (10 mL) and water (50 mL). The organic phase was separated and washed with water (2 x 100 mL). To the organic phase was added 48% hydrobromic acid (5 mL) and methanol (50 mL), the dichloromethane was removed under reduced pressure and the precipitated biladiene was filtered

and washed with ethyl acetate.

The biladiene was dissolved in DMSO (65 mL) and pyridine (5 mL), the solution was allowed to stand in the dark open to the air for 5 days. The product (0.88g, 61.8%) was filtered, washed with methanol and dried.

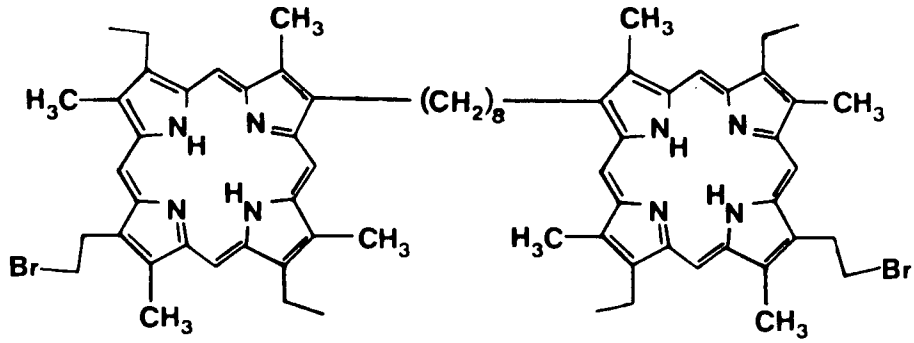
Anal: Calc. for $C_{72}H_{86}N_8O_4$: C, 76.67; H, 7.69; N, 9.94. Found: C, 76.50; H, 7.77; N, 9.74%.

^{1}H NMR: (270 MHz) (δ, $CDCl_3$/TFA), 1.35 (bs, 4H, $-(CH_2)_3(C\underline{H}_2)_2(CH_2)_3-$); 1.55 (bs, 4H, $-(CH_2)_2C\underline{H}_2(CH_2)_2C\underline{H}_2(CH_2)_2-$); 1.70 (m, 10H, overlap $CH_2C\underline{H}_3$ & $-CH_2C\underline{H}_2(CH_2)_4C\underline{H}_2CH_2-$); 2.04 (s, 6H, $COC\underline{H}_3$); 3.59 (s, 12H, $C\underline{H}_3$); 3.66 (s, 6H, $C\underline{H}_3$); 3.69 (s, 6H, $C\underline{H}_3$); 4.10 (m, 12H, overlap $-C\underline{H}_2(CH_2)_6C\underline{H}_2-$ & $C\underline{H}_2CH_3$); 4.59 (t, J6.5Hz, 4H, $C\underline{H}_2CH_2O-$); 4.96 (t, J6.5Hz, 4H, $C\underline{H}_2CH_2O-$); 10.59, 10.61, 10.66, 10.72 (s, 4H, meso $\underline{H}$).

Visible Spectrum (CH_2Cl_2)

λ_{max} (nm)	397	497	533	567	620
peak ratio	42.66	3.22	2.38	1.61	1.00

Bis 1,8-{12-(2-bromoethyl)-7,12-diethyl-3,8,13,18-tetramethylporphin-2-yl}-octane (170)



Bis 1,8- 12-(2-acetoxyethyl)-7,17-diethyl-3,8,13,18-tetramethylporphin-2-yl octane (169) (20mg, 0.02 mmole) was deprotected with 5% sulfuric acid/methanol. The hydroxyethylporphine formed was dissolved in a solution of triphenylphosphite dibromide (150mg, 0.3 mmole) in dry dichloromethane (15 mL). After 2 hours the reaction was quenched by pouring into water (30 mL). The organic layer was separated, washed with water (30 mL x 3), evaporated under reduced pressure and chromatographed on activity IV silica with dichloromethane as eluent. The product (13.5g, 65%) was crystallised from dichloromethane/methanol.

Anal: Calc. for $C_{68}H_{80}N_8Br_2.H_2O$: C, 68.78; H, 6.96; N, 9.44. Found: C, 68.25; H, 6.96; N, 8.82%.

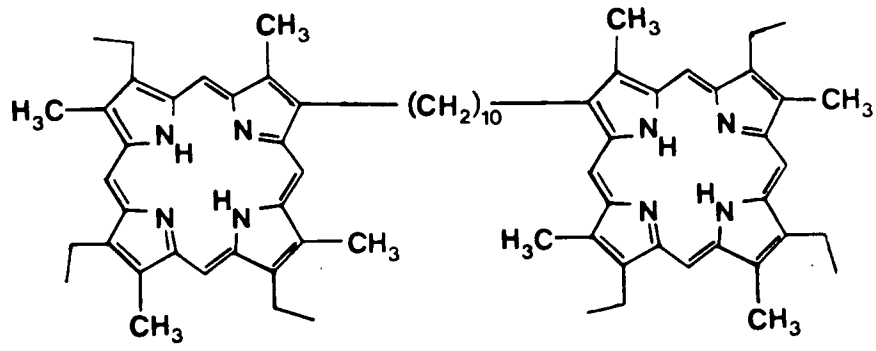
^{1}H NMR: (δ, $CDCl_3$); 1.41 & 2.03 (bs, 12H, $-CH_2(C\underline{H}_2)_6CH_2-$); 1.72 (t, J7.5Hz, 12H, $CH_2C\underline{H}_3$); 3.60 (s, 12H, $C\underline{H}_3$); 3.67

(s, 6H, $C\underline{H}_3$); 3.70 (s, 6H, $C\underline{H}_3$); 4.08 (m, H, overlap, $C\underline{H}_2CH_3$, $C\underline{H}_2(CH_2)_6C\underline{H}_2$ and $C\underline{H}_2CH_2Br$); 4.70 (t, J7.5Hz, 4H, $CH_2C\underline{H}_2Br$); 9.60, 9.62, and 9.67 (3s, 8H, meso H).

Visible Spectrum (CH_2Cl_2) :

λ_{max} (nm)	398	497	535	568	621
peak ratio	38.57	3.00	2.18	1.57	1.00

Bis 1,10-(7,12,17-triethyl-3,8,13,18-tetramethylporphin-2-yl) decane (178)



Method A.

Cyclohexene (2 mL) was added to a solution of 5'-bromo-5-bromomethyl-3',4-diethyl-3,4'-dimethyl dipyrromethene hydrobromide (173) (0.5g, 1.04 mmole) in dry dichloromethane (50 mL) and the solution was evaporated to dryness under reduced pressure.

The resulting solid and 1,10-bis(3'-ethyl-3,4',5-trimethyl-dipyrromethene-4-yl) decane dihydrobromide (140) (0.36g, 0.5 mmole) were dissolved in dry dichloromethane (50 mL) treated with stannic chloride (2 mL) and left for 2 hours. The bright orange/red solution was quenched with 48% hydrobromic acid (10 mL) and methanol (5 mL). The organic phase was washed with water (3 x 100 mL). Ethyl acetate (50 mL), 48% hydrobromic acid (5 mL) and methanol (5 mL) were added and the dichloromethane removed under reduced pressure. The

biladiene crystallised as a red/brown solid, was filtered, washed with ethyl acetate and dried.

The biladiene was dissolved in DMSO (100 mL) and pyridine (20 mL) then left in the dark, open to the atmosphere for 5 days. The product (0.303g, 42.6%) formed as a purple scum, was filtered, washed with methanol and dried.

Method B

Compound (177a) (10mg, 0.008 mmole) was dissolved in formic acid (20 mL) and hydrogenated over PdO (1mg) until 10% of the absorbance had been lost in the visible spectrum. The solution was then filtered and evaporated to dryness under reduced pressure. The solid was chromatographed on activity IV silica gel eluted with dichloromethane. The fast running band was shown to be identical to the product above by tlc, mass spectra, and ^{1}H NMR.

Anal: Calc. for $C_{70}H_{86}N_8$: C, 80.88; H, 8.34; N, 10.78; Found: C, 81.38; H, 8.20; N, 10.56%.

^{1}H NMR: (δ, $CDCl_3$/TFA): -3.10 (bs, 4H, N$\underline{H}$); 1.29, 1.41 and 1.61 (3bs, 12H, $-(CH_2)_2(C\underline{H}_2)_6(CH_2)_2-$); 1.73 (m, 12H, $CH_2C\underline{H}_3$); 2.07 (m, 4H, $CH_2C\underline{H}_2(CH_2)_6C\underline{H}_2CH_2$); 3.60 (s, 12H, $C\underline{H}_3$); 3.64 (s, 12H, $C\underline{H}_3$); 4.10 (bm, 16H, overlap, $C\underline{H}_2(CH_2)_8C\underline{H}_2$ and $C\underline{H}_2CH_3$); 9.47, 9.48, 9.49 and 9.50 (4s, 8H, meso H).

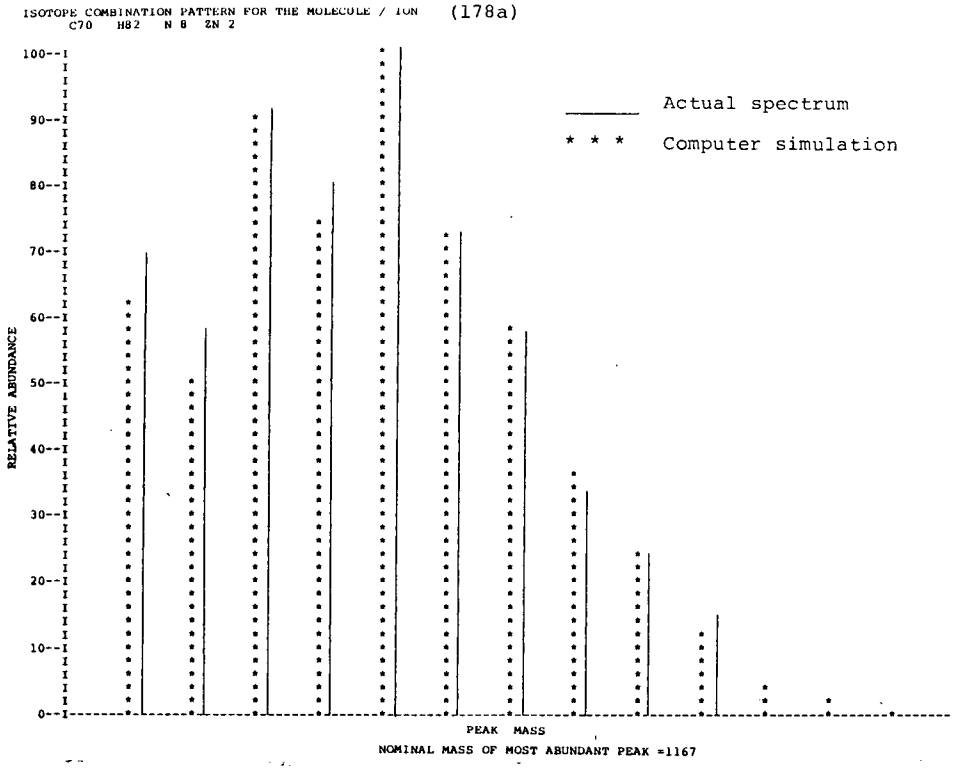
^{13}C NMR: (δ, $CDCl_3$/5%TFA): 144.567, 143.439, 142.322, 141.825, 141.497, 138.221, 137.893 (32C, α- and β-carbons); 98.481

(8C, meso-carbons 5-, 10-, 15-, 20-C), 32.253 (2C, chain 2', 9'C); 30.008 (2C, chain 3',8'C); 29.523 (2C, chain 4',7'C); 29.438 (2C, chain 5', 6'C); 26.877 (2C, chain 1', 10'C); 20.167 (4C, $-\underline{C}H_2CH_3$); 16.284 (4C, $-CH_2\underline{C}H_3$); 11.904, 11.770 (8C, β-CH_3).

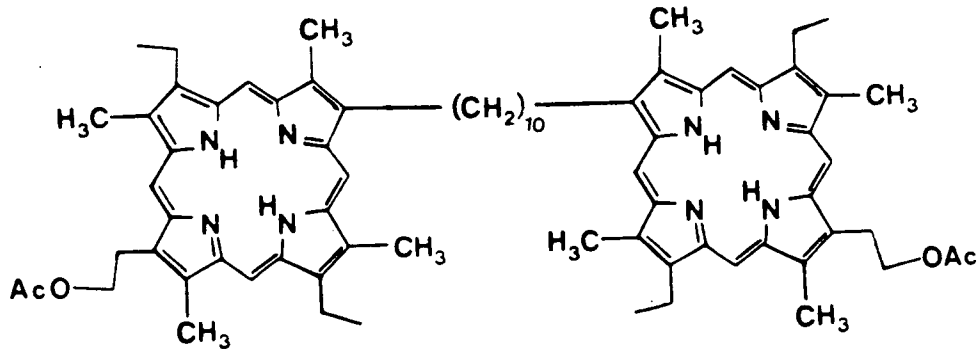
Visible Spectrum (CH_2Cl_2) :

λ_{max} (nm)	400	497	532	566	620
peak ratio	70.43	2.87	2.63	2.22	1.00

Mass Spectrum



Bis-1,10{12-(3-acetoxypropyl)-7,17-diethyl-3,8,13,18-tetramethylporphyrin-2-yl}decane. (179)



Cyclohexene (3 mL) was added to a solution of 4-(3-acetoxypropyl)-5'-bromo-5-bromomethyl-3,4'-dimethyldipyrromethene hydrobromide (158) (2.8g, 5.06 mmole) in dry dichloromethane (100 mL); the solution was evaporated to dryness under reduced pressure. The resulting solid and 1,10-bis (3'-ethyl-3,4,5'trimethyldipyrromethene-4-yl) decane dihydrobromide (140) (1.8g, 2.47 mmole) were dissolved in dry dichloromethane (500 mL) and treated with stannic chloride (5 mL).

After standing for 1½ hours the bright orange/red solution was quenched with 48% hydrobromic acid (10 mL) in methanol (50 mL). The solution was then washed with water (500 mL x 3) and a mixture of hydrobromic acid (5 mL), methanol (5 mL) and ethyl acetate (50 mL) was added. The dichloromethane was removed under reduced pressure until a deep red brown biladiene precipitated. This was filtered, washed with ethyl acetate and dried.

The biladiene was dissolved in DMSO (100 mL), pyridine (25 mL) and left open to the atmosphere in the dark for 5 days. The porphyrin formed as a purple scum and was filtered and washed with methanol. The product (1.95g, 66.7%) was recrystallised from dichloromethane/methanol. An analytical sample was produced by metallating the porphyrin with zinc and drying at 120°C/.01 Torr for 4 days.

Deprotection of the alcohol was carried out in 5% sulfuric acid/methanol, extracted with dichloromethane, washed with water and crystallised from methanol in 95% yield.

Anal: Calc. for $C_{76}H_{94}N_8O_4$: C, 77.12; H, 8.01; N, 9.47.
Found: C, 76.50; H, 8.02; N, 9.29%.
Calc. for $C_{76}H_{90}N_8O_4Zn_2 \cdot H_2O$: C, 68.77; H, 6.98; N, 8.44:
Found: C, 68.62; H, 7.10; N, 8.20%.

^{1}H NMR (400 MHz): (δ, $CDCl_3$/TFA); 1.24 (bs, 4H, $-(CH_2)_4-C\underline{H}_2-C\underline{H}_2(CH_2)_4$); 1.37 (bs, 4H, $-(CH_2)_3-C\underline{H}_2-(CH_2)_2-C\underline{H}_2-(CH_2)_3-$); 1.56 (m, 4H, $-(CH_2)_2-C\underline{H}_2-(CH_2)_4-C\underline{H}_2-(CH_2)_2-$); 1.69 & 1.71 (2t, 12H, $-CH_2C\underline{H}_3$); 2.14 (m, 4H, $-CH_2-C\underline{H}_2-(CH_2)_6-C\underline{H}_2-CH_2$); 2.26 (s, 3H, $-OCOC\underline{H}_3$); 2.54 (m, 4H, $-CH_2C\underline{H}_2CH_2CO_2CH_3$); 3.60 (s, 6H, $-C\underline{H}_3$); 3.64 (s, 6H, $-C\underline{H}_3$); 4.15 (q, overlap, 8H, $-C\underline{H}_2CH_3$); 4.20 (t, overlap, 4H, $-C\underline{H}_2-(CH_2)_8-C\underline{H}_2-$); 4.28 (t, J6Hz, 4H, $-CH_2C\underline{H}_2CH_2CO_2CH_3$); 4.47 (t, J6Hz, 4H, $-C\underline{H}_2CH_2CH_2CO_2CH_3$); 10.60, 10.63, 10.65 (4s, 8H, meso H).

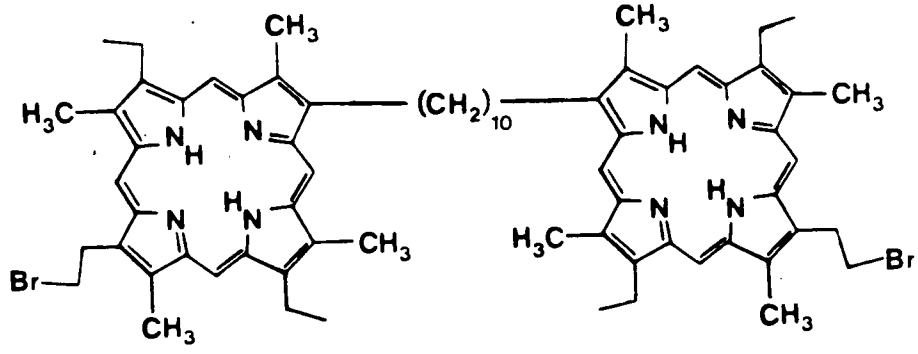
^{13}C NMR: (δ, 5% TFA/$CDCl_3$): 174.148 (2C, -COO); 144.590, 143.446, 142.508, 142.384, 142.026, 141.791, 141.529, 141.433,

140.950, 138.344, 138.220, 137.889, 137.792 (32C, α - and β- carbons); 98.632, 98.329 (4C, meso-carbons 5-, 10-, 15-, and -20C); 64.835 (2C, $-CH_2CH_2\underline{C}H_2-O-$); 32.238 (2C, chain 2', 9'C); 30.694 (2C, $-CH_2\underline{C}H_2CH_2-O-$); 29.991 (2C, chain 3', 8'C); 29.508 (2C, chain 4', 7'C); 29.439 (2C, chain 5', 6'C); 26.888 (2C, chain 1', 10'C); 23.124 (2C, $-\underline{C}H_2CH_2CH_2-O-$); 20.987 (2C, $\underline{C}H_2CO$); 20.159 (4C, $-\underline{C}H_2CH_3$); 16.243 (4C, $-CH_2\underline{C}H_3$); 11.927, 11.872, 11.721 (8C, β-CH_3).

Visible Spectrum (CH_2Cl_2):

λ_{max} (nm)	399	496	532	567	619
peak ratio	48.75	3.0	3.0	2.57	1.00

1,10-Bis{12-(3-bromopropyl)-7,17-diethyl-3,8,13,18-tetramethylporphinato zinc}-decane (181a)



Bromine (100mg, 0.63 mmole) in dichloromethane (10 mL) was added slowly with swirling to an ice cold solution of triphenylphosphite (200mg, 0.64 mmole) in dichloromethane (10 mL). 1,10-Bis{7,17-diethyl-12-(3-hydroxypropyl)-3,8,13,18-tetramethylporphin-2-yl}decane (180) (150mg, 0.14 mmole) was dissolved in the triphenylphosphite dibromide solution and stirred for 30 mins. The solution was washed with water (2 x 30 mL), sat. zinc acetate in methanol solution was added (1 mL), and the solution washed once again with water (30 mL) and with sat. sodium chloride solution (30 mL).

The solvent was removed under reduced pressure and the solid dissolved in the minimum THF diluted with dichloromethane (2 mL) and chromatographed on activity IV silica gel with dichloromethane solvent. When allowed to stand the product (120mg, 65.1%) crystallised from the dichloromethane solution; the bright orange solid was filtered, washed with dichloromethane and dried.

Anal: Calc. for $C_{72}H_{86}N_8Br_2Zn_2 2H_2O$. C, 62.21; H, 6.53; N, 8.06: Found: C, 61.80; H, 6.35; N, 8.00%.

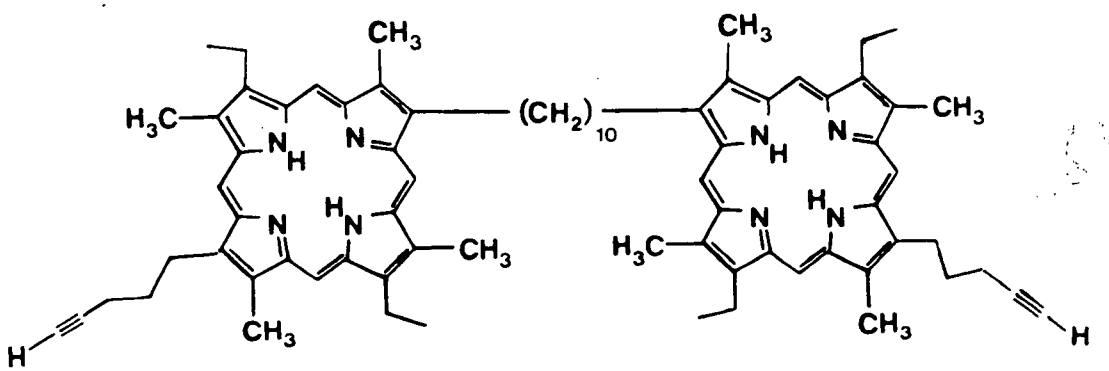
^{1}H NMR: (δ, $CDCl_3$/TFA) 1.30 (bs, 4H, $-(CH_2)_4-C\underline{H}_2C\underline{H}_2(CH_2)_4-$); 1.41 (bs, 4H, $-(CH_2)_3-C\underline{H}_2-(CH_2)_2-C\underline{H}_2(CH_2)_3-$); 1.62 (bs, 4H, $-(CH_2)_2-C\underline{H}_2-(CH_2)_4-CH_2-(CH_2)_2$); 1.72 and 1.74 (2t, J7.5Hz, 12H, $-CH_2C\underline{H}_3$); 2.09 (m, 4H, $-CH_2-C\underline{H}_2-(CH_2)_6-C\underline{H}_2-CH_2$); 2.71 (m, 4H, $-CH_2C\underline{H}_2C\underline{H}_2Br$); 3.65 (s, 12H, $-CH_3$); 3.67 (t, J7Hz, 4H, $-CH_2CH_2C\underline{H}_2Br$); 3.71 (s, 12H, $-C\underline{H}_3$); 4.11 (q, J7.5Hz, 8H, $-C\underline{H}_2CH_3$); 4.16 (t, J7.5Hz, 4H, $-C\underline{H}_2-(CH_2)_8-C\underline{H}_2-$); 4.38 (t, J7.5Hz, 4H, $-C\underline{H}_2CH_2CH_2Br$); 10.66, 10.67, 10.68 and 10.87 (4s, 8H, meso H).

^{13}C NMR (δ, 5% TFA/$CDCl_3$): 145.332, 145.271, 144.167, 142.492, 142.383, 141.958, 141.776, 141.679, 141.606, 141.449, 139.240, 138.985, 138.913, 138.524 (32C, α and β -carbons); 99.064, 98.858, 98.736 (4C, meso-carbons 5-, 10-, 15-, 20-C); 34.401, 33.126 (4C, $-CH_2\underline{C}H_2\underline{C}H_2Br$); 32.313 (2C, Chain 2', 9'C); 30.093 (2C, Chain 3', 8'C); 29.571 (2C, Chain 4', 7'C); 29.450 (2C, Chain 5', 6'); 26.914 (2C, Chain 1', 10'C); 24.596 (2C, $-\underline{C}H_2CH_2CH_2Br$); 20.191 (4C, $-\underline{C}H_2CH_3$); 16.284, 16.248 (4C, $-CH_2\underline{C}H_3$); 12.013, 11.904, 11.673 (8C, β-CH_3).

Visible Spectrum (CH_2Cl_2) :

λ_{max} (nm)	399	497	532	566	620
peak ratio	33.33	2.90	2.07	1.41	1.00

1,10-Bis{12-(pent-4-yne)-7,17-diethyl-3,8,13,18-tetramethylporphinato-zinc}-decane (182a)



The C_{10} bis-bromopropylporphinato zinc (181a) (49mg, 0.036 mmole) was dissolved in DMSO (15 mL) and treated with excess lithium acetylide ethylenediamine. The solution was left to stir at room temperature protected from moisture for 3 hours. The mixture was then poured into water (50 mL) and extracted with dichloromethane (50 mL) and THF (10 mL). The solution was washed with water (2 x 30 mL) and finally with sat. sodium chloride solution (30 mL). The solvent was removed under reduced pressure and the solid dissolved in the minimum volume of THF diluted with dichloromethane (2 mL) and chromatographed on activity IV silica gel with dichloromethane eluent.

The fast running band was collected and crystallised from dichloromethane/pet. ether to yield product (31.5mg, 70.0%).

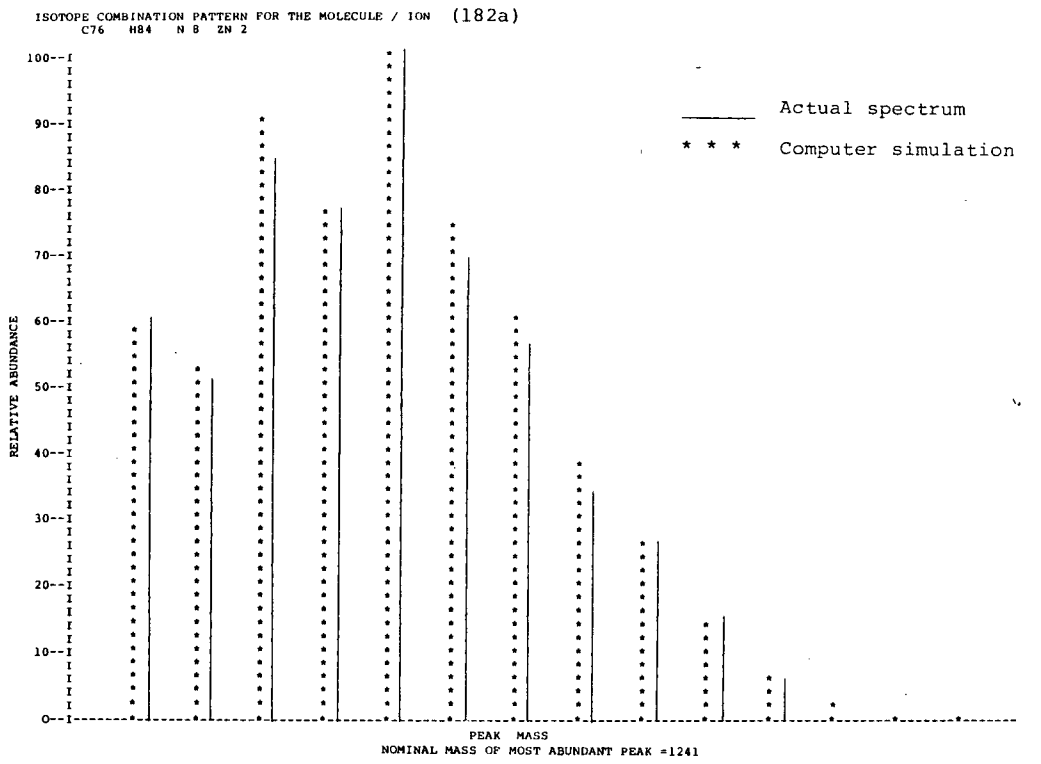
Anal: Calc. for $C_{76}H_{86}N_8Zn_2.2H_2O$: C, 71.41; H, 7.10; N, 8.77. Found: C, 71.18; H, 6.93; N, 8.14%.

^{1}H NMR: (δ, $CDCl_3$, TFA) 1.32 (bs, 4H, $-(CH_2)_4\underline{CH_2}\underline{CH_2}(CH_2)_4-$); 1.42 (bs, 4H, $-(CH_2)_3\underline{CH_2}(CH_2)_2\underline{CH_2}(CH_2)_3-$); 1.63 (bs, 4H, $-(CH_2)_2\underline{CH_2}(CH_2)_4\underline{CH_2}(CH_2)_2-$); 1.78 (t, J7.5Hz, 12H, $-CH_2\underline{CH_3}$); 2.12 (m, 4H, $-CH_2\underline{CH_2}(CH_2)_6\underline{CH_2}CH_2-$); 2.72 (m, 4H, $-CH_2\underline{CH_2}CH_2C{\equiv}CH$); 3.65 (s, 12H, $-C\underline{H_3}$); 3.71 (t, J7Hz, $CH_2CH_2\underline{CH_2}C{\equiv}CH$); 3.72 (s, 12H, $-C\underline{H_3}$); 4.09 (q, J7.5Hz, 8H, $-\underline{CH_2}CH_3$); 4.15 (t, J7.5Hz, 4H, $-\underline{CH_2}(CH_2)_8\underline{CH_2}-$); 4.45 (t, J7.5Hz, 4H, $-\underline{CH_2}CH_2CH_2C{\equiv}CH$); 10.59, 10.64, 10.65 and 10.72 (4s, 8H, meso H).

Visible Spectrum (CH_2Cl_2);

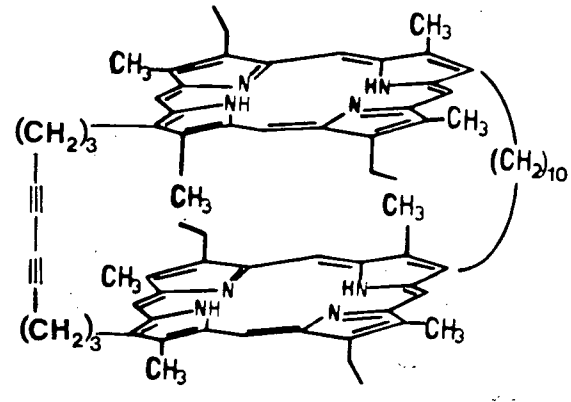
λ_{max} nm	398	495	533	565	620
peak ratio	31.43	2.70	1.95	1.30	1.00

Mass Spectrum



3.9 Synthesis of Doubly Linked Porphyrins

2,2'-Decamethylene-12,12'-deca'4,6-diynedi(7,17-diethyl-3,8,13,18-tetramethylporphinato zinc) (183a)



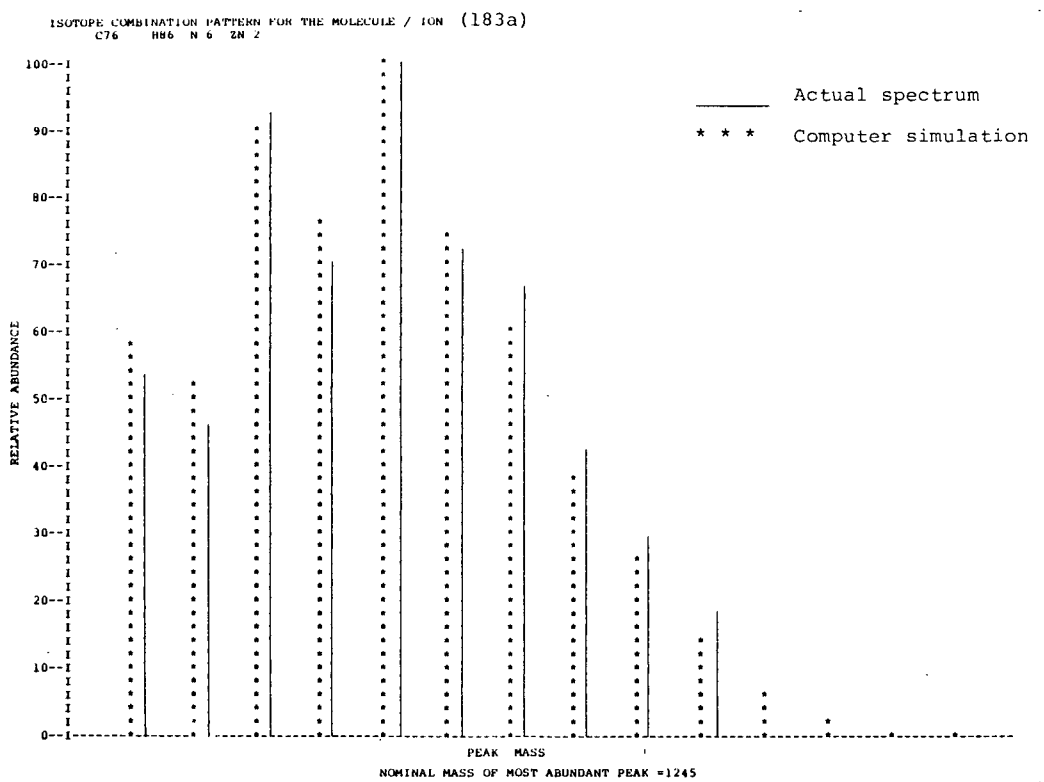
To a stirred solution of cuprous chloride (0.1g, 1.0 mmole) in methanol (80 mL) and pyridine (80 mL) was added a solution of bis-1,10{7,17-diethyl-3,8,13,18-tetramethyl-12(pent-4-yne) porphinatozinc-2-yl} decane (182a) (25mg, 0.02 mmole) in THF (50 mL) over a seven hour period using a syringe pump. The solution was washed with water (3 x 100 mL) and sat. sodium chloride solution (100 mL). The organic phase was evaporated under reduced pressure, and the solid dissolved in dichloromethane and chromatographed on activity IV silica gel with dichloromethane as eluent. The first fast moving band was starting material (12mg); the second slower band was eluted with 2% methanol/dichloromethane. The solvent was removed under reduced pressure and product (1mg, 4%) obtained as a dark red solid.

^{1}H NMR: (270 MHz): (δ, $CDCl_3$/TFA) 1.05, 1.14 and 1.30 (3bs, 12H, $(CH_2)_2(C\underline{H}_2)_6(CH_2)_2$); 1.38 (2t, 12H, $CH_2C\underline{H}_3$); 1.68 (m, 4H, $CH_2C\underline{H}_2(CH_2)_6C\underline{H}_2CH_2$); 1.94 (2m, 8H, $C\underline{H}_2C\underline{H}_2C$ $CC\underline{H}_2C\underline{H}_2$); 2.91 (s, 12H, CH_3); 2.95 (2s, 12H, CH_3); 3.30 (m, 12H, CH_3); 3.44 (m, 4H, $C\underline{H}_2(CH_2)_2C$ $C(CH_2)_2C\underline{H}_2$); 8.52 (4s, 8H, meso H).

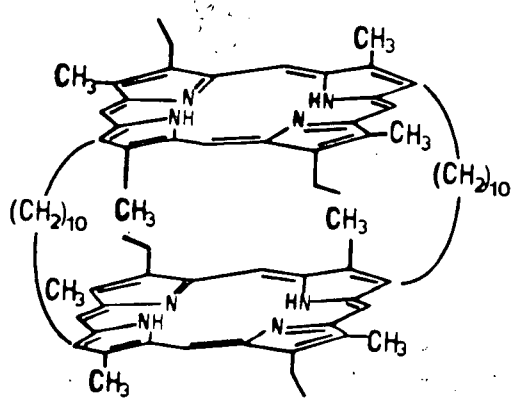
Visible Spectrum (CH_2Cl_2) :

λ_{max} (nm)	399	(378)	500	535	594	622
peak ratio	31.42	shoulder	3.16	2.25	1.69	1.00

Mass Spectrum



2,2',12,12'-Bisdecamethylenedi-(7,17-diethyl-3,13,18-tetramethylporphin) (185)



Method A.

Cyclohexene (2 mL) was added to a solution of 1,10-bis(5'-bromo-5-bromomethyl-3'-ethyl-3,4'-dimethyldipyrromethene-4-yl) decane dihydrobromide (159) (0.53g, 0.5 mmole) in dry dichloromethene (100 mL) and the solution evaporated to dryness under reduced pressure. The resultant solid and 1,10-bis-(3'ethyl-3,4',5-trimethyldipyrromethene-4-yl)decane dihydrobromide (140) (0.364g, 0.5 mmole) were dissolved in dry dichloromethane (1,400 mL) and added dropwise to a stirring solution of stannic chloride (25 mL) in dry dichloromethane (500 mL) over a period of 6 hours. When the addition was complete the solution was left for a further 1 hour before being quenched with 48% hydrobromic acid (25 mL) and washed with water (3 x 500 mL). To ensure complete removal of the tin, the solution was further treated with TFA (10 mL) and washed with water (500 mL). The solution was reduced in volume (approximately 150 mL), DMSO (200 mL) and pyridine (20 mL) were added and the solution left to stand open to the air for 5 days.

The porphyrin was filtered, washed with methanol and dried. The porphyrin was then dissolved in dichloromethane, filtered to remove polymeric material and chromatographed on activity IV silica gel with 5% ethyl acetate/dichloromehtane as eluent. The product (31mg, 5.5%) was recrystallised from dichloromethane/pet/ether.

Method B.

A solution of 2,2'-decamethylene-12,12'-deca-4,6-diynedi (7,17-diethyl-3,8,13,18-tetramethylporphinato zinc) (183a) (10mg, 0.008 mmole) in formic acid (5mL) and THF (2 mL) was hydrogenated over palladium oxide for 6 hours. The solution was extracted with dichloromethane (30 mL), washed with water (30 mL), treated with zinc acetate.methanol solution and washed again with water (30 mL x 2) and with sat. sodium chloride solution. The solvent was removed under reduced pressure and the solid chromatographed on activity IV silica gel with dichloromethane eluent. The product (~0.5mg, 5%), obtained by removing the solvent on a vacuum pump overnight, was shown to be identical to the product from method A by tlc, having a much larger R_f than the starting material, mass spectra, visible spectra and ^1H NMR.

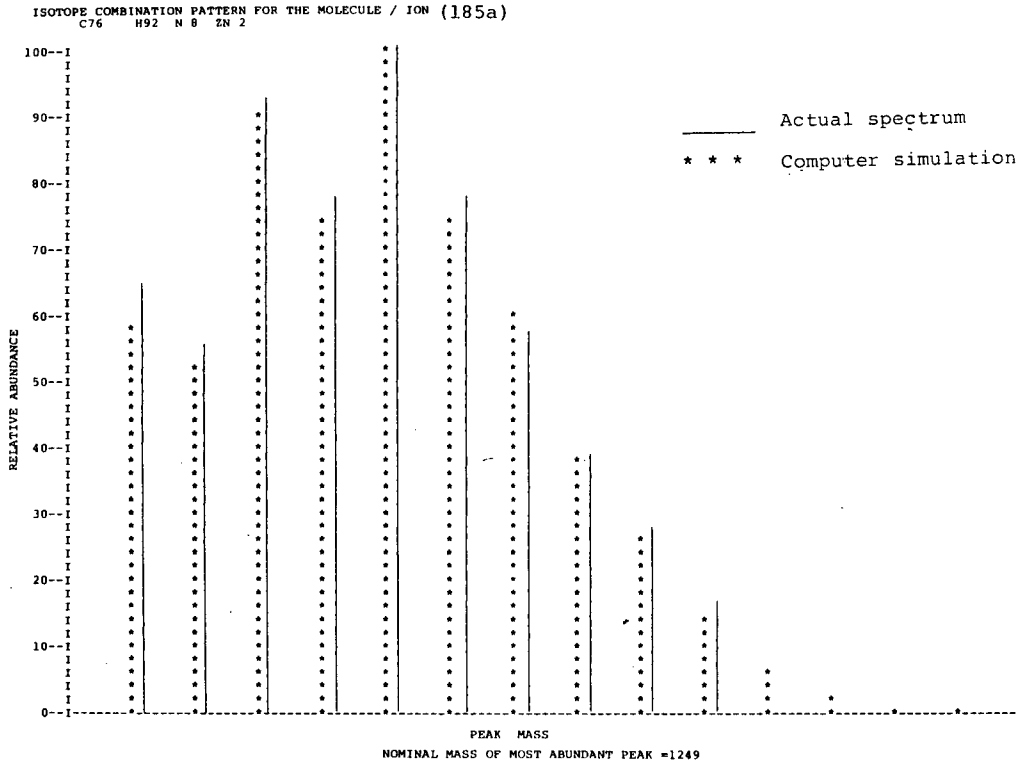
Anal: Calc. for $C_{76}H_{92}N_8Zn_2$: C, 73.12; H, 7.43; N, 8.98; Found: C, 72.85; H, 7.40; N, 8.69%.

^{1}H NMR: (400 MHz) (δ,$CDCl_3$/TFA) -4.93 (bs, 2H, N$\underline{H}$); -4.45 (bs, 2H, N$\underline{H}$); 0.59, 0.69 and 8.95 (3bs, 24H, $(CH_2)_2(C\underline{H}_2)_6(CH_2)_2$); 1.47 (bs, 8H, $CH_2C\underline{H}_2(CH_2)_6C\underline{H}_2CH_2$); 1.63 (t, J8Hz, 12H, $CH_2C\underline{H}_3$); 3.49 (s, 12H, CH_3); 3.55 (s, 12H, CH_3); 4.03 (m, 16H, overlap $C\underline{H}_2CH_3$ and $C\underline{H}_2(CH_2)_8C\underline{H}_2$); 10.47 (s, 4H, meso $\underline{H}$); 10.51 (s, 4H, meso $\underline{H}$).

Visible Spectrum (CH_2Cl_2) :

λ_{max} (nm)	390	(382)	500	532	568	621
peak ratio	31.86	shoulder	3.02	2.05	1.49	1.00

Mass Spectrum



CHAPTER 4

SPECTRAL DATA

4.1 ^{1}H NMR Spectra

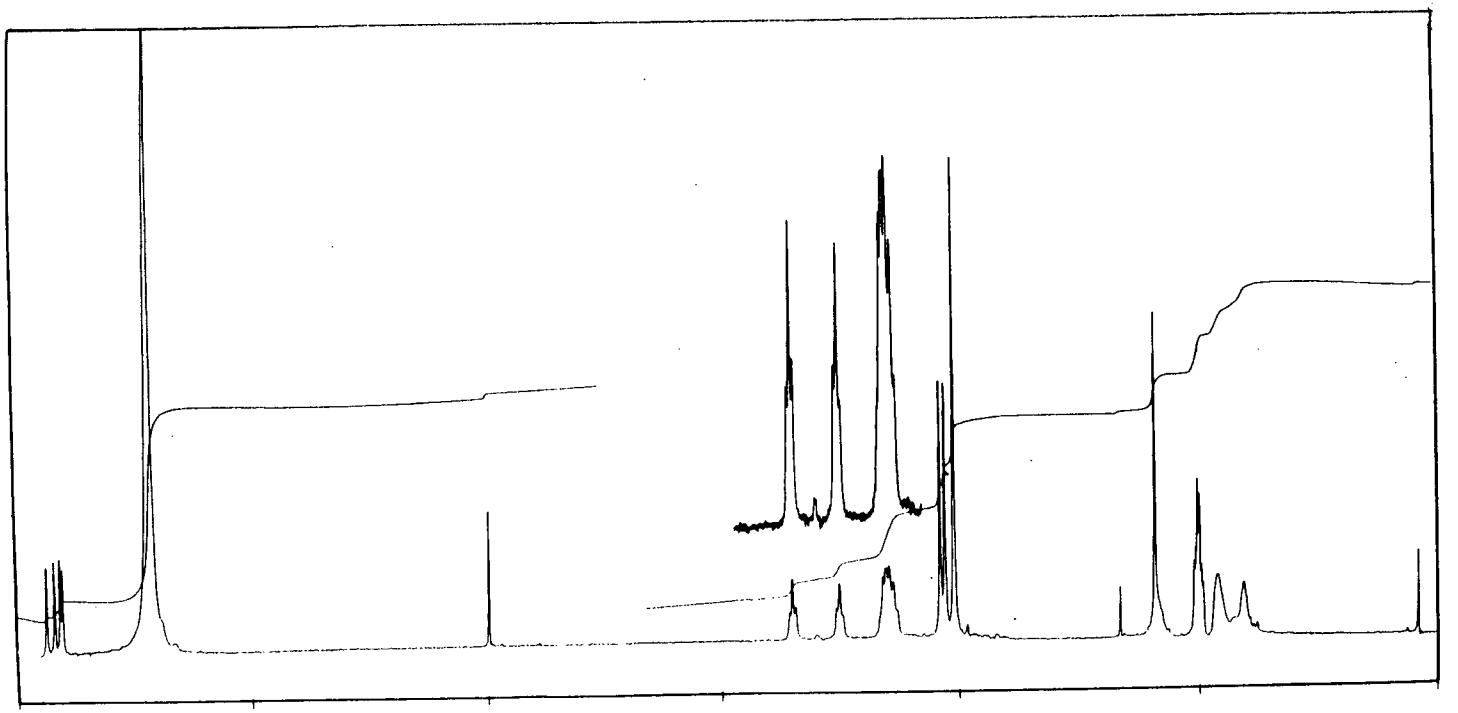


FIGURE 28: 270 MHz ^{1}H NMR Spectrum of (169)

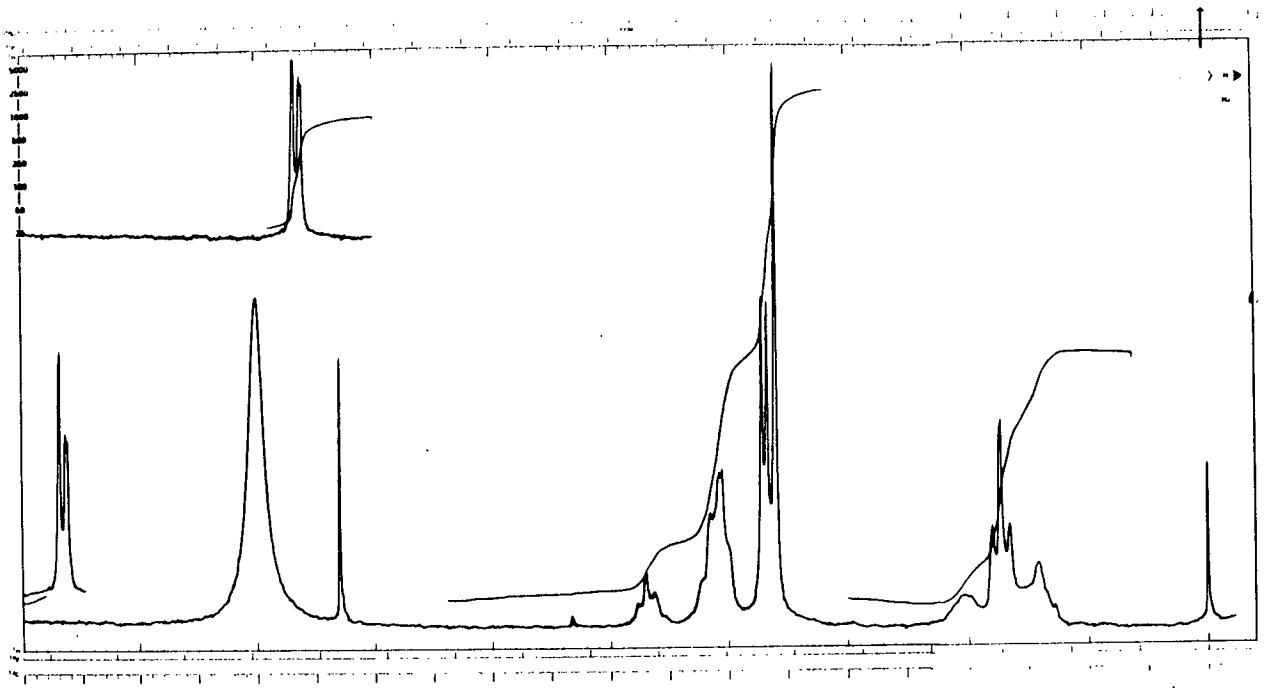


FIGURE 29: 100 MHz ^{1}H NMR Spectrum of (170)

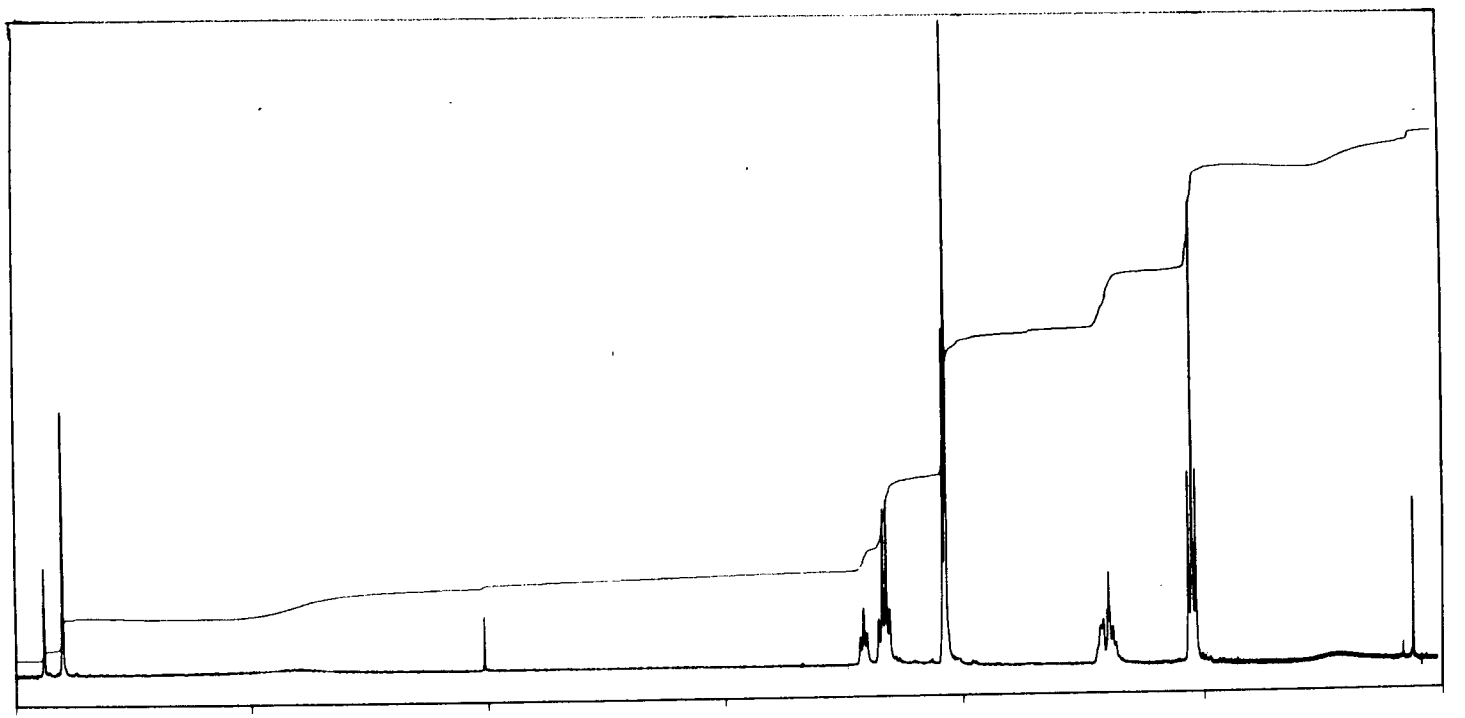


FIGURE 30: 270 MHz ^{1}H NMR Spectrum of (171)

FIGURE 31: 400 MHz ^{1}H NMR Spectrum of (172)

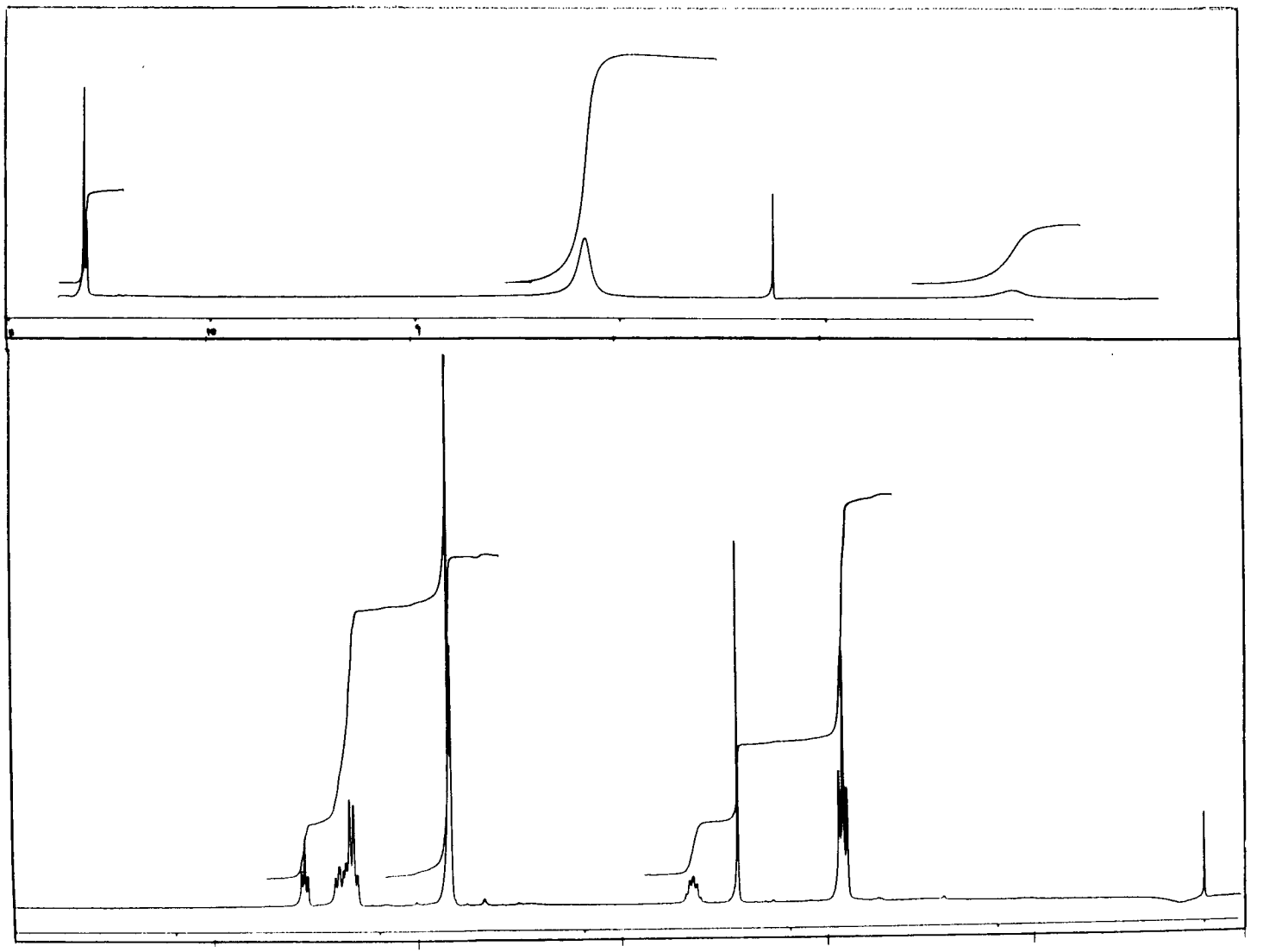


FIGURE 32: 400 MHz ^{1}H NMR Spectrum of (173)

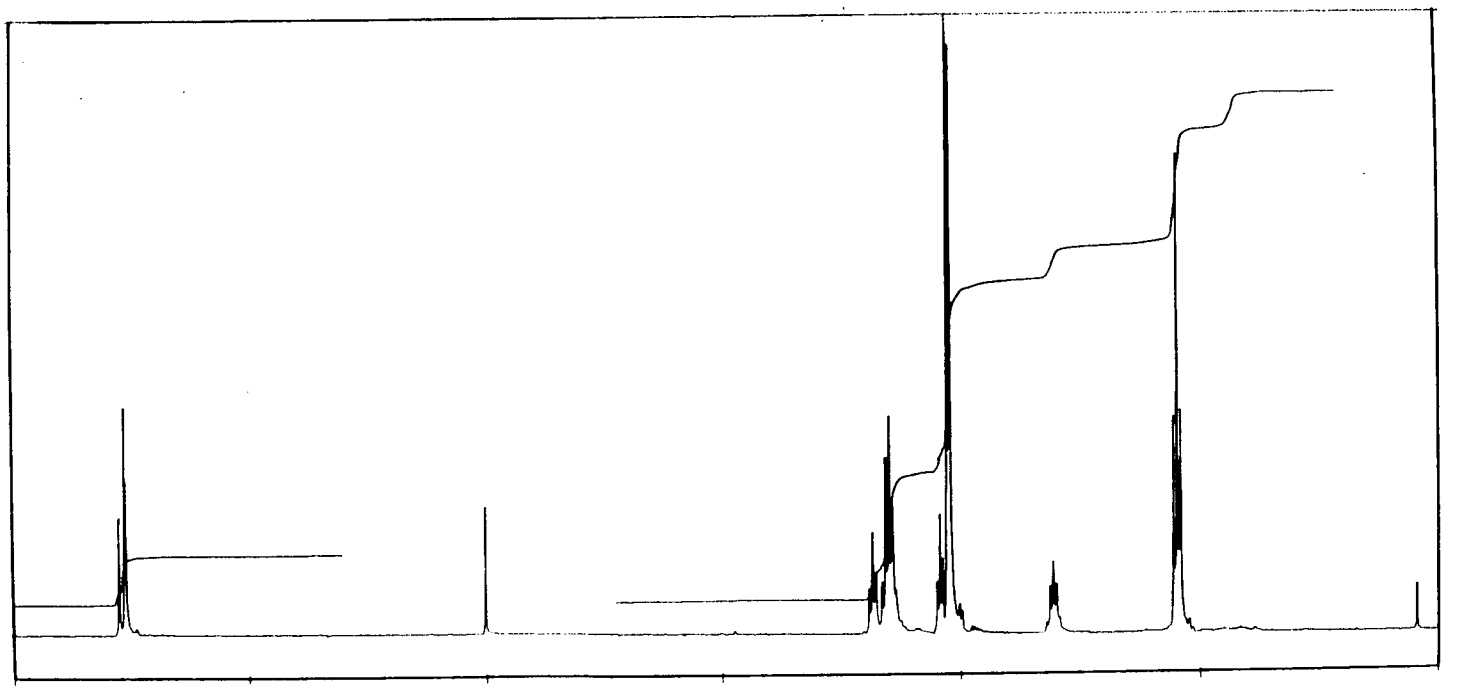


FIGURE 33: 270 MHz ^{1}H NMR Spectrum of (175)

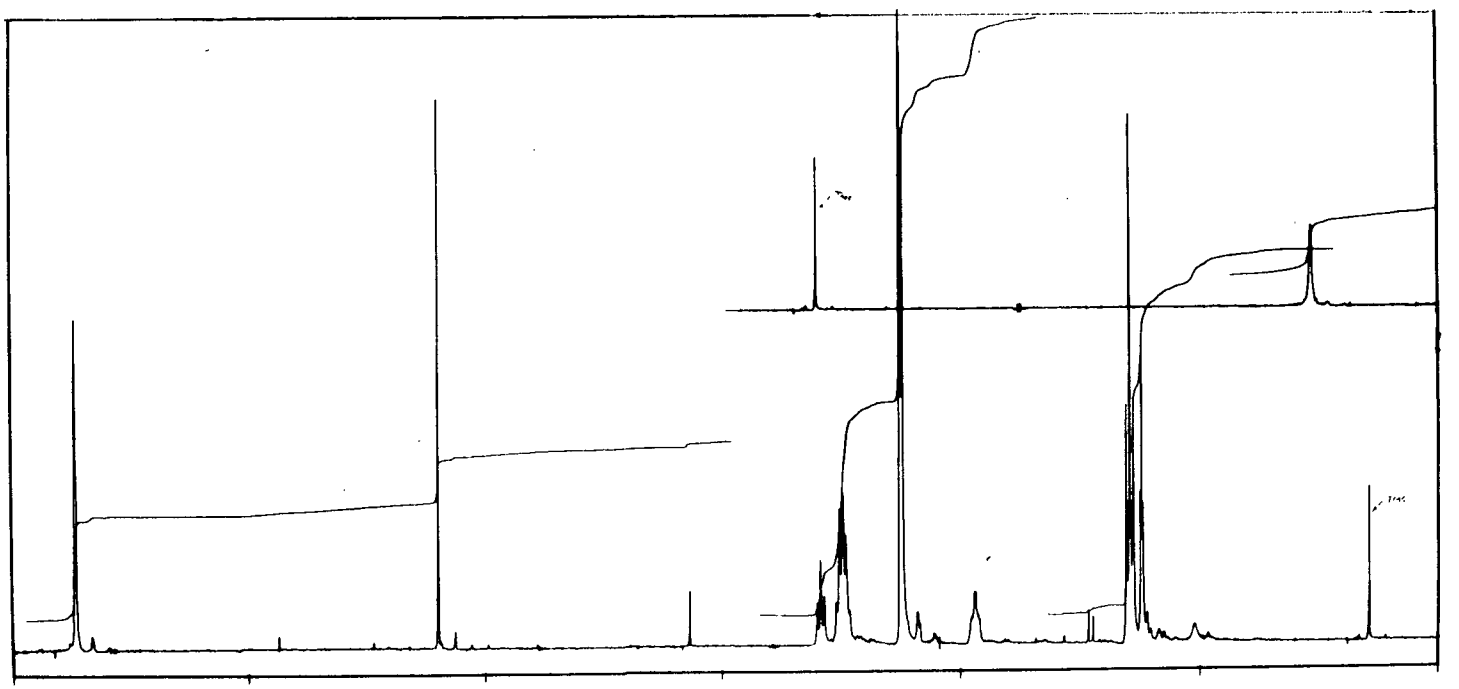


FIGURE 34: 270 MHz ^{1}H NMR Spectrum of (176)

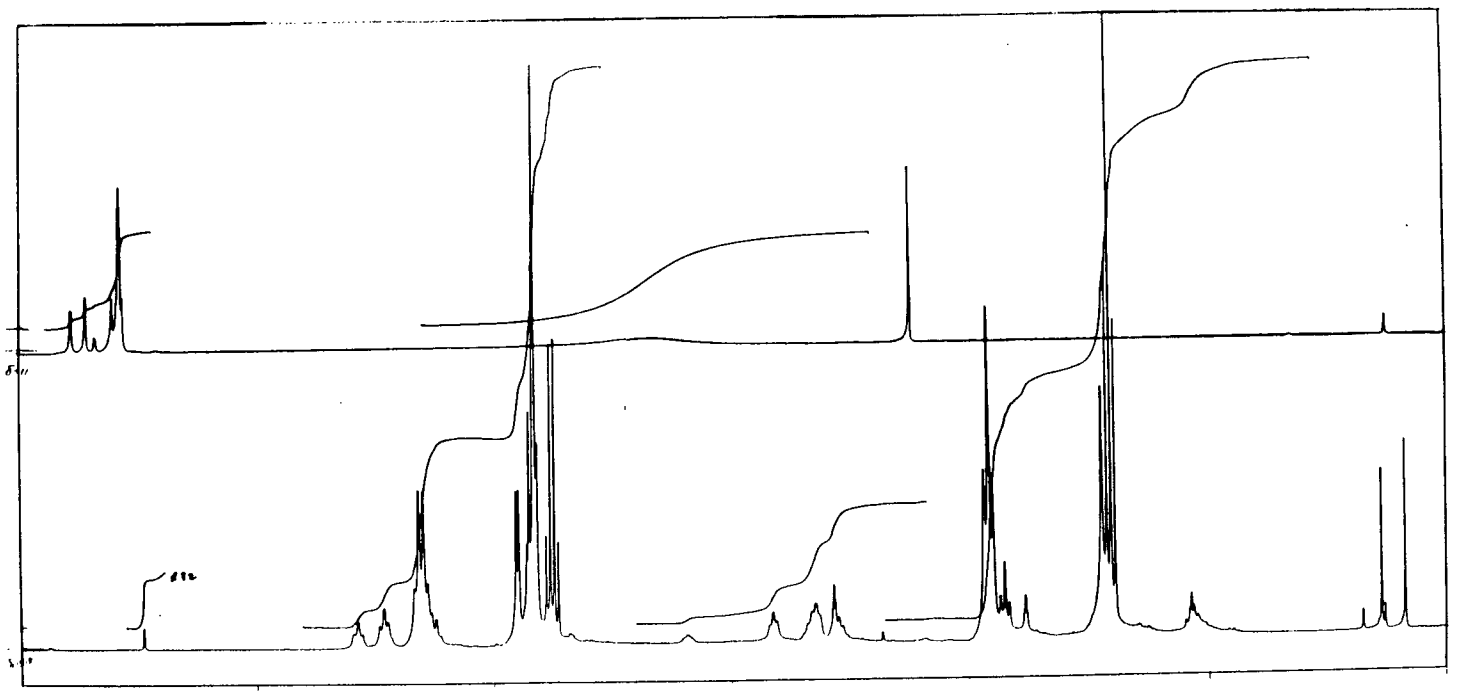


FIGURE 35: 400 MHz ^{1}H NMR Spectrum of (177)

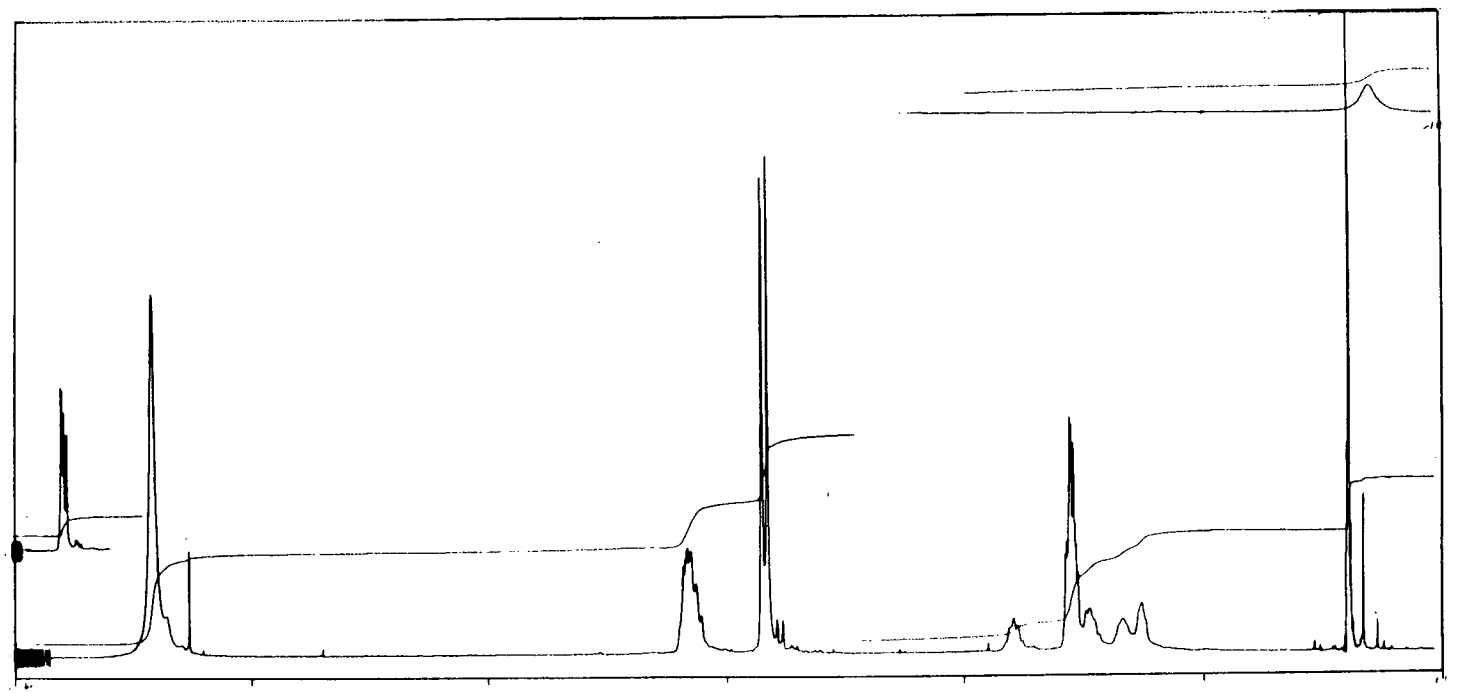


FIGURE 36: 270 MHz ^{1}H NMR Spectrum of (178)

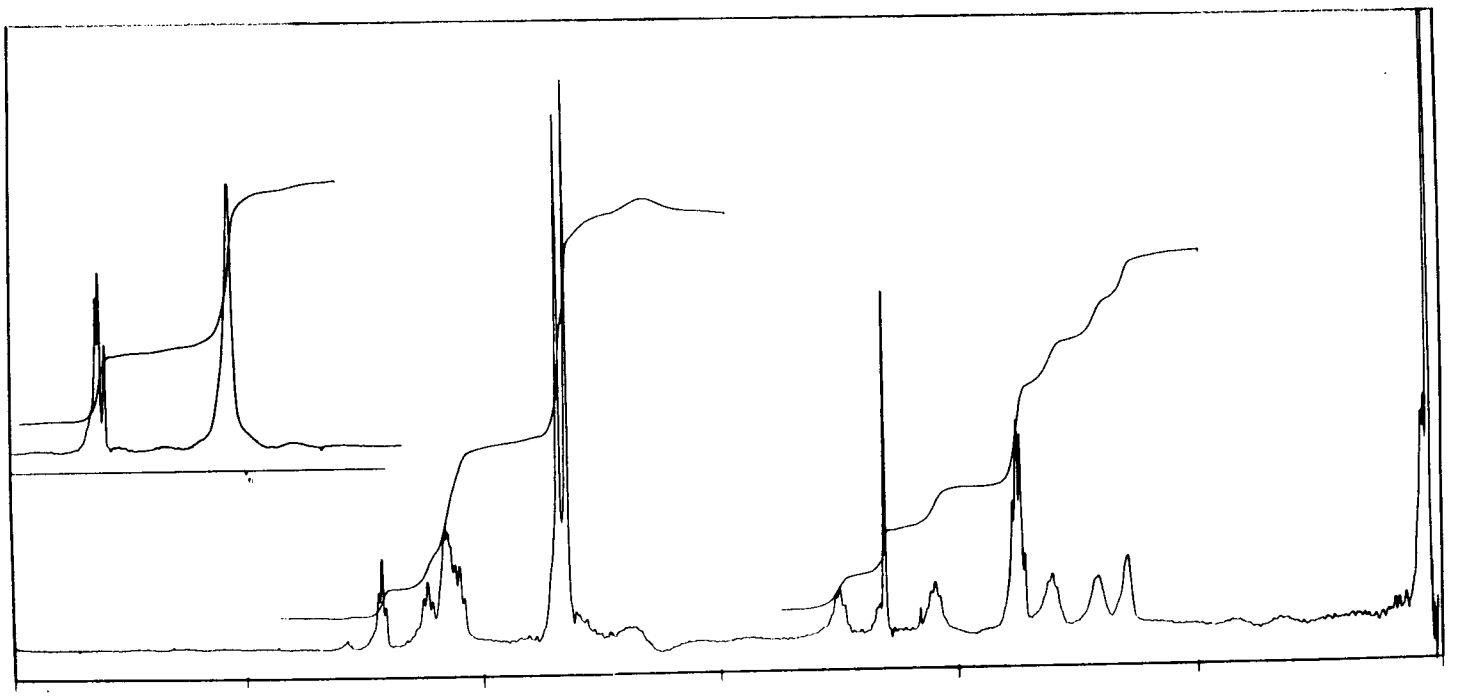


FIGURE 37: 400 MHz ^{1}H NMR Spectrum of (179)

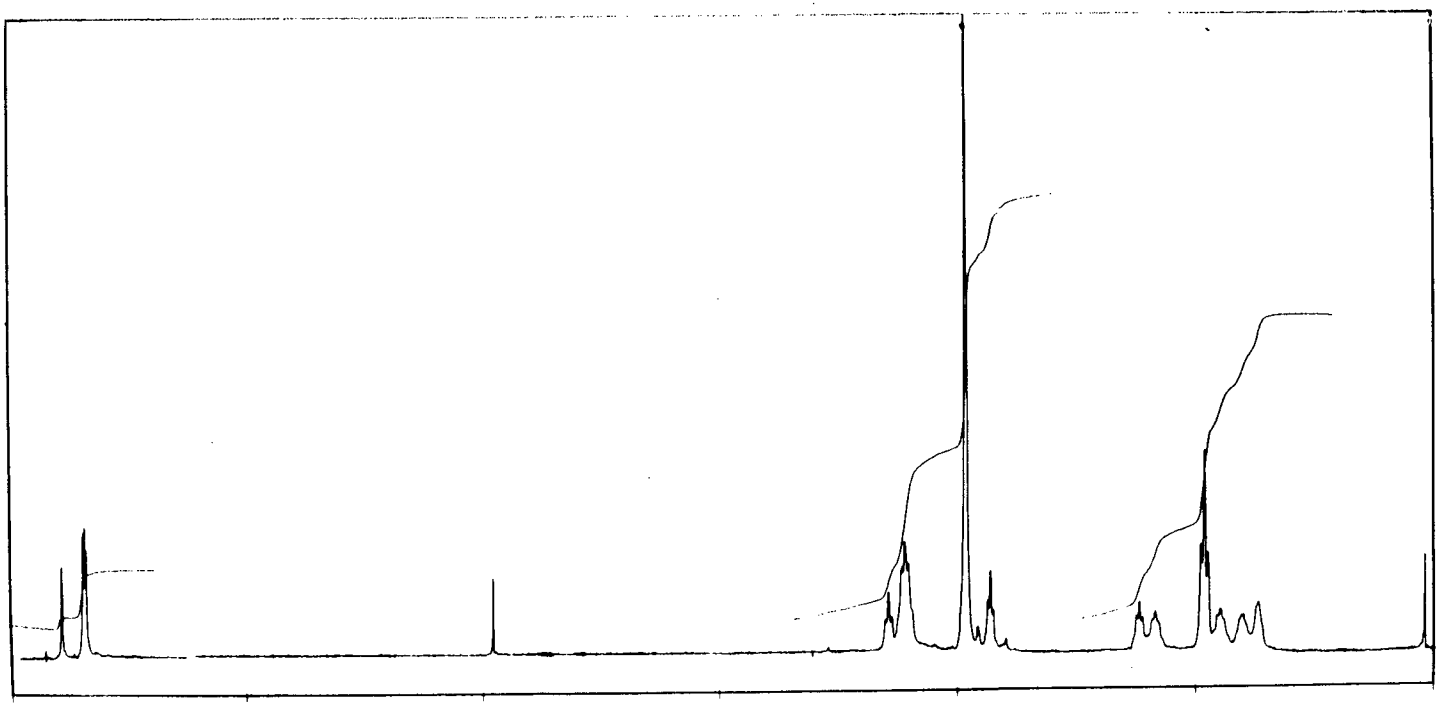


FIGURE 38: 270 MHz ^{1}H NMR Spectrum of (180)

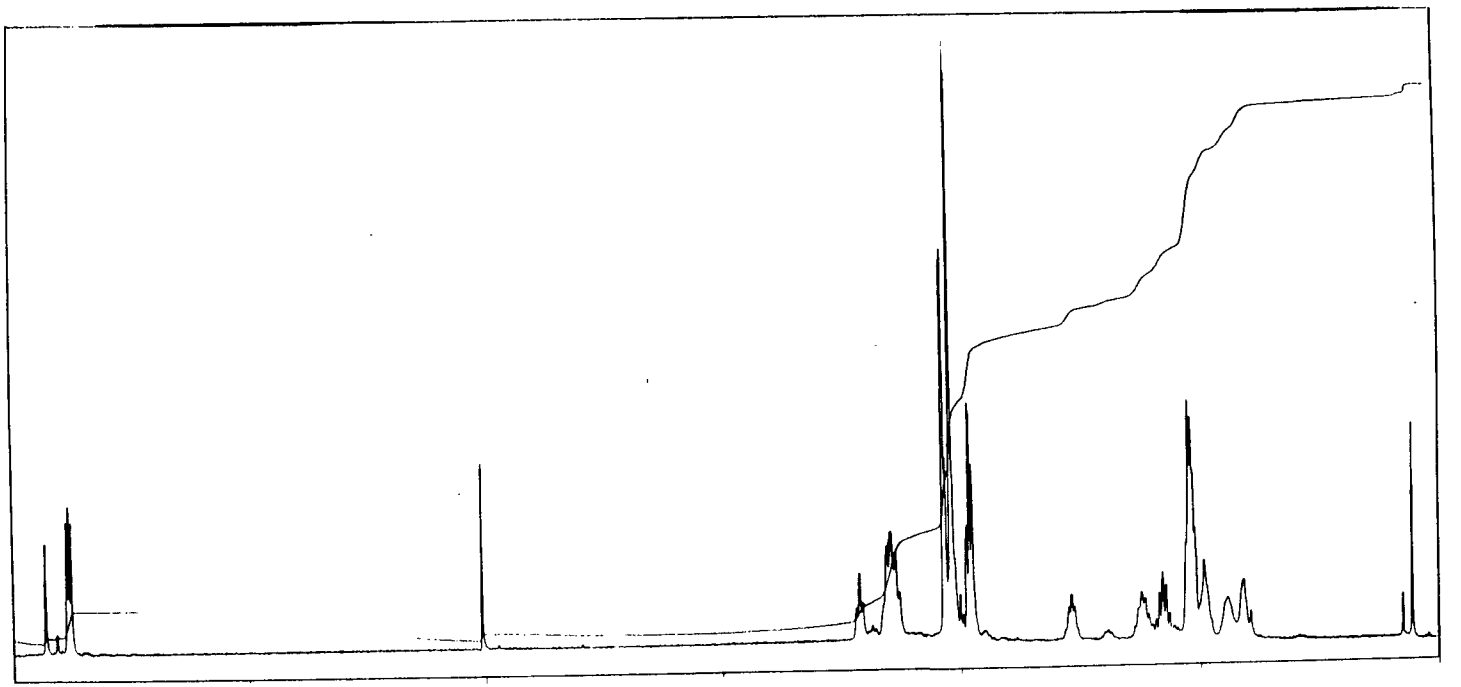


FIGURE 39: 270 MHz ^{1}H NMR Spectrum of (181)

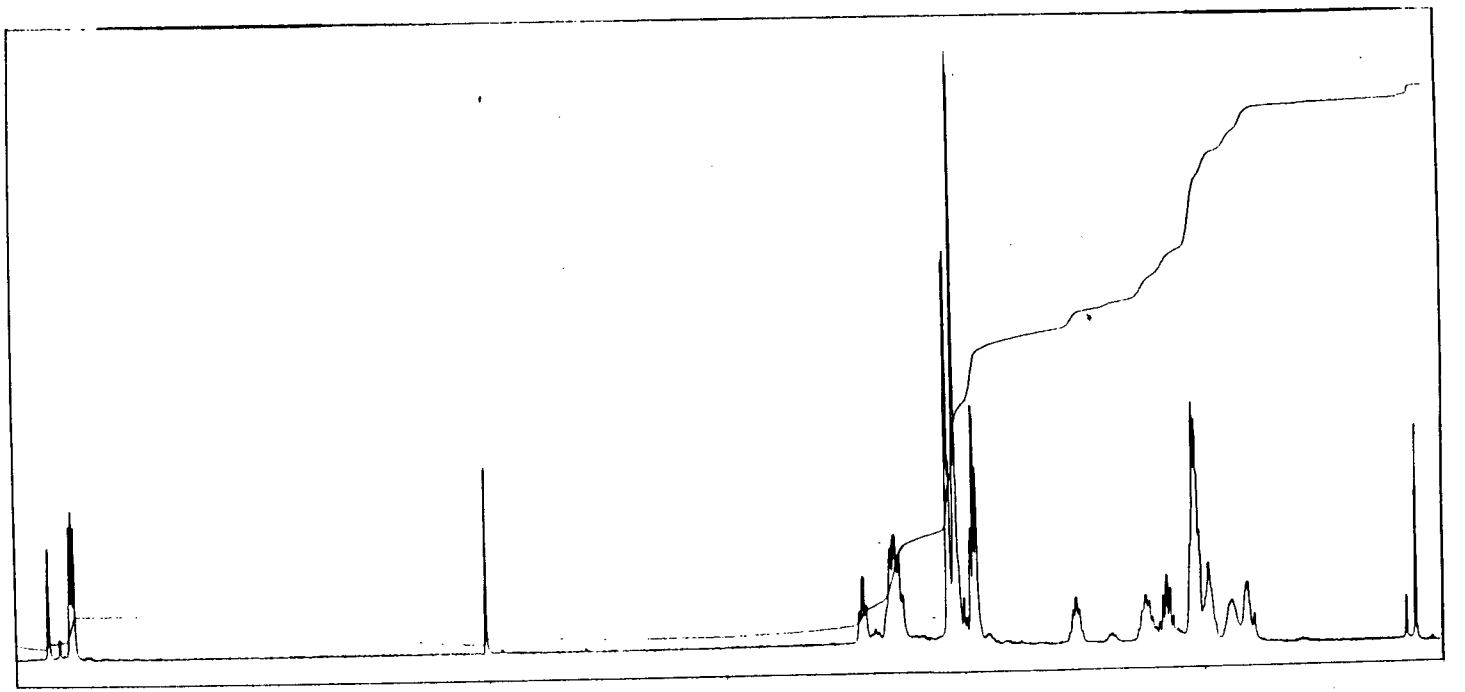


FIGURE 40: 270 MHz ^{1}H NMR Spectrum of (182)

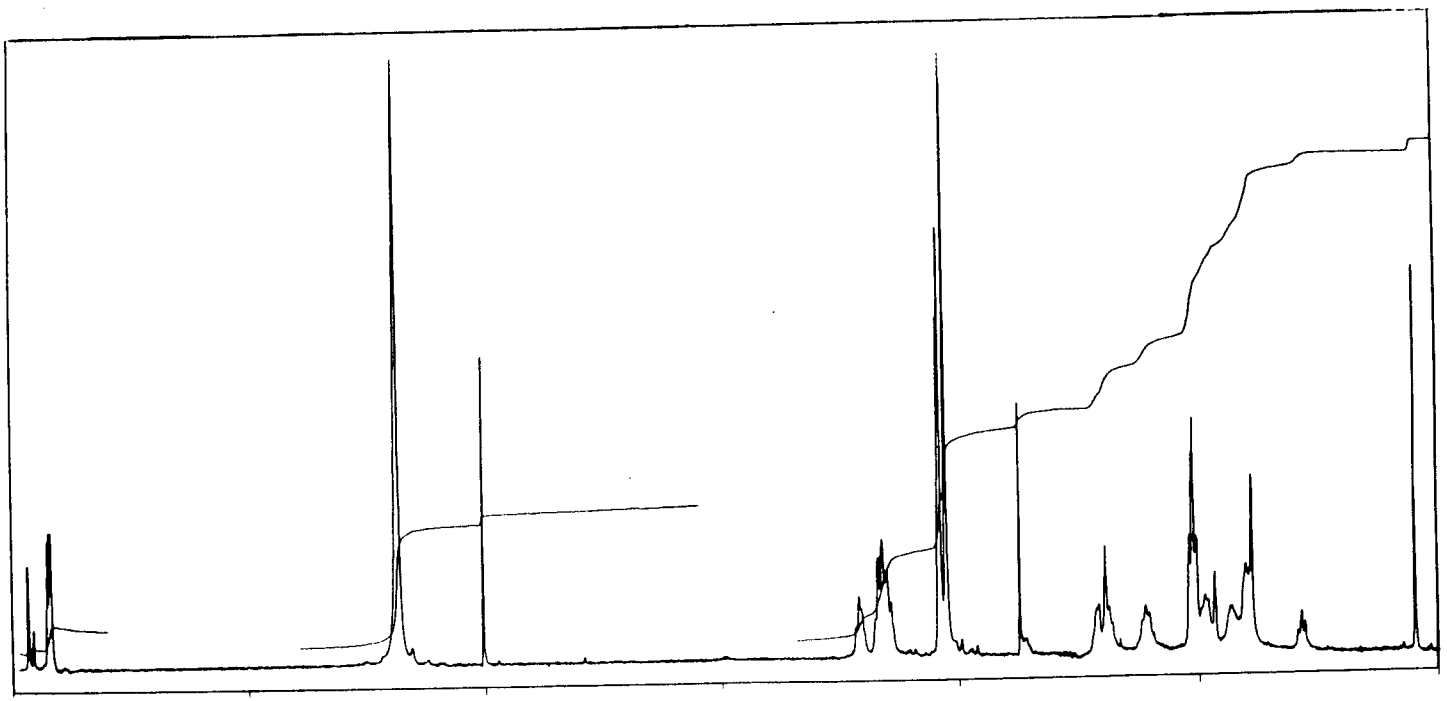


FIGURE 41: 270 MHz ^{1}H NMR Spectrum of (183)

FIGURE 42: 400 MHz ^{1}H NMR Spectrum of (185)

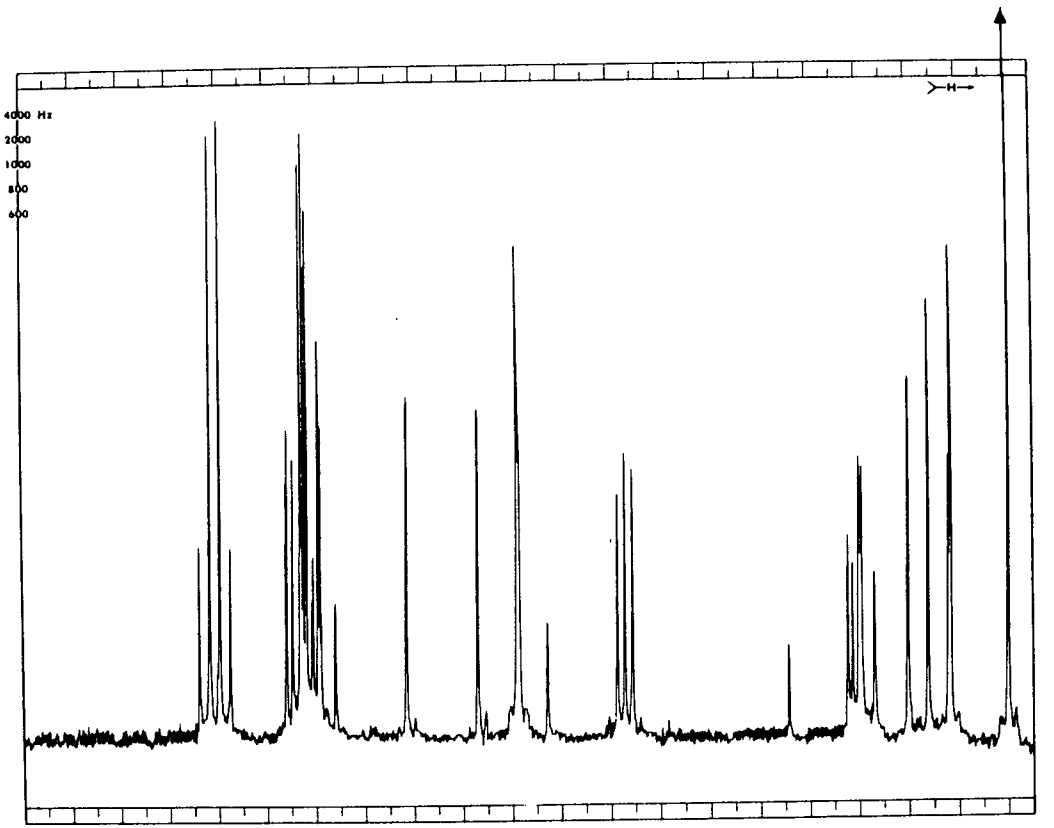


FIGURE 43: 20 MHz ^{13}C NMR Spectrum of (168)

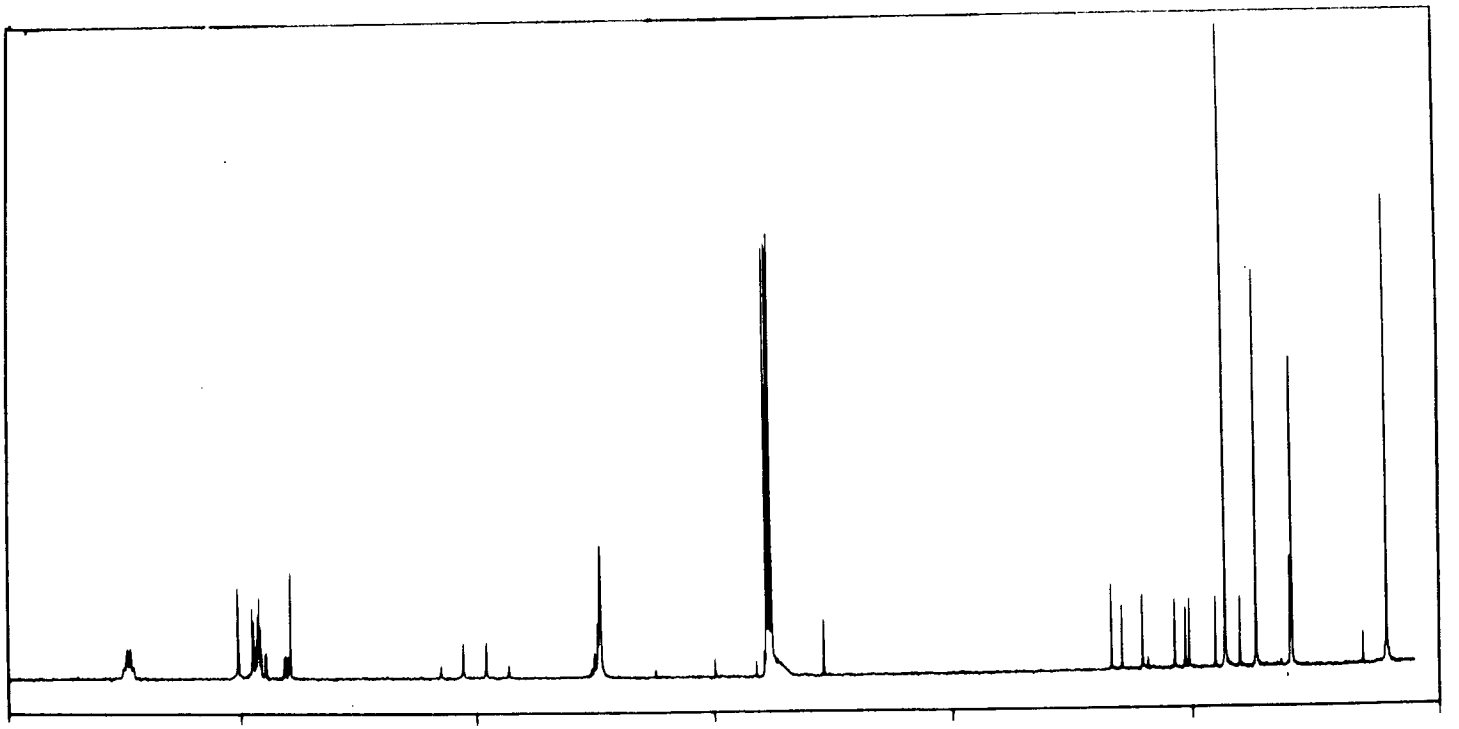


FIGURE 44: 100.6 MHz ^{13}C NMR Spectrum of (171)

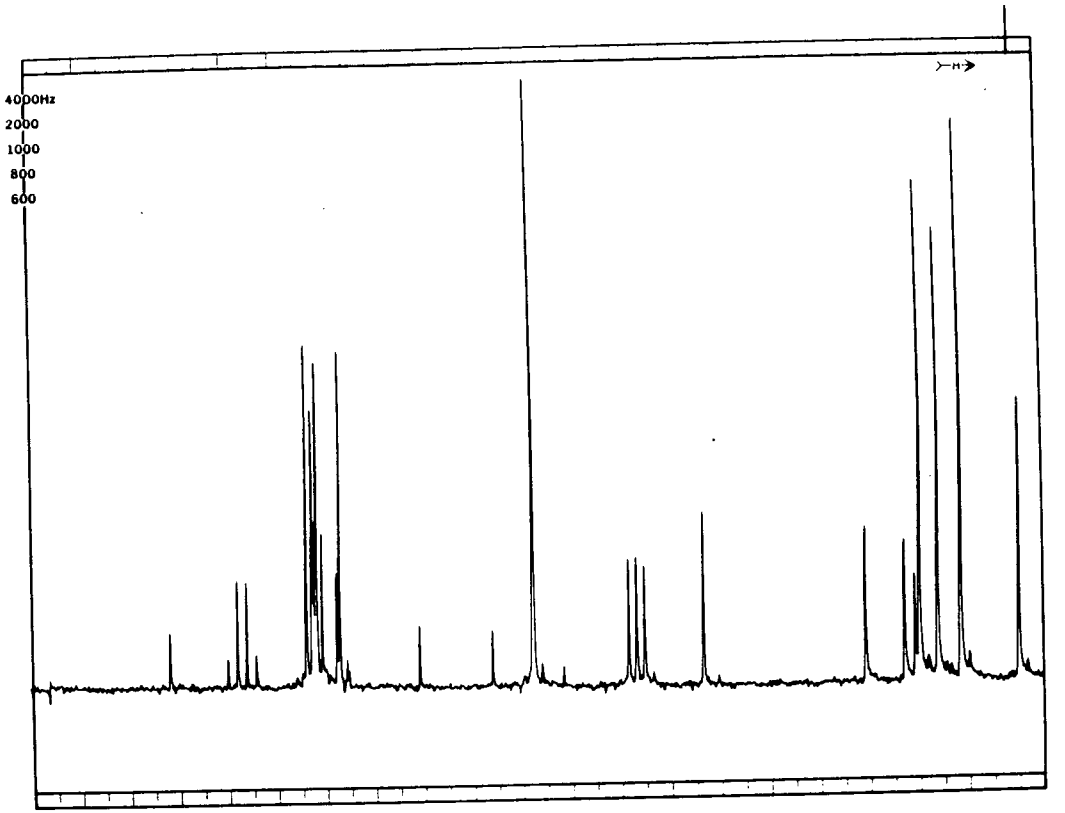


FIGURE 45: 20 MHz ^{13}C NMR Spectrum of (172)

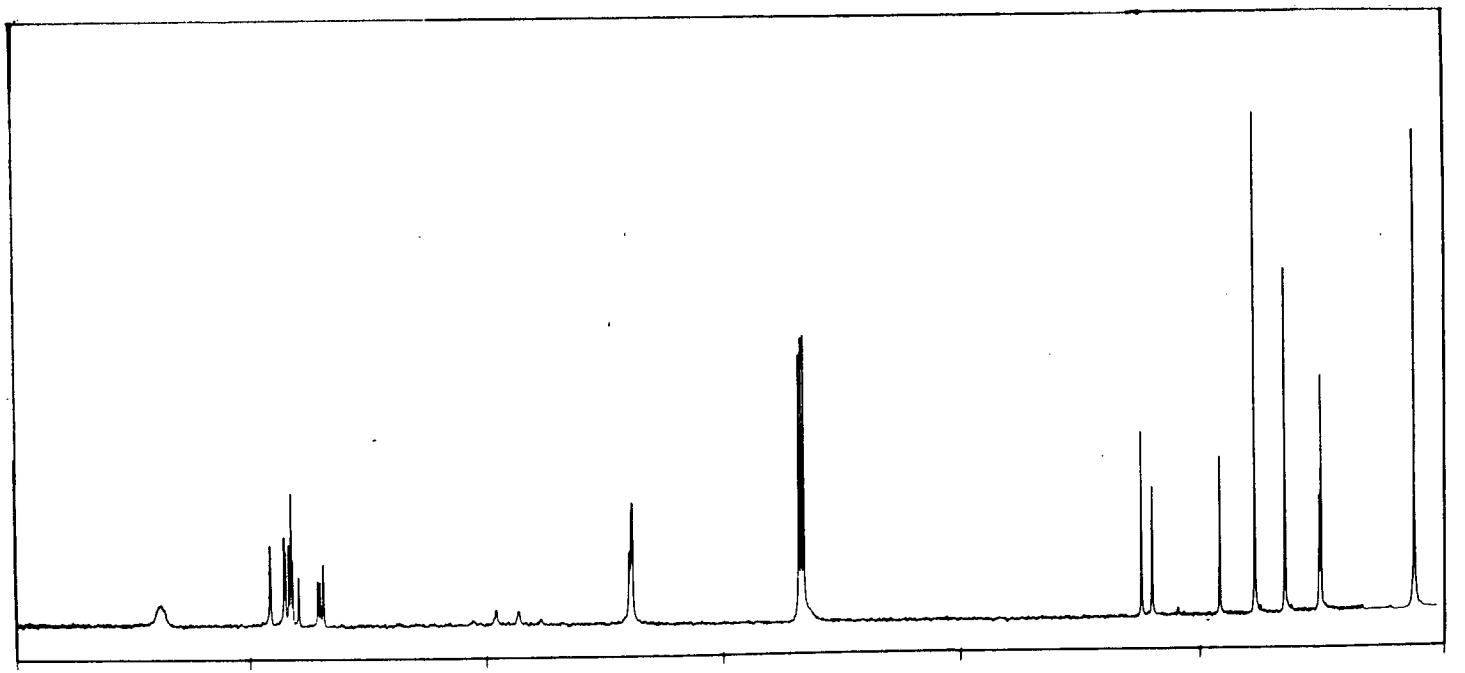


FIGURE 46: 100.6 ^{13}C NMR Spectrum of (173)

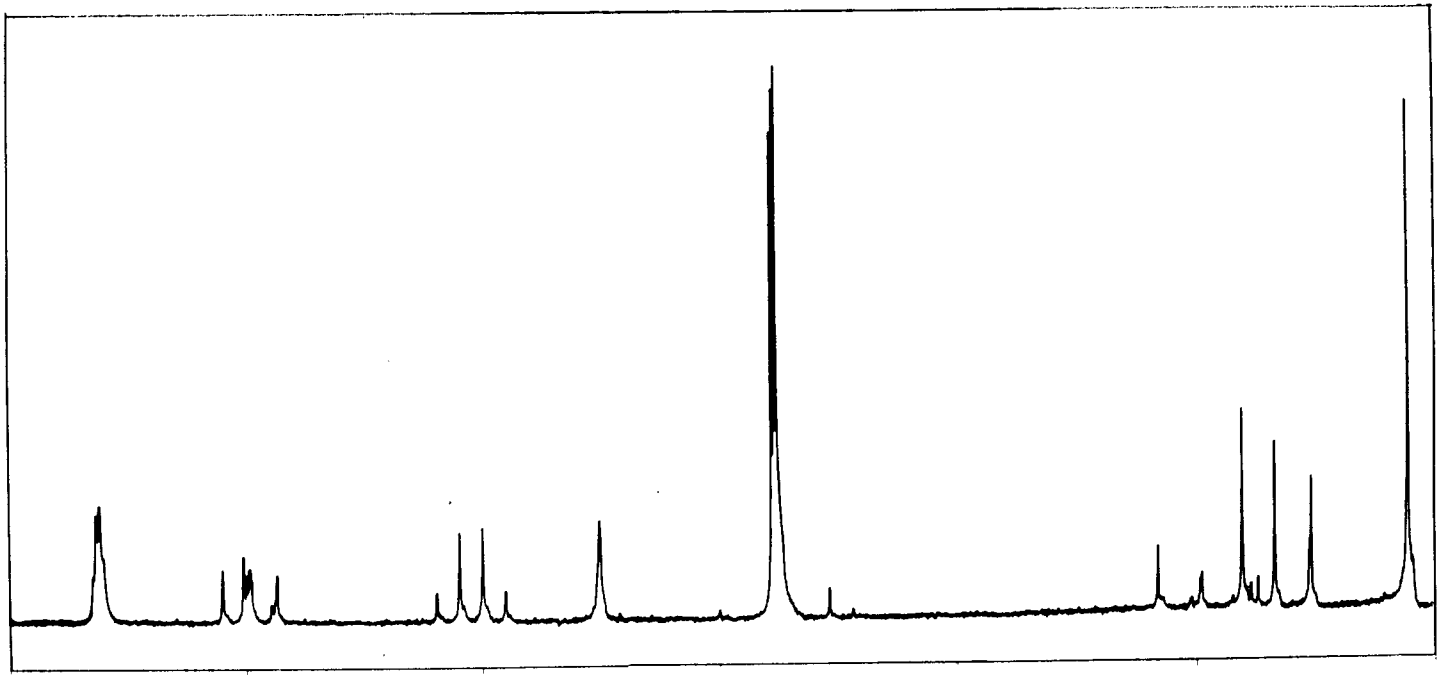


FIGURE 47: 100.6 MHz ^{13}C NMR Spectrum of (177)

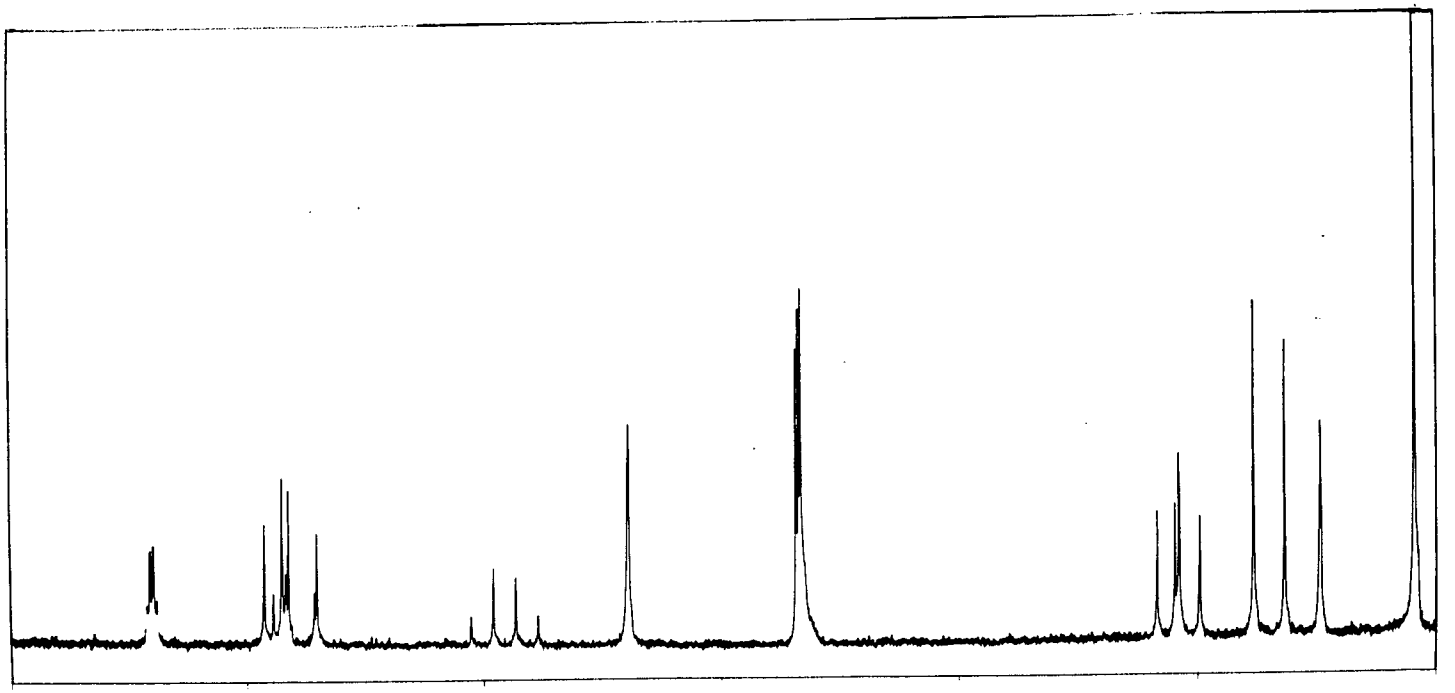


FIGURE 48: 100.6 MHz ^{13}C NMR Spectrum of (178)

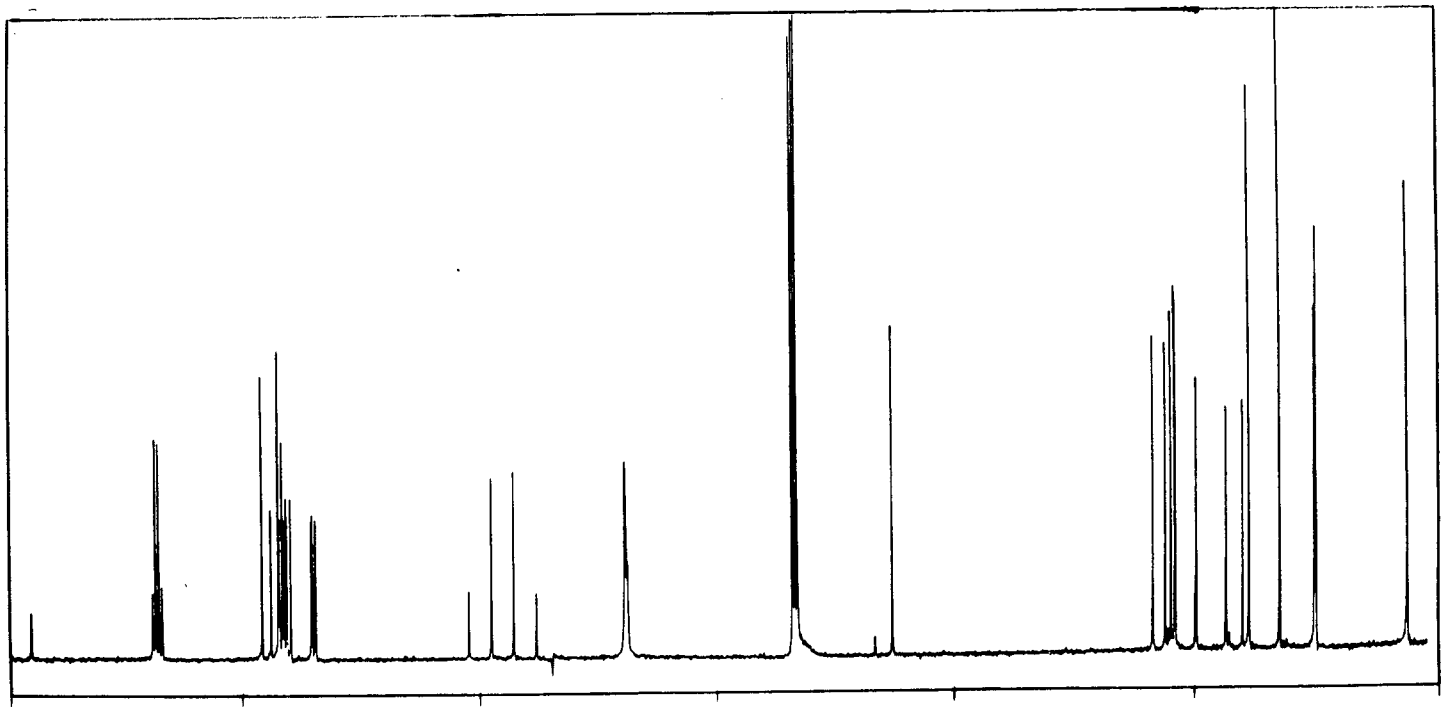


FIGURE 49: 100.6 MHz ^{13}C NMR Spectrum of (179)

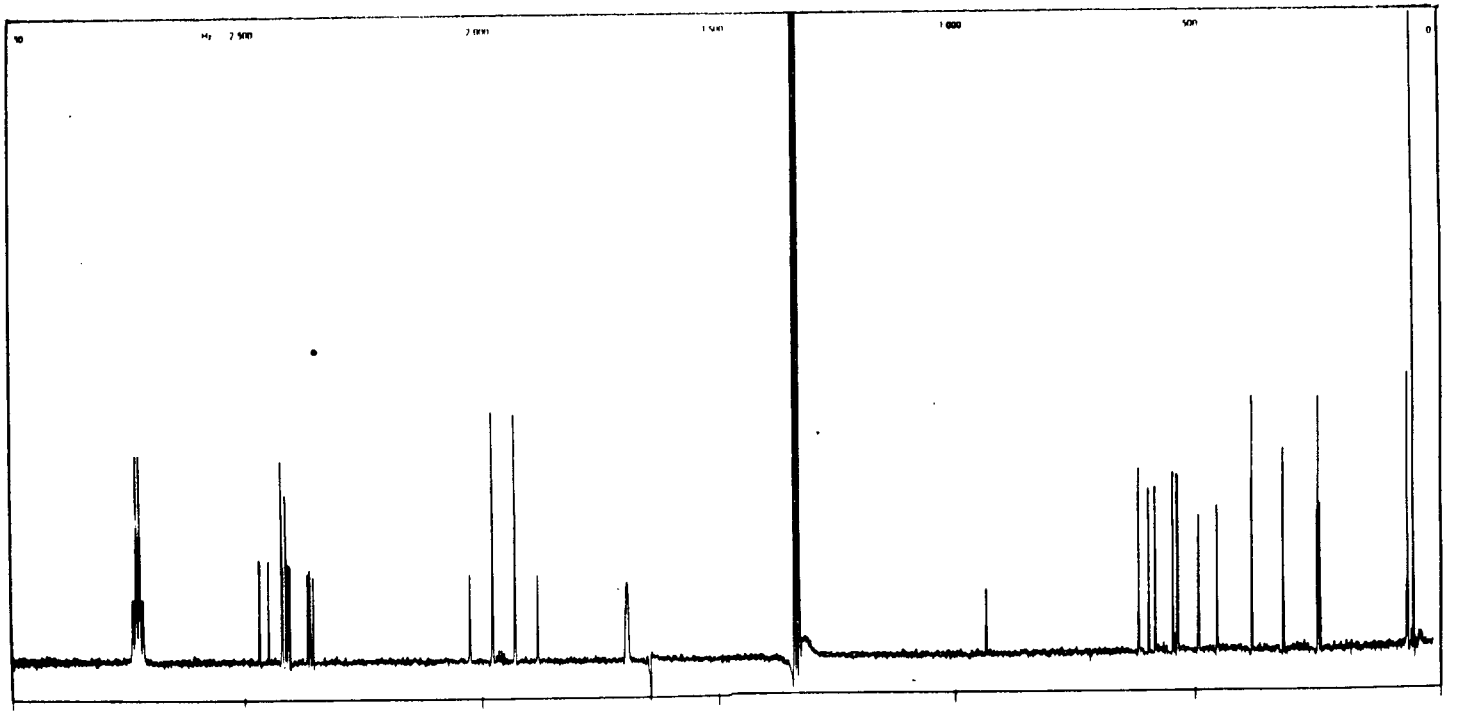


FIGURE 50: 100.6 MHz ^{13}C NMR Spectrum of (181)

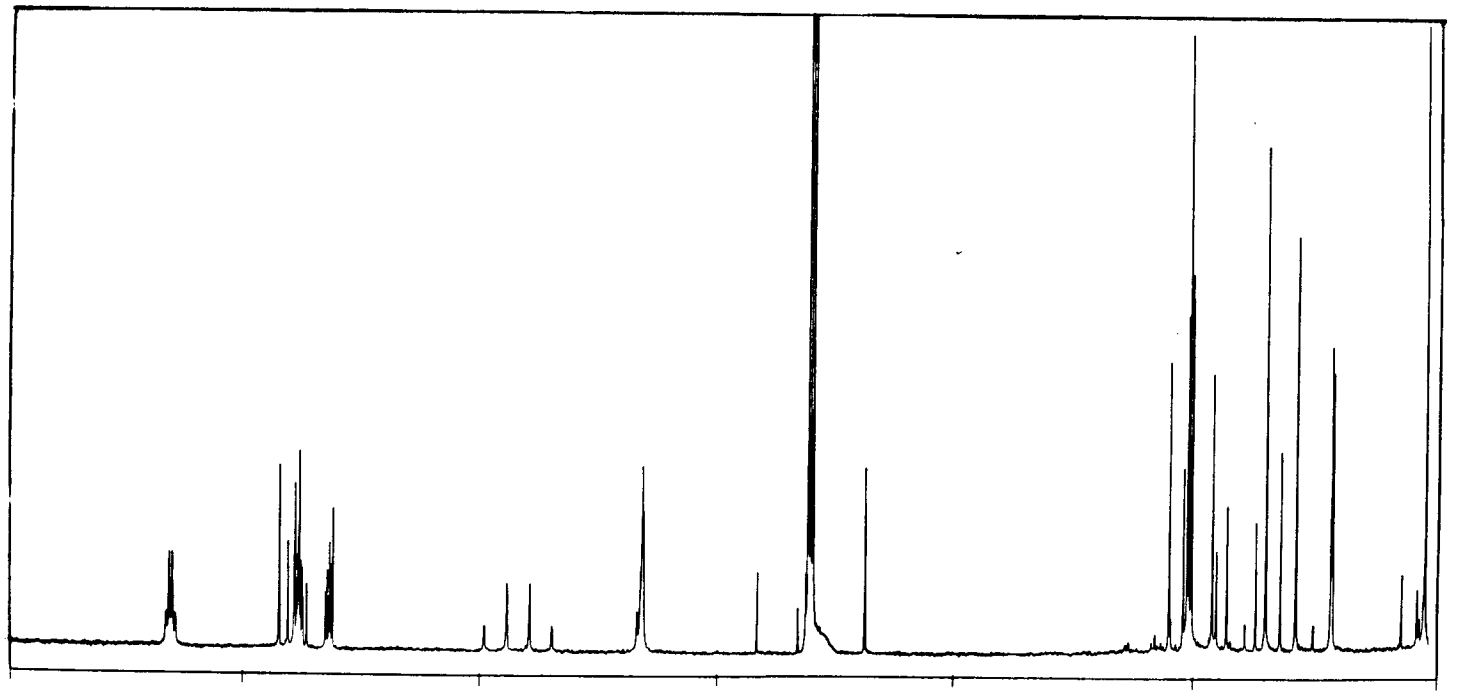


FIGURE 51: 100.6 MHz ^{13}C NMR Spectrum of (182)

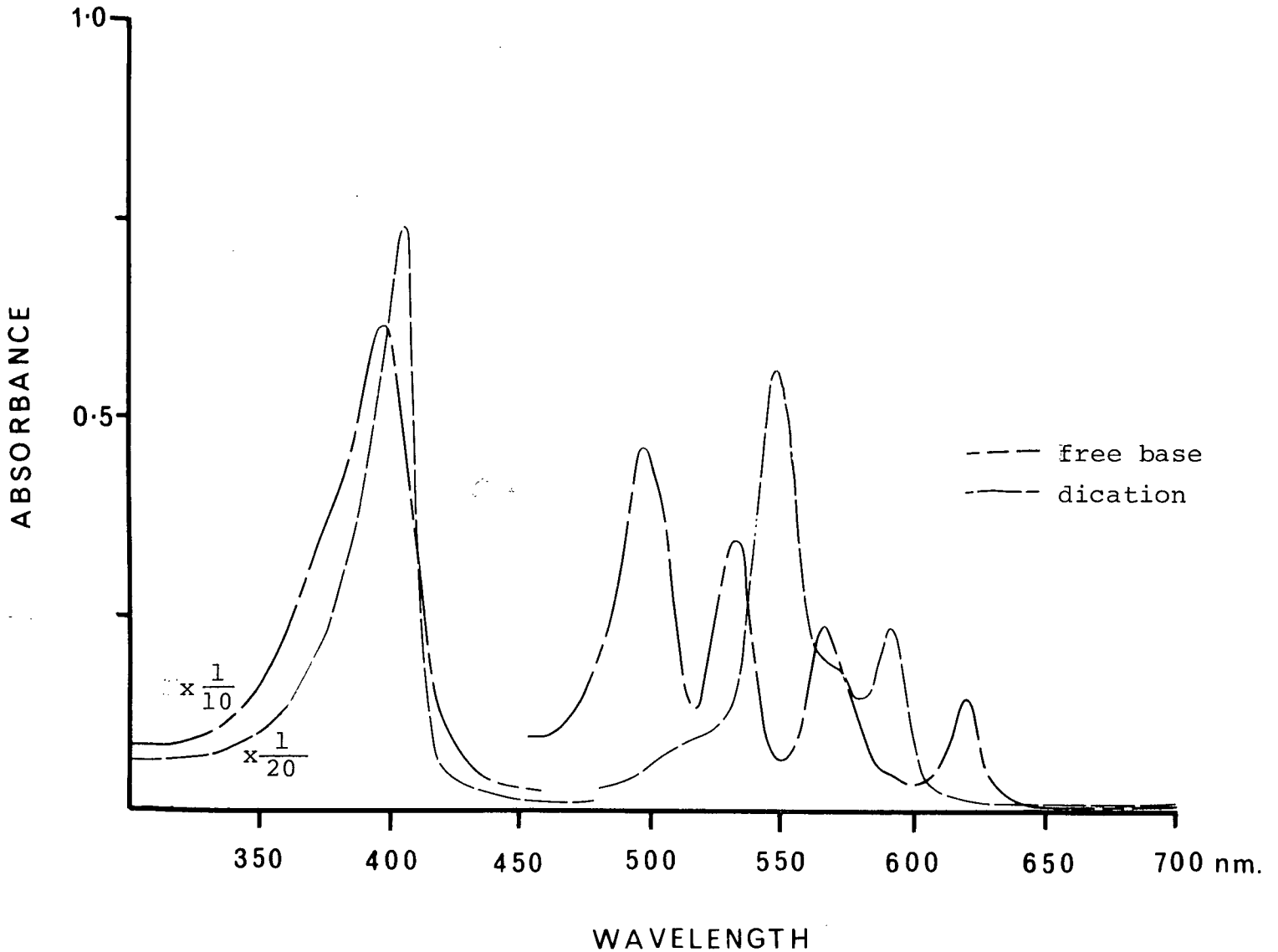


FIGURE 52: Electronic Absorption Spectrum of (169)

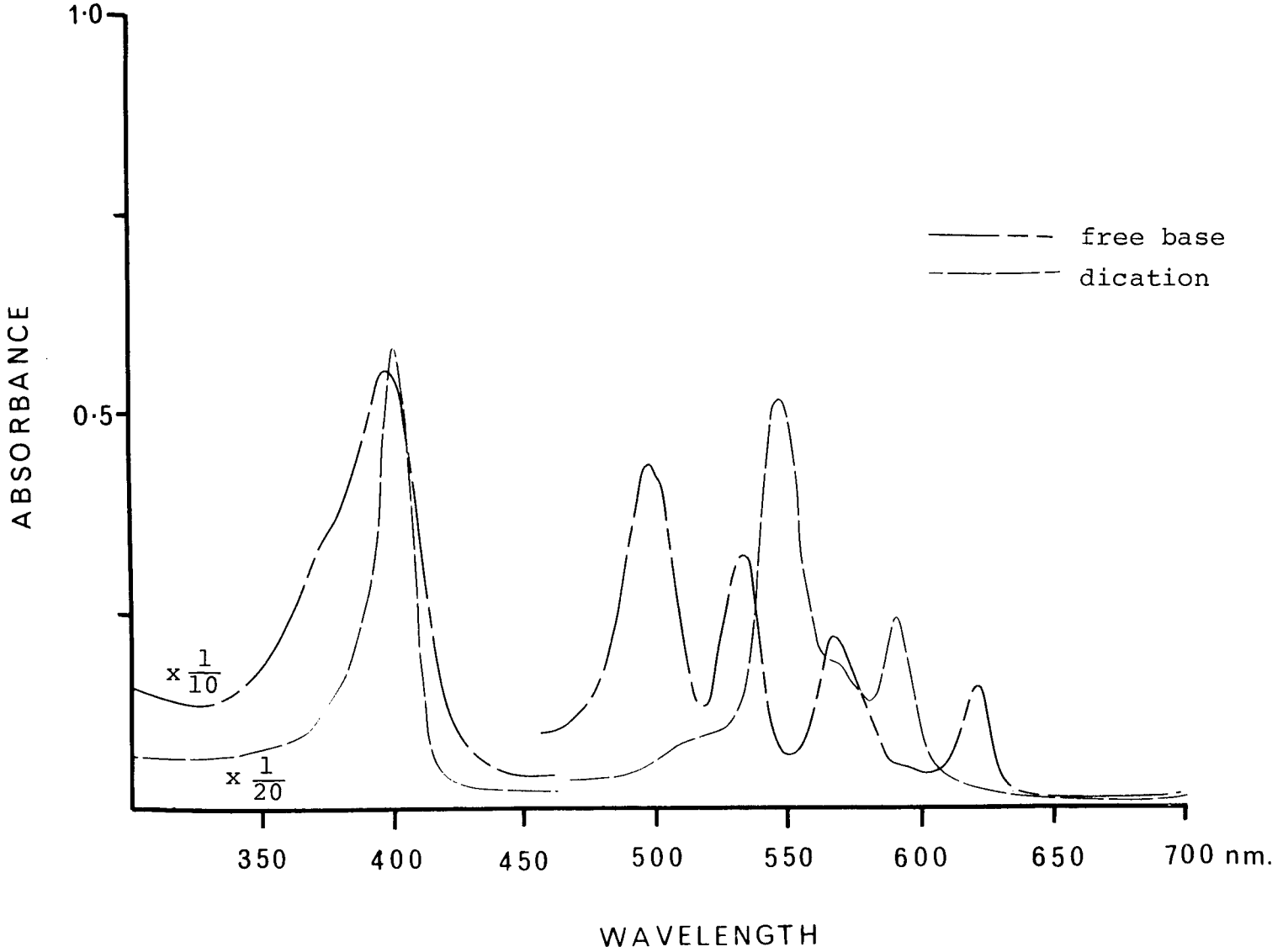


FIGURE 53: Electronic Absorption Spectrum of (170)

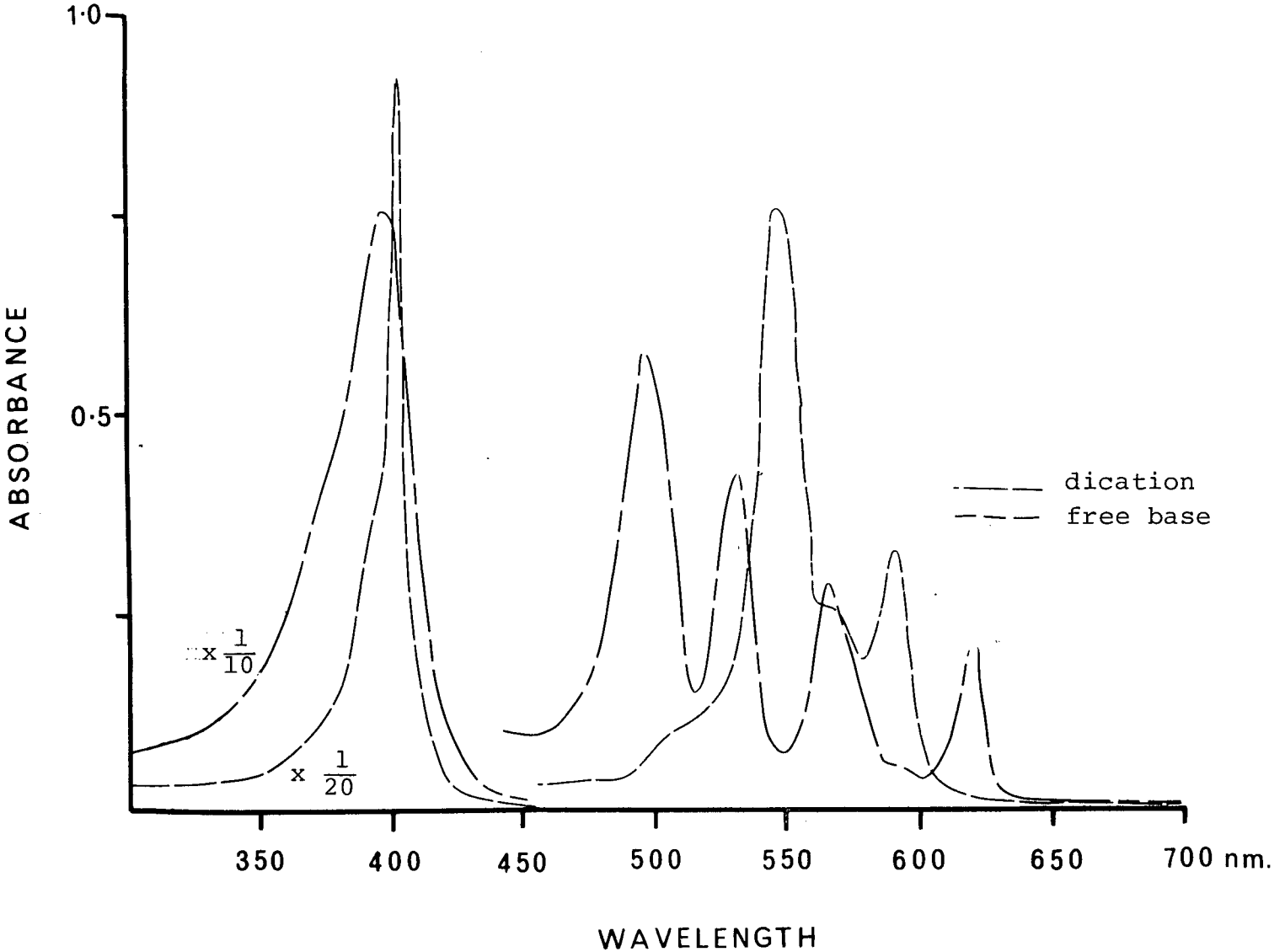


FIGURE 54: Electronic Absorption Spectrum of (171)

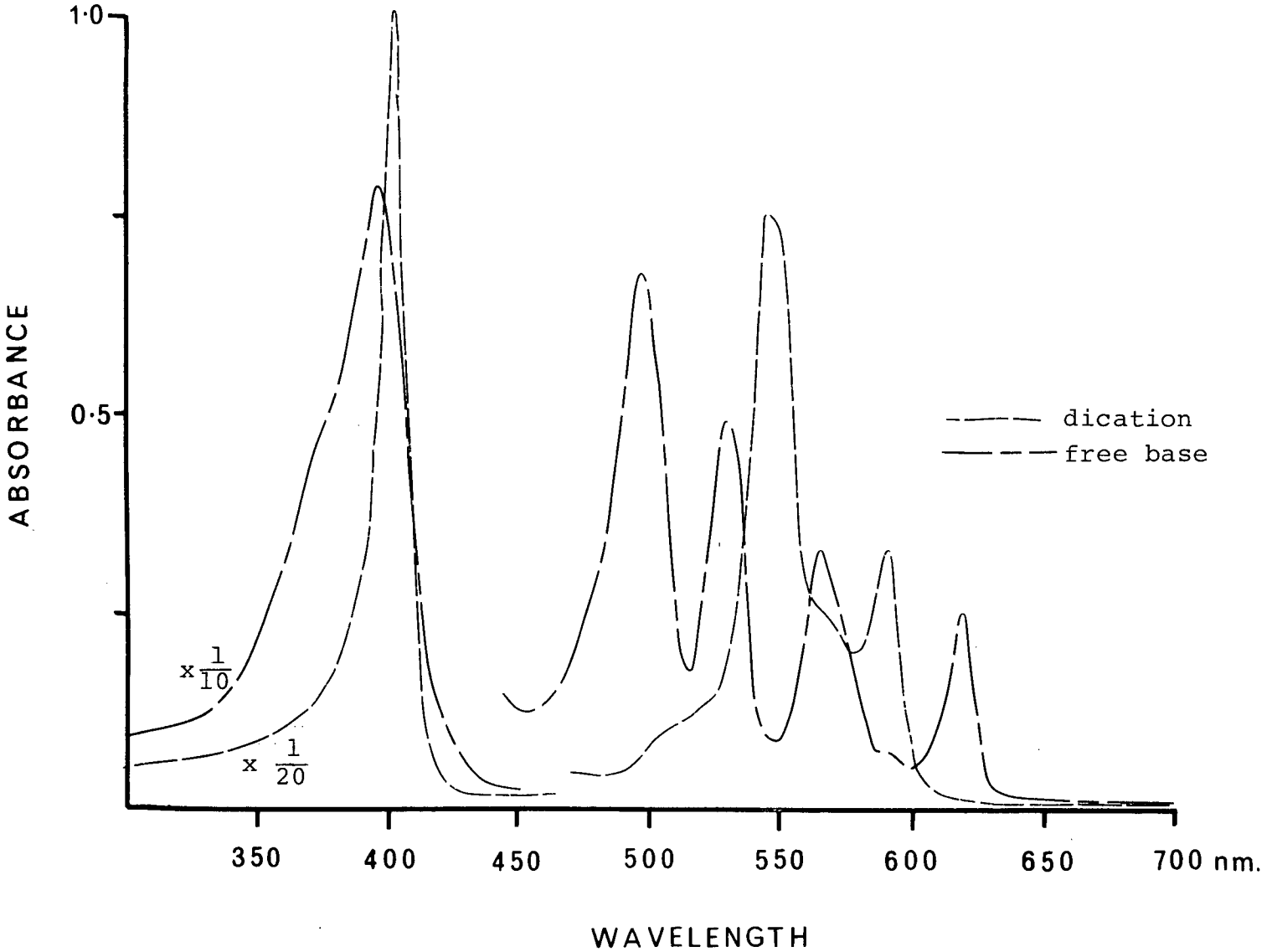


FIGURE 55: Electronic Absorption Spectrum of (172)

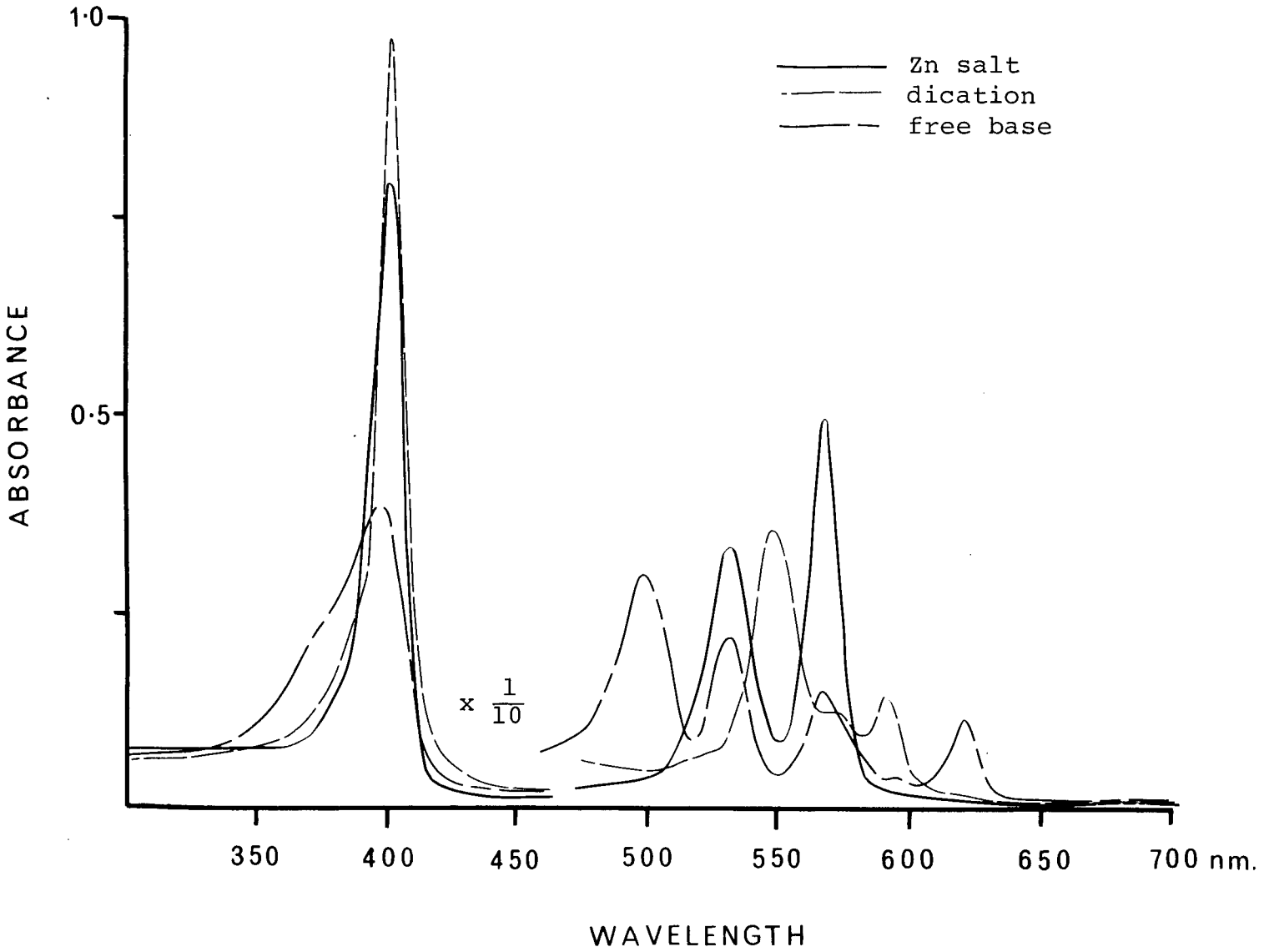


FIGURE 56: Electronic Absorption Spectrum of (175)

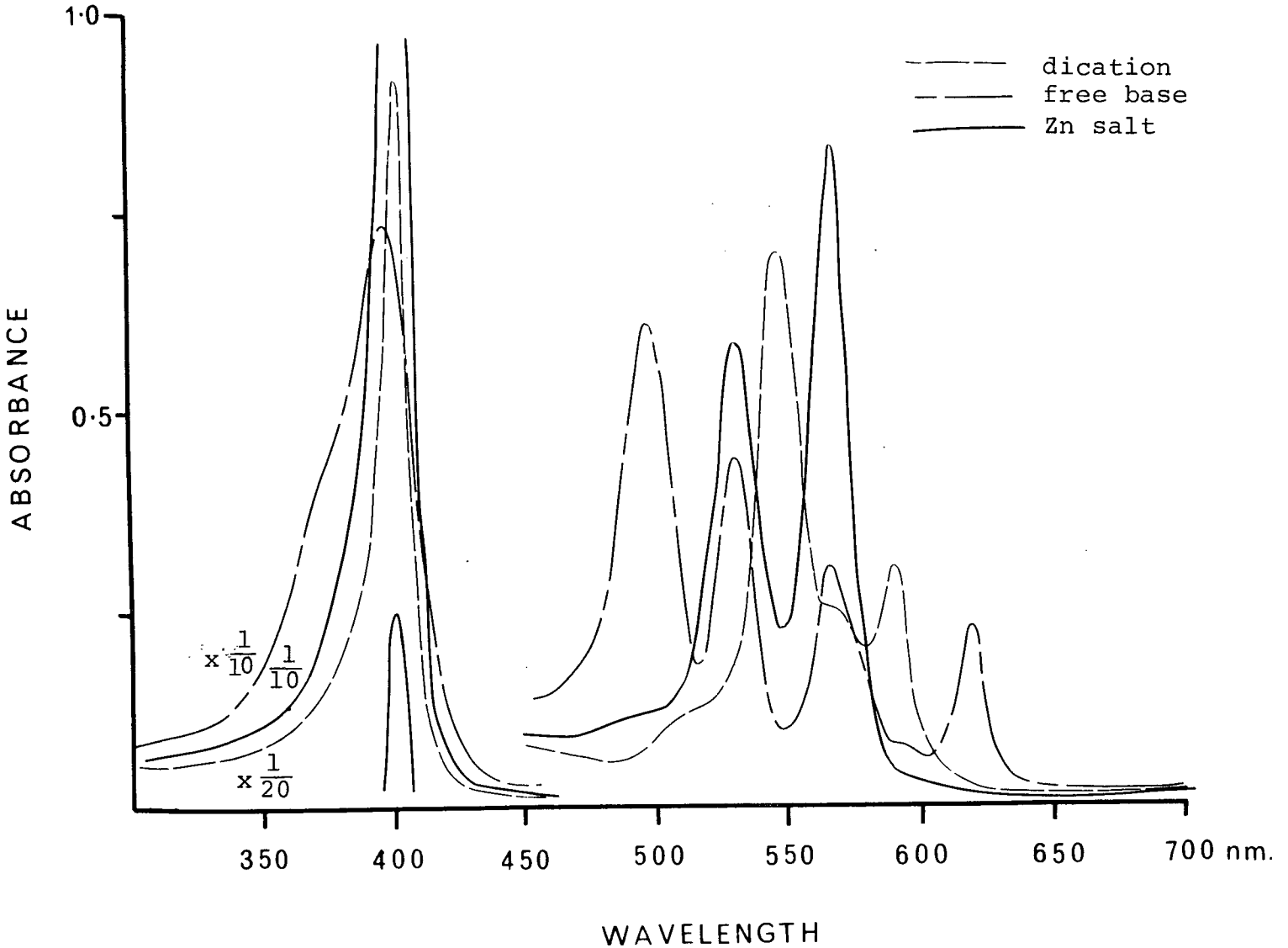


FIGURE 57: Electronic Absorption Spectrum of (177)

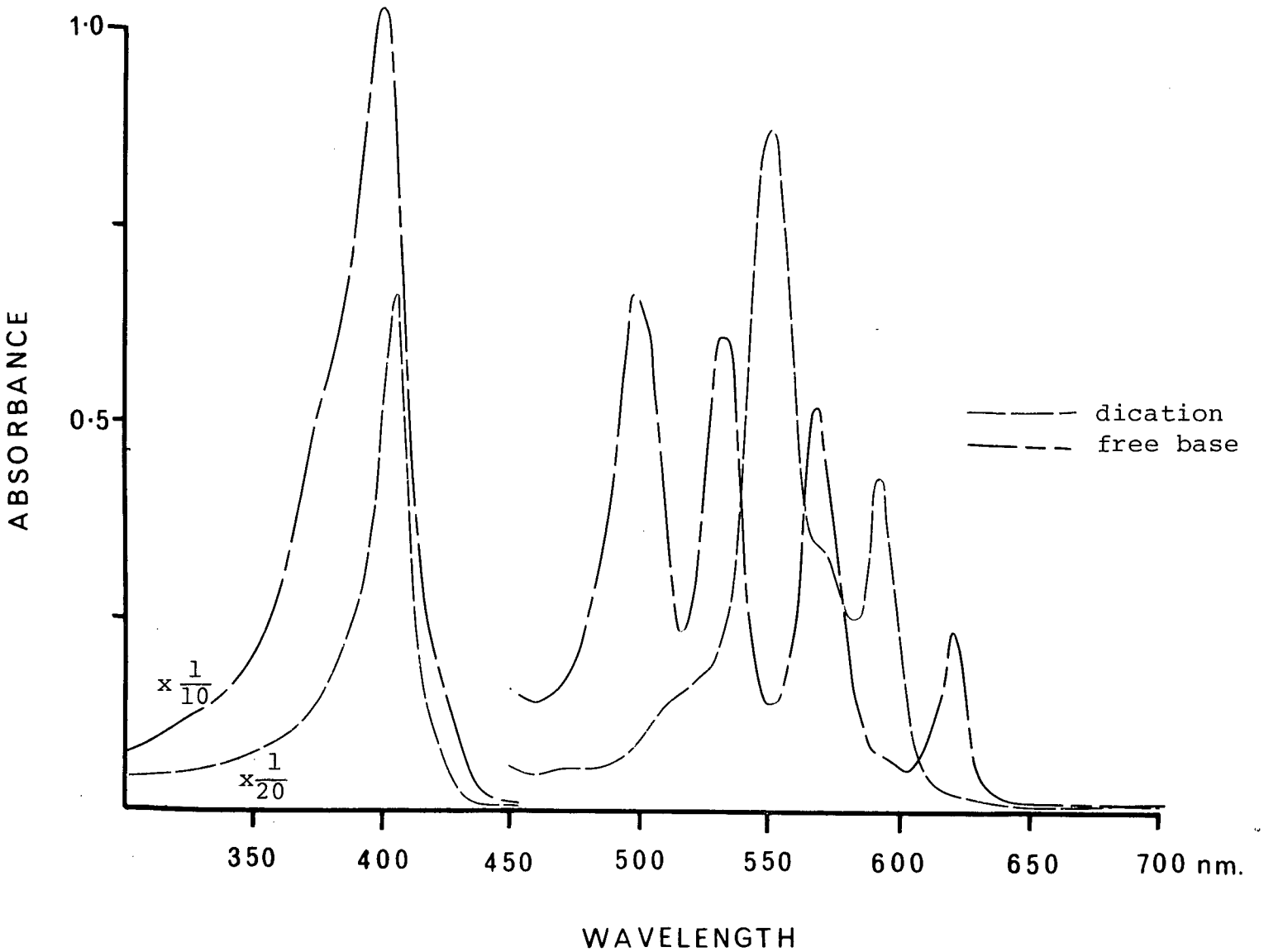


FIGURE 58: Electronic Absorption Spectrum of (178)

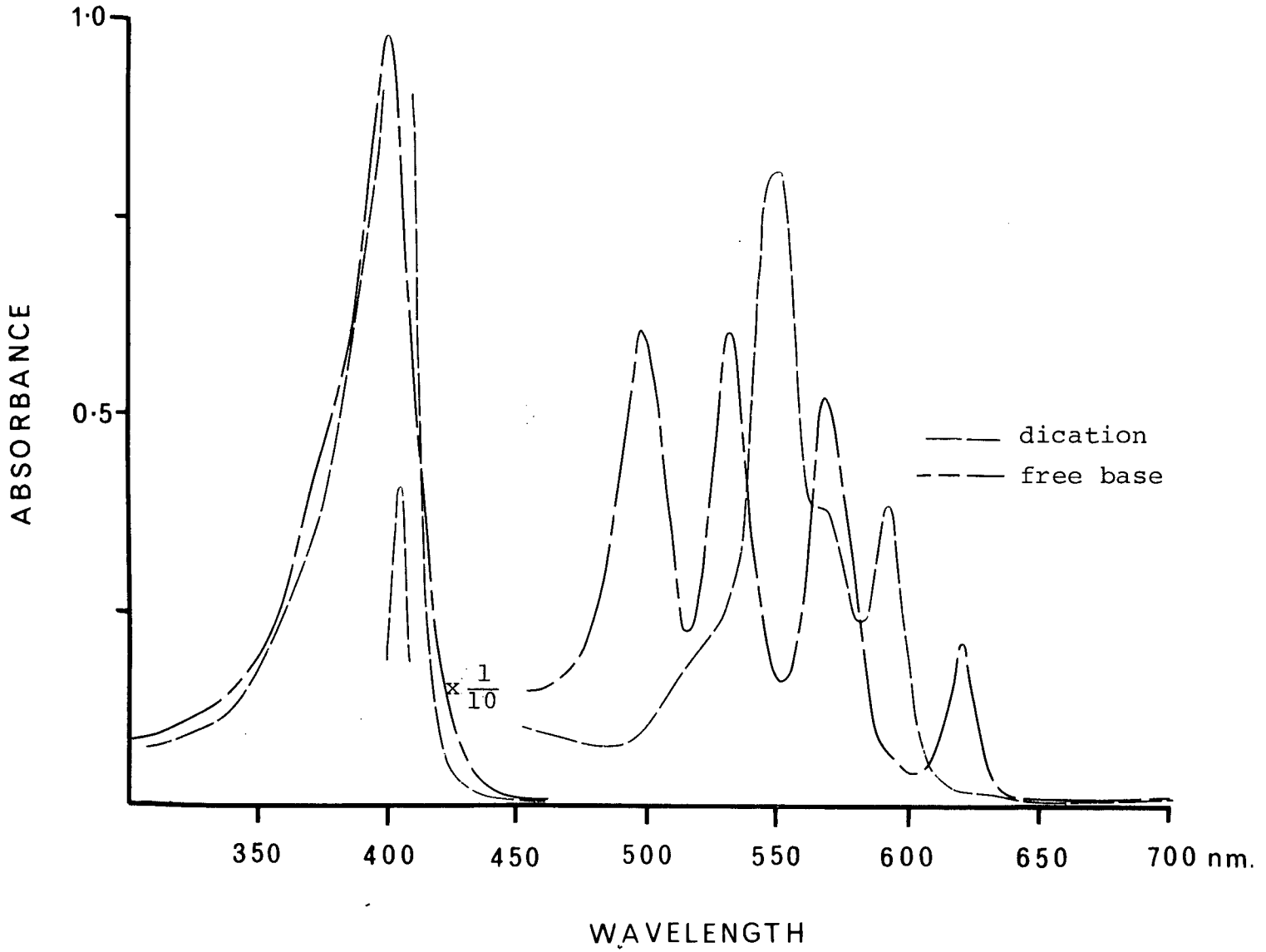


FIGURE 59: Electronic Absorption Spectrum of (179)

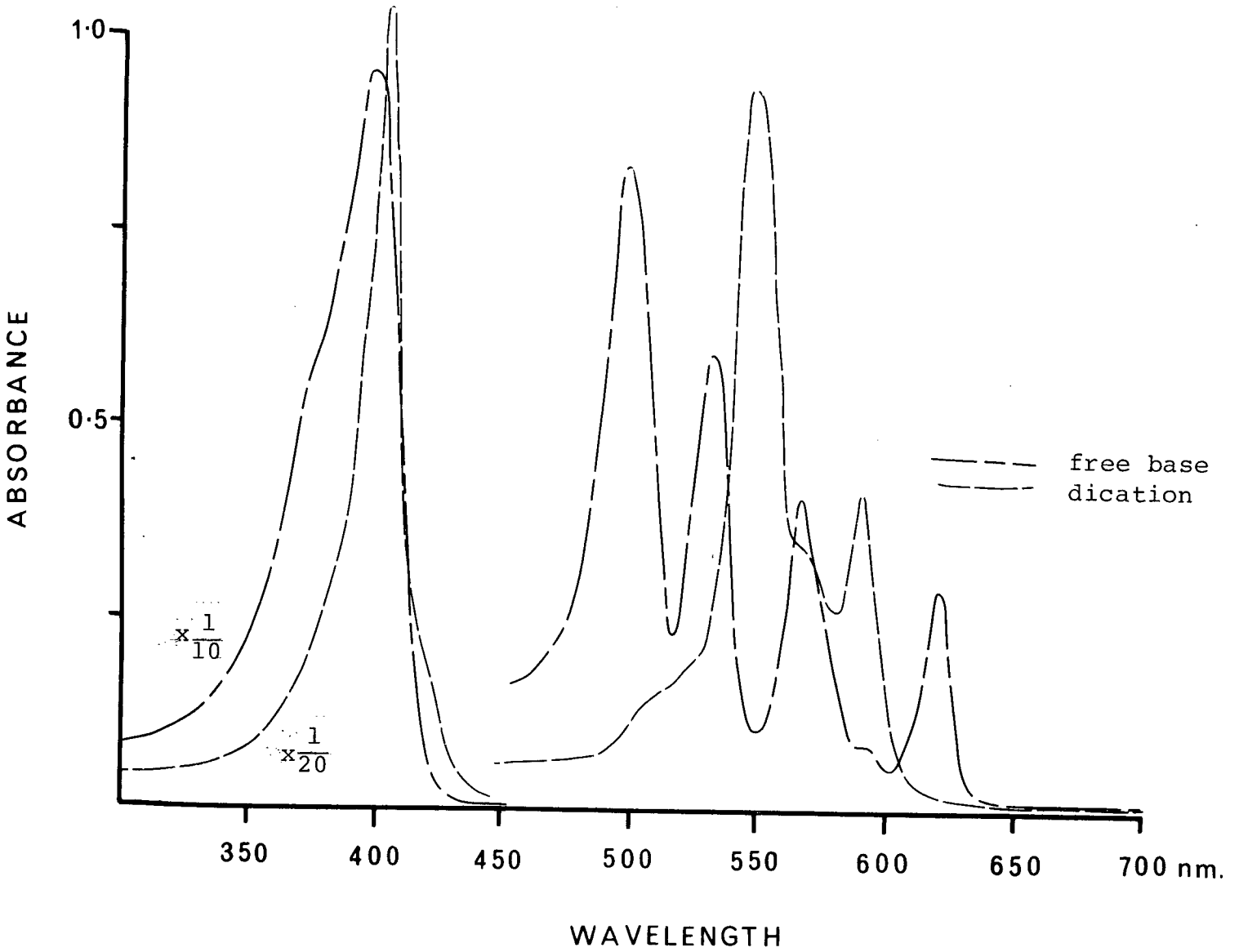


FIGURE 60; Electronic Absorption Spectrum of (181)

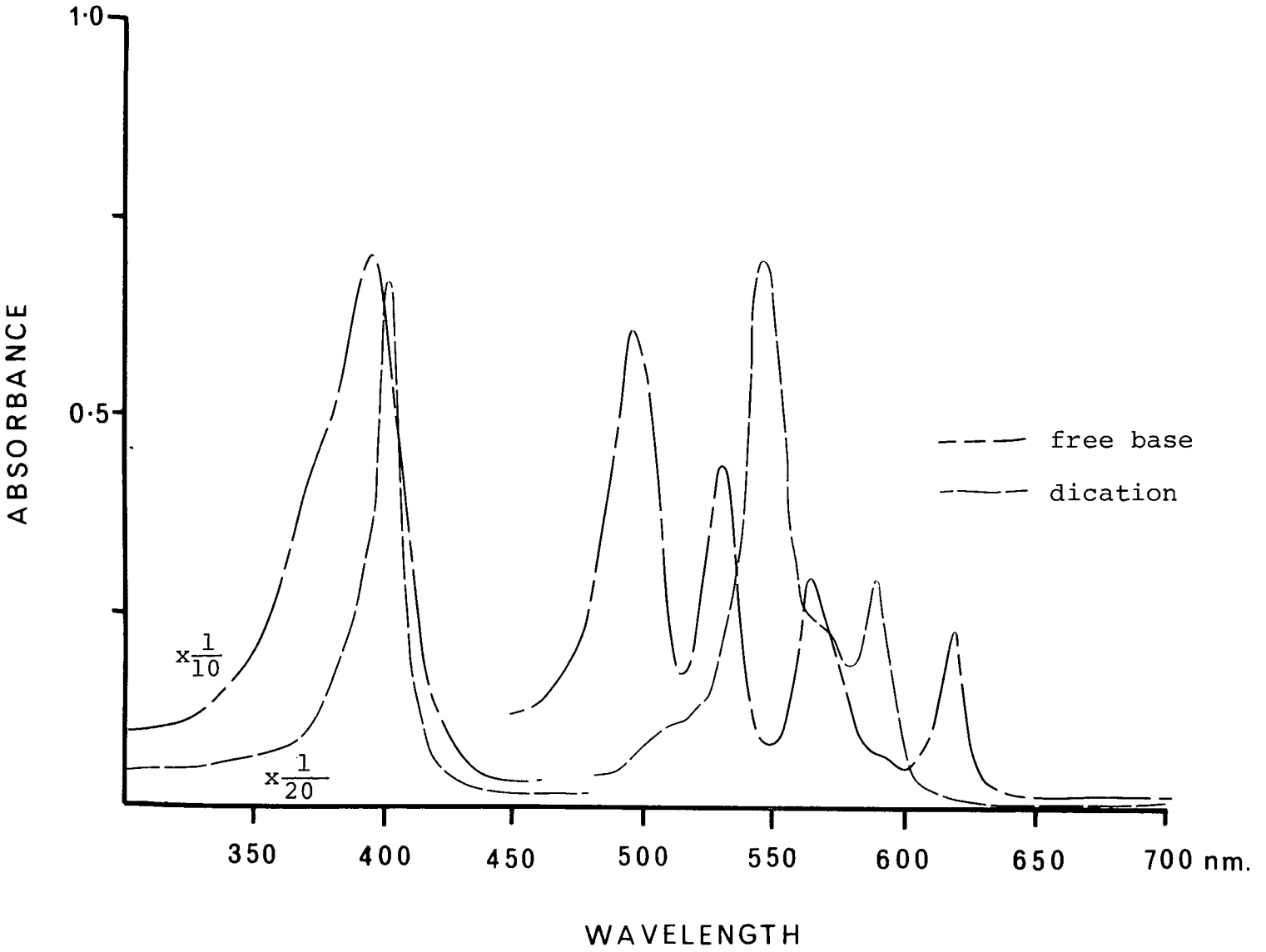


FIGURE 61: Electronic Absorption Spectrum of (182).

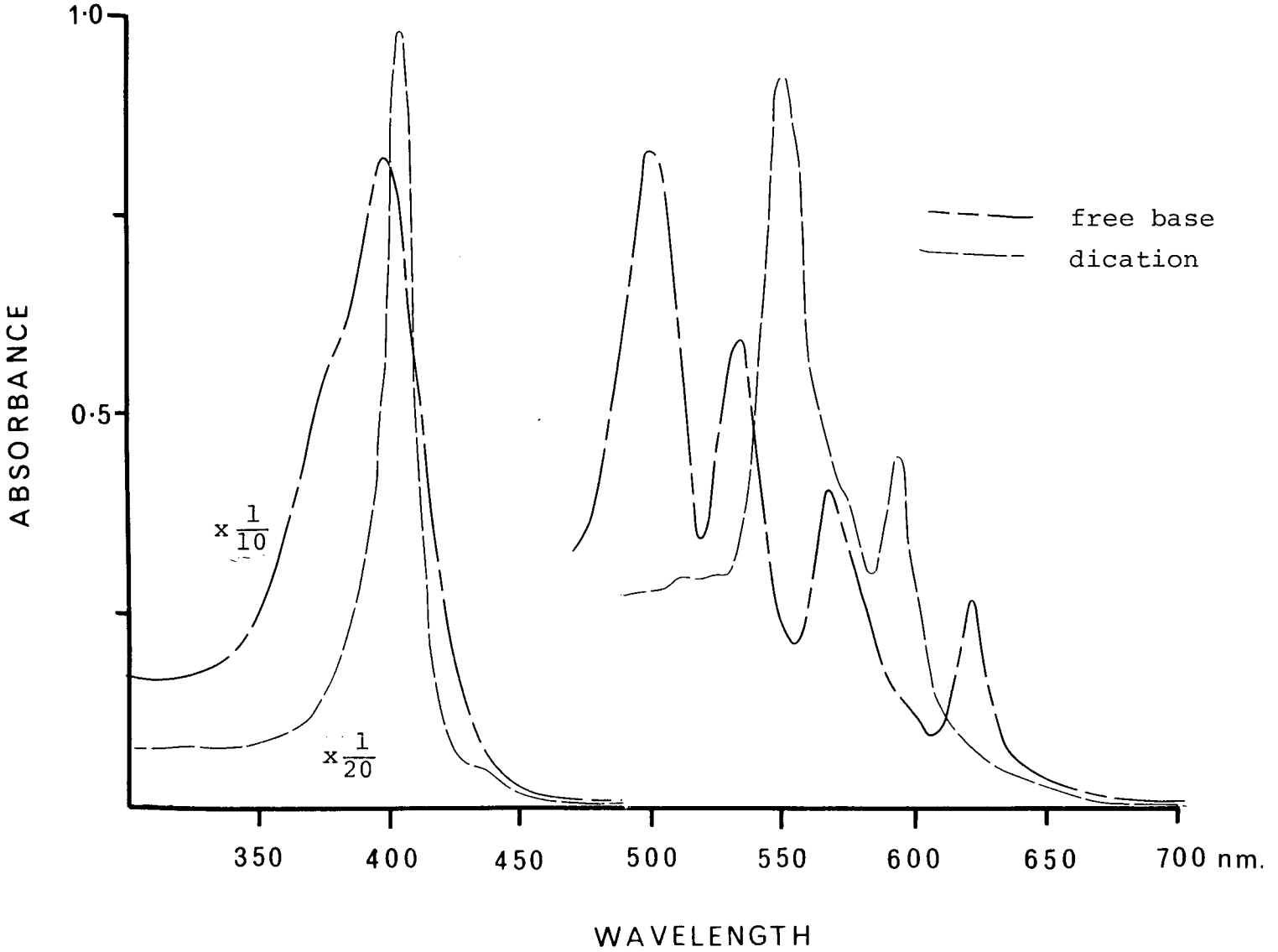


FIGURE 62: Electronic Absorption Spectrum of (183)

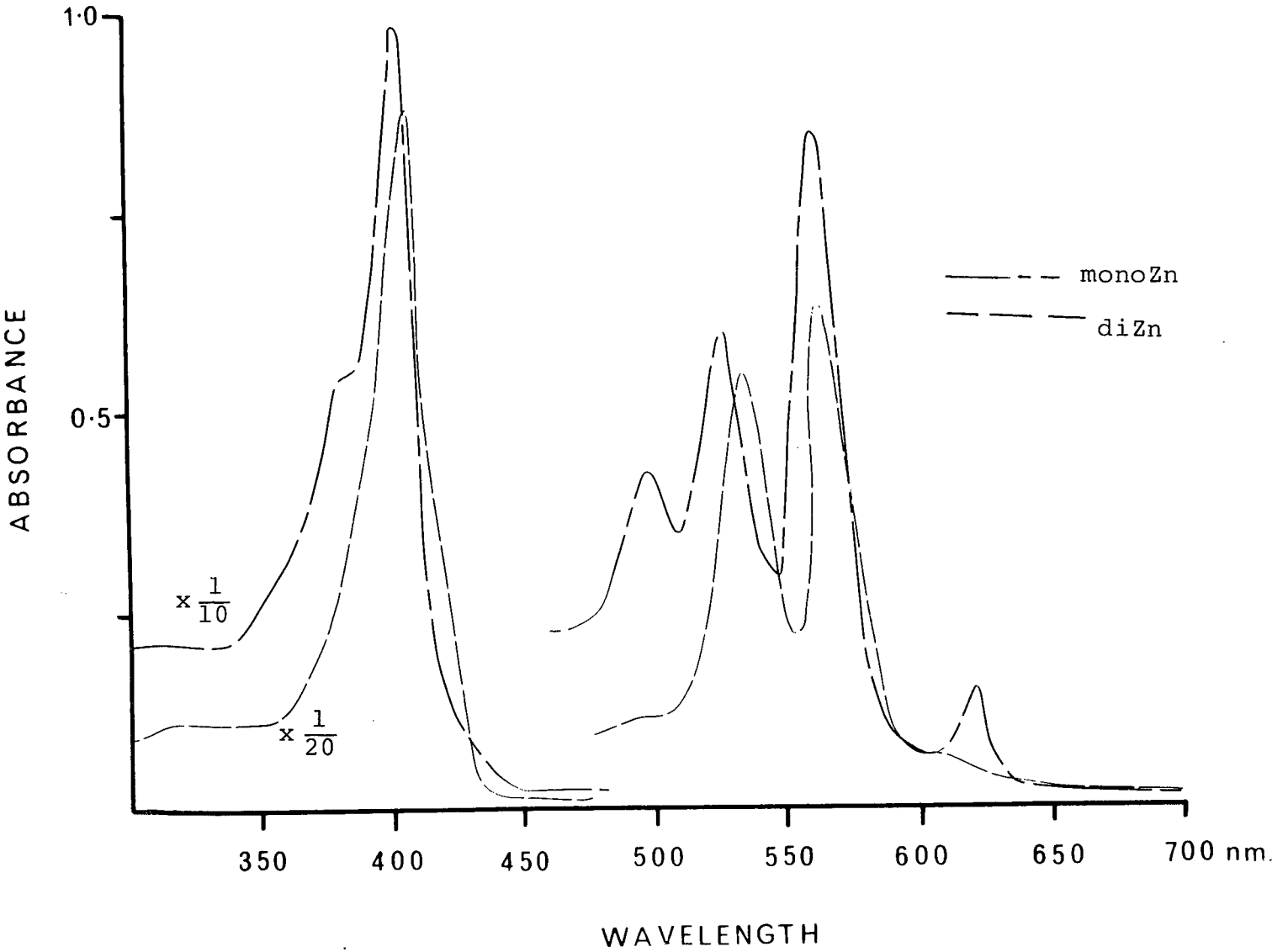


FIGURE 63: Electronic Absorption Spectrum of (183a)

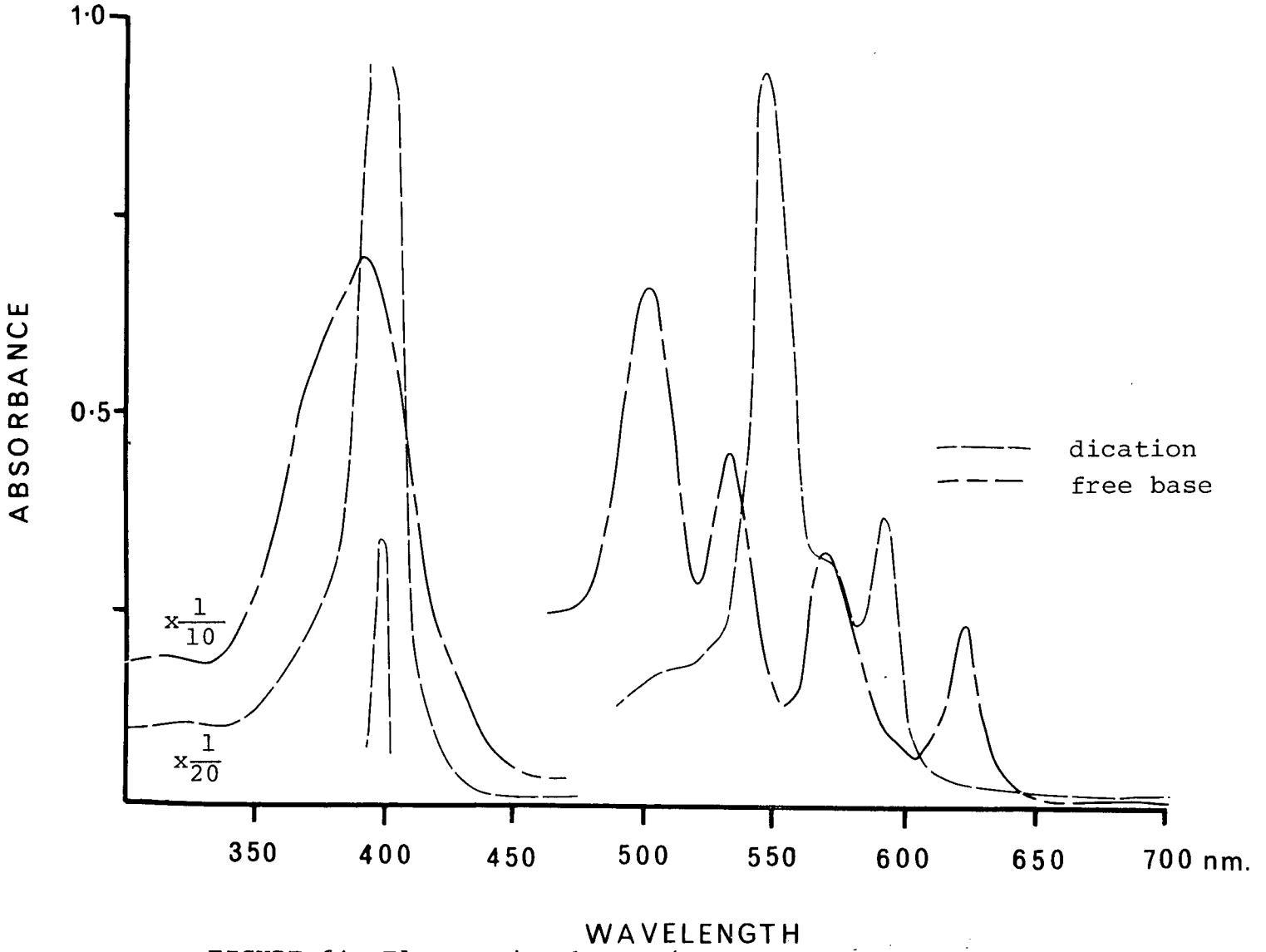


FIGURE 64: Electronic Absorption Spectrum of (185)

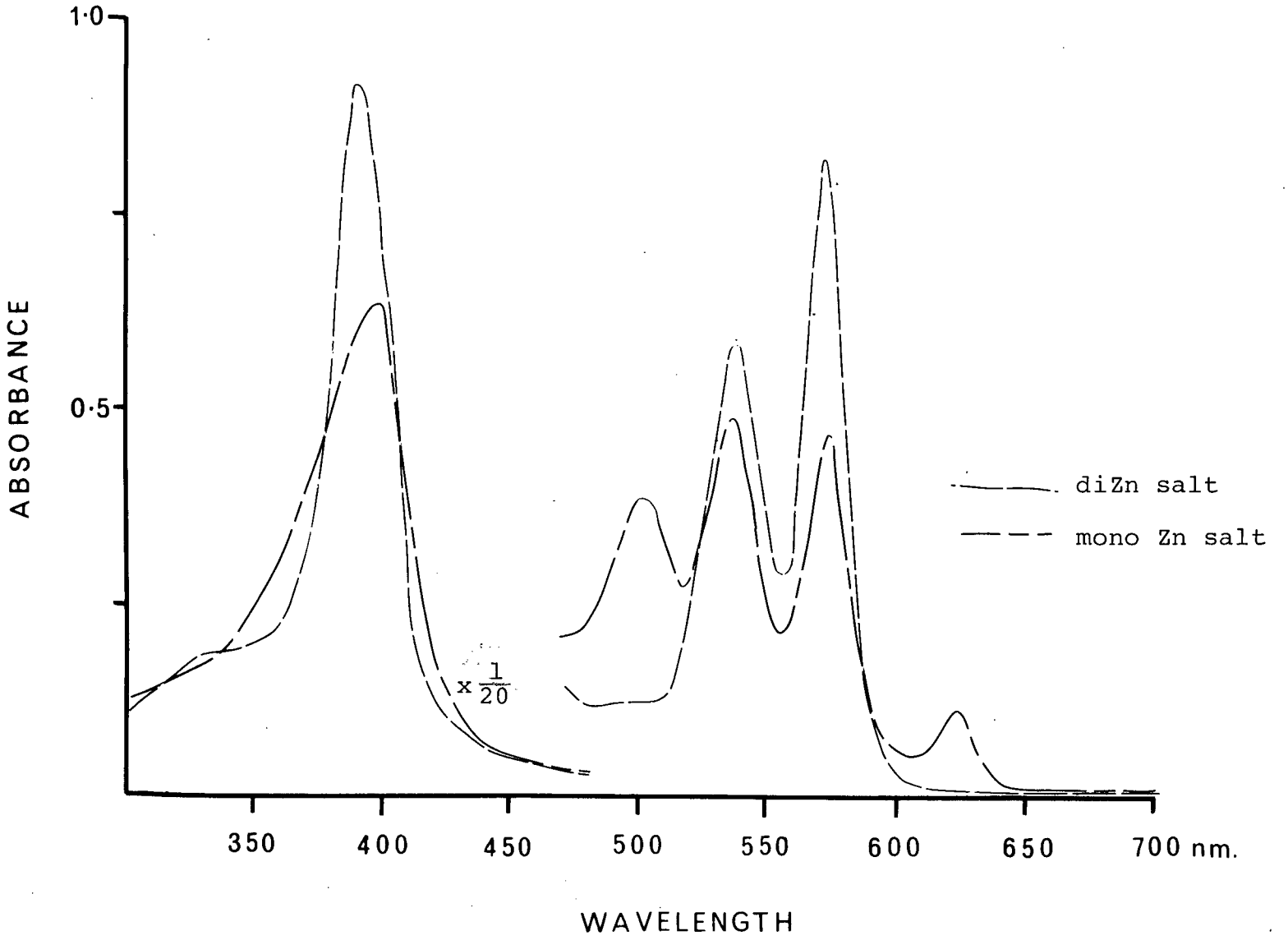


FIGURE 65: Electronic Absorption Spectrum of (185a)

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