SYNTHESES OF POLYPYRROLIC MACROCYCLES

by

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ABSTRACT

Pentaphyrins are pentapyrrolic macrocycles containing five bridging methine groups between the five pyrrolic subunits. The syntheses of decamethylpentaphyrin 71, 2-ethoxycarbonyl-3,7,8,12,13,17,18,22,23-nonamethylpentaphyrin 74, 2-ethoxycarbonyl-3,7,8,22,23-pentamethyl-12,13,17,18-tetraethylpentaphyrin 75, 3,12-dimethoxycarbonylethyl-2,7,8,-13,17,18,22,23-octamethylpentaphyrins 29 and the zinc complexes of 71 and 74 are described.

The physical properties of the pentaphyrins show them to be aromatic like sapphyrins, porphyrins and corroles. This aromaticity is reflected in the large shielding of the NH protons and the deshielding of the methine protons in the nmr spectra and by their optical spectra, which exhibit Soret and visible bands similar to sapphyrins and porphyrins.

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ABBREVIATIONS

Abbreviations which may appear are (in random order)

^{13}C nmr	=	Carbon-13 nuclear magnetic resonance
DMF	=	N,N-dimethylformamide
EI	=	electron impact
Et	=	ethyl
FAB	=	fast atom bombardment
^{1}H nmr	=	proton nuclear magnetic resonance
Hz	=	Hertz
Lit	=	literature
M.P.	=	melting point
Mol. Wt.	=	molecular weight
Ph	=	phenyl
PMe	=	methoxycarbonylethyl
p-TSOH	=	para-toluenesulfonic acid
TFA	=	trifluoroacetic acid
THF	=	tetrahydrofuran
TLC	=	thin layer chromatography
Uncorr	=	uncorrected
Uv	=	ultraviolet

Abbreviations in NMR Assignments

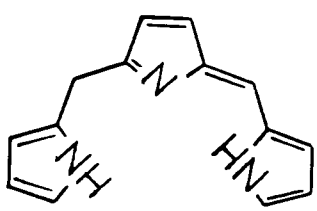
S	=	singlet
d	=	doublet
t	=	triplet
q	=	quartet
m	=	multiplets
bs	=	broad singlet

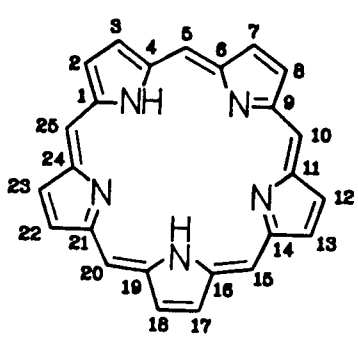
NOMENCLATURE

In this work, several terms of nomenclature are used interchangeably.

Dipyrromethane = 2,2'-Dipyrrolylmethane

Tripyrrne = Tripyrromethane (= 2,5-bis-(2-pyrrolylmethyl)-pyrrole)

Tripyrrene = 

Pentaphyrin = 

ACKNOWLEDGMENTS

I am very grateful to Professor David Dolphin for his encouragement and guidance during the course of this work. It has been a rewarding experience and my sincere thanks goes to him.

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A special thanks to my wife, Kate, and son, Jeremy.

1. INTRODUCTION AND LITERATURE REVIEW

The increasing interest in polypyrrole macrocycles is justified by the central role which porphyrin and its derivatives play in several essential biological processes. A further influence which fostered the development of porphyrin chemistry has been the interest in the theoretical aspects of aromaticity such as the extent to which modification and expansion of cyclic systems of conjugated double bonds is possible while still retaining aromatic character. The porphyrin which occurs naturally as prosthetic groups of biological molecules, haemoglobin and myoglobin is a tetrapyrrolic macrocycle with the pyrrole units linked to one another by methine bridges. The basic porphyrin nucleus (1) is shown in figure 1. The dihydro- and tetrahydroderivatives of the porphyrin nucleus are known as chlorin (2) and bacteriochlorin (3) respectively and are the parent macrocycles of a variety of plant pigments known as chlorophylls and bacteriochlorophylls. The corrin (4), another naturally occuring cyclic tetrapyrrole with one direct link between two

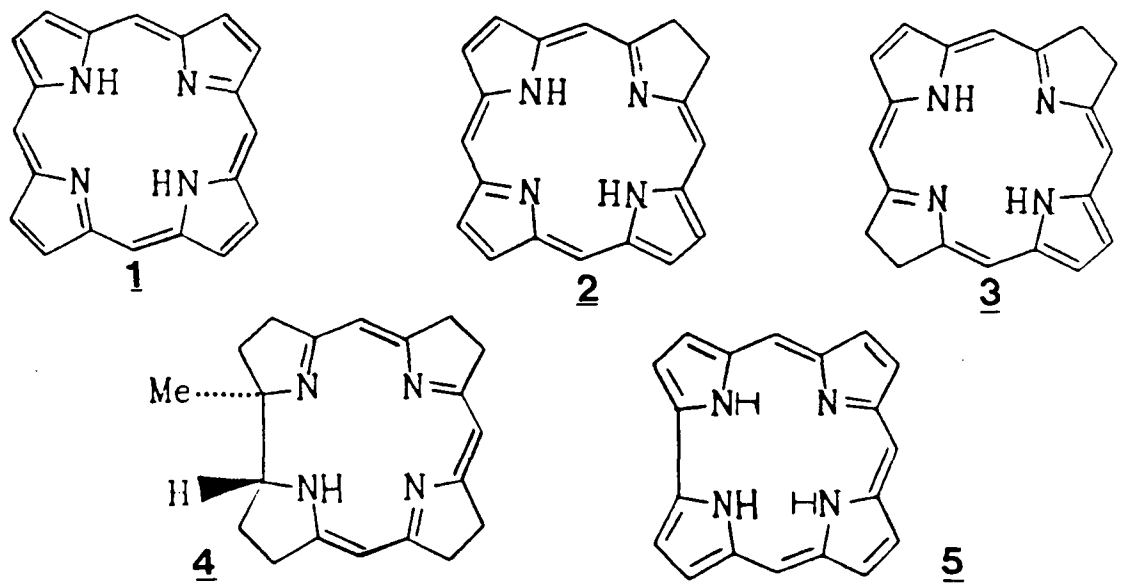
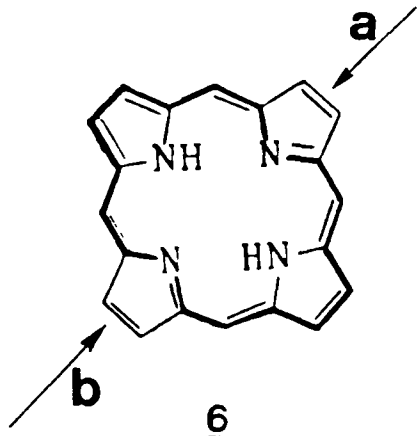


Figure 1. Nomenclature of tetrapyrrolic macrocycles

pyrrole units, is the parent macrocycle of the B_{12} coenzyme. The tetradehydro derivative of the corrin nucleus is the corrole (5).

The extreme stability of these tetrapyrrolic macrocycles has been attributed to their aromaticity with the exception of corrin (4) which is not aromatic. Aromaticity may be defined in a number of different ways[1,2] and several different methods have been proposed for the measurement of aromatic character. Classically, aromaticity has been correlated with the presence of an "aromatic sextet"[3], the stability and the chemical reactivity of the compound. Clearly, chemical reactivity is not a ground state property of the compound but one dependent on the energy difference between the ground state and the transition state for the chemical change involved. Huckel's rule[4] predicts that planar, monocyclic conjugated systems of trigonally hybridized atoms having a closed shell configuration of $(4n + 2)\pi$ - electrons will possess stability, i.e., will be aromatic. Thus, aromaticity is a function of the electronic nature of the system, and not a property of the stability or chemical reactivity. Elvidge and Jackman[5,6] define aromatic compounds as those which will sustain an induced ring current. The magnitude of the ring current will be a function of the delocalisation of π-electrons around the ring and therefore a measure of aromaticity.

The porphyrin macrocycle is a highly conjugated system and a number of resonance forms can be written for it. There are 22 π-electrons in the carbon skeleton, but only 18 of these are included in any one delocalization pathway (6). Thus the cross-conjugated



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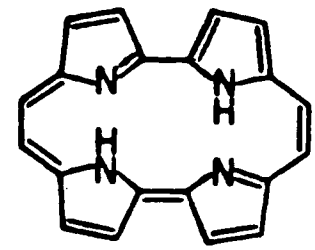

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double bonds (shown by arrows a,b) can be reduced without disturbing the aromaticity of the macrocycle. Chlorin (2) with one (arrow a) of the peripheral double bonds reduced and bateriochlorin with two (arrows a,b) reduced, both retain their aromaticity since the conjugated 18 π-electron system is maintained. Similarly, the corrole nucleus is aromatic and one peripheral double bond can be reduced while still maintaining its aromaticity. However, the corrin nucleus is neither aromatic nor planar. Porphycene 7, a porphyrin-like macrocycle, have been synthesized and found to be aromatic.[7]

A number of physical methods are currently used to measure the extent of π-electron delocalization, and hence aromatic character. These include nmr spectroscopy, uv-visible spectroscopy and x-ray crystallography. These and other techniques have been tested on the 18 π-electron porphyrin system known to be aromatic.

One manner in which the π-electron delocalization manifests itself is in sustaining of ring currents when placed in an external magnetic

field. Thus the presence of a ring current is an indication of aromaticity. Aromatic compounds in nmr spectroscopy exhibit chemical shifts of protons such that those inside the ring are strongly shielded due to the ring current opposing the applied field (thus diamagnetic) and appear shifted upfield from position expected on electronic considerations. Protons outside the ring are strongly deshielded, the ring current strengthening the external field, and therefore appear downfield from the expected for olefinic protons. Studies on porphyrins[8] by nmr spectroscopy clearly indicate the presence of a ring current. The parent porphrin (1) in trifluoroacetic acid exhibits resonances at -4.48 for the NH protons, 9.98 for the eight β-protons and 11.22δ for the meso-protons[9] (δ = 0 ppm for TMS).

A major difference between aromatic systems and conjugated cyclic or non-cyclic polyenes is the fact that in the non-aromatic systems, the carbon-carbon bond lengths are alternately long and short in accordance with the alternate single and double bonds, whereas in the aromatic compounds, all the bonds are of the same length - i.e. of the same bond order character. This bond order is unique (resulting in bond lengths intermediate between those for single and double bonds) and not simply a relationship between single and double bonds. In order to obtain this bond order, there must be maximum overlap between the axially oriented p-orbitals and this requires that the ring be planar. X-ray crystallographic studies on prophine (1) and some other porphyrin systems have shown[10] this to be the case.

Porphyrins are highly colored compounds having absorption bands in the visible region (400-700 nm) with varying relative intensities

depending on the peripheral substituents on the nucleus[11,12], solvent system[13] and molecular aggregation[14]. One of these bands near the ultraviolet region (ca 400 nm) is more intense, $\varepsilon \approx 10^4\ M^{-1}\ cm^{-1}$ in order of magnitude stronger than the other visible bands. This 'Soret' band, named after the discoverer, is characteristic of the macrocyclic conjugation and the rupture of the macrocycle results in the disappearance of this band. The aromatic character in porphyrin macrocycles has also been confirmed by measurement of their heats of combustion[15].

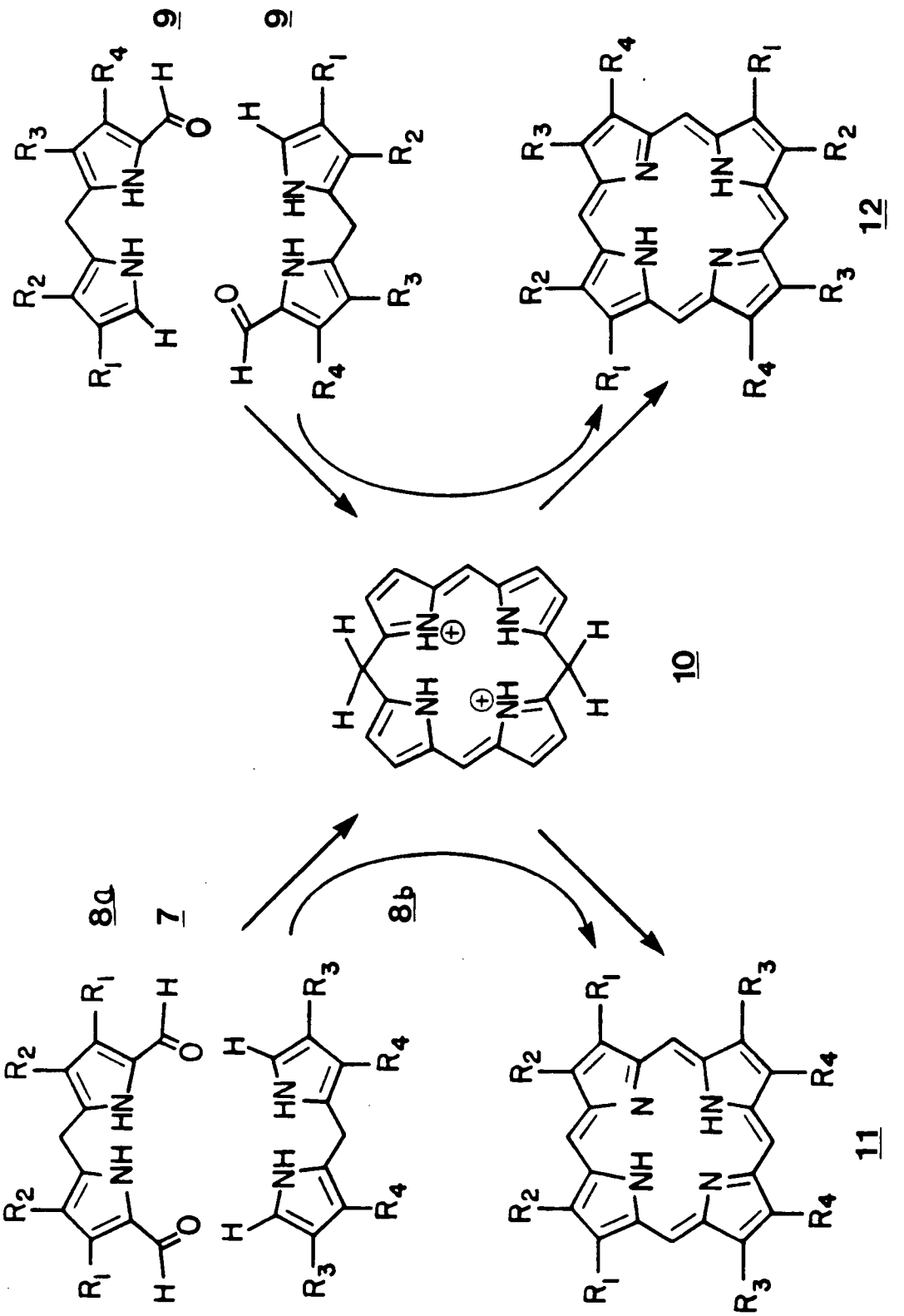
In the laboratory, as well as in nature, porphyrins are synthesized from pyrroles, which in turn are readily obtained from acyclic precursors. The porphyrin macrocycle can be constructed in three fundamentally different ways. They are: (a) The single step condensation of monopyrroles[16]. (b) The coupling of two dipyrrolic intermediates, commonly referred to as a "2 + 2" synthesis[17]. (c) The stepwise condensation of individual pyrroles, leading to a linear tetrapyrrole and a final head to tail cyclisation[18].

Method (a) has very limited synthetic value, primarily due to the symmetric nature of the porphyrins produced and also due to the limit on the type of substituents that can be introduced. Methods (b) and (c), together form the major route to porphyrins as well as other related macrocycles since it is now possible to synthesize systems with diverse peripheral substituents in the required relative orientations.

A synthetic route of great value in porphyrin syntheses has been that developed independently by Woodward[19] and MacDonald[20] which involves the use of the well-known reaction whereby 2-formylpyrroles condense with acid and 2-unsubstituted pyrroles to afford efficiently the stable

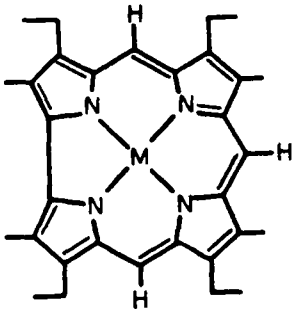
2,2'-dipyrromethemium salts. The extension of this reaction to porphyrin synthesis (Scheme 1) involves the coupling of dipyrromethane dialdehyde 8a with bis-α-free dipyrromethane 8b in the presence of hydriodic acid in acetic acid solution to produce an intermediary porphodimethene 10 which upon oxidation gives the final porphyrin 11 or 12. The synthetic analogue of 8b, the dicarboxy derivative can also be used since it decarboxylates during acid catalysed cyclization. One particular catalyst which has been used intensively is p-toluenesulfonic acid. Using this catalyst, Kenner et al.[21] cyclised a porphyrin in methanol. The addition of zinc acetate afforded the isolation of the products as the zinc complex. The acid strength of the reaction medium affects rearrangement of the bipyrrolic units leading to isomers. This rearrangement has been avoided by the use of methanol-methylene chloride (1:30) mixtures [22(a,b,c)]. The physical and chemical properties of the porphyrins and their related macrocycles have been dealt with extensively in the serial volume "The Porphyrins"[12].

The first isolation of metal derivatives of corrole 13 was reported by Johnson and Price[23]. These syntheses resulted from the reaction of formaldehyde and aqueous ethanolic hydrogen chloride with the palladium complex of 5,5"-Bis(5'-bromo-3,3'-diethyl-4,4'-dimethyldipyrromethene) 14, originally prepared by Fisher and Stachel[24]. However it was shown that this reaction gave the metalloxocorroles 15 instead[25].



SCHEME 1

Since the original claim for a corrole synthesis had not been fulfilled, Woodward and Bauer[26] directed their efforts toward such a synthesis.



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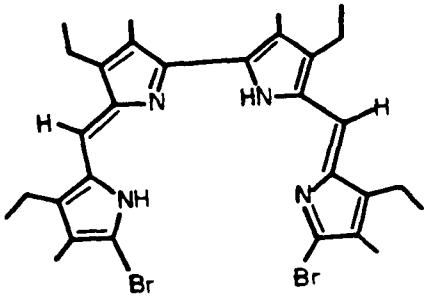

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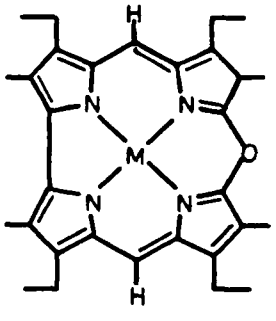

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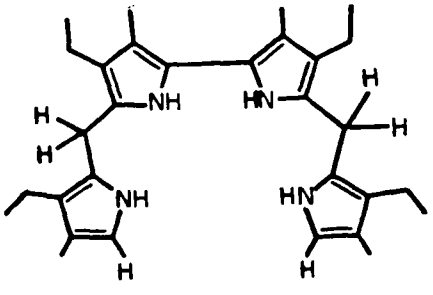

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To synthesize an authentic corrole, Woodward and Bauer treated the free base bi(dipyrromethene) 16, obtained by demetallation and catalytic hydrogenation of 14, with formic and hydrobromic acids. The product, a blue glass isolated in low yield exhibited an intense Soret band in the visible spectrum at 458 nm. However, Johnson and Kay[27] had by now prepared authentic samples of corroles by the photochemical cyclization of dideoxybiladienes-ac 17. The electronic spectra of the corroles reported by Johnson[28] showed a Soret band at ~400 nm clearly different from that

observed for the "corrole" prepared by Woodward and Bauer which led to the reinvestigation of the compound. The compound was found to form a diperchlorate salt, whereas corroles underwent only mono-N- protonation. The empirical formula of the diperchlorate salt proved to be

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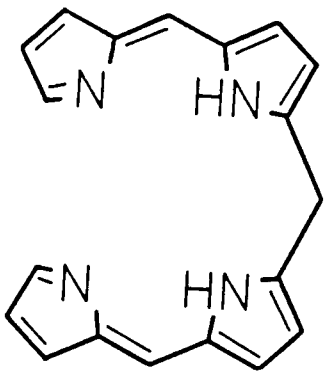
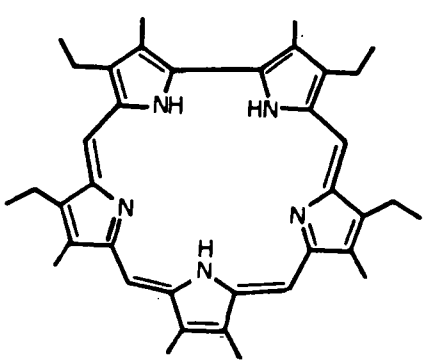


consistent with a mono-hydrate diperchlorate salt containing five pyrrolic units, and not four. Accordingly, the structure of this compound was concluded to be 18, and because of the crystalline form and brilliant blue color (reminiscent of sapphires), was called sapphyrin. This macrocycle is analogous in structure to a corrole with one direct link between pyrroles.

18

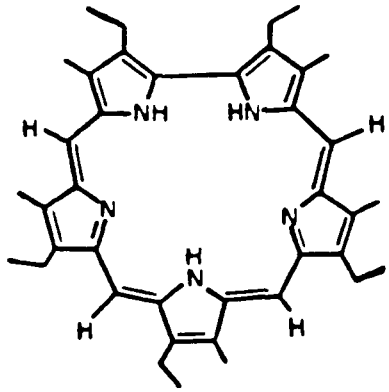


The sapphyrin macrocycle 18 was the first polypyrrolic macrocycle isolated containing more than four pyrrole rings. The presence of a very intense Soret-like absorption band (458 nm) and ring-current induced nmr shifts (downfield for the external methine protons, upfield from the reference standard tetramethylsilane for the NH protons) indicate that the sapphyrin system, which can be formally written as containing 22 conjugated π-electrons (4n + 2, n = 5) is aromatic.

The first syntheses of a pentapyrrolic macrocycle generated interest in other workers for other macrocycles with different substituents and heteroatoms. Thus in 1972 Broadhurst et al. investigated sapphyrin-like macrocycles and reported the synthesis of dioxasapphyrin[29] with a bifuran moiety replacing the bipyrrole. The same authors also reported the synthesis of thiasapphyrin, with one thiophene moiety replacing a pyrrole and pentaethylsapphyrin[30] 19 all of which were aromatic and contained the intense Soret type band in their visible spectra. King and Woodward[31] also synthesizes a 22 π-electron macrocycle which they called smaragdyrin (smaragdus:emerald) 20. Johnson and co-workers[30] also attempted to synthesize this system which they called norsapphyrin. They did in fact succeed with syntheses of the dioxanorsapphryins (or dioxasmaragdyrins) 21 a,b). A series of heteroatom-bridged annulenes containing furan and thiophene have also been synthesized by Voldhardt[32]. Bauer et al.[26] reported the synthesis of decamethylsapphyrin 22.

The formation of 18 was first rationalised as proceeding through the condensation of two molecules of 16 with formic acid followed by α-pronation and bond cleavage to give sapphyrin. Another method of

preparation utilized 16 and 2,5-diformyl-3,4-dimethylpyrrole. The



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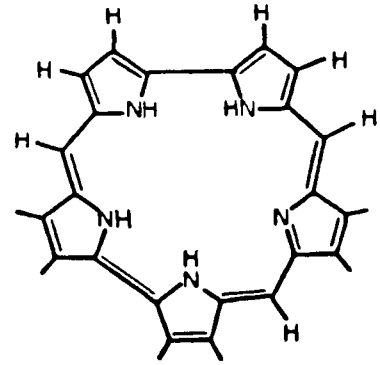

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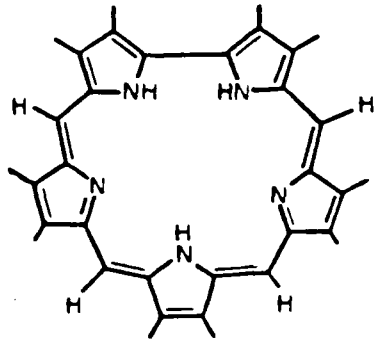

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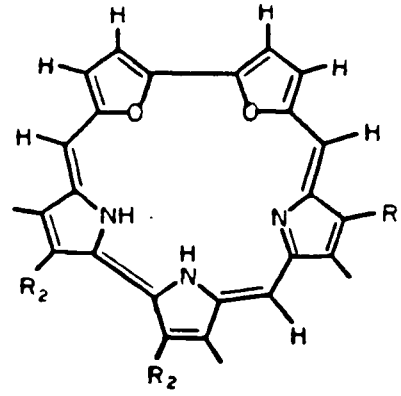
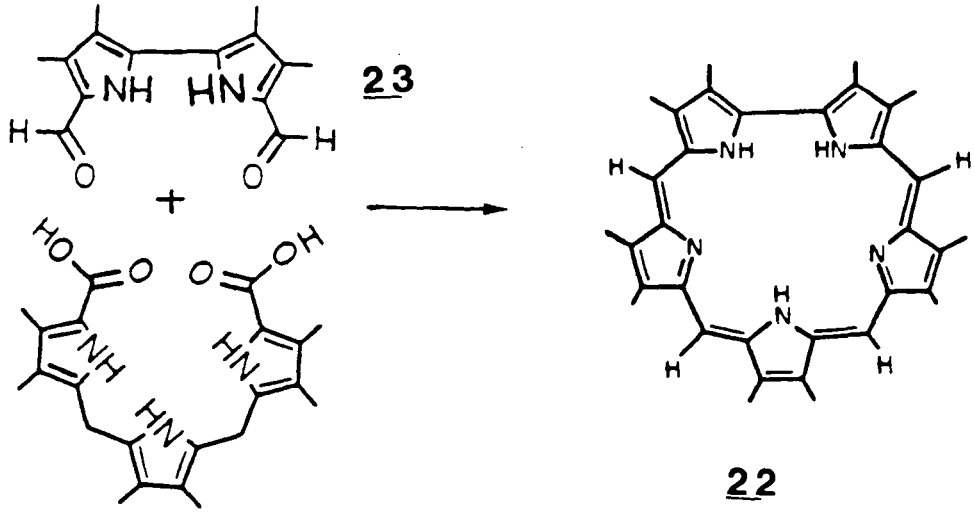


21a: $R_1 = H$, $R_2 = CH_3$
b: $R_1 = R_2 = C_2H_5$

decamethylsapphyrin 22 was also synthesized efficiently utilizing the coupling of bipyrroledicarboxaldehyde 23 with tripyrrane diacid 24 by the agency of p-toluenesulfonic acid in oxygenated ethanol (Scheme 2) a process analogous to MacDonald's 2 + 2 coupling of porphyrin (Scheme 1). In a similar procedure, hexamethylsapphyrin was prepared from 5,5'-diformyl-2,2'-bipyrrole and tripyrrane diacid in excellent yield.

Metal complexes of decamethylsapphyrin 25 have also been reported and in some cases isolated[26]. When a methanolic solution of

decamethylsapphyrin and the acetate salts of nickel, iron, cadium,



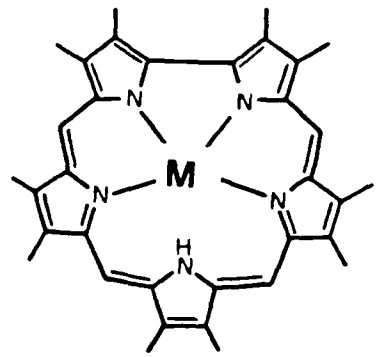
23

24

22

SCHEME 2

manganese, cobalt and zinc were heated in the presence of sodium acetate, metal complexes were formed as indicated by spectral changes. The complexes of cobalt and zinc have been isolated as crystalline solids. The same publication reported the unsuccessful attempts to synthesize uranyl and lead complexes. Despite the large "hole" in the centre of dioxanorsapphyrin it was found not to form metal complexes with uranyl ions which are known to form pentagonal bipyramids[33]. Superphthalocyanide 26, a uranyl moiety coordinated to five subunit Pentakis-(2-iminoisoindoline) was first reported by Bloor et al.[34] and in 1974



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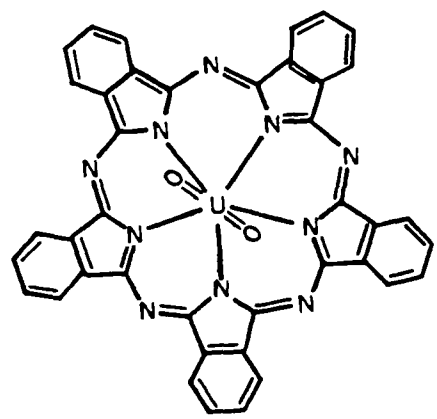
Day et al.[35] reported the synthesis of the same compound with improved chemical analysis. Attempts to displace the uranyl ion with acid or other metal ions invariably resulted in contraction of the macrocycle[36].



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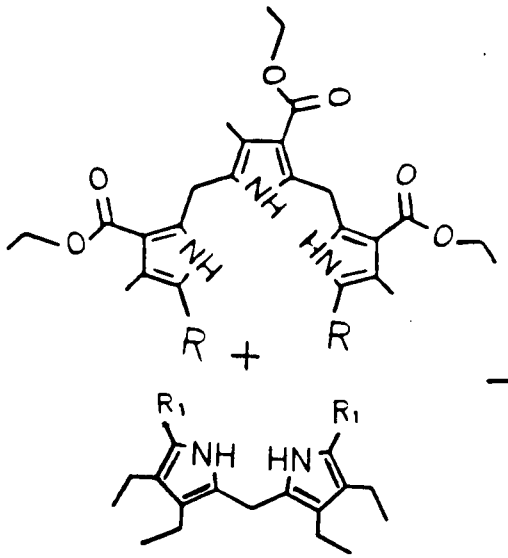
The success of the Harvard group in their syntheses of those sapphyrin macrocycles and the metal derivatives encouraged them to undertake a project to attempt the synthesis of the pentapyrrole analog of porphyrin. This project was aimed at the syntheses of decamethylpentapyrrole and other pentapyrrole macrocycles[37]. Employing the "3 + 2"

coupling analogous to MacDonald's "2 + 2" coupling (see Scheme 1), tripyrrane diacid and dialdehyde 27 (a & b) were used with dipyrromethane dialdehyde and the diacid 28 (a & b) respectively in the presence of catalytic amounts of p-toluenesulfonic acid in oxygenated ethanol and methanol (see Scheme 3). The coupling reactions were followed and monitored using electronic absorption for several days and in some cases for weeks, yielding porphyrins instead of the pentapyrrole macrocycles. Another attempt[38] was made to synthesize these pentapyrrole macrocycles in methylene chloride with anhydrous hydrogen chloride gas. The same porphyrin products as reported earlier[37] were obtained. Franck and co-workers[39] attempted to synthesize penta- and hexapyrrolic macrocycles directly by condensation of the tri- and tetrapyrroles with dipyrromethane dialdehydes in oxygenated methanol in the presence of hydrogen bromide (in acetic acid). In spite of the very mild reaction conditions, porphyrins were obtained accompanied by elimination of pyrrole units. Using the same starting pyrroles Franck[40] attempted again the syntheses of penta- and hexapyrrole macrocycles in glacial acetic acid at room temperature in the presence of 0.25% hydriodic acid. The result was not different from those reported earlier[39].

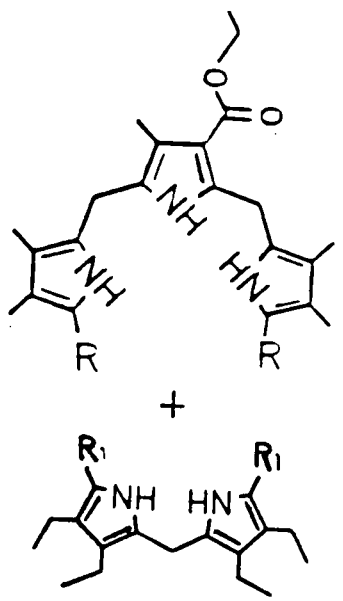
The first successful synthesis of pentapyrrolic macrocycle analogous to the porphyrins, ie. having five pyrrole rings with five methine bridges, was reported by Gossauer and Rehausen[41]. The five membered macrocycle for which they suggested the trivial name pentaphyrin 29, was obtained by the condensation of the dipyrromethane 30 with the tripyrrane dialdehyde 31 using methylene chloride as solvent and HBr in



PORPHYRIN

27 a: R=CHO, R_1=CO_2H

b: R=CO_2H, R_1=CHO



PORPHYRIN

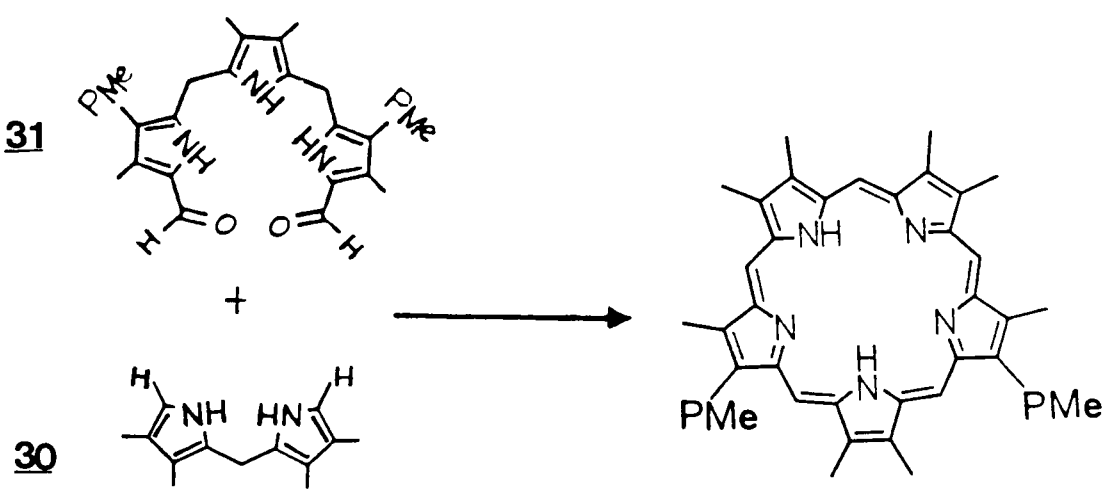
28 a: R=CO_2H, R_1=CHO

b: R=CHO, R_1=CO_2H

SCHEME 3

acetic acid as catalyst with oxidation of the initial cyclization product with chloranil (Scheme 4).

For a long time now work in our group[37,38] in attempting to shed light to various aspects of the pentaphyrin system was hampered by the failure of the precursors or systems to cyclize. This work was therefore undertaken in order to synthesize several pentaphyrins with different peripheral substituents and investigate the effects of those groups on cyclization yields, spectral properties and metalation and thereby complete the work already started in this group.



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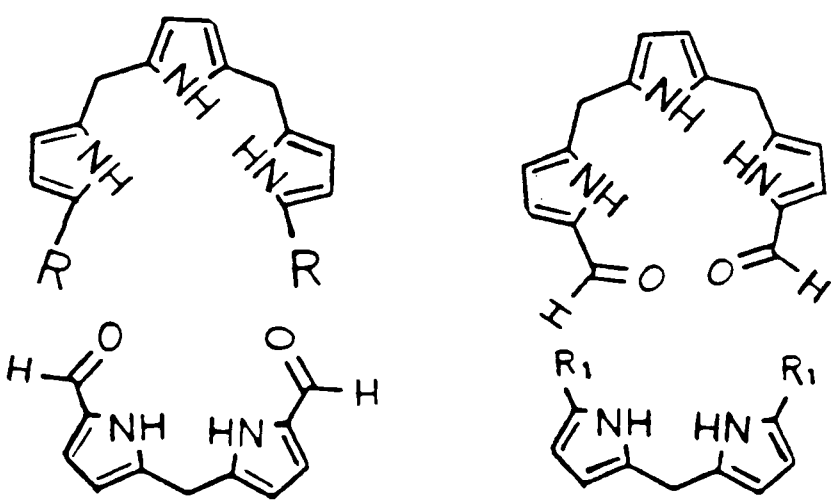
SCHEME 4

2. RESULTS AND DISCUSSIONS

2.1 SYNTHETIC STRATEGY

In the syntheses of pentapyrrolic macrocycles from pyrrolic precursors, the 3 + 2 condensation analogous to the MacDonald's 2 + 2 porphyrin synthesis (Scheme 1) can be employed. This condensation method plus the 4 + 1 condensation were used in the sapphyrin syntheses. In as much as linear tetrapyrroles (tetrapyrranes or bilanes) without electron-withdrawing stabilization on each pyrrole ring are difficult to handle, or even synthesize, most attention was directed to possible 3 + 2 synthesis. The syntheses of these macrocycles require "formylpyrroles" as the electrophilic component. Hence the two relevant 3 + 2 approaches involve the coupling of either a terminally unsubstituted tripyrrane with a dipyrromethane dialdehyde (Case A) or the reaction of 5,5'-unsubstituted dipyrromethane with a tripyrrane dialdehyde (Case B) as illustrated in figure 2.



A R=H or CO_2H B R=H or CO_2H

Figure 2. The 3 + 2 mode of approaches in Pentaphyrin Syntheses

In general di-α-unsubstituted tripyrranes and dipyrromethanes without electron-withdrawing groups are very unstable and require special handling procedures. Moreover, they are obtained by sublimation from their diacids at high temperatures with possibility of fragmentation due to the presence of catalyst used in the sublimation. Due to the above reasons, it was decided that the use of the dicarboxylic acid instead of the di-α-unsubstituted dipynomethane would be more appropriate. The tripyrrane or dipyrromethane dicarboxylic acid, apart from its relatively stable nature, readily undergoes decarboxylation under the acid conditions used for cyclization. Of the two relevant 3 + 2 approaches, (figure 1), case B has been found to be the only route to the synthesis of the pentapyrrolic macrocycle[41]. Most of the unsuccessful attempts in the synthesis of the pentapyrrole macrocycles [37,38,39,41] utilized the coupling of dipyrromethane dialdehydes and di-α-unsubstituted tripyrranes (figure 1, case A) resulting in only porphyrin formation without even traces of the desired pentapyrrolic product. In fact Gossauer et al.[41] initially failed in their attempt using these precursors. Thus the "diformyl" must be on the tripyrrolic unit rather than the dipyrromethane component in order to cause cyclization leading to the required macrocycle.

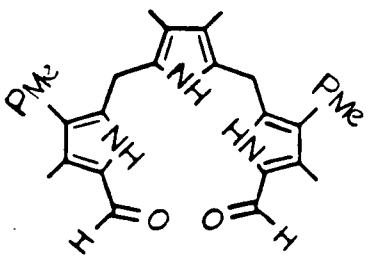
Generally, the free base dipyrromethenes and tripyrrenes dialdehydes are very unstable and thus, tripyrrenes cannot be used as such for case B. However, tripyrrenes can be a convenient source of tripyrranes when properly reduced. One of the target molecules is the decamethyl-derivative of our macrocycle and so it was found convenient to use the tetramethyldipyrromethane dicarboxylic acid 32 and hexamethyl-tripyrrane dialdehyde 33. The effect of an electron-withdrawing group on

the macrocycle was also considered. Tripyrranes, very vulnerable to random acid-catalysed fragmentation in the absence of electron-withdrawing groups, become the obvious choice for the introduction of this group. Thus, a tripyrrane whose central pyrrolic nucleus would be as deactivated as possible to internal fragmentation was considered. This required the presence of at least one electron-withdrawing group on the central pyrrolic unit, and for such a group, the ester group, ethoxycarbonyl was chosen.

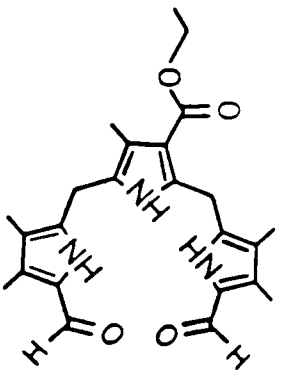
We decided to change the β-substituents of our diacid from the tetramethyl to the tetraethyl, couple it with the tripyrrane monoester dialdehyde 34 and find out how it would affect the macrocycle. Apart from being unstable in comparison to the tetramethyl, the tetraethyl analog would be much soluble. The use of several differently substituted pyrroles for the cyclization would also provide markers for some possible fragmentation modes should the reaction give only porphyrins and polymers.

It was decided to start this present work by first synthesizing the macrocycle reported in literature[41] using improved methods.

Therefore, the tripyrrane dialdehydes and dipyrromethane dicarboxylic acids to be synthesized are shown in figure 3.



31



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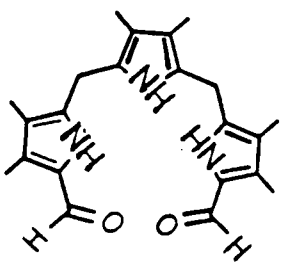
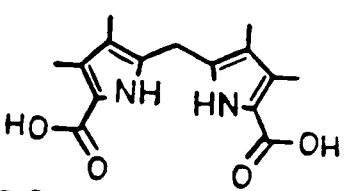
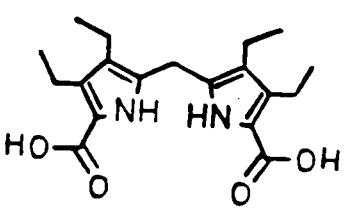


33



32



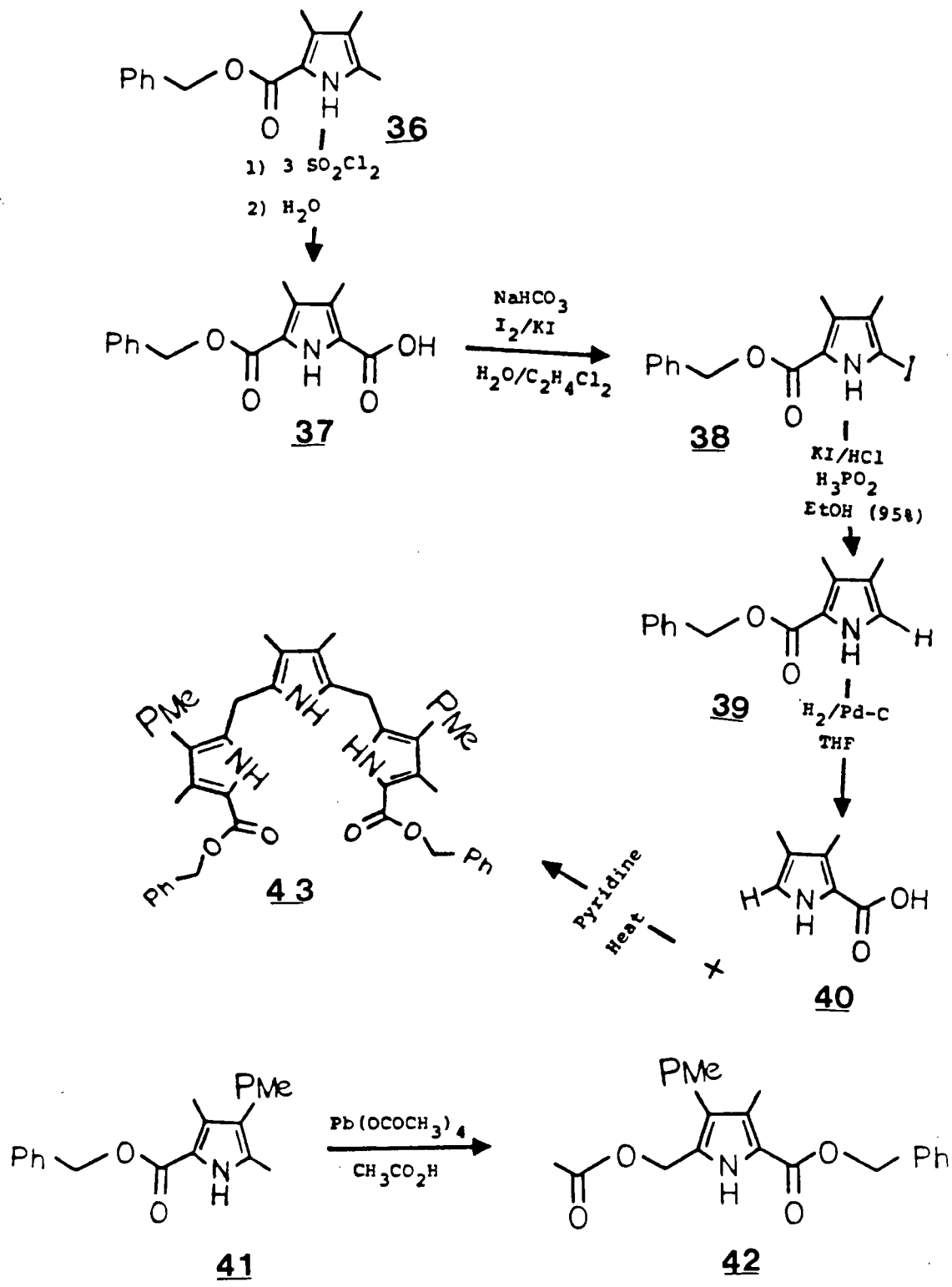
35

Figure 3. Intermediates for the syntheses of macrocycles

2.2 SYNTHESIS OF INTERMEDIATES

The essential basic pyrroles used in the preparation of the primary precursors, (dipyrromethane diacids and tripyrrane dialdehydes), were available in our laboratory. These had been previously synthesized from acyclic precursors using standard procedures[37]. Their purity was checked by melting point and spectroscopic analysis prior to use.

The synthesis of the tripyrrane 43 is outlined in Scheme 5. The trimethylpyrrole 36 was converted to its α-carboxypyrrole 37 derivative by treating 36 in dry ether with surfuryl chloride and hydrolysing the intermediate trichloro product. To prepare compound 40 an important precursor for the synthesis of tripyrrane 43 the α-carboxypyrrole 37 was first transformed to the α-free pyrrole by decarboxylation. This decarboxylation was obtained by an indirect iodination procedure (via 38) which gives high yields and pure products. In practise, the decarboxylative iodination of 37 was carried out in the two phase system of dichloroethane and water, using sodium bicarbonate to solubilize the starting material as its anion. The dichloroethane extracts the iodopyrrole 38 as it is formed, preventing the formation of solid pyrrole-iodine charge-transfer complexes[43]. Since the molecular iodine complexes cannot form, the iodine taken in excess (in aqueous potassium iodide) was rapidly added. The product was isolated from the organic phase after destroying the excess iodine with bisulfite. The yield of the recrystallised product was 80%. The subsequent deiodination was carried out by the use of hydriodic acid (a mixture of potassium iodide and


Ph
O
N
H
O
36
1) 3 SO_2Cl_2
2) H_2O
OH
37
$NaHCO_3$
I_2/KI
$H_2O/C_2H_4Cl_2$
38
KI/HCl
H_3PO_2
EtOH (95%)
39
H_2/Pd-C
THF
40
Pyridine
Heat
43
PMe
41
$Pb(OCOCH_3)_4$
CH_3CO_2H
42

SCHEME 5

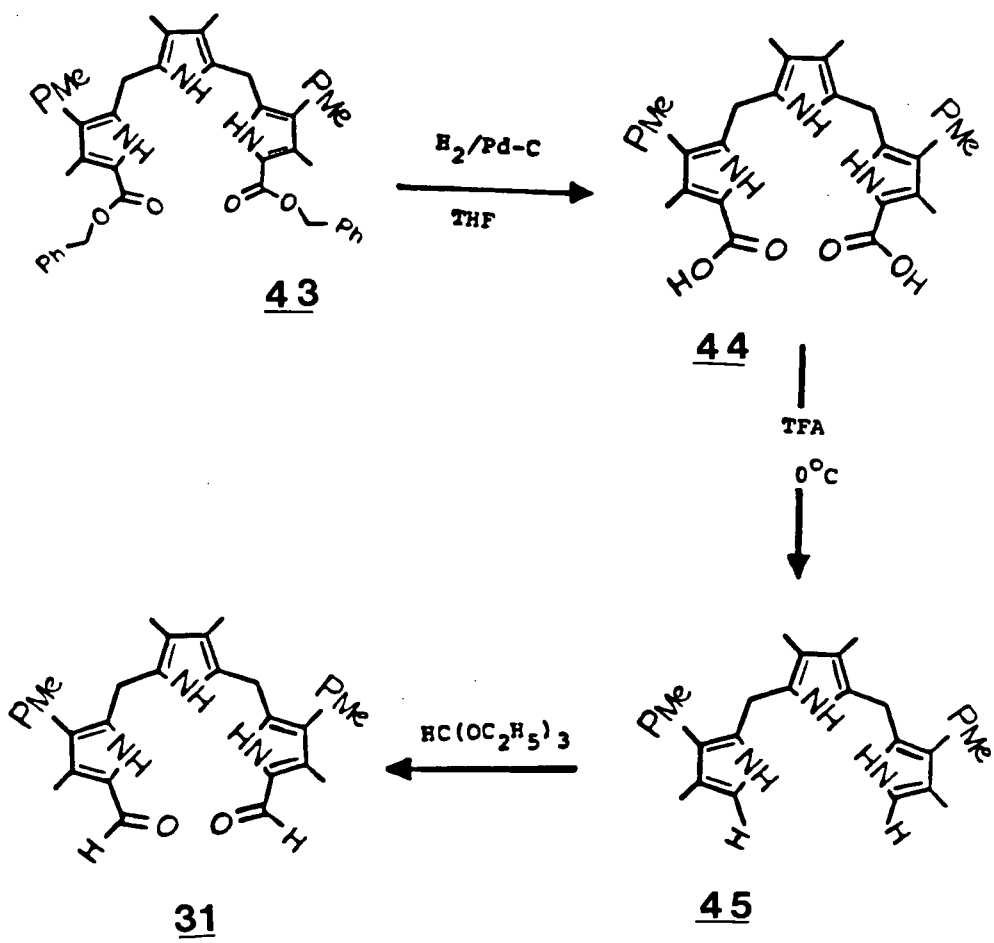
concentrated hydrochloric acid). The α-free pyrrole 39 was purified by chromatography and obtained in greater than 85% yield.

The 2-benzyloxycarbonyl-3,4-dimethylpyrrole 39 was next subjected to hydrogenation in order to cleave the benzyl ester group. The debenzylation was carried out in tetrahydrofuran at room temperature and atmospheric pressure using 10% palladium on charcoal as the catalyst to obtain the α-carboxy-α-free pyrrole 40 in over 95% yield. It was used as it is in the next step. The 2-benzyloxycarbonyl-4-methoxycarbonylethyl -3,5-dimethylpyrrole 41 was acetylated using one equivalent of lead tetraacetate in acetic acid[44]. The resulting product 42 was recrystallized from methylene chloride-hexane to give a fluffy solid in approximately 60% yield.

Having synthesized pyrroles 40 and 42 the next step was the preparation of the symmetrical tripyrrane 43. This was effected via the method used by Clezy and Liepa[45]. The pyrroles 40 and 42 in pyridine solution were heated on a steam-bath overnight. The precipitate obtained was crystallized from ethanol to give colorless plates in approximately 31% yield.

Scheme 6 outlines the conversion of the tripyrrane dibenzyl ester 43 to the tripyrrane dialdehyde 35 required for coupling. Tripyrrane 43 was hydrogenated as in compound 39 and the resulting crude tripyrrane dicarboxylic acid 44 formylated[46].

Thus the diacid 44 dissolved in trifluoroacetic acid with stirring near 0° C under argon atmosphere, underwent rapid decarboxylation. After 15 minutes, triethylorthoformate was added, reacting with the newly produced bis α-free tripyrrane 45. The product was dissolved in methylene



43 44 45 31

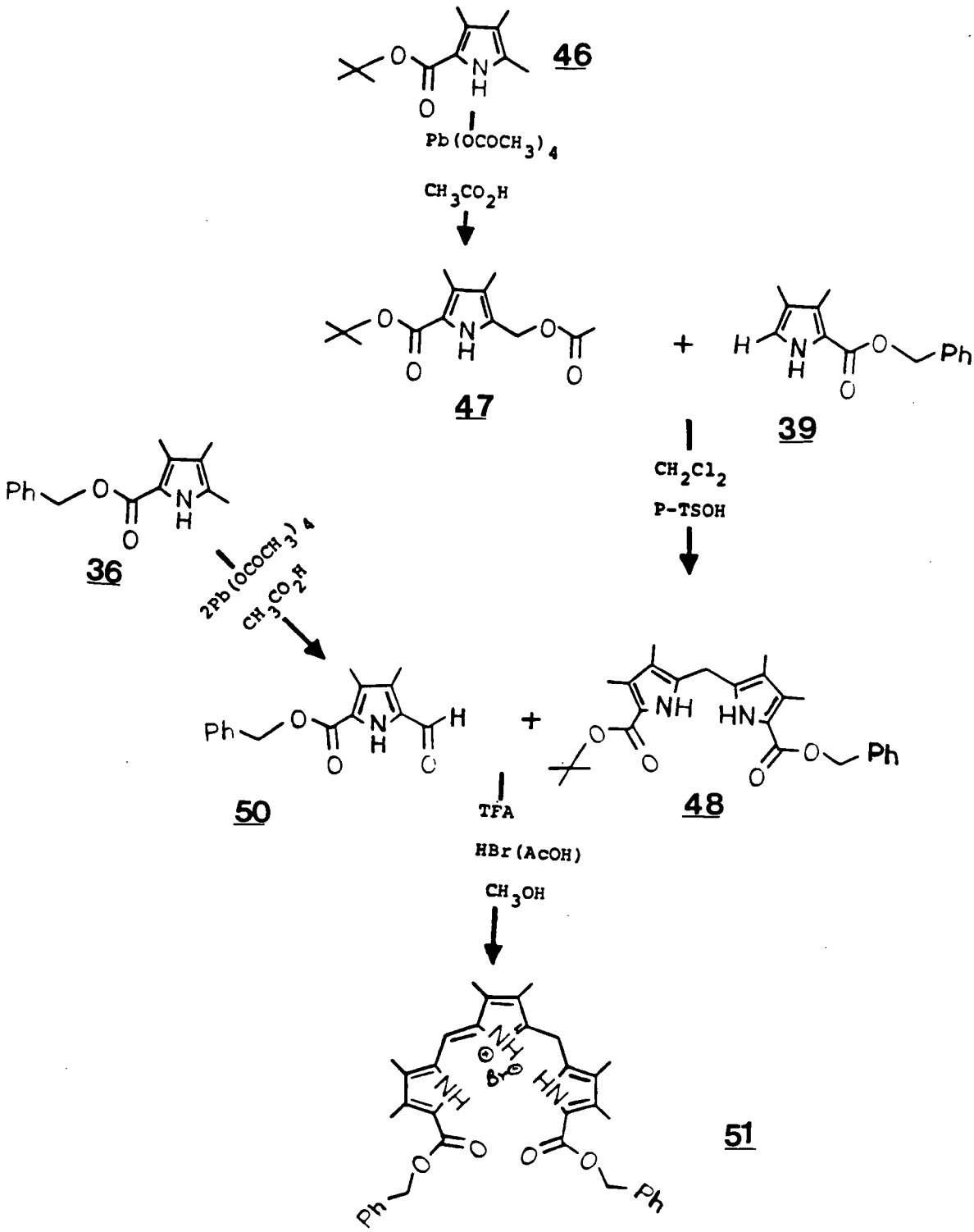
SCHEME 6

chloride and recrystallized from methanol to give the tripyrrane dialdehyde 31 in about 43% yield.

The synthesis of tripyrrane 33 was accomplished via the tripyrrin 51 whose synthesis is outlined in Scheme 7.

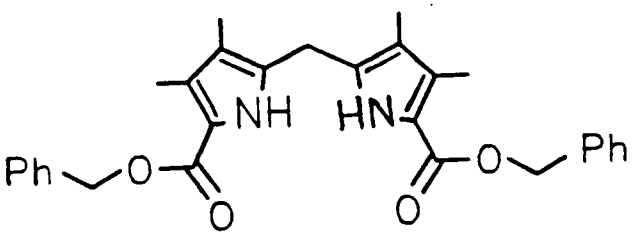
Esters requiring milder and different means of removal have become established as the functionalities of choice for many applications. These include the t-butyl esters, readily deprotected in strong acid and benzyl esters, which on catalytic hydrogenolysis afford the carboxypyrroles under mild, neutral conditions. The key intermediate here, therefore, is the dipyrromethane 48 with t-butyl and benzyl esters at 5 and 5' positions allowing manipulation of the two positions independently. Pyrrole 47 was obtained by treatment of pyrrole 46 with one equivalent of lead tetraacetate in glacial acetic acid and recrystallized from hexane.

For the coupling of pyrrole monoesters, MacDonald et al.[47] have devised a procedure whereby a bromomethylpyrrole or an acetoxymethylpyrrole is refluxed with an α-unsubstituted pyrrole in sodium acetate buffered acetic acid. Smith and collaborators[44] have synthesized dipyrromethanes using acetoxymethylpyrrole and α-unsubstituted component by boiling them in glacial acetic acid to a temperature of 120-130° C. The main draw-back in a synthesis of this type is the possibility of self-condensation of the bromomethyl or acetoxymethyl component via a solvolytic process to give the symmetrical dipyrromethane. The milder reaction conditions used by Battersby et al.[48] were employed here since less decomposition products were obtained. The pyrrole 47 in methylene chloride was added dropwise over a twenty minute period to a solution of


46
Pb(OCOCH3)4
CH3CO2H
47
39
CH2Cl2
P-TSOH
36
2Pb(OCOCH3)4
CH3CO2H
50
48
TFA
HBr(AcOH)
CH3OH
51

SCHEME 7

the α-unsubstituted pyrrole 39 in methylene chloride containing catalytic quantity of P-toluenesulfonic acid, under a nitrogen atmosphere. The resulting oil obtained dissolved in methylene chloride and petroleum ether to produce a white powder approximately 10% yield which was shown by nmr to be the symmetrical dibenzylester 49. After filteration, the filtrate and the washings were evaporated and recrystallized from warm petroleum either to produce the required dipyrromethane mixed esters 48 in approximately 84% yield.

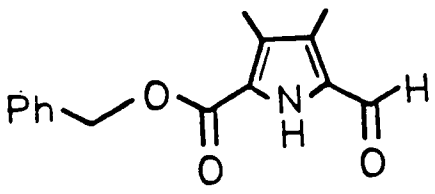


49

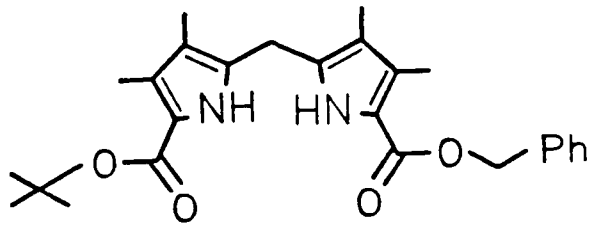
The oxidation of α-methylpyrrole 36 to the corresponding formylpyrrole 50 can be achieved in different ways. The usual oxidants are sulfuryl chloride, tertiary butyl hypochloride or lead tetraacetate[16] and the reaction conditions are similar to those used for monooxidation, except that two equivalents are used. With sulfuryl chloride, a lack of selectivity coupled with a competing reaction with ether solvent often leads to incomplete oxidation and formation of symmetrical dipyrromethane from the intermediary chloromethylpyrrole upon hydrolsyis. This can be avoided by the use of methylene chloride as the only solvent and performing the oxidation at high dilution near 0°C. Lead tetraacetate[49] requires heating to induce the second equivalent to react. It may be taken in considerable excess, as it cannot oxidize α-pyrrlmethyls beyond the aldehyde stage (presumably due to in-situ

decomposition of the diacetoxymethylpyrrole to the free aldehyde and acetic anhydride). Thus, 2-benzyloxycarbonyl-3,4,5-methylpyrrole 36 was dissolved in glacial acetic acid and one equivalent of lead tetraacetate added fairly rapidly. This allows the exothermicity of the reaction to heat up the solution which allows the second equivalent of oxidant to react promptly. A temperature of 70-80° C was maintained on a steam-bath with occasional manual swirling until all the solids were dissolved. Water was added to crystallize out the product. The product was recrystallized from methylene chloride-hexane to give solid of 73% yield of compound 50.

For certain purposes, t-butyl esters may be deprotected and the resulting carboxylic acid decarboxylated by dissolution in triflouroacetic acid. Clezy[50] has established that bis-α-free dipyrromethenes are stable ion this solvent for up to a week at room temperature. Kenner et al.[16] have routinely used trifuoroacetic acid to cleave t-butylesters 48. In the synthesis of tripyrrin hydrobromide 51 the reported method of Smith et al.[51] was used. Compound 48 was treated with neat trifluoroacetic



50



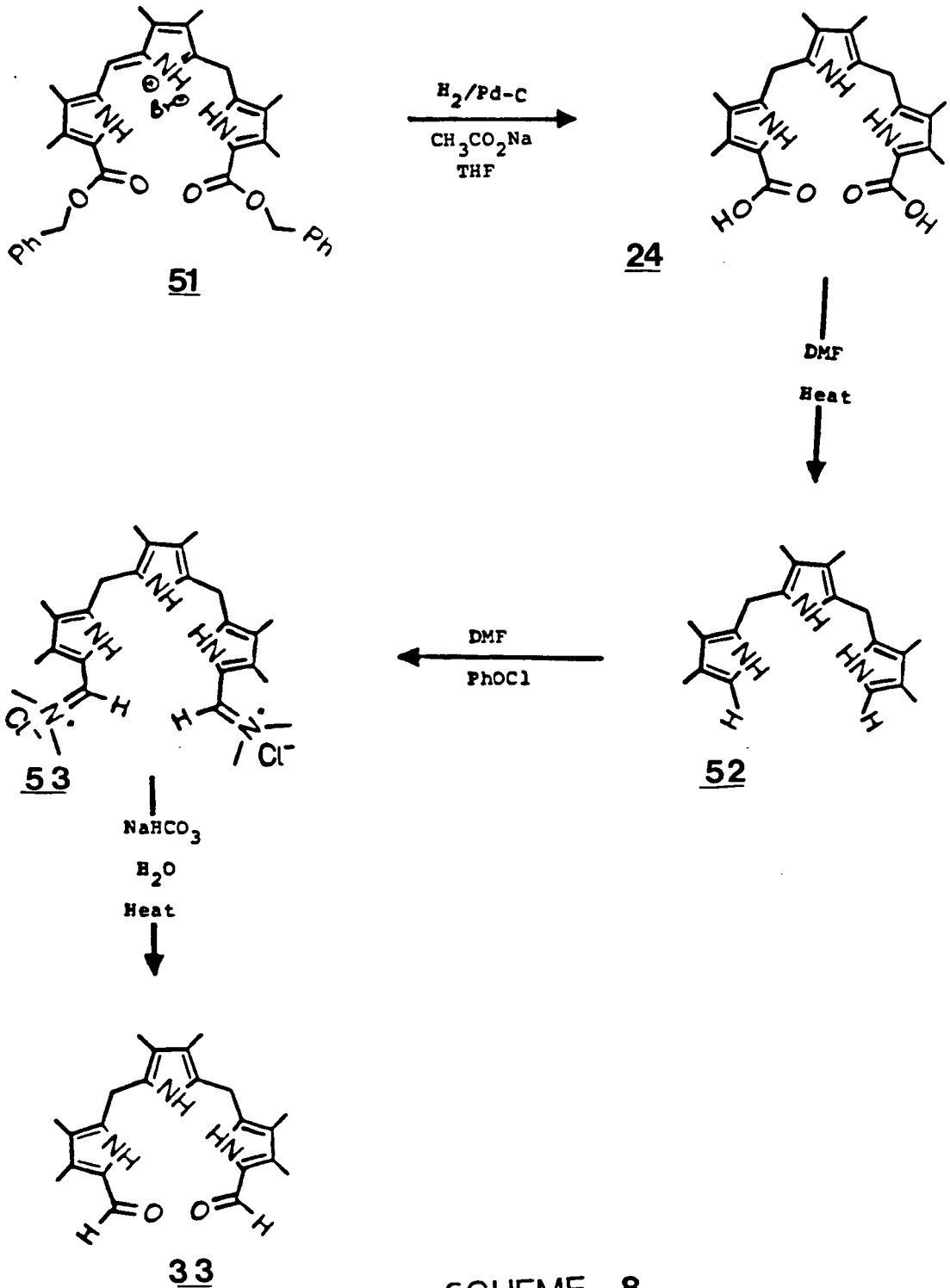
48

acid with stirring under a nitrogen atmosphere at ambient temperature for about 5 minutes. The formylpyrrole 50 previously dissolved in methanol was added all at once. The reddish solution was stirred for an additional 90

minutes period followed by the addition of hydrogen bromide in acetic acid (30-32%) and ether. The fluffy reddish solid, separated out after 15 minutes stirring, was filtered, washed with ether and air dried to give 76% yield of tripyrrin hydrobromide 51.

To obtain tripyrrane dialdehyde 33 (Scheme 8) the tripyrrin hydrobromide 51 was catalytically hydrogenated in order to cleave the benzyl ester groups and to hydrogenate the double bond. The reaction was carried out in tetrahydrofuran with few drops of triethylamine and sodium acetate, at room temperature and atmospheric pressure using 10% palladium on charcoal as the catalyst. The tripyrrane diacid 24 was obtained as a red powder. The crude tripyrrane diacid 24 was subjected to thermal decarboxylation without further purification.

Several high boiling solvents are generally used for this purpose of which dimethylformamide has a distinct advantage over the others for this work. It's reflux temperature of 153° C is sufficient not only to decarboxylate the tripyrrane but also to remove any remaining toluene (the byproduct of hydrogenolysis of the benzyl esters), from the crude starting material. Furthermore dimethylformamide is one of the reagents used in the next reaction, i.e. the Vilsmeier formylation and therefore it is not necessary to isolate the decarboxylated product. The decarboxylation of 24 in dimethylformamide was followed by uv spectroscopy. The starting material exhibited a single absorption band at approximately 285 nm. After one hour of reflux, this band was observed to be removed completely indicating the completion of the decarboxylation. The reaction mixture was cooled and the produce 52 used in the dimethylformamide solution for the formylation reaction.

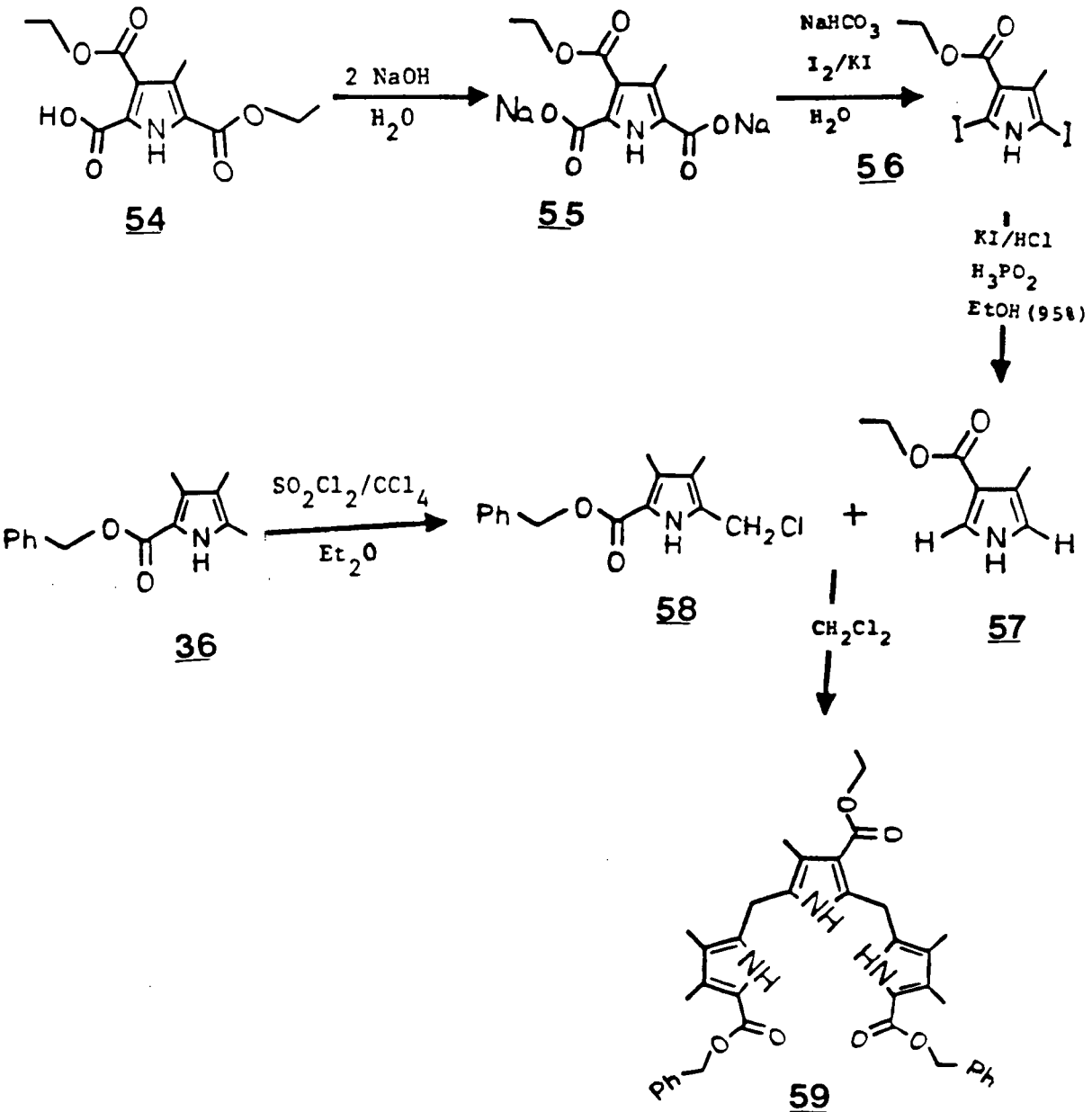


51 24 52 53 33

SCHEME 8

The introduction of the formyl group was effected by the Vilsmeier reaction[52] whereby the bis-α-unsubstituted tripyrrane 52 in dimethylformamide solution is treated with phosphorous oxychloride or benzoyl chloride[53]. This is known to proceed via an iminium salt of the type 53. The iminium salt could be isolated in crystalline form if benzoyl chloride is used and this can subsequently be hydrolysed in aqueous base to give the tripyrrane dialdehyde 33. A weakly basic medium is usually provided for the hydrolysis by using sodium bicarbonate or sodium acetate[52,53]. The formylation of tripyrrane 52 was effected using benzoyl chloride, the iminium salt was not isolated but hydrolysed directly in aqueous sodium bicarbonate (pH 8-9). The precipitate was dissolved in methylene chloride and recrystallized from methanol to give 33 as an orange solid.

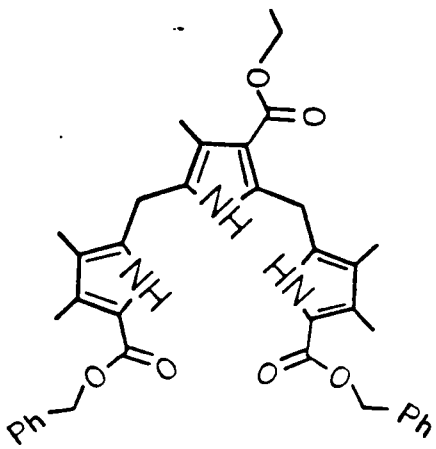
The synthesis of tripyrrane 59 is outlined in Scheme 9. The pyrrole 54 used as the precursor to the central unit of compound 59 was saponified readily to the disodium salt 55 by heating with two equivalents of sodium hydroxide. To maximize the yield, the resulting solution of the disodium salt was iodinated directly as before to give the diiodopyrrole 56 as a dense granular crystalline solid. This was deiodinated, without further purification, directly to the diα-free pyrrole 57 as described for pyrrole 38 (Scheme 5). The di-α-free pyrrole 57 reacted spontaneously in methylene chloride at room temperature with two equivalents of the α-chloromethylpyrrole 58 to give the tripyrrane 59. The α-chloromethylpyrrole 58 in turn was prepared by sulfuryl chloride oxidation of 2-benzyloxycarbonyl-3,4,5-trimethyl- pyrrole 36 in carbon


2 NaOH
H_2O
$NaHCO_3$
I_2/KI
H_2O
KI/HCl
H_3PO_2
EtOH (95%)
SO_2Cl_2/CCl_4
Et_2O
CH_2Cl_2
54
55
56
57
58
59
36

SCHEME 9

tetrachloride. The tripyrrane 59 was obtained from the reaction mixture, together with the symmetrical dipyrromethane 49 and was isolated in pure form by preferential crystallization using tetrahydrofuran-methanol. The yield was only 39%. The tripyrrane 59 was catalytically hydrogenated to give the diacid 60 (Scheme 10). The same process used to obtain compound 33 was used in obtaining compound 34 except that, the decarboxylation of 60 took about 2 hours and the formylation was achieved by using phosphorous oxychloride.

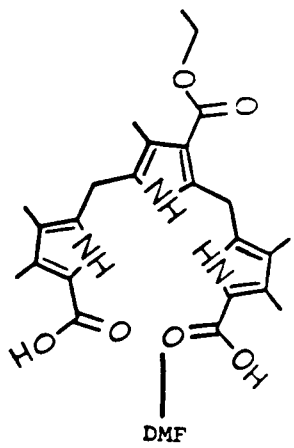
With the tripyrrane dialdehydes ready, the next step was the syntheses of dipyrromethane diacids for the coupling reactions. With the pyrrole 63 in hand, transbenzylation was considered. Transbenzylation is a useful reaction in pyrrole chemistry due to its high yields and the ease of removal of the benzyl esters when required. Thus the syntheses of dipyrromethane diacids 32 and 35 are illustrated in Scheme 11. The pyrrole 64 was obtained in greater than 90% yield from its ethyl ester analog 63 by transesterification in redistilled benzyl alcohol at refluxing temperature using sodium benzyloxide as a catalyst[54,55]. A slight modification of Clezy and Liepa procedure[45] was used in the preparation of the dipyrromethane. 2-Benzyloxycarbonyl-3,4-diethyl-5-methyl pyrrole 63 was acetylated in the usual manner in glacial acetic acid with lead tetraacetate. After precipitating the product 65 with water, it was filtered, and dissolved in 80% glacial acetic acid and heated to reflux. The reaction was followed with tlc, and when all the starting materials had reacted to give a single product on tlc, the reaction mixture was cooled and water added to precipitate the product. The product was collected and recrystallized from ethanol to give solids



59

H_2/Pd-C

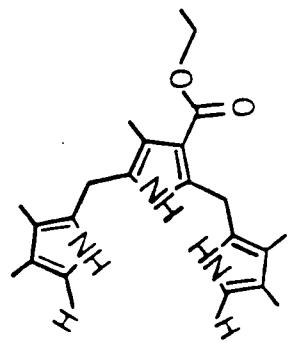
THF



DMF

60

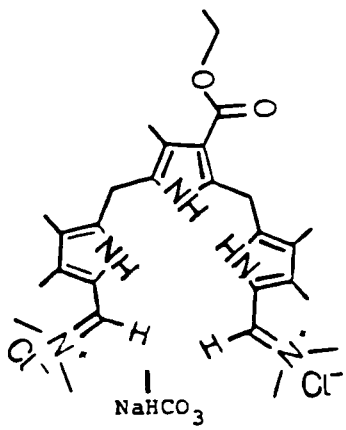
Heat



61

DMF

$POCl_3$

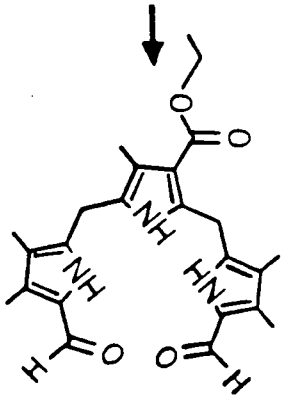


$NaHCO_3$

H_2O

62

Heat

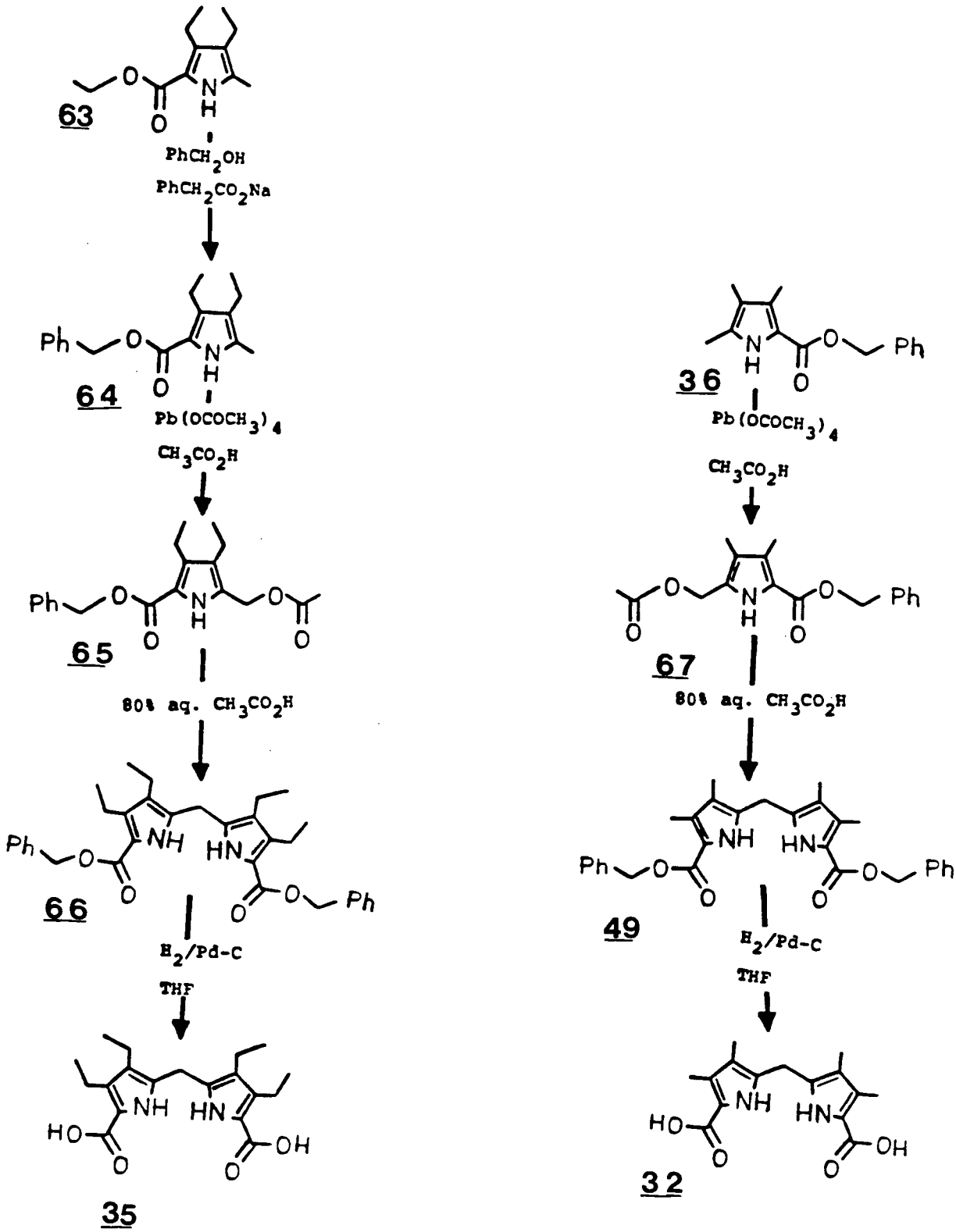


34

SCHEME 10

in 76% yield of 66. In a similar way the dibenzyl ester 49 was prepared from pyrrole 36 through 67.

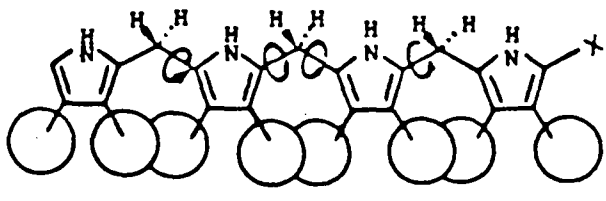
The dibenzyl ester 66 was converted to the diacid 35 by catalytic hydrogenation in tetrahydrofuran at room temperature and atmospheric pressure. When the uptake of hydrogen ceased, the catalyst was filtered off and the filtrate made up to known volume and stored in the fridge in the dark due to the unstable nature of diacid 34. The diacid 32 was prepared by hydrogenolsis of the dibenzyl ester 49 in the same way as 66. With the diacid 32 after filtration, the solvent was evaporated on the rotary evaporator at room temperature. The light-yellowish solid was stored in the fridge in the dark and used as it was for the cyclization reaction without purification.


63
PhCH2OH
PhCH2CO2Na
64
Pb(OCOCH3)4
CH3CO2H
65
80% aq. CH3CO2H
66
H2/Pd-C
THF
35
36
Pb(OCOCH3)4
CH3CO2H
67
80% aq. CH3CO2H
49
H2/Pd-C
THF
32

SCHEME 11

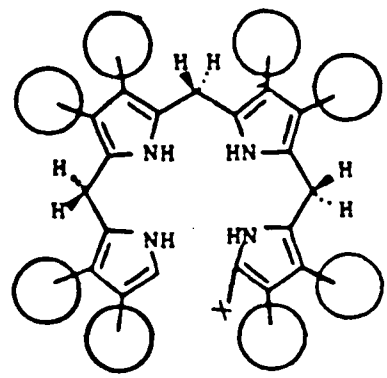
2.3 SYNTHESIS OF THE MACROCYCLES

The exclusive formation of porphyrins and non cyclic polymeric products in attempts to synthesize the pentapyrrolic macrocycle from dipyrromethane dialdehyde and the di-α-unsubstituted tripyrrane precursors has already been mentioned. It must be added that the formation of porphyrins is not limited to the aforementioned pyrroles but was also observed during this work. This was easily detected by uv-visible spectroscopy in monitoring the reaction and by the characteristic fluorescence of porphyrins on the plates under long wavelength uv light. Franck et al.[39] attributed this behaviour to the strong preference for porphyrin formation compared to the pentaphyrin macrocycle. This preference is explained by the strong destabilizing steric interaction of the side chain in the β-position in the linear conformation 68 of the open-chain tetrapyrrole porphyrin precursors. The helical conformation 69 is thought to provide the prerequisites for ring closure to afford porphyrins due to reduction in such interactions.



68

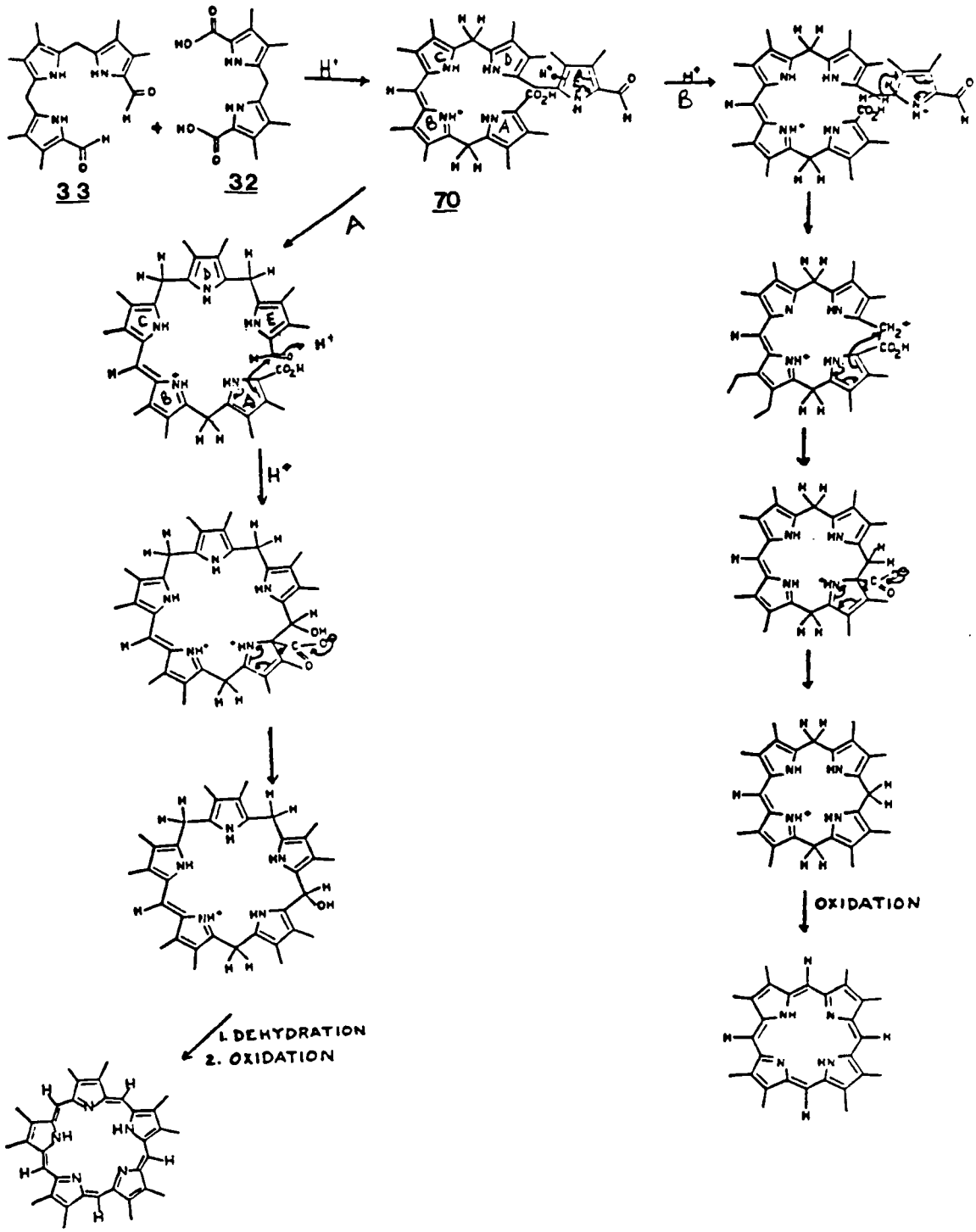
X = CHO



69

Thus, a possible mechanism for the pentaphyrin and the preferred porphyrin formation can be derived as illustrated in Scheme 12. If tripyrrane dialdehyde 33 couples with dipyrromethane diacid 32 in acidic medium, a helical conformation of pentapyrrole 70 results with two possible modes for cyclization. First, there is a high probability of protonation at the electron-rich α-position of the pyrrole ring E with the resultant elimination of formylpyrrole and subsequent cyclization and oxidation to give the porphyrin (route B). The second (route A) is the protonation of the aldehyde on the ring E followed by cyclization, dehydration and oxidation to give the required pentaphyrin. Thus, the porphyrins which appear as a natural product is extremely favored in its formation.

In many of the attempted syntheses of the pentaphyrrin macrocycle, a stream of air was bubbled or allowed to diffuse through the reaction mixture and the end product resulting in porphyrin without any traces of pentaphyrin. This was noted to be the case in this work when air accidentally diffused through the reaction mixture. Thus oxygen, the main oxidizing agent in the syntheses of porphyrins in the laboratory possibly favors exclusive production of porphyrin probably through route B (scheme 12). In the pentaphyrin synthesis, the bridging carbons of the tripyrrolic unit must be at the methane oxidation level since methenes would be promoted under acidic coupling conditions and thus be effectively non-nucleophilic. This has also been observed in the sapphyrrin syntheses.



SCHEME 12

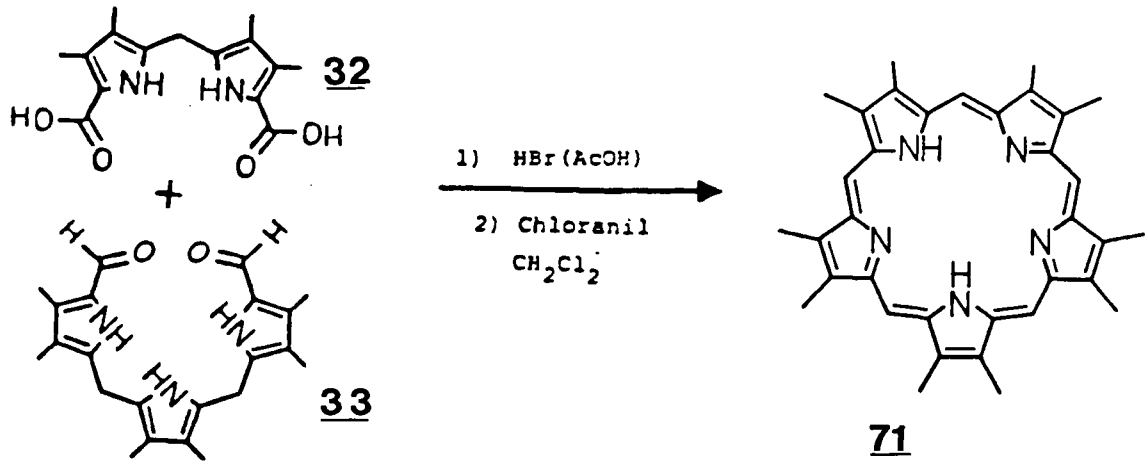
To effect the coupling, the reaction was carried out at high dilution to minimize linear polymerization. The reaction was also carried out a room temperature to minimize random fragmentation. Since little is known about the sensitivity of these macrocycles to light, they were protected from light from the coupling reaction through work up to the final product (cf with intermediates in porphyrin synthesis).

In a typical reaction, dipyrromethane diacid 32 (Scheme 13) was suspended in methylene chloride (which has been "degased" by bubbling argon through for 2 hours) and stirred for 20 minutes under argon. Tripyrrane dialdehyde 33 was added and the reaction mixture stirred for an additional 15 minutes after which HBr in acetic acid (30-32%) (catalytic quantity) was added to effect the condensation. The color of the reaction mixture passed through a series of changes, the original yellowish solution quickly turning orange and subsequently to red (also observed in dipyrromethene coupling passing through the porphodimethenes). The reaction mixture was allowed to stir for 2 hours, the oxidizing agent, chloranil added and the reaction-solution was stirred further for 36 hours. The reaction was monitored using electronic absorption; the visible and the near-ultraviolet regions of the spectrum were found most useful.

From the uv-visible spectra of the reaction mixture, a successful reaction becomes evident 30 minutes after the addition of the acid catalyst, HBr (in acetic acid). A characteristic band around 450-460 nm, the Soret is a definite sign of the formation of the pentaphyrin. Also present in almost equal intensity, at times, to the above mentioned band is another band around 480-490 nm. On the addition of the oxidizing

agent, tetrachlorobenzoquinone, there is a shift of the 480-490 nm band to 500 nm which, at times, competes with the Soret band in intensity. In most cases the intensity of the Soret increased appreciably compared to the other band which was found to be due to polymeric pyrroles.

The solvent was evaporated to dryness in vacuo to give a dark brown residual product. Tlc studies showed that ethyl acetate was a good eluting solvent in that most of the porphyrinic and other byproducts are "washed off" leaving the desired product and other impurities as a



SCHEME 13

dark-green band at the origin. Thus preparative chromatography using silica gel with fluorescent indicator and ethyl acetate as the eluent was used. After properly drying the plates, the dark-greenish fraction which stayed at the origin was scraped and eluted with methylene chloride-methanol (10:1). (The solubility of the decamethylpentaphyrin was found to be quite different from the others in being less soluble, and thus, the polarity of the solvent had to be increased to methylene chloride-methanol (5:1)). The solvent was evaporated off and the residual product was twice chromatographed on a column using silica gel and eluted with 5% methanol in methylene chloride. The green fraction was collected and the solvent evaporated to give an orange decamethylpentaphyrin 71 of about 21% yield. All the pentaphyrins synthesized during the course of this work could not be subjected to combustion analysis due to the inability of obtaining solid samples.

The zinc complexes of pentaphyrins 71 and 74 were also prepared. The "acetate method"[62(a,b)] using anhydrous zinc acetate was employed in this syntheses. The choice of solvent was methanol in which both the pentaphyrins and zinc acetate are readily soluble. A methanolic solution of pentaphyrin with anhydrous zinc acetate and sodium acetate was stirred for 5 hours and allowed to stand at room temperature for three days. The reaction was monitored by uv-visible spectroscopy. Spectral changes

indicated that pentaphyrins, like porphyrins and sapphyrin, form metal complexes. A yield of 66.8% and 54% was obtained for compounds 72 and 73 respectively.

3. EXPERIMENTAL

3.1 GENERAL METHODS

Melting point determination were obtained using a 6548-J17 microscope equipped with a Thomas Model 40 micro hot stage

Elemental analysis was performed by Mr. P. Borda of the Micro Analytical Laboratory, UBC

Electronic absorption spectra in the uv and visible region were recorded using a Cary 17 spectrometer

^{1}H nmr spectra of the pentaphyrrins were recorded at 400 MHz using a Bruker WH-400 spectrometer. All the intermediates were generally recorded at 100 MHz with a Varian XL-100 Fourier-transform spectrometer

^{13}C nmr spectra were recorded at 75 MHz on the Varian XL-300

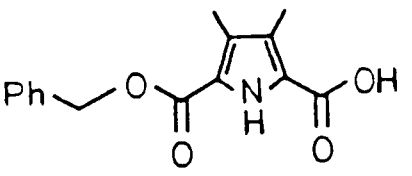
Mass spectra were recorded on a Varian MAT CH4-B spectrometer or a Kratos/AEI MS-902

Thin layer chromatography was carried out using precoated silica gel GF plates (Analtech, 250 μ)

Preparative chromatography was carried out using silica gel GF (Analtech, 20 x 20 cm, 2000 μ)

Column chromatography was carried out using silica gel GF60 (230-400, Merck)

3.2 STARTING MATERIALS

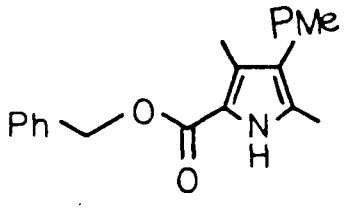


Mol. Formula $C_{15}H_{15}NO_4$ Mol. Wt. 273.3

M.P. 211-213° C Lit[56]: 212-214° C

Mass Spectrum: m/e (relative intensity) 273(17), 91(100)

^{1}H nmr: (δ,$DMSO_4$-d_6) 2.30(6H,S), 5.37(2H,S), 7.43(5H,S), 9.42(1H,NH), 11.52(1H,S,COOH)

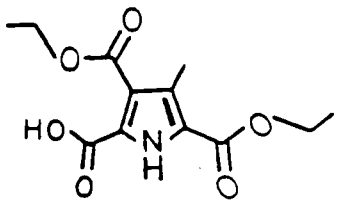


Mol. Formula $C_{18}H_{21}NO_4$ Mol. Wt. 315.3

M.P. 98-99° C Lit[57]: 99-101° C

Mass Spectrum: m/e (relative intensity) 315(19), 242(29), 91(100)

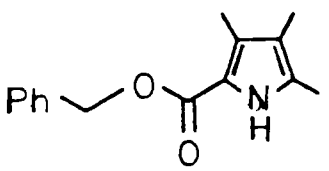
^{1}H nmr: (δ,$CDC\ell_3$) 2.22(3H,S), 2.31(3H,S), 2.38(2H,q,J=7.5Hz), 2.67(2H,q,J=7.5Hz), 3.68(3H,S), 5.30(2H,S), 7.39(5H,S), 8.50(1H,br,NH)



Mol. Formula $C_{12}H_{15}NO_6$ Mol. Wt. 269.2

M.P. 149-151° C Lit[58]: 150° C

^{1}H nmr: (δ,$CDC\ell_3$) 1.40(3H,t,J=7Hz), 1.48(3H,t,J=7Hz), 2.62(3H,S), 4.41(2H,q,J=7.5Hz), 4.52(2H,q,J=7.5Hz), 10.25(1H,br,N<u>H</u>), 14.80(1H,S,COO<u>H</u>)

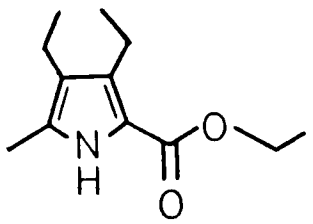


Mol. Formula $C_{15}H_{17}NO_2$ Mol. Wt. 243.3

M.P. 117-118° C Lit[26]: 119-120° C

Mass Spectrum: m/e (relative intensity) 243(31), 109(13), 91(100)

^{1}H nmr: δ($CDC\ell_3$) 1.91(3H,S), 2.18(3H,S), 2.28(3H,S), 5.99(2H,S), 7.36(5H,m), 8.61(1H,bs,N<u>H</u>)

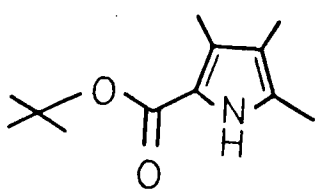


Mol. Formula $C_{12}H_{19}NO_2$ Mol. Wt. 209.3

M.P. 76-77° C Lit[37]: 75° C

Mass Spectrum: m/e (relative intensity) 209(46), 194(45), 148(100)

^{1}H nmr: (δ,$CDC\ell_3$) 1.03(3H,t,J=7Hz), 1.38(3H,t,J=7Hz), 2.25(3H,S), 2.40(2H,q,J=7.5Hz), 2.70(2H,q,J=7.5Hz), 8.72(1H,bs,NH)



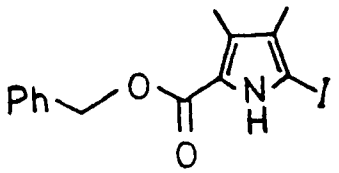
Mol. Formula $C_{12}H_{19}NO_2$ Mol. Wt. 209.3

M.P. 136-138° C Lit[59]: 137-138° C

Mass Spectrum: m/e (relative intensity), 209(17), 153(54), 135(100)

^{1}H nmr: (δ,$CDC\ell_3$) 1.10(9H,S), 1.93(3H,S), 2.20(3H,S), 2.25(3H,S), 8.83(1H,bs,NH)

3.3 SYNTHESES OF INTERMEDIATES



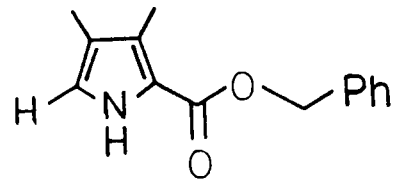
2-Benzyloxycarbonyl-5-iodo-3,4-dimethylpyrrole (38)

5-Benzyloxycarbonyl-3,4-dimethyl-2-carboxylic acid (8.2 g, 0.03 moles) 37, sodium bicarbonate (10.1 g, 0.12 moles), water (60 mL) and dichloroethane (60 mL) were placed in an erlenmeyer flask and heated on a hot plate while stirring. The starting material dissolved with effervescence. When the temperature of the solution reached 71° C, a solution of iodine (8.9 g, 0.035 moles), sodium iodide (9.0 g, 0.06 moles) and water (60 mL) was added within 10 minutes by the aid of a dropping funnel. The solution was refluxed for one hour and the excess iodine was destroyed with sodium bisulfite (a pale yellow color remained in the organic layer while the aqueous layer turned colorless). The organic phase was separated, filtered and evaporated to dryness. The crude product was redissolved in ethanol (100 mL) and the solid was reprecipitated by adding water, collected by filtration and washed with 50% ethanol-water followed by water to give 5.7 g (53.5%). The mother liquors were concentrated for a second crop of 2.8 g (26.5%).

M.P.: 125-126° C Lit[42]: 126-128° C Mol. Wt.: 355.2

^{1}H nmr: (δ,$CDC\ell_3$) 1.98(3H,S), 2.33(3H,S), 5.33(2H,S), 7.39(5H,S), 8.88(1H,br)

Mass Spectrum: m/e (relative intensity) 355(m^+,19), 228(6), 91(100), 65(15)



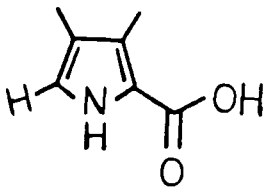
2-Benzyloxycarbonyl-3,4-dimethylpyrrole (39)

2-Benzyloxycarbonyl-5-iodo-3,4-dimethylpyrrole (21.3 g, 0.06 moles) 38 was dissolved in 95% ethanol (150 mL) by warming on a steam bath. A solution of potassium iodide (11.6 g, 0.07 moles) in water (20 mL) and concentrated hydrochloric acid (25 mL) was added liberating iodine. 50% aqueous hypophosphorous acid (40 mL) was added to discharge the iodine color and the reaction mixture heated on the steam bath for 20 minutes. The solution was cooled, methylene chloride (150 mL) and water (100 mL) added, the organic phase isolated and dried (Na_2SO_4). The solvent was evaporated under reduced pressure and the residual product dissolved in methylene chloride (15 mL) and chromatographed on silica gel using methylene chloride as the eluting solvent. All of the colored impurities remained at the origin and the α-free pyrrole eluted out clean as a pale yellow liquid. The solvent was evaporated and the product crystallized out from Hexane. The yield of the α-free pyrrole was 11.7 g (85.2%).

M.P.: 74-75° C Lit.[58]: 64-66° C Mol. Wt.: 229.3

^{1}H nmr: (δ,$CDC\ell_3$) 2.03(3H,S), 2.30(3H,S), 5.31(2H,S), 6.66(1H,d) 7.40(5H,S), 8.70(1H,br)

Mass Spectrum: m/e (relative intensity) 229(m^+,32), 138(24), 91(100), 65(24)



2-carboxy-3,4-dimethylpyrrole (40)

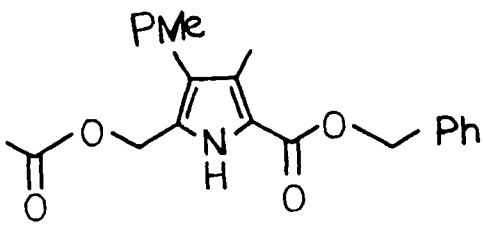
2-Benzyloxycarbonyl-3,4-dimethylpyrrole (4.6 g, 0.02 moles) 39 in THF (100 mL) was stirred overnight under hydrogen in the presence of 10% palladium on charcoal (400 mg). When the uptake of hydrogen ceased, the catalyst was filtered and the solution checked by TLC for any unconverted starting material. The solvent was evaporated off, in vacuo, leaving pure white product. Yield 2.65 g (95.3%).

M.P.: decompose around 178-179° C Lit[61]: 180° C (sublime)

Mol. Wt. 139.1

^{1}H nmr: (δ,DMSO-d_6): 1.90(3H,S), 2.15(3H,S), 6.65(1H,d), 11.0(1H,S), 9.50(1H,bs)

Mass Spectrum: m/e (relative intensity) 139(m^+,74), 121(59), 94(71)



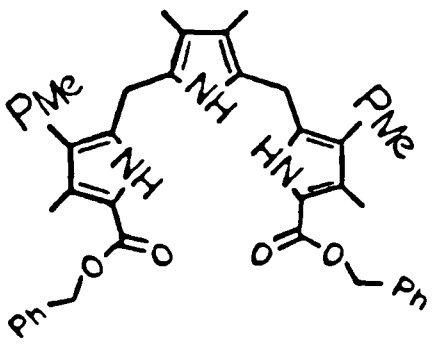
2-Acetoxymethyl-5-Benzyloxycarbonyl-3(2-methoxycarbonylethyl)-4-methylpyrrole (42)

2-Benzyloxycarbonyl-3(2-methoxycarbonylethyl)-3,5-dimethyl-pyrrole (13.8 g, 44 mmoles) 41 was dissolved in glacial acetic acid (150 mL) and lead tetraacetate (21.0 g, 47 mmoles) was added all at once. The mixture was swirled manually and warmed on a steam bath to 60° C to complete the reaction. Ethylene glycol (5 mL) was added. The reaction mixture was cooled and diluted with water (500 mL) to precipitate the product which was filtered and dissolved in methylene chloride (150 mL). The organic phase was separated, filtered, dried ($MgSO_4$) and concentrated. The product was recrystallized from hexane. Yield 10.5 g (64%).

M.P.: 109-110° C Lit.[57]: 111-112° C Mol. Wt.: 373.4

^1H nmr: (δ,$CDC\ell_3$), 2.07(3H,S), 2.30(3H,S), 2.50(2H,q,J=7.5Hz), 2.75(2H,q,J=7.5Hz), 3.68(3H,S), 5.05(2H,S), 5.30(2H,S), 7.40(5H,S), 9.10(1H,S).

Mass Spectrum: m/e (relative intensity) 373(m^+,8), 313(15), 179(15), 91(100), 65(19)



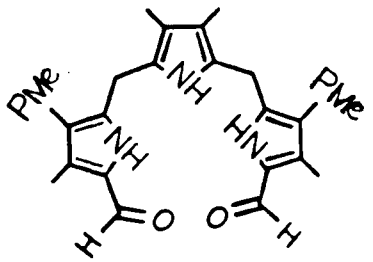
2,5-Bis[(5-benzyloxycarbonyl-3-(2-methoxycarbonylethyl)-4-methylpyrrol-2-yl)-methyl]-3,4-dimethylpyrrole (43)

2-Acetoxymethyl-5-benzyloxycarbonyl-3-(2-methoxycarbonylethyl)-4-methylpyrrole (6.0 g, 0.016 moles) 42 and 2-carboxy-3,4-dimethylpyrrole (1.5 g, 0.011 moles) 40 were dissolved in pyridine (10 mL) and heated overnight on the steam bath. Ice cold water (50 mL) was added and the tarry precipitate triturated with a small quantity of warm ethanol. The product was filtered after 6 hours and twice recrystallized from ethanol. Yield 2.4 g (30.8%).

M.P.: 140-141° C Lit[45]: 139-141° C Mol. Wt.: 721.8

^{1}H nmr: (δ,$CDC\ell_3$) 1.98(6H,S), 2.23(6H,S), 2.35(4H,q,J=7.5Hz), 2.60(4H,q,J=7.5Hz), 3.58(6H,S), 3.63(4H,S), 4.74(4H,S), 7.28(10H,S), 8.25(1H,S), 9.25(2H,S)

Mass Spectrum: m/e (relative intensity) 721(m^+,10), 313(16), 198(12), 184(12), 91(100), 65(28)



2,5-Bis[(5-formyl-3(2-methoxycarbonylethyl)-4-methylpyrrol-2-yl)-methyl]-3,4-dimethylpyrrole (31)

2,5-Bis[(5-benzyloxycarbonyl-3-(2-methoxycarbonylethyl) -4-methylpyrrol-2-yl)-methyl]-3,4-dimethylpyrrole (0.65 g, 0.9 mmole) in THF (80 mL) was stirred overnight under hydrogen (1 atmosphere) 43 in the presence of 10% palladium on charcoal (200 mg). When the uptake of hydrogen ceased, the catalyst was filtered through a celite plug and the solution checked by the TLC for any unconverted starting material. The solvent was evaporated off, in vacuo, leaving a red powder 44, and was used as is, in the next reaction.

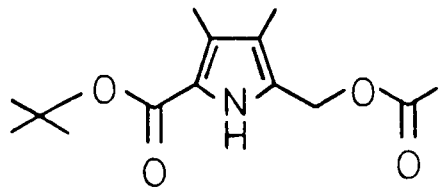
Compound 44 was dissolved in trifluoroacetic acid (5 mL) at 0° C under argon. After 15 minutes of stirring, triethylorthoformate (3 mL) was added in 3 portions. The honey-yellow color of the solution turned black instantaneously. After another 5 minutes at 0° C and 20 minutes at room temperature, trifluoroacetic acid was evaporated in vacuo. The residual product was neutralized with ice cold sodium bicarbonate solution and the water phase was twice extracted with methylene chloride (50 mL). The solution was dried ($MgSO_4$) and evaporated at room temperature and the

product recrystallized from methylene chloride-methanol mixture. The yield of the dialdehyde was 200 mg (42.6%).

M.P.: 186-188° C Mol. Wt.: 509

^{1}H nmr: (δ,$CDC\ell_3$) 2.00(6H,S), 2.25(6H,S), 2.43(2H,q,J=7.5Hz), 2.68(2H,q,J=7.5Hz), 3.68(6H,S), 3.87(4H,S), 9.00(1H,bs), 9.25(2H,bs), 9.91(2H,bs)

Mass Spectrum: m/e (relative intensity) 509(m^+,100), 422(30), 301(98), 227(38), 207(44), 199(20)



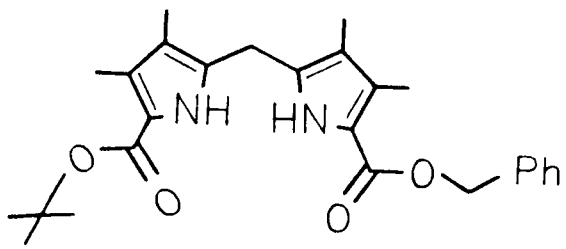
5-Acetoxymethyl-2-t-butoxycarbonyl-3,4-dimethylpyrrole (47)

2-Carbo-t-butoxy-3,4,5-trimethylpyrrole (11.1 g, 0.053 moles) 46 in glacial acetic acid (50 mL) was treated with lead tetraacetate (2.47 g, 0.056 moles) in several portions. The reaction mixture was swirled manually and the reaction was complete within 15 minutes (checked by TLC) with evolution of considerable heat. Ehtylene glycol (5 mL) was added and the mixture diluted slowly with water (100 mL) to precipitate the product, which was filtered and thoroughly washed with water. The wet product was dissolved in methylene chloride (100 mL). The organic layer was filtered, dried ($MgSO_4$) and evaporated to dryness. The residue was recrystallized from methylene chloride-hexane. Yield 11.88 g (84%)

M.P.: 126-128° C Lit[56]: 126-127 Mol. Wt. 267.3

^1H nmr: (δ,$CDCl_3$) 1.58(9H,S,C($\underline{CH_3}$)$_3$), 2.00(3H,S), 2.06(3H,S), 2.23(6H,S), 5.02(2H,S), 9.89(1H,br,N$\underline{H}$)

Mass Spectrum: m/e (relative intensity) 267(m^+,36), 211(46), 168(16), 152(99.7), 151(100), 133(48)



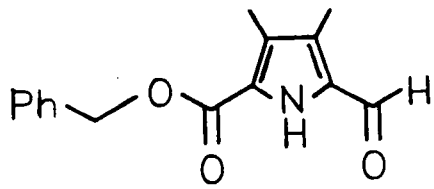
5-Benzyloxycarbonyl-5'-t-butoxycarbonyl-3,3',4,4'-tetramethyl-2,2'-dipyrromethane (48)

5-Acetoxymethyl-2-carbo-t-butoxy-3,4-dimethylpyrrole (5.3 g, 0.02 moles) 47 in methylene chloride (80 mL) was added dropwise over a 20 minutes period, to a solution of 2-benzyloxycarbonyl-3,4-dimethylpyrrole (4.6, 0.02 moles) 39 containing toluene-p-sulfonic acid (10 mg). After being stirred at room temperature under argon for 90 minutes, the solution was washed with saturated bicarbonate and water, dried ($MgSO_4$) and evaporated off. The resulting oil was crystallized from methylene chloride-petroleum ether (35-60° C). The powder so obtained was found to be more of the symmetrical dipyrromethane by nmr. The filtrate was evaporated, and the residue taken into warm petroleum ether and kept in the fridge overnight. The crystals were filtered and air dried. Yield 7.32 g (84%)

M.P.: 133-134° C Lit[26]: 132-134° C Mol. Wt.: 436.5

^1H nmr: $\delta(CDCl_3)$ 1.52(9H,S), 1.92(6H,S), 2.23(3H,S), 2.28(3H,S), 3.81(2H,S), 5.27(2H,S), 7.37(5H,S), 8.54(1H,S), 8.75(1H,S)

Mass Spectrum: m/e (relative intensity) 436 (m^+,22), 380(32), 227(20), 185(20), 151(56), 91(100)



5-Benzyloxycarbonyl-5-formyl-3,4-dimethylpyrrole (50)

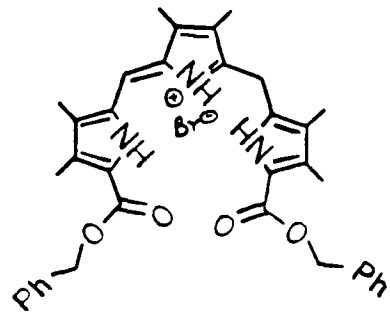
2-Benzyloxycarbonyl-3,4,5-trimethylpyrrole (10.9 g, 0.045 moles) 36 was dissolved in glacial acetic acid (200 mL) and lead tetraacetate (41 g, 0.092 moles) was added in portions over a 30 minute period. The mixture was then heated on a steam bath for 45 minutes and ethylene glycol (5 mL) added.

Water (200 mL) was added slowly to the hot solution to hydrolyze the diacetate. When crystallization set in, the suspension was further diluted with water (200 mL). The precipitate was filtered, washed with water and dissolved in methylene chloride (100 mL). The solution was again water-washed, dried ($MgSO_4$) and filtered and evaporated. The residual product was twice recrystallized from methylene chloride-hexane. Yield 8.4 g (73%)

M.P.: 120-121° C Lit[58]: 119-120° C Mol. Wt.: 257.3

^1H nmr: $\delta(CDC\ell_3)$ 2.30(6H,S), 5.35(2H,S), 9.80(1H,S,CHO), 9.37(1H,S,NH)

Mass Spectrum: m/e (relative intensity) 257(m^+,19), 166(12), 91(100), 67(14)



5-(5-Benzyloxycarbonyl-3,4-dimethylpyrrol-2yl-methyl)-5'-benzyl-carbonyl-3,3',4,4'-tetramethyl-2,2'-dipyrromethene Hydrobromide (51)

5-Benzyloxycarbonyl-5't-butoxycarbonyl-3,3',4,4'-tetramethyl-2,2'-dipyrromethane (1.3 g, 3 mmoles) 48 in a 100 mL round bottom flask was treated with trifluoroacetic acid (5 mL) with stirring under a nitrogen atmosphere at room temperature for 5 minutes. The formylpyrrole (0.77 g, 3 mmoles) 50 previously dissolved in methanol (60 mL) was added at once. The red solution was stirred an additional 90 minutes followed by the addition of 30-32% hydrogen bromide in acetic acid (1 mL), and ether (25 mL). Continual stirring for 15 minutes resulted in the formation of reddish-orange crystals. The precipitate was filtered, washed with ether and air dried, to give a yield of 1.59 g (76%).

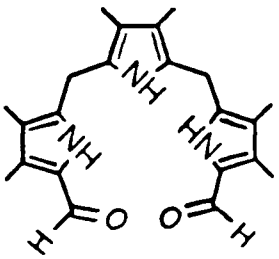
M.P.: 197-199° C Mol. Wt.: 656.6

^{1}H nmr: (δ,$CDC\ell_3$) 2.03(3H,S), 2.06(3H,S), 2.25(6H,S), 2.86(6H,S), 4.50(2H,S), 5.29(2H,S,$C_6H_5\underline{CH_2}$), 5.50(2H,S,$C_6H_5\underline{CH_2}$), 7.30(10H,S,$\underline{C_6H_5}CH_2$), 7.50(1H,d=C$\underline{H}$), 10.67(1H,S,N$\underline{H}$), 12.45(1H,S,N$\underline{H}$), 14.86(1H,S,N$\underline{H}$)

Mass Spectrum: m/e (relative intensity) 577(8), 336(24), 241(26), 108(43), 91(100), 65(31)

Anal. Cald. for $C_{36}H_{38}N_3BrO_4$: C,65.86; H,5.83; N,6.40; Br,12.17.

Found: C,66.21; H,5.95; N,6.43; Br,12.00



2,5-Bis(5-formyl-3,4-dimethylpyrrol-2-yl-methyl)-3,4-dimethylpyrrole (33)

Tripyrrin hydrobromide (1.4 g, 2.2 mmoles) 51 was dissolved in THF (600 mL) and hydrogenated at atmospheric pressure and room temperature in the presence of triethylamine (5 drops), sodium acetate (3 g) and 10% palladium on charcoal (200 mg). Hydrogen uptake was complete in one hour but was allowed to stir overnight. The catalyst was filtered through a celite plug and the filtrate was evaporated to dryness at reduced pressure. The crude product 24 was used, as is, in the next reaction.

In an apparatus consisting of a 150 mL erlenmeyer flask fitted with a claisen adapter and an argon inlet, DMF (5 mL) was heated to reflux. To the boiling DMF, under argon, were added four successive 5 mL DMF portions of the bis-α-carboxypyrrole. A drop of the solution before heating was diluted with methylene chloride and a uv absorption spectrum was recorded, showing a single absorption band at λ 286 nm. The mixture was refluxed under argon, the original reddish solution turned dark brown. The decarboxylation was over in 30 minutes as the absorption

band at 286 nm had disappeared. The solution still under argon was chilled in ice and used in the next reaction.

Benzoyl chloride (2.0 g, 14.2 mmole) was added rapidly dropwise to the above reaction mixture and was stirred for 30 minutes to ensure complete reaction and left to stand at room temperature for two hours. Water (60 mL) and sodium bicarbonate (2.0 g, much excess) were added to the reaction mixture and was heated on steam bath for one hour, during which time the product coagulated into crystalline lumps. The mixture was cooled, the solid filtered, washed with water and recrystallized from methylene chloride-methanol go tive a yield of 0.61 g (75.9%).

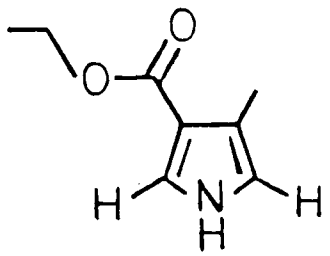
M.P.: >240° C Mol. Wt. 365.5

^{1}H nmr: (δ,$CDC\ell_3$) 1.98(6H,S), 2.28(6H,S), 2.48(6H,S), 3.93(4H,S), 8.02(1H,S), 9.29(1H,S), 9.43(1H,S), 10.05(1H,S), 10.18(1H,S)

Mass Spectrum: m/e (relative intensity) 365(m^+,2), 258(77), 229(24, 201(36), 136(100), 123(30), 108(40), 94(36)

Anal. Calcd. for $C_{22}H_{27}N_3O_2$: C,72.31; H,7.44; N,11.50

Found: C,71.97; H,7.32; N,11.48



3-Ethoxycarbonyl-4-methylpyrrole (57)

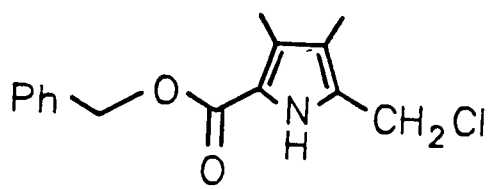
2-4-Bis-ethoxycarbonyl-5-carboxy-3-methylpyrrole (12.0 g, 0.045 moles) 54 and sodium hydroxide (3.6 g, 0.09 moles) in water (90 mL) were heated on the steam bath for 2 hours, after which time the pH had fallen to 8-9. The solution was diluted with water (180 mL), sodium bicarbonate (4.5 g, 0.54 moles) was added and the solution warmed to approximately 60° C. A solution of iodine (22.9 g (0.09 moles)) in sodium iodine (25 g) and water (125 mL) was added fairly rapidly causing mild effervescence and the deposition of dense granular light tan solids. The mixture was kept warm for 2 hours to ensure complete iodination. The solids were filtered off, washed with water and the wet-crude filter-cake was warmed with 95% ethanol (110 mL) on the steam bath, dissolving to give fairly light brown solution. To this solution was added, potassium iodide (6 g), concentrated hydrochloric acid (5.4 mL) and 50% hypophosphorous acid (50 mL) in that order. The mixture was heated for 20 minutes to ensure complete reduction. The enthanol was evaporated off, the residue dissolved in methylene chloride (100 mL) and rinsed with aqueous sodium bicarbonate and water. The organic phase was filtered, dried ($MgSO_4$) and evaporated to dryness. The residual black oil was dissolved in methylene chloride (20 mL) and chromatographed on silica gel using methylene chloride as the eluting solvent. All the colored impurities remained at

the origin and the di-α-free pyrrole was eluted as a pale yellow liquid. The solvent was evaporated to give solid of yield 6.2 g (89.9%).

M.P.: 72-74° C Lit[60]: 73° C Mol. Wt.: 153.2

^{1}H nmr: δ($CDC\ell_3$) 1.35(3H,t,J=7.0Hz), 2.3(3H,S), 4.3(2H,q,J=7.5Hz), 6.5(1H,m)

Mass Spectrum: m/e (relative intensity), 153(m^+,43), 149(20), 124(34), 108(100)



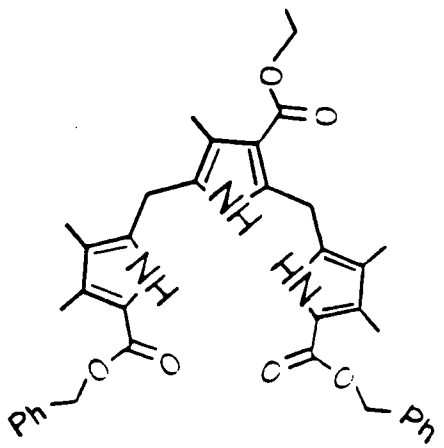
2-Benzyloxycarbonyl-5-chloromethyl-3,4-dimethylpyrrole (58)

2-Benzyloxycarbonyl-3,4,5-trimethylpyrrole (24.3 g, 0.1 moles) 35 was suspended in anhydrous diethyl either (250 mL) and stirred at room temperature, a solution of sulfuryl chloride (13.8 g, 8.3 mL, 0.1 moles=13.5 g) in carbon tetrachloride (20 mL) was added dropwise over a 15 minute period. The addition of reagent caused a yellow color to form and all the starting material dissolved. When the reagent was about half added, a fluffy white product began to crystallize out and the mixture became thick. After standing for 45 minutes, the solids were filtered off and rinsed with ether, then hexane. The product 13.1 g (47.2%) was stored in the dark.

M.P.: 143-144° C (decomposed) Lit[37]: 144-145° C (decomposed)

Mol. Wt.: 335.8

^{1}H nmr: (δ,$CDC\ell_3$) 2.01(3H,S), 2.26(H,S), 4.55(2H,S), 5.33(2H,S), 7.36(5H,S), 9.20(1H,bs)



2,5-Bis-(5-benzyloxycarbonyl-3,4-dimethylpyrrol-2-yl-methyl)-3-ethoxycarbonyl-4-methylpyrrole (59)

2-Benzyloxycarbonyl-5-chloromethyl-3,4-dimethylpyrrole (12.0 g, 43 mmoles) 58 and 3-ethoxycarbonyl-4-methylpyrrole (3.3 g, 22 mmoles) 57 were dissolved in methylene chloride (60 mL) and stirred for 15 minutes at room temperature. The solvent was boiled down to a small volume on a steam bath with the solution turning red. Methanol (50 mL) was added and the boiling continued until amost all the methylene chloride was boiled off. The reaction mixture was cooled, the precipitate filtered and washed with methanol. The product was found to be a mixture of the desired product and 5,5'-benzyloxycarbonyl-3,3',4,4'-tetramethyl-2,2'-dipyrromethane 68, a byproduct.

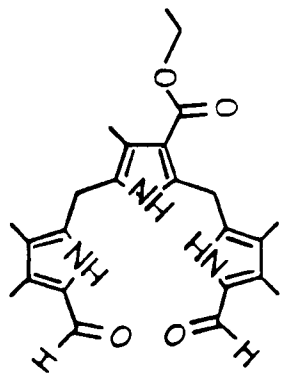
The mixture was dissolved in methylene chloride (50 mL) and diluted with hot petroleum ether (35°-60° C) (100 mL), causing the dipyrromethane to crystallize. The solution was cooled in the refrigerator to complete the crystallization, filtered and the byproduct rinsed with more petroleum ether. The yield of byproduct was 0.8 g. The

filtrate and washings, were evaporated to dryness and the resulting solids redissolved in tetrahydrofuran (25 mL). Methanol was added to the boiling solution to displace the tetrahydrofuran. The solution was cooled, the crystals were filtered, washed with methanol and air dried. Yield 5.5 g (39.3%).

M.P.: 181-182° C Lit[37]: 184-187.5° C Mol. Wt.: 635.7

^{1}H nmr: (δ,$CDC\ell_3$) 1.38(3H,t,J=7.0), 1.75(3H,S), 1.83(3H,S), 2.40(3H,S), 2.46(6H,S), 3.38(2H,bS), 4.1-4.5(8H,m), 7.25(10H,m), 9.58(1H,S,NH), 10.93(1H,S,NH), 11.52(1H,S,NH)

Mass Spectrum: m/e (relative intensity) 635(m^+,3), 594(60), 436(100), 315(41), 91(90)



2-5-Bis-(-5-formyl-3,4-dimethylpyrrol-2-yl-methyl)-3-ethoxy-carbonyl-4-methylpyrrole (34)

2,5-Bis-(5-benzyloxycarbonyl-3,4-dimethylpyrrol-2-yl-methyl)-3-ethoxycarbonyl-4-methylpyrrole 59 (1.3 g, 2 mmoles) and 10% palladium on charcoal (200 mg) were stirred overnight under hydrogen (1 atmosphere at room temperature) in tetrahydrofuran (150 mL). When the uptake of hydrogen ceased, the catalyst was filtered off through a celite plug, rinsed with tetrahydrofuran and the filtrates were evaporated to dryness in vacuo at 30° C leaving the bis-carboxypyrrole as a pale yellow solid. The crude product was used, as is, in the next reaction.

In an apparatus consisting of a 50 mL erlenmeyer flask fitted with a claisen adapter and an argon inlet, DMF (5 mL) was heated to reflux. To the boiling DMF under argon, were added three successive 5 mL portions of the bis-carboxypyrrole in DMF. A drop of this solution was diluted with methylene chloride and a uv absorption spectrum was recorded, showing a single absorption band at λ 286 nm. The mixture was refluxed under argon, the originally colorless solution turned dark brown and at every 30 minutes, a drop was removed into methylene chloride and the uv spectrum

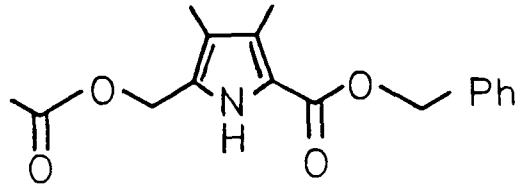
recorded. The absorption band at 286 nm was reduced to just a shoulder in one hour but a further half-hour of heating did not remove this completely. The solution was cooled in ice and used in the next reaction.

To an ice-cooled solution of DMF (5 mL), phosphorous oxychloride (0.46 mL) was added and magnetically stirred. The Vilsmeier reagent thus prepared, was treated, rapidly and dropwise, with the chilled DMF solution of the bis-α-free pyrrole prepared above. Once the addition was complete, the solution was stirred for a further half-hour to ensure the completion of the reaction. The solution was poured into crushed ice. Solid sodium bicarbonate was added, carefully with stirring, until the solution was weakly basic to pH paper and then heated on the steam bath (the solution became acidic again and more bicarbonate had to be added). The hot solution was filtered to remove a few brown particles and heated until the solution turned turbid and a grey colored solid separated out. The heating was continued for a further half-hour, the mixture cooled and the solid filtered and washed with water. The product was recrysallized in methylene chloride-methanol. The yield was 0.78 g (92%).

M.P.: 220-221° C Lit[37]: 221-221.5° C Mol. Wt.: 423.5

^{1}H nmr: (δ,$CDCl_3$) 1.36(3H,t,J=7.0Hz,$C\underline{H}_3CH_2$), 1.95(3H,S), 1.97(3H,S), 2.20(3H,S), 2.21(3H,S), 2.29(3H,S), 3.79(2H,S), 4.30(2H,q,J=7.0Hz,$CH_3C\underline{H}_2$), 4.31(2H,S), 8.97(1H,S, CHO), 9.01(1H,S,C<u>H</u>O), 10.06(1H,<u>S</u>,N<u>H</u>), 10.97(1H,S,N<u>H</u>), 11.03(1H,S,N<u>H</u>)

Mass Spectrum: m/e (relative intensity) 423(m^+,100), 300(59), 287(45), 254(53), 213(38), 136(57)



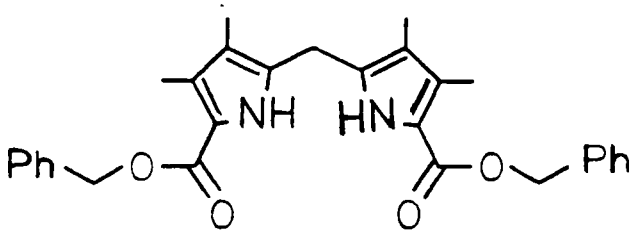
5-Acetoxymethyl-2-benzyloxycarbonyl-3,4-dimethylpyrrole (67)

2-Benzyloxycarbonyl-3,4,5-methylpyrrole (12.5 g; 51 mmole) 36 was dissolved in glacial acetic acid (100 mL) and lead tetraacetate (23.7 g, 53.5 mmole) was added all at once. The mixture was swirled manually and warmed on a steam bath to about 60° C to complete the reaction. The reaction mixture was allowed to cool and water added until there was no milkiness. The precipitate was filtered and washed with water. About 0.5 g of the wet product was dissolved in methylene chloride, filtered, dried ($MgSO_4$), concentrated and recrystallized from hexane.

M.P.: 115-116° C Mol. Wt.: 301.3

^1H nmr: (δ,$CDCl_3$) 2.01(3H,S), 2.08(3H,S), 2.26(3H,S), 5.01(2H,S), 5.31(2H,S), 7.38(5H,S), 8.94(1H,br)

Mass Spectrum: m/e (relative intensity) 301(m^+,3), 168(15), 91(100), 65(12)



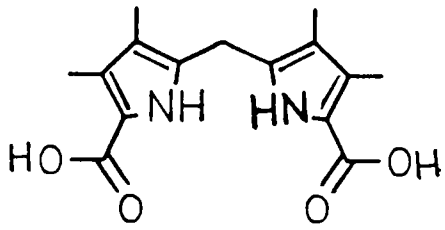
5-5'Bisbenzyloxycarbonyl-3,3',4,4'-tetramethyl-2,2'-dipyromethane (49)

The 5-acetoxymethyl-2-benzyloxycarbonyl-3,4-dimethylpyrrole 67 was dissolved in acetic acid-water (80-20, 1 L) and heated to reflux for 2 hours . After checking the reaction mixture by TLC for complete conversion of starting material, the reaction mixture was allowed to cool, and diluted with water until there was no appearance of milkiness. The precipitate was filtered, washed with water and recrystallized from ethanol. The yield was 9.0 g (75%).

M.P.: 177-179° C Mol. Wt.: 470.5

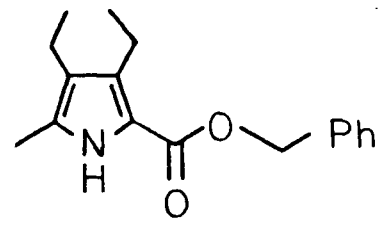
^{1}H nmr: (δ,$CDC\ell_3$) 2.00(6H,S), 2.30(6H,S), 3(2H,S), 5.23(4H,S,$C_6H_5\underline{CH_2}$), 7.37(10H,S,$C_6\underline{H_5}CH_2$), 9.08(2H,S,$\underline{NH}$)

Mass Spectrum: m/e (relative intensity) 470(m^+,20), 149(19), 91(100), 65(16)



5,5'-Biscarboxy-3,3',4,4'-tetramethyl-2,2'-dipyrromethane (32)

5,5'-Bisbenzyloxycarbonyl-3,3',4,4'-tetramethyl-2,2'-dipyrromethane 49 (2.3 g, 4.9 mmoles) in THF (100 mL) was stirred overnight under hydrogen (1 atmosphere) in the presence of 10% palladium on characoal (200 mg). When the uptake of hydrogen ceased, the catalyst was filtered through a celite plug and the solution checked by TLC for any unconverted starting material. The solvent was evaporated off, in vacuo, leaving the biscarboxypyrrole as a pale yellowish solid. Because of the unstable nature of this compound, it was not analysed. The flask was wrapped with foil and kept in the fridge.



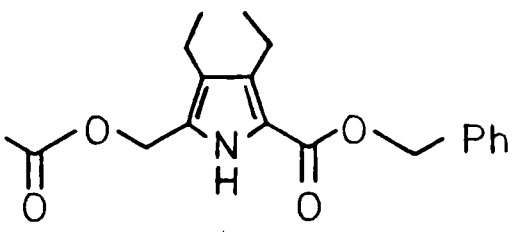
2-Benzyloxycarbonyl-3,4-diethyl-5-methylpyrrole (64)

2-Carboethoxy-3,4-diethyl-5-methylpyrrole (50 g, 0.24 moles) 63 was dissolved in redistilled benzyl alcohol (100 mL) and heated to reflux under nitrogen in an erlenmeyer flask equipped with a claisen adapter and a nitrogen inlet on the side arm and a thermometer suspended in the flask. To prevent heat losses, the whole apparatus was wrapped with aluminum foil. A few drops of sodium benzyloxide catalyst (prepared by dissolving sodium metal in redistilled benzyl alcohol) were added to the refluxing solution when the temperature reached 209° C causing a temperature drop and evolution of ethanol vapours. When the reaction subsided more catalyst was added. The procedure was repeated until no further reaction was observed and the temperature of the refluxing solution was again that of benzylalcohol (209° C). The hot solution was then poured into a quenching mixture of methanol (400 mL) and glacial acetic acid (10 mL). Water (400 mL) was gradually added while stirring. The clear pale yellow solution turned pink, and white granular material precipitated from the solution and the suspension was allowed to sit overnight. The product was filtered, washed with 40% methanol-water and then with water. The crude solid was recrystallized from methanol to give 55.4 g (83.5%) yield.

M.P.: 72-73° C Lit[37]: 72-73° C Mol. Wt.: 271

^{1}H nmr: (δ,$CDC\ell_3$) 1.03(3H,t,J=7.0Hz), 1.10(3H,t,7.0Hz), 2.14(3H,S), 2.38(2H,q,J=7.5Hz), 2.70(2H,q,J=7.5Hz), 2.72(2H,q,J=7.5Hz), 7.36(5H,S), 8.72(1H,bs)

Mass Spectrum: m/e (relative intensity) 271(m^+,28), 180(36.5), 162(39), 91(100)



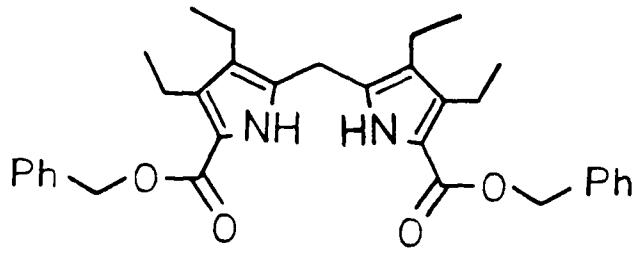
5-Acetoxymethyl-2-benzyloxycarbonyl-3,4-diethylpyrrole (65)

2-Benzyloxycarbonyl-3,4-diethyl-5-methylpyrrole (27.1 g, 0.1 moles) 64 was dissolved in glacial acetic acid (200 mL) and lead tetraacetate (48 g, 0.1 mole = 44.3 g) was added all at once. From this point, the reaction was carried out as described for compound 67.

M.P.: 113-115° C Lit[59]: 113.5-115° C Mol. Wt.: 329.4

^{1}H-nmr: (δ,$CDC\ell_3$) 1.10(6H,t,J=7.0Hz,$C\underline{H}_3CH_2$), 2.08(3H,S), 2.44(2H,q,J=7.5Hz,$CH_3C\underline{H}_2$), 2.91(2H,q,J=7.5Hz,$CH_3C\underline{H}_2$), 5.00(2H,S,$CH_3CO_2C\underline{H}_2$), 5.30(2H,S,$C_6H_5C\underline{H}_2$), 7.38(5H,S), 7.99(1H,bs)

Mass Spectrum: m/e (relative intensity) 329(m^+,16), 177(39), 163(30), 120(48), 91(100)



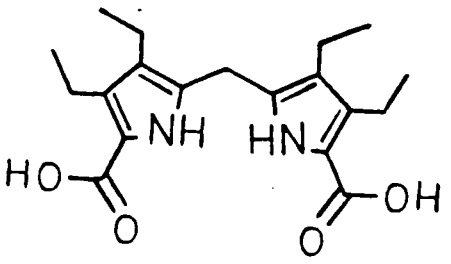
5,5'-Bisbenzyloxycarbonyl-3,3',4,4'-tetraethyl-2,2'-dipyrromethane (66)

The 5-acetoxymethyl-2-benzyloxycarbonyl-3,4-diethylpyrrole 65 was dissolved in acetic acid-water (80-20, 200 mL) and heated to reflux for 2 hours. From this point, the reaction and purification was carried out as described for compound 49. The yield was 20.3 g (77.2%).

M.P.: 119-120° C Lit[59]: 119.5-120.5° C Mol. Wt.: 526.6

^{1}H nmr: (δ,$CDC\ell_3$) 1.03(6H,t,J=7.5Hz), 1.20(6H,t,J=7.5Hz), 2.41(4H,q,J=7.5Hz,$C\underline{H}_2CH_3$), 2.73(44,q,J=7.5Hz,$C\underline{H}_2CH_3$), 3.83(2H,S), 5.28(4H,S,$C_6H_5C\underline{H}_2$), 7.36(10H,S,$\underline{C_6H_5}CH_2$-), 8.72(2H,bs,$N\underline{H}$)

Mass Spectrum: m/e (relative intensity) 526(m^+,17), 269(54), 178(23), 91(100)

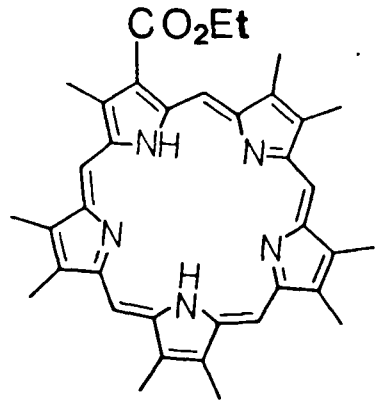


5,5'-Biscarboxy-3,3',4,4'-tetraethyl-2,2'-dipyrromethane (35)

5,5'-Bisbenzyloxycarbonyl-3,3',4,4'-tetraethyl-2,2'-dipyrromethane (1.1 g, 2 mmoles) 66 in THF (100 mL) was hydrogenated as for compound 49.

As the product, dicarboxylic acid is very unstable, the filtrate was made up to 250 mL of THF, wrapped in foil and stored in the fridge, without analysing it.

3.4 SYNTHESES OF PENTAPHYRIN



2-Ethoxycarbonyl-3,7,8,12,13,17,18,22,23-nonamethylpentaphyrin (74)

Dipyrromethane diacid (34.3 mg, 0.12 mmole) 32 was dissolved in methylene chloride (300 mL) under argon (in a 1 L round bottomed schlenk flask) which has been "degased" by bubbling argon through for 2 hours. After stirring the mixture for 30 minutes, the tripyrrane dialdehyde (50 mg, 0.12 mmole) 34 was added. The solution was stirred for 10 minutes and acidified with HBr in acetic acid (0.9 mL) (30-32%). The color of the reaction mixture changed from yellow to pinkish-red and then to red which did not change with stirring for 2 hours. Chloranil (280 mg) was added to effect oxidation and the reaction mixture was stirred for a further 36 hours. The development of the reaction was followed by uv-visible spectroscopy. The solvent was evaporated off on a rotary evaporator and the residual product chromatographed (preparative TLC) using silica gel GF plates (Analtech) with fluorescent indicator and ethyl acetate as eluent. After properly drying the plates, the dark green fraction at the origin was scraped and eluted with methylene chloride-methanol (10:1). The solvent was evaporated off, and the residual product, twice

chromatographed using 5% methanol in methylene chloride. The green fraction was collected and the solvent evaporated to give a yield of 18.0 mg (26.1%). A preparation on a 5.9×10^{-2} mmole scale gave 31.9% yield.

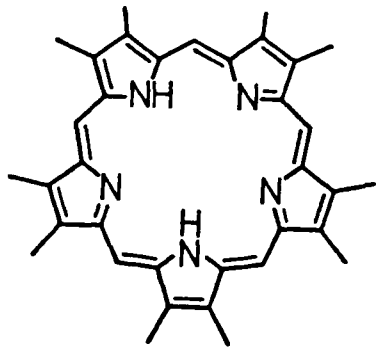
^{1}H nmr: (δ,TFA/$CDCl_3$) 1.95(3H,t,J=7Hz,$\underline{CH_3}CH_2$), 4.13(6H,S,$\underline{CH_3}$), 4.15(12H,S,$\underline{CH_3}$), 4.19(6H,S,$\underline{CH_3}$), 4.51(3H,S,$\underline{CH_3}$), 5.18(2H,q,J=7.5Hz,$CH_3\underline{CH_2}$), 11.91(2H,bs,meso-$\underline{H}$), 12.00(1H,bs,meso-$\underline{H}$), 12.12(1H,bs,meso-H), 13.29(1H,bs,meso-H), -4.33(1H,S,$N\underline{H}$), -4.63(1H,S,$N\underline{H}$), -4.70(1H,S,$N\underline{H}$), - 4.76(1H,S,$N\underline{H}$), -4.80(1H,S,$N\underline{H}$).

^{13}C nmr: (δ,30%TFA/$CDCl_3$) 12.751. 12.881(9C,$\underline{C}H_3$), 29.808(1C,$CH_2\underline{C}H_3$), 64.579(1C,$O\underline{C}H_2CH_3$), 97.584, 97.644, 99.464, 101.226, 101,623(5C meso carbons), 131.511, 136.547, 137.989, 138.443, 140.286, 140.336, 140.609, 141.695, 141.921, 142.056, 142.381, 143.802 (20C,α-β-carbons), 165.489(1C,C=0)

Mass Spectrum: EI m/e (relative intensity) 587(m^++2, 4.7), 588(m^++3, 2.6) 480(41), 452(11), 422(23), 108(100)

FAB m/e m+1=586, m+2=587

(0.2 mL TFA/CH_2Cl_2)	$\lambda_{max(nm)}$	365	458	595	645	715
	log ϵ_{max}	3.99	5.68	3.66	4.27	4.01
(0.1 mL Et_3N/CH_2Cl_2)	$\lambda_{max(nm)}$	345	450	642		
	log ϵ_{max}	4.53	4.73	4.01		



Decamethylpentaphyrin (71)

The synthesis and purification was carried out on 71 as described for compound 74. Tripyrrane dialdehyde 33 (50 mg, 1.3×10^{-4} moles) and dipyrromethane diacid 32 (40 mg, 1.3×10^{-4} moles) were used, to give a yield of 12 mg (21%).

^{1}H nmr: (δ,TFA/$CDCl_3$) 4.41(30H,S,$\underline{CH_3}$), 12.49(5H,S,meso-$\underline{H}$), -5.52(5H,S,N$\underline{H}$)

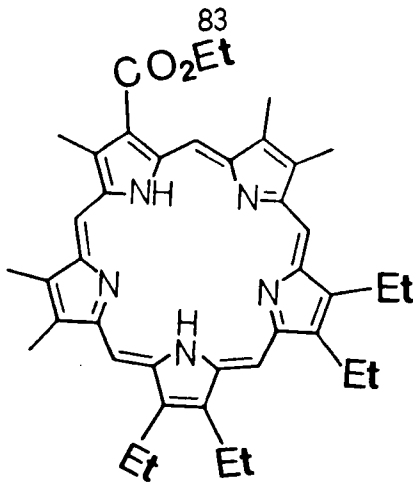
^{13}Cnmr: (δ,TFA): 14.478(10C,$\underline{C}H_3$), 102.009(5C,meso-$\underline{C}$), 142.740(10C,βC), 147.328(10C,αC)

Mass Spectrum: EI m/e (relative intensity) 484(3), 476(3)

FAB m/e m+1=528, m+2=529

UV-Visible Spectrum:

(0.2 mL TFA/CH_2Cl_2)	$\lambda_{max(nm)}$	380	455	595	645	705
	log ε_{max}	3.77	4.77	2.95	3.89	3.55
(0.1 mL Et_3N/CH_2Cl_2)	$\lambda_{max(nm)}$	395	425	474	670	
	log ε_{max}	4.09	4.09	4.05	3.31	



2-Ethoxycarbonyl-3,7,8,22,23-pentamethyl-12,13,17,18-tetraethylpentaphyrin (75)

The dipyrromethane diacid 35 (0.12 mmole, 15.2 mL of the stock solution in THF) was taken into 1 L round-bottomed schlenk flask and the solvent evaporated off on a rotary evaporator at room temperature, and allowing argon into the flask at the end. Methylene chloride (300 ml) was added to the diacid and the solution "degassed" by bubbling argon through for 2 hours.

The tripyrrane dialdehyde (50 mg, 0.12 mmole) 34 was added and the mixture stirred for 10 minutes. From this point, the synthesis and purification was carried out as described for 74. The yield was 21.0 mg (28%).

^{1}H nmr: (δ, TFA/$CDCl_3$) 2.05(3H,t,J=7Hz,$CO_2CH_2\underline{CH_3}$), 2.17(12H,m,$CH_2\underline{CH_3}$), 4.26(3H,S,$C\underline{H_3}$), 4.27(3H,S,$C\underline{H_3}$), 4.33(6H,S,CH_3), 4.65(3H,S,CH_3), 4.75(8H,m,$\underline{CH_2}CH_3$), 5.30(2H,q,J=7.5Hz,)$O\underline{CH_2}CH_3$), 12.16(2H,S,meso-H), 12.23(1H,S,meso-H), 12.40(1H,S,meso-H),

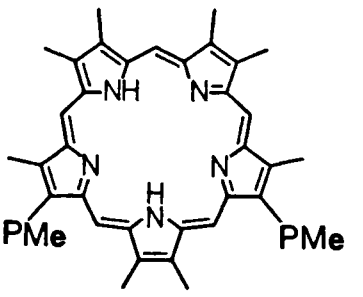
13.43(1H,S,meso-H), -4.23(1H,bs,NH), -4.48(1H,S),
-4.55(1H,bs,NH), -4.58(1H,bs,NH), -4.61(1H,bs,NH)

^{13}C-nmr: (δ,30%TFA/$CDCl_3$): 13.037, 14.498, 17.598, 17.695, 17.875, 20.747, 20.800, 27.285, 29.710(14C), 63.792(1C,OCH_2CH_3), 96.167, 96.529, 98.452, 101.170, 101.683, (5C, meso C), 131.509, 136.220, 137.713, 138.247, 139.689, 140.105, 140.529, 141.093, 141,431, 141.613, 142.289, 142.523, 143.083, 144.086, 147.846, 158.060, 148,649 (20C, α- and β-carbons), 164.782.

Mass Spectrum: EI m/e (relative intensity) 641(m^+,1.8), 642(m^++2, 12.7), 645(m^++4.12), 536(100), 508(52), 478(63), 122(87), 108(91)
FAB m/e m+1+642, m+2=643

UV-Visible Spectrum:

(0.2 mL TFA/CH_2Cl_2)	$\lambda_{max(nm)}$	370	463	603	652	721
	log ε_{max}	5.10	6.18	4.67	4.96	4.79
(0.1 mL Et_3N/CH_2Cl_2)	$\lambda_{max(nm)}$	350	450	645		
	log ε_{max}	5.21	5.44	4.74		



3,12-Dimethoxycarbonylethyl-2,7,8,13,17,18,22,23-octamethylpentaphyrin (29)

The synthesis and purification was carried out as described for compound 74. Tripyrrane dialdehyde 31 (50 mg, 0.1 mmoles) and dipyrromethane diacid (34mg, 0.11 mmoles) 32 were used. Yield 18 mg (27%).

^{1}H nmr: (δ,30%TFA/$CDCl_3$) 3.68(4H,b,$\underline{CH_2CH_2}CO_2CH_3$), 3.79(6H,S,$CO_2\underline{CH_3}$), 4.38(6H,S,$\underline{CH_3}$), 4.41(12H,S,$\underline{CH_3}$), 4.42(6H,S,$\underline{CH_3}$), 5.26(4H,b,$\underline{CH_2CH_2}CO_2CH_3$), 12.47(1H,S,meso-H), 12.48(2H,S, meso-H), 12.55(2H,S,meso-H), -5.10(2H,bs,N$\underline{H}$), -5.17(1H,S,N$\underline{H}$), 5.29(1H,S,N$\underline{H}$), -5.22(H,bs,N$\underline{H}$)

^{13}C nmr: (δ,TFA) 11.742, 11.870(bC,$\underline{CH_3}$), 21.912(4C,$\underline{CH_2CH_2}CO_2CH_3$), 53.557(2C,O$\underline{CH_3}$), 99.4888. 99.111, 98.850(5C,meso-$\underline{C}$), 139.458 139.889, 140.258, 140.317, 140.647, 144,700, 144.899, 144.929, 145.090, 145.194(10C,α,β,β$\underline{C}$), 179.989(1C,$\underline{CO}$)

Mass Spectrum: EI m/e (relative intensity) 674(m^++2,36), 566.6(100), 494.5(89), 421.5(44), 108(78)

FAB m/e,m+1=672, m+2=673

UV-Visible Spectrum:

(0.2 mL TFA/CH_2Cl_2)	$\lambda_{max(nm)}$	375	458	590	645	706
	log ε_{max}	4.06	5.95	3.63	3.94	3.66
(0.1 mL Et_3N/CH_2Cl_2)	$\lambda_{max(nm)}$	345	462	635		
	log ε_{max}	4.56	4.78	3.76		

Zinc decamethylpentaphyrrin (72)

Decamethylpentaphyrin 71 (20 mg. 3.8×10^{-5} moles) was dissolved in spectra grade methanol (20 mL) and stirred in the dark for 5 minutes. A saturated solution of zinc acetate in methanol (1 mL) and anhydrous sodium acetate (100 mg) were added and the resulting reaction mixture was stirred at room temperature for 5 hours and allowed to stand at room temperature for 3 days. Uv-visible spectroscopy was used to follow the reaction. Methylene chloride (50 mL) was added, the solution washed twice with water (15 mL) dried over anhydrous magnesium sulfate and evaporated at room temperature in vacuo to give a yield of 15 mg (67%).

Mass Spectrum: EI m/e (relative intensity) 591(3), 484(100, 108(32)

FAB m/e 591, 592

UV-Visible Spectrum: $\lambda_{max(nm)}$ 388 395 468 495 600 628 655

Zinc 2-Ethoxycarbonyl-3,7,8,12,13,17,18,22,23-nonamethylpentaphyrin (73)

2-Ethoxycarbonyl,3,7,8,12,13,17,18,22,23-nonamethylpentaphyrin 74 (15 mg, 2.6×10^{-5} moles) is dissolved in methanol. Saturated solution of zinc acetate (1 mL) and anhydrous sodium acetate (100 mg) was added and the reaction carried out as in compound 72.

Mass Spectrum: EI m/e (relative intensity) 542(12), 514(3), 484(5)
FAB m/e 649, 650

UV-Visible Spectrum: $\lambda_{max(nm)}$ 362 398 474 485 485 465 590

4. SPECTRAL ASSIGNMENTS

4.1 ^{1}H NMR DATA OF THE PENTAPHYRINS

The proton nmr spectra of the four pentaphyrins synthesized during the course of this work are illustrated in figures 4-7. The nmr spectrum of each pentaphyrin was recorded in deuterochloroform-trifluoroacetic acid (1:1 v/v) using deuterochloroform as the internal standard reference. The chemical shifts of decamethylpentaphyrin 71, exhibited a singlet resonance at δ 12.49 corresponding to a set of five methine (meso) protons. The ten peripheral methyl groups were observed as a singlet at δ 4.41 while the inner N-H protons were shifted upfield as a singlet at δ -5.52. These chemical shifts of decamethylpentaphyrin compare well with the characteristics exhibited in the nmr spectrum of octamethylporphyrin (in TFA) (δ 10.98, 3.78, -4.82)[63] for methine, methyl and N-H protons respectively.

With pentaphyrin 74, the five methine protons gave signals in the ratio of 2:1:1:1 at δ 11.91, 12.00, 12.17 and 13.29 respectively while compound 75 were at δ 12.16, 12.23, 12.40 and 13.43 with the same ratio as of compound 71. The effect of the ester side chain on compounds 74 and 75 is evident in the way it affects the resonance of the NH protons in comparison to compound 71. Whereas the NH protons of compounds 74 and 75 exhibited resonance between δ ~ -4.2 to -4.8, that of compound 71 is at δ -5.5, showing the deshielding ability of the ester side chain.

The methyl and methylene protons of ethoxycarbonyl, the ester side chain of compound 74, gave a triplet of δ 1.95 and quartet at 5.18 respectively. The same protons of the ester side chain of compound 75 gave a triplet at δ 2.05 and a quartet at δ 5.30 respectively. The

protons of the nine methyl groups of compound 74 exhibited a ratio of 2:4:2:1 at δ 4.13, 4.15, 4.19 and 4.51. For compound 75, the methylene protons of the ethyl groups exhibited a broad multiplet at δ 4.75 and another multiplet at δ 2.12 to 2.21 with the highest peak at δ 2.17 for the methyl protons. The five peripheral methyl groups showed resonance at δ 4,26, 4.27, 4.33, 4.65 of ratio 1:1:2:1.

The chemical shifts of compound 29 compared well with that of data published in literature[41]. Despite the presence of the two propionic ester side chain, the NH protons resonance occur between δ ~ -5.1 to -5.2 with a ratio of 2:1:1:1 very close to that of compound 71. Thus the ester side chains have small deshielding effect on the NH protons. The five meso protons were observed as singlets with a ratio of intensities 1:2:2 at δ 12.47, 12.48, 12.55. The eight peripheral methyl groups gave singlets of ratio 1:2:1 at δ 4.38, 4.41 and 4.42.

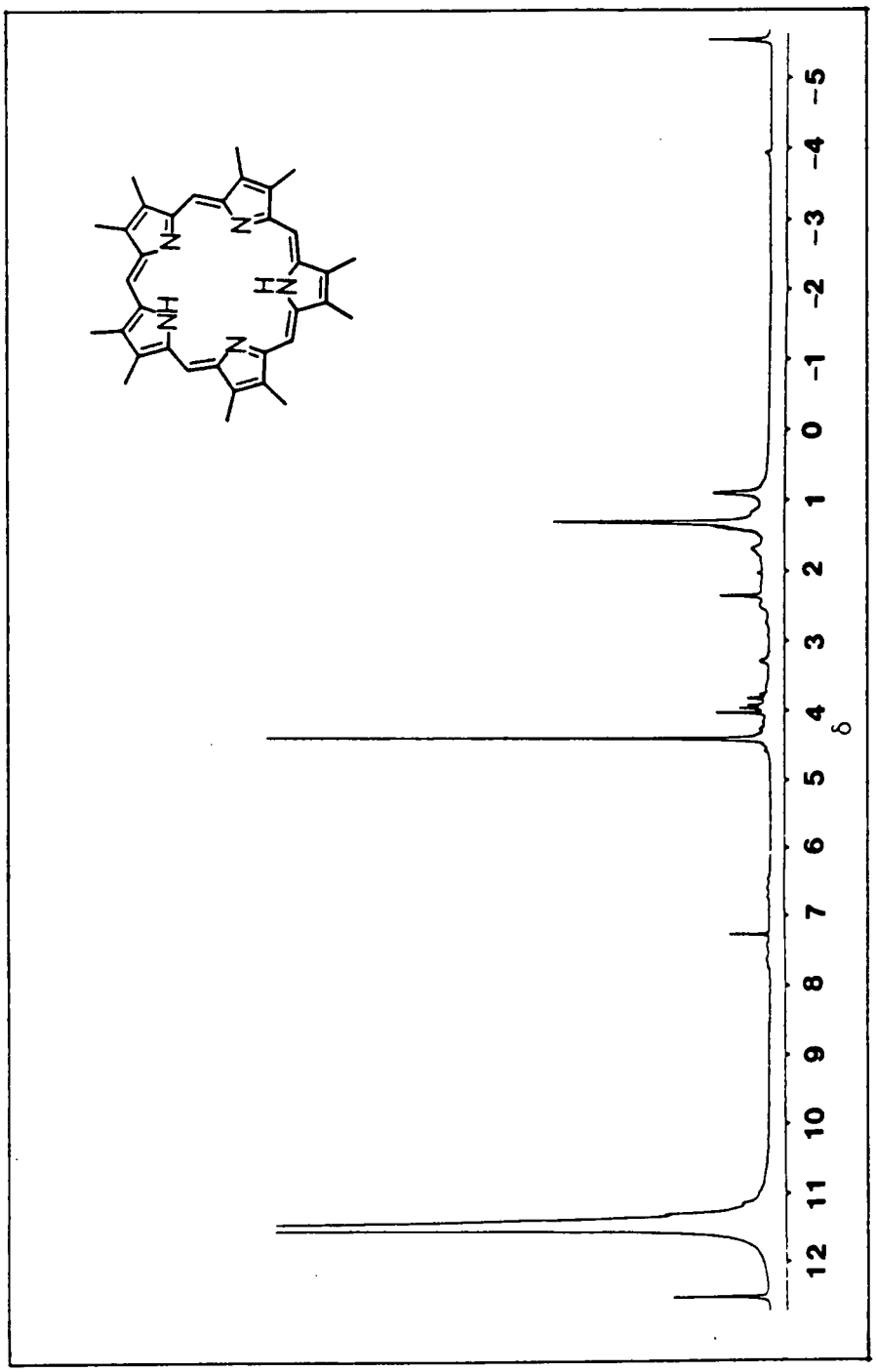


Figure 4: ^{1}H nmr Spectrum of 71 in 50% TFA-$CDCl_3$

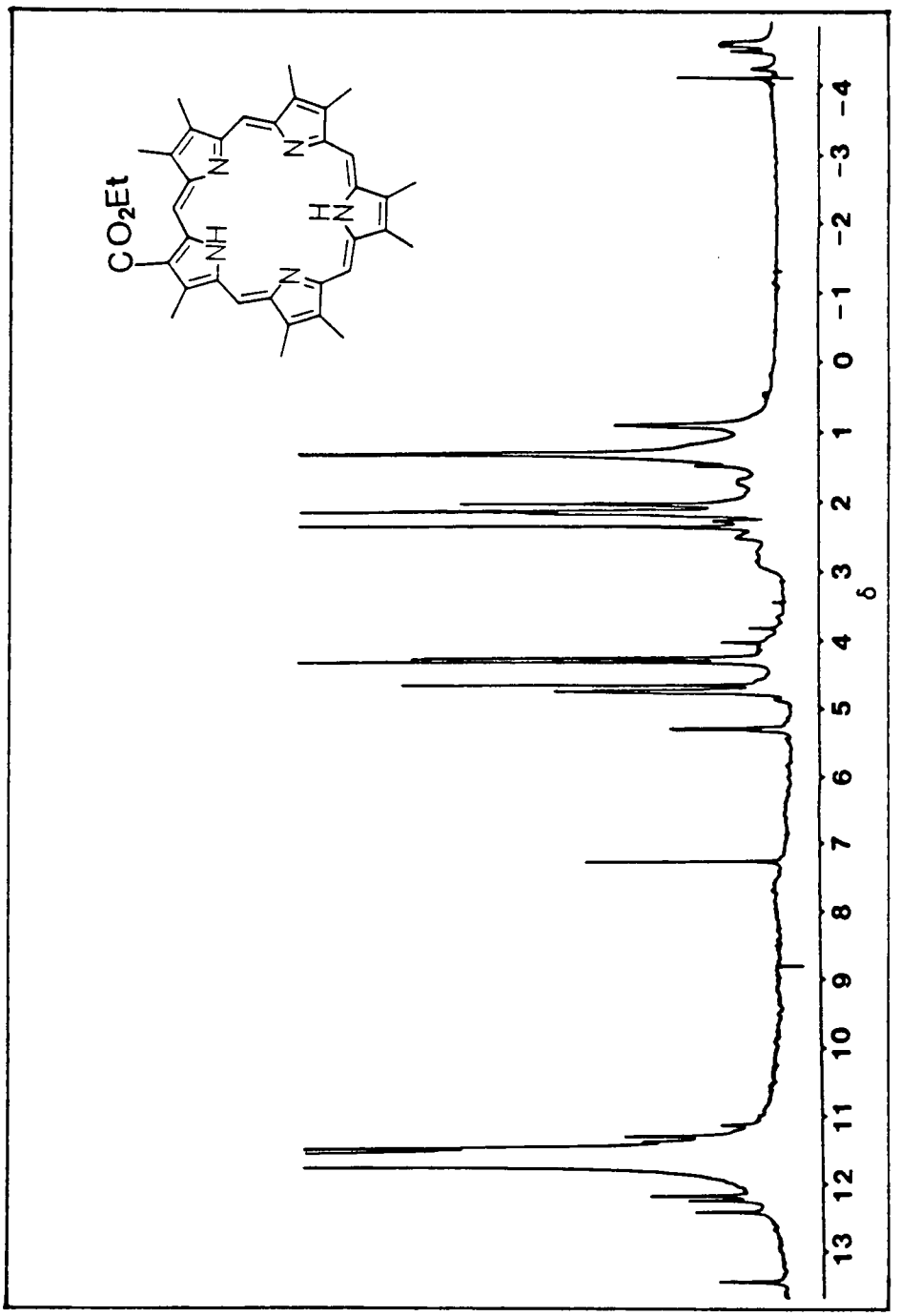


Figure 5: ^{1}H nmr Spectrum of 74 in 50% TFA-$CDCl_3$

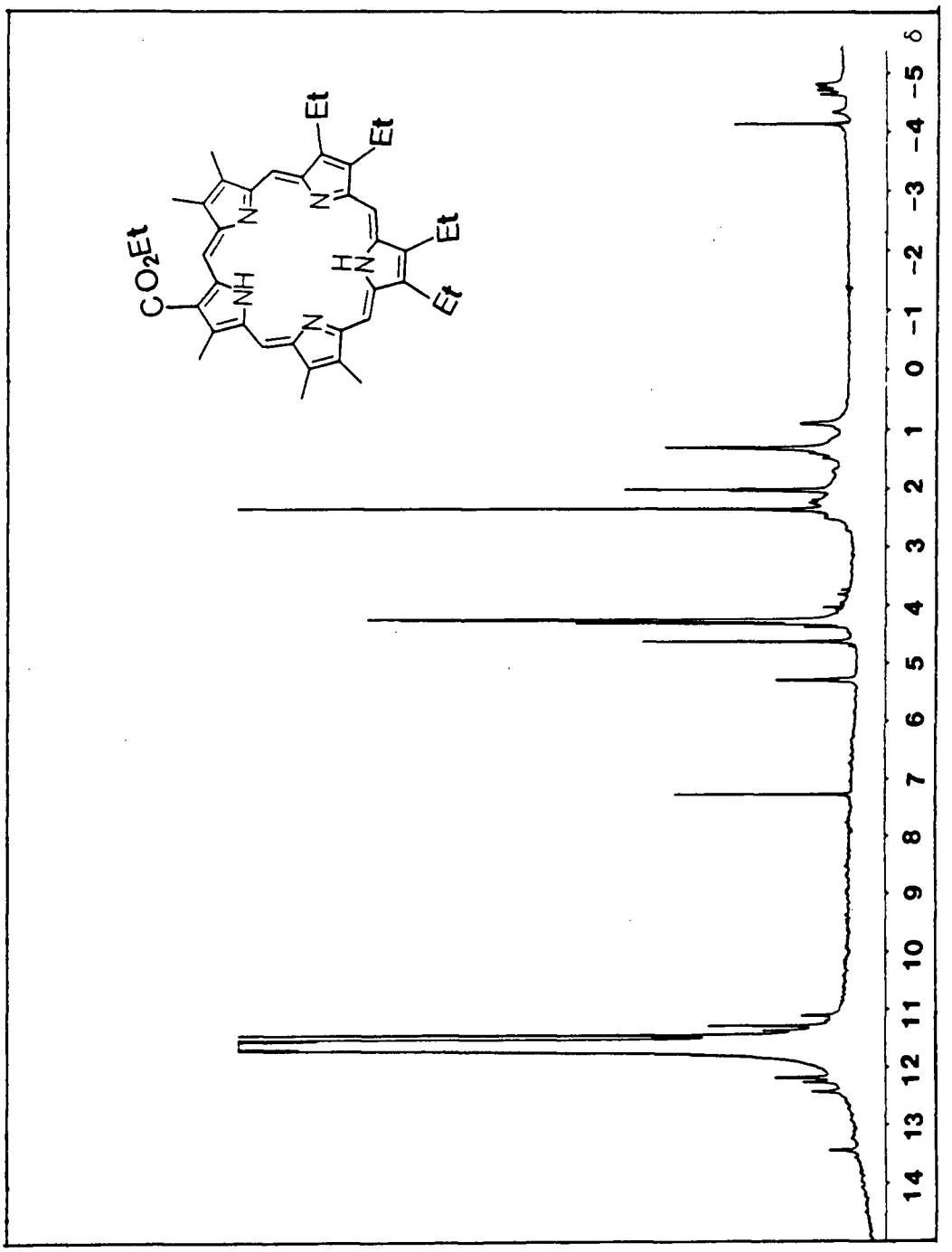


Figure 6: ^1H nmr Spectrum of 75 in 50% TFA-$CDCl_3$

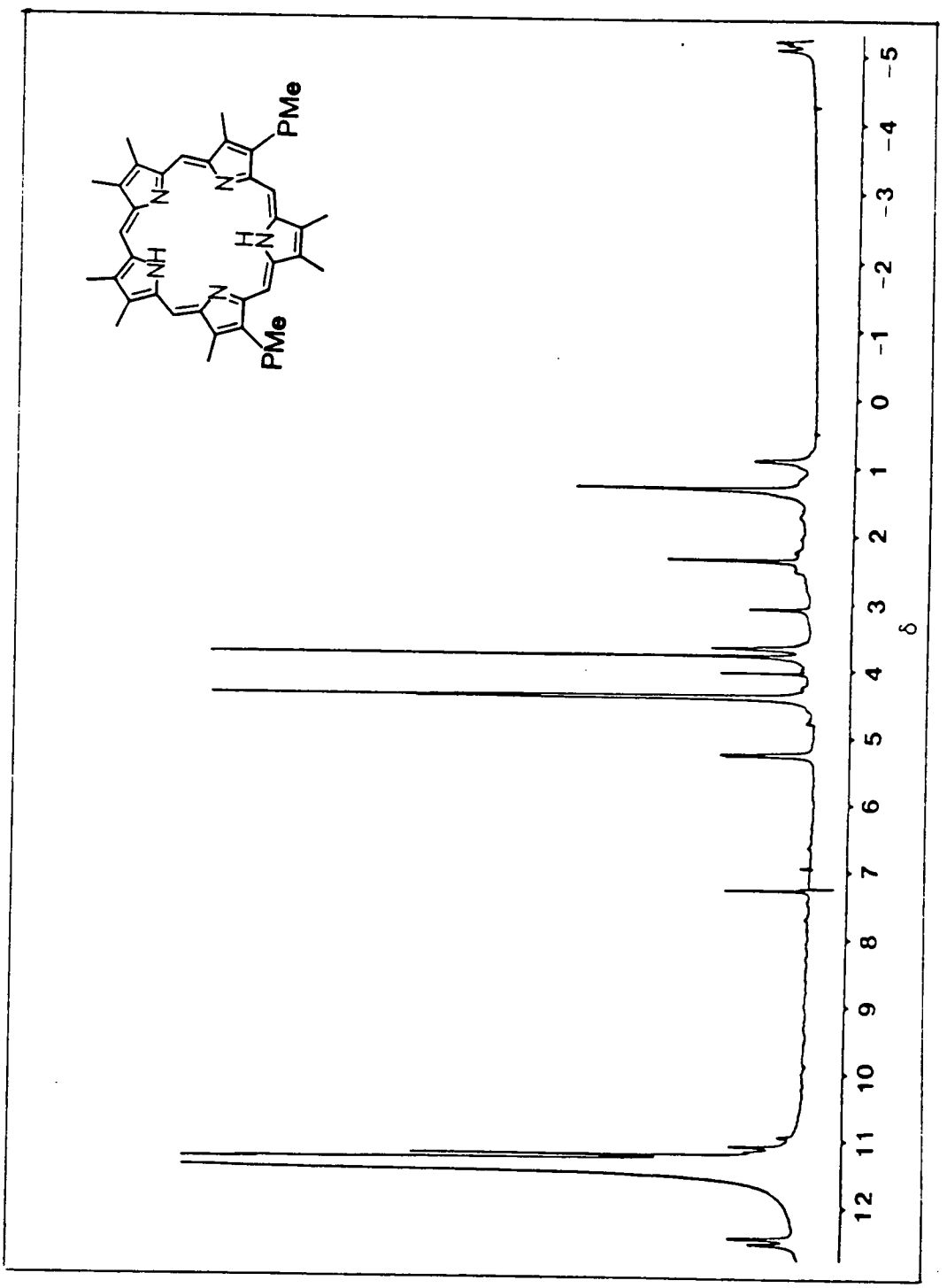


Figure 7: ^{1}H nmr Spectrum of 29 in 50% TFA-$CDCl_3$

4.2 ^{13}C-NMR DATA OF THE PENTAPHYRINS

^{13}C nmr spectroscopy was used in this work primarily for the purpose of supplementing proton nmr data in the characterization of the pentaphyrins synthesized. These are illustrated in figures 8-11. The solvent used was trifluoroacetic acid except for compounds 74 and 75 where 30% trifluoroacetic acid in deuterochloroform was used (v/v). All the compounds were found to be unstable in acid.

The ^{13}C resonances of the pentaphyrin, like porphyrins could be divided into three major groups; (1) the α- and β-pyrrolic carbons, (2) the meso or methine carbons and (3) the aliphatic carbons of the substituents. The simplest of these pentaphyrin, decamethylpentaphyrin 71 exhibited only two resonances in the aromatic region at δ ~142.7 and δ ~147.3 ppm probably due to β- and α-carbons respectively. The five meso carbons as expected gave only one peak at δ ~102 ppm while the ten peripheral methyl carbons gave a resonance at δ ~14.5 ppm.

The five meso carbons of pentaphyrin 29 gave three resonances at δ ~98.9, ~99.1, ~99.5 ppm. The methoxy carbon was observed at δ ~53.6 ppm with the carbonyl exhibiting resonance at δ ~180 ppm. Pentaphyrin 74 meso carbons gave five peaks at δ ~97.5, ~97.6, ~99.5, ~101.2 and ~101.6 ppm with the methylene carbon of the ethoxy appearing at δ ~64.6 ppm and the carbonyl of the same side chain exhibiting resonance at δ ~165.5 ppm. Like pentaphyrin 74, pentaphyrin 75 methine carbons also gave five peaks at δ ~96.2, 96.5, 98.5, ~101.2 and ~101.7 ppm. The carbonyl and methylene carbons of the ethyloxycarbonyl side chain gave resonances at δ ~164.8 and ~63.8 ppm respectively.

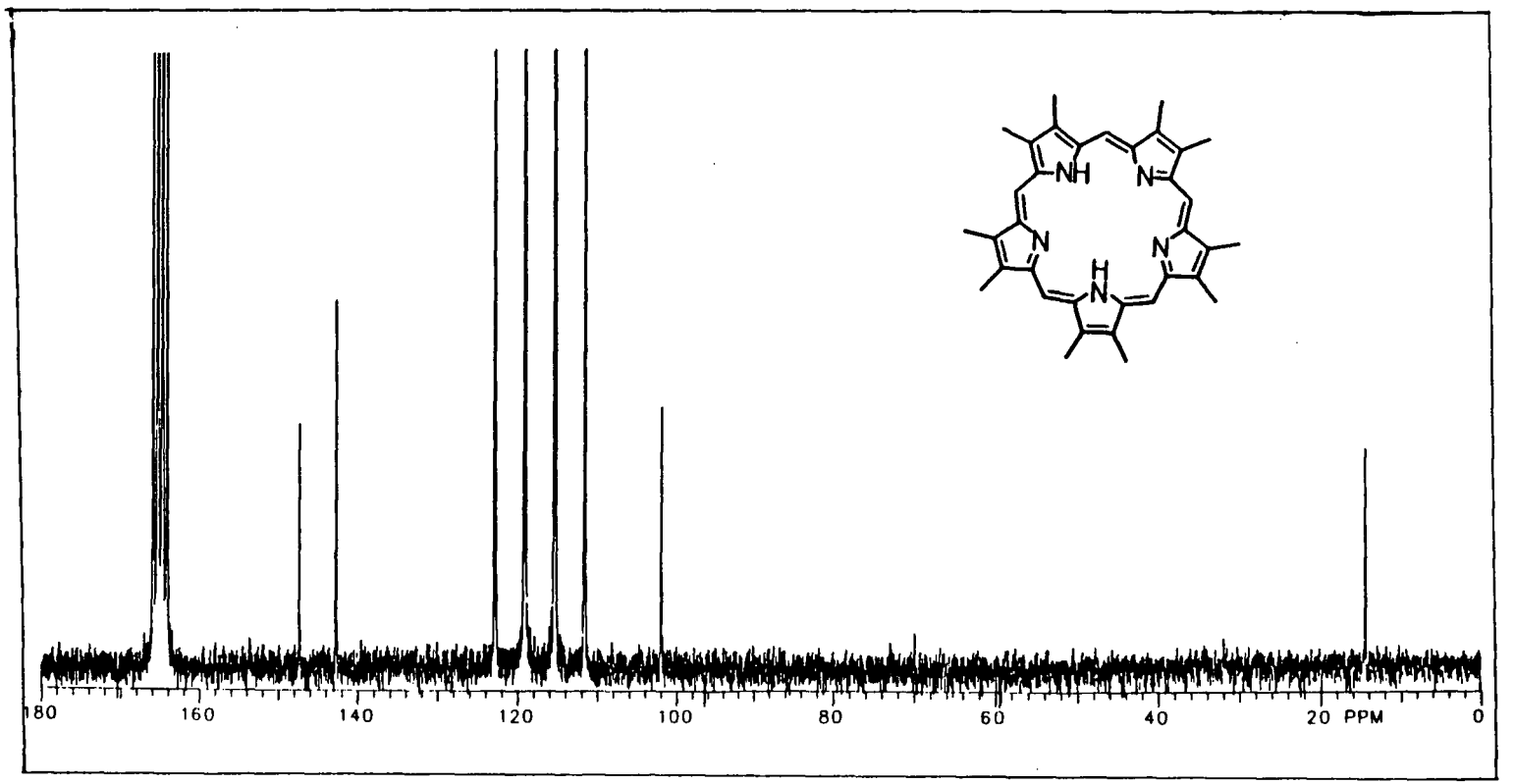


Figure 8: ^{13}C nmr Spectrum of 71 in TFA

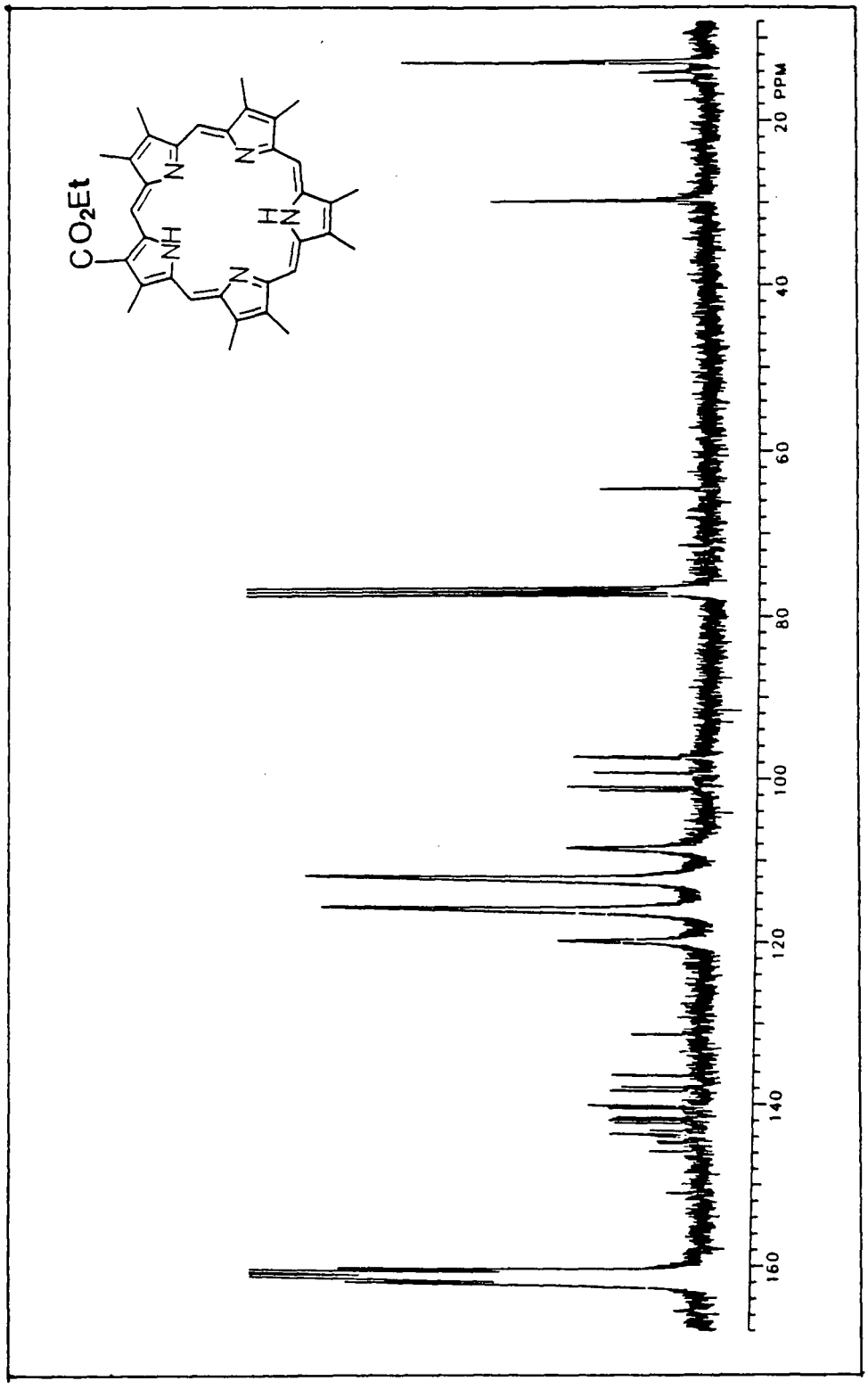


Figure 9: ^{13}C nmr Spectrum of 74 in 30% TFA-$CDCl_3$

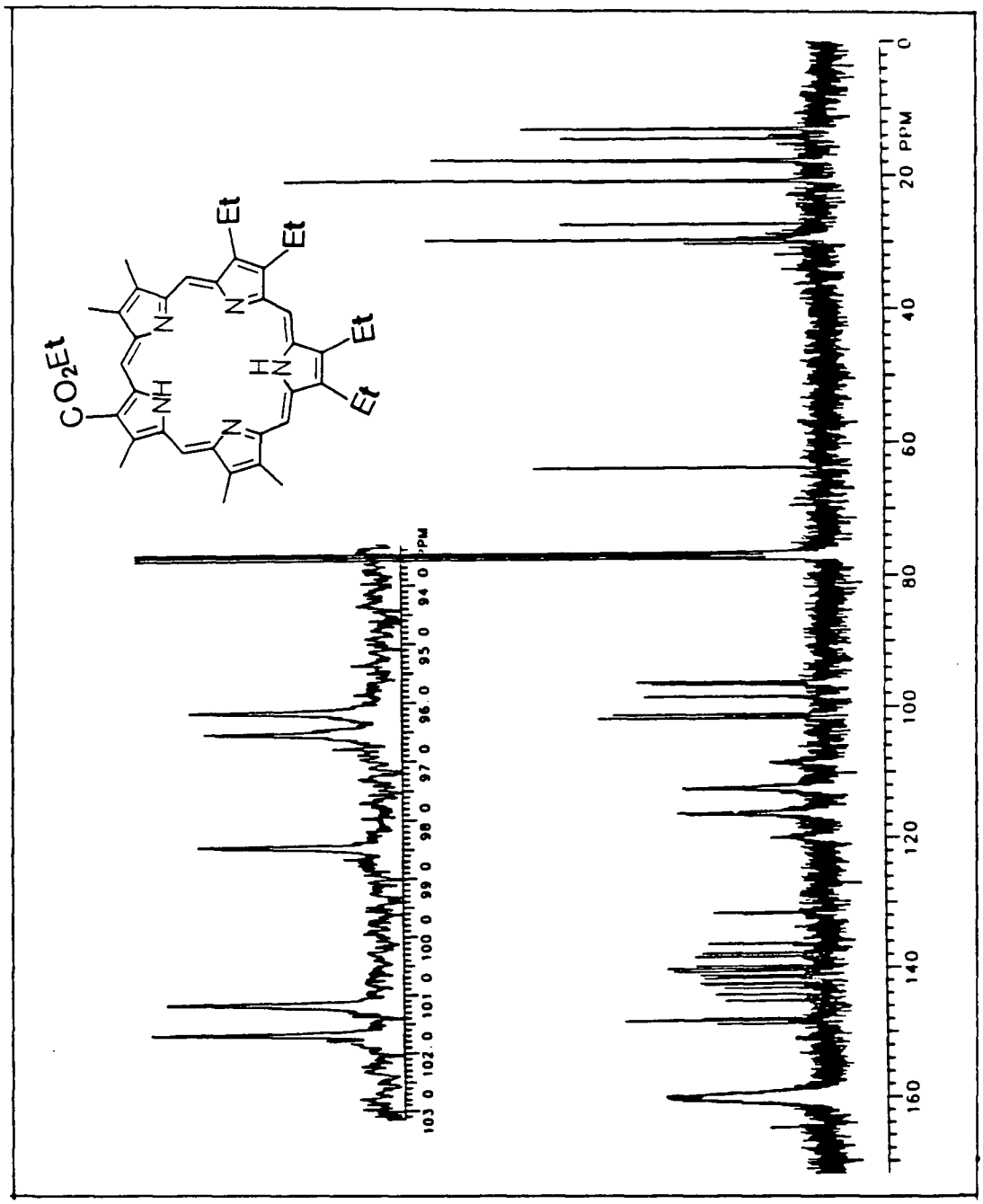


Figure 10: ^{13}C nmr Spectrum of 75 in 30% TFA-$CDCl_3$

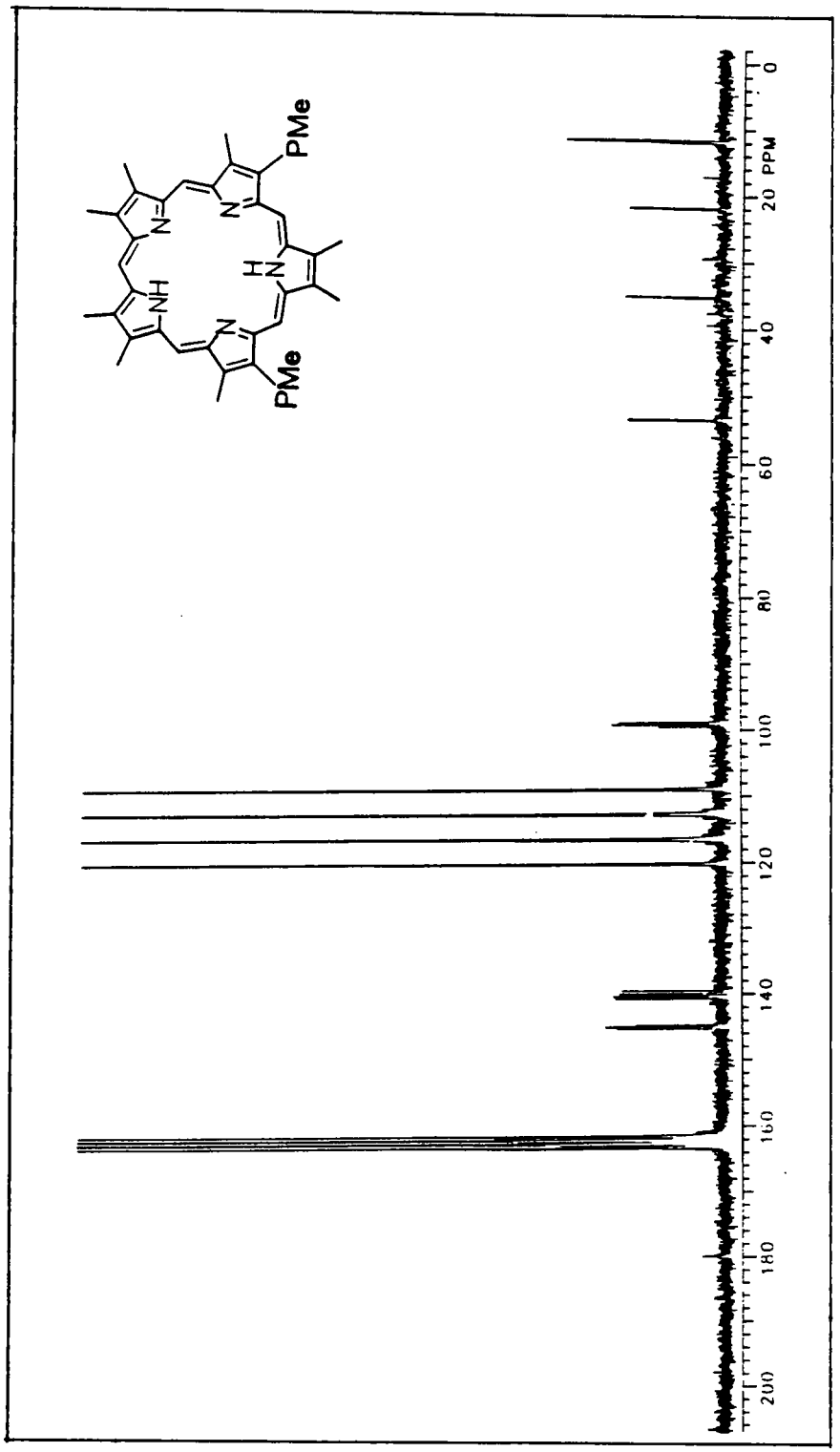
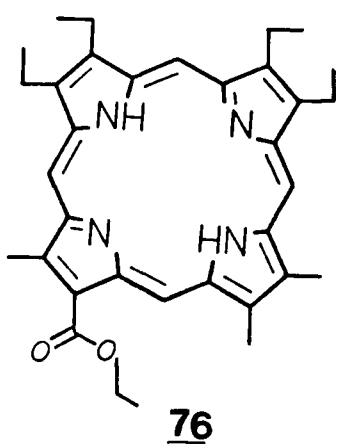


Figure 11: ^{13}C nmr Spectrum of 29 in TFA

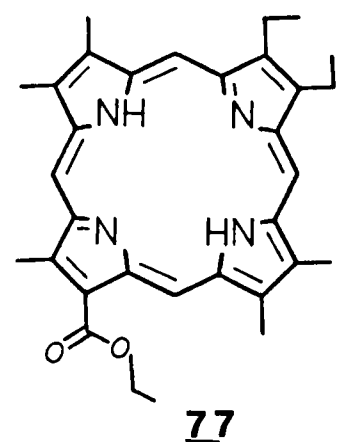
4.3 MASS SPECTRA OF PENTAPHYRINS AND DERIVATIVES

All the pentaphyrins and the metal derivatives of two of them synthesized during the course of this work were subjected to the fast atom bombardment and electron impact ionization in the mass spectrometer and the spectral are illustrated in figures 12-17.

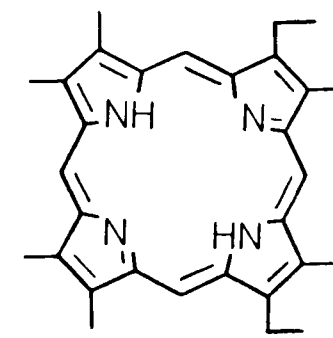
The fast atom bombardment of the pentaphyrin 75 exhibited a peak at 642 corresponding to the m+1 peak, and m+2 peak at 643. Electron impact ionization of this compound showed an interesting pattern. The parent peak was exhibited at 641(m^+) plus m+1, m+2, m+3, and m+4 peaks with the highest being m+2 and m+4 (12.66% and 12.16% of base peak respectively). This high m/e, up to m+3 was not surprising, reflecting the basicity of the pentaphyrin chromophore and probably protonation within the mass spectrometer[64]. The same behaviour was also found when sapphyrin was subjected to mass spectrometric investigation[26]. Three different intense peaks were surprisingly exhibited at m/e 536 (base peak), 508 (51.33% of base peak) and 478 (62.52% of base peak). These three peaks were calculated to be the parent peaks (m^+) of porphyrins 76, 77 and 78 respectively.



76



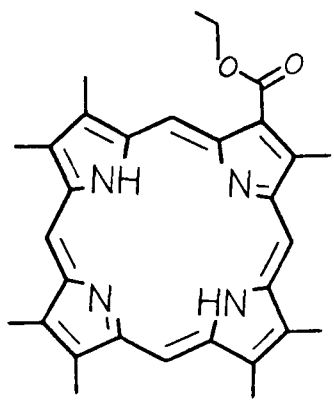
77



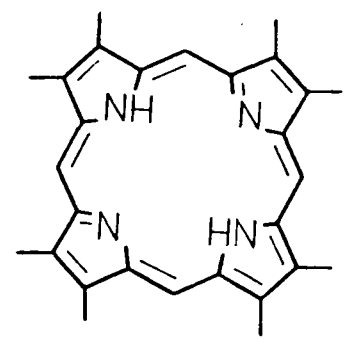
78

Since this pentaphyrin contains three different pyrroles, the nucleus apparently rearranges to porphyrin nucleus with a loss of a monopyrrolic fragment for the three different masses. Peaks at m/e 704 and 697 corresponding to m+1 peaks of copper and iron complexes of the pentaphyrin were also exhibited. Also exhibited were copper and iron complexes of the porphyrins.

All the other pentaphyrins exhibited the same fragmentation pattern as described above. With pentaphyrin 74 the m+1 and m+2 peaks were observed at 586 and 587 respectively in the fast atom bombardment. Instead of the parent peak at 585 (m^+), a 4.7% of base peak at 587 corresponding to m+2 was exhibited with m+3 and m+4 (with 2.6% and 2.8% of base peak respectively). Another feature is the peaks at 480 and 422 (41.45% and 22.70% of base peak) corresponding to the m^+ peaks of monoethoxycarbonylheptamethylporphyrin 79 and octamethylporphyrin 80. Peaks were also exhibited for iron and copper complexes of the pentaphyrin 74 and the porphyrins.

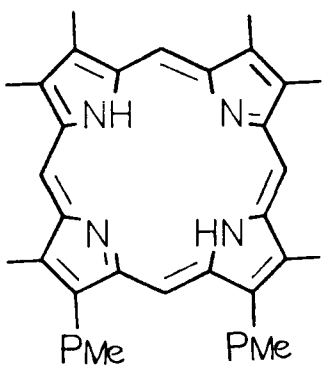


79

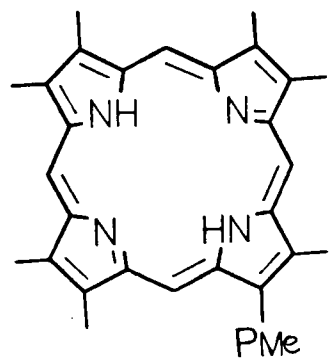


80

The fast atom bombardment of compound 29 exhibited the m+1 and m+2 peaks at 672 and 673 respectively. The electron impact ionization exhibited the m+1, m+2 and m+3 peaks with the m+2 and m+3 peaks being 35.69% and 19.22% of base peaks respectively. The m+1 peaks with copper and iron were exhibited. As usual, with two different pyrroles making up the pentaphyrin nucleus, two different types of porphyrin peaks were exhibited. The base peak of m/e 566.5 correspond to porphyrin 81 while the porphyrin 82 with m^+ at m/e 494.5 had 89% intensity of the base peak. The copper and iron complexes of these porphyrins had 19.1% and 11.8% (relative to the base peaks) intensities.



81



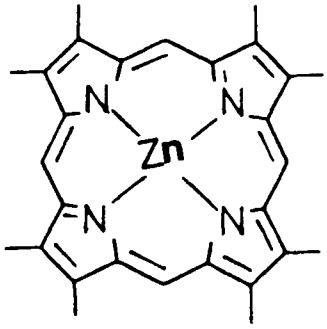
82

With decamethylpentaphyrin 71, the m+1 and m+2 peaks at m/e 528 and 529 respectively were exhibited with fast atom bombardment. Electron impact ionization exhibited peaks at m/e 476 and 484 with no m^+ or m+1 peak of the pentaphyrin. The observed peaks, m/e 476 and 484, correspond to the m^+ and m+1 peaks of iron and copper complexes of octamethylporphyrin 80.

It must be noted that the presence of both copper and iron in the spectra is more probably due to the scavenging of metal ions by the pentaphyrins from the ion source in the spectrometer[65]. The same behaviour has been observed in our laboratory with metal-free porphyrin mass spectra.

In the fast bombardment, zinc decamethyl-pentaphyrin 72 exhibited peaks at m/e 591 and 592. One interesting feature with the electron impact ionization is that it exhibited a peak at m/e 591 of about 2.7 % intensity of the base peak. The base peak happened to be at m/e 484, the mass of zinc octamethylporphyrin 83. The pattern at m/e 484 was the same for 591. Thus, the complex, like the metal free pentaphyrin nucleus, rearranges giving a zinc complex of the porphyrin with a loss of monopyrrolic fragment. The zinc complex of decamethylsapphyrin was observed to behave in the same way[26].

For compound 73, peaks at m/e 649 and 650 were exhibited with the fast atom bombardment. With electron impact ionization, peaks at m/e 649 and 651 were exhibited. Like compound 72, this complex nucleus rearranges to give the complex of porphyrins 79 and 80 at m/e 542 and 484 respectively.



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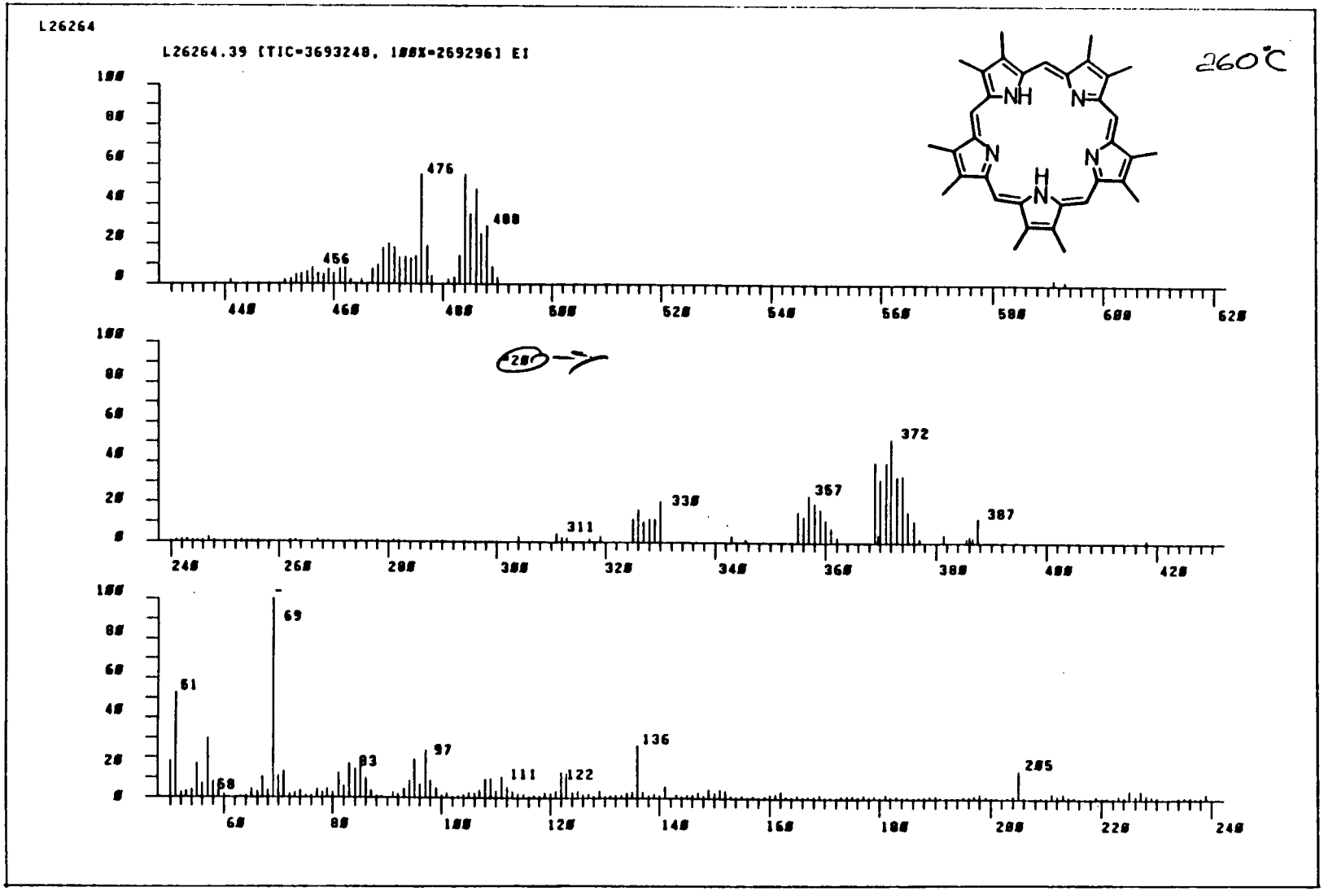


Figure 12: Mass Spectra of 71

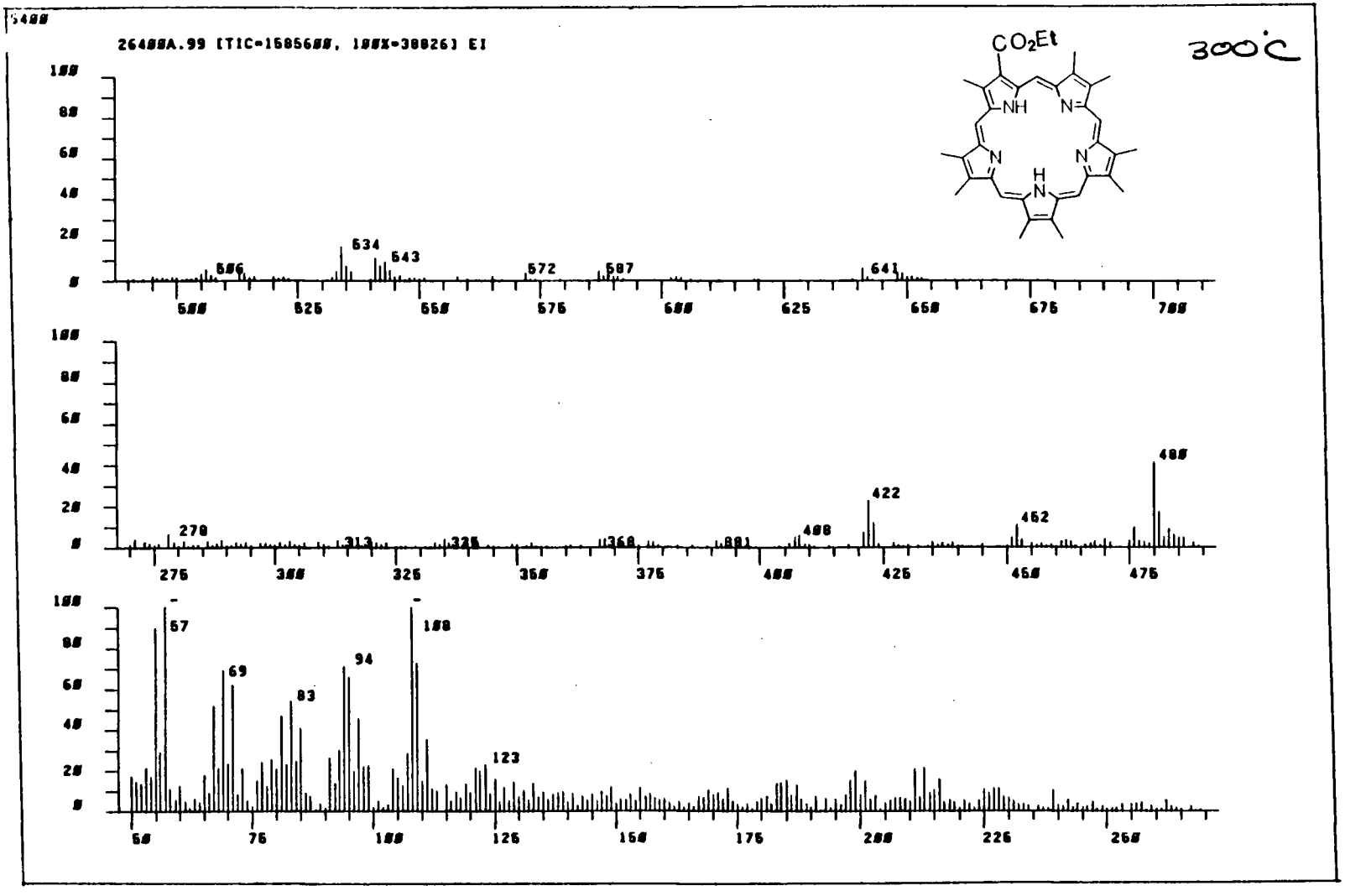


Figure 13: Mass Spectra of 74

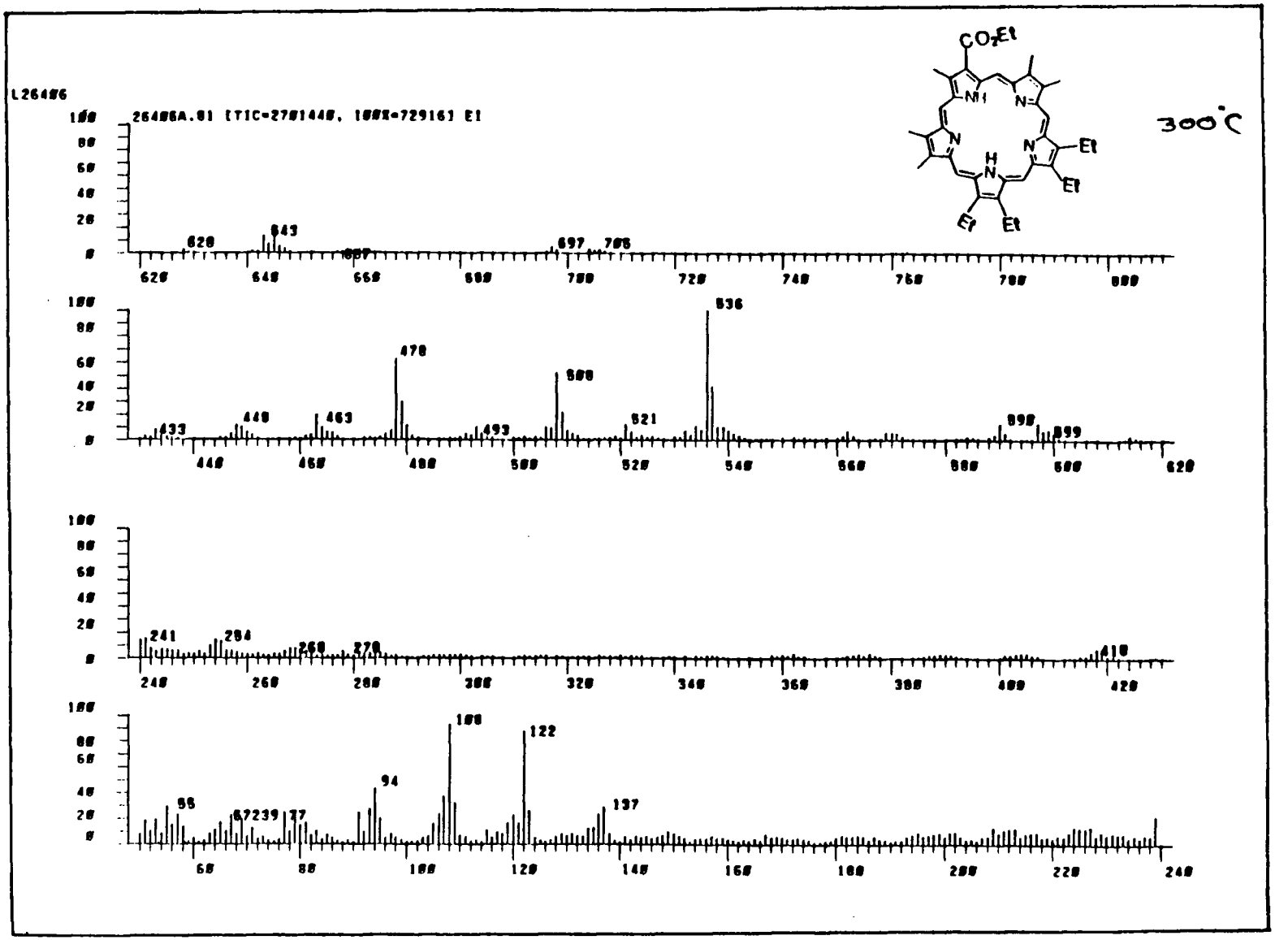


Figure 14: Mass Spectra of 75

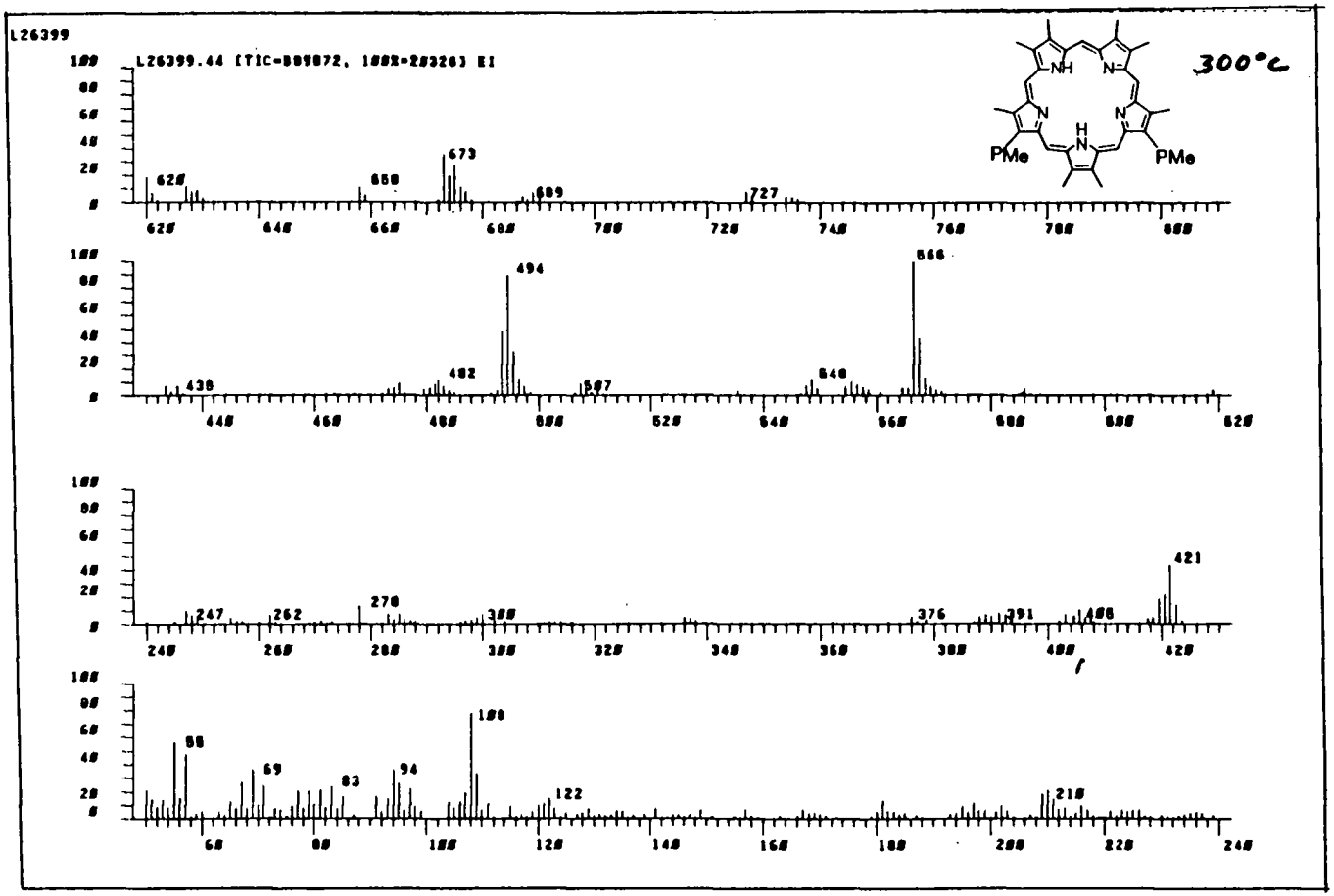


Figure 15: Mass Spectra of 29

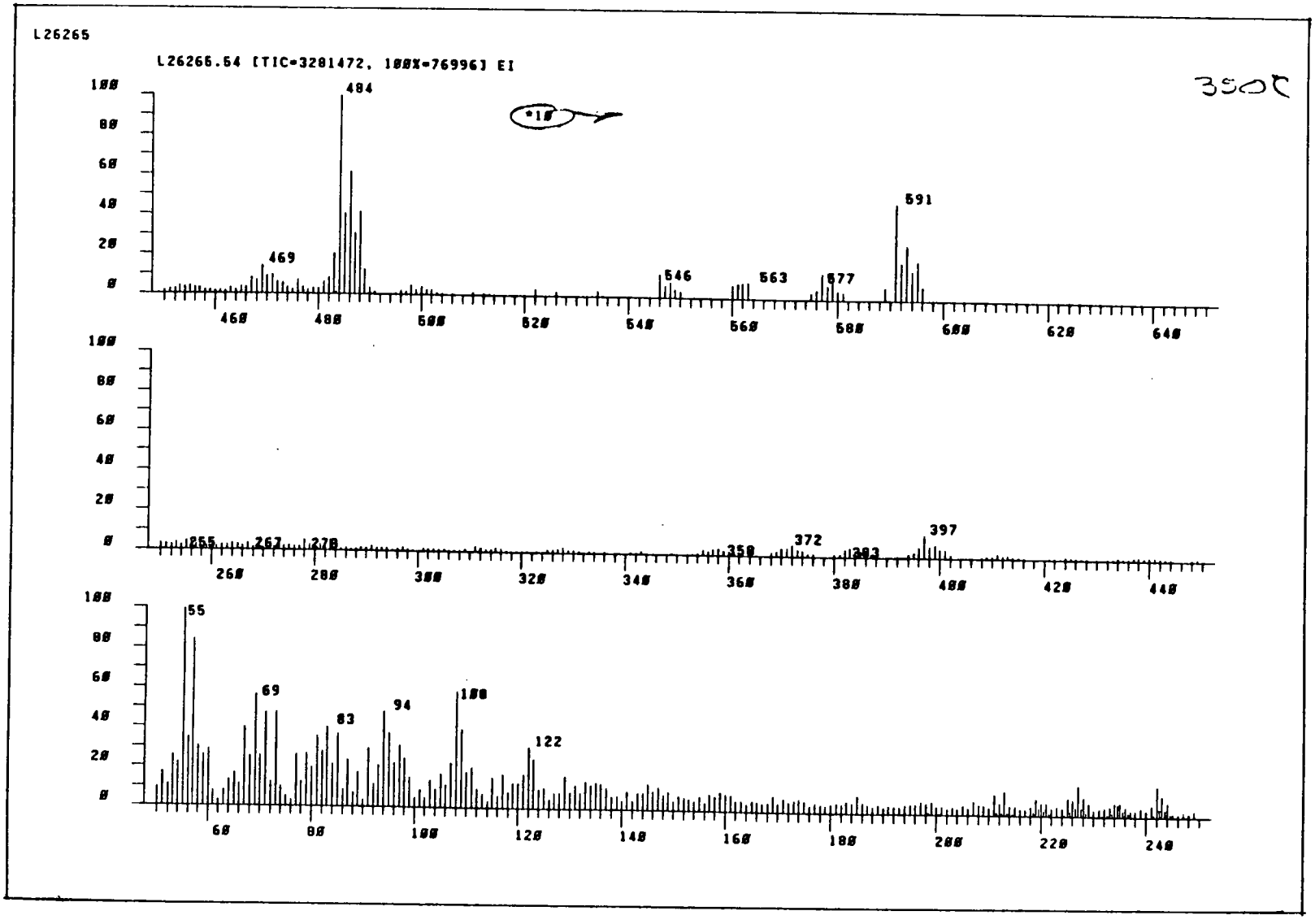


Figure 16: Mass Spectra of 72

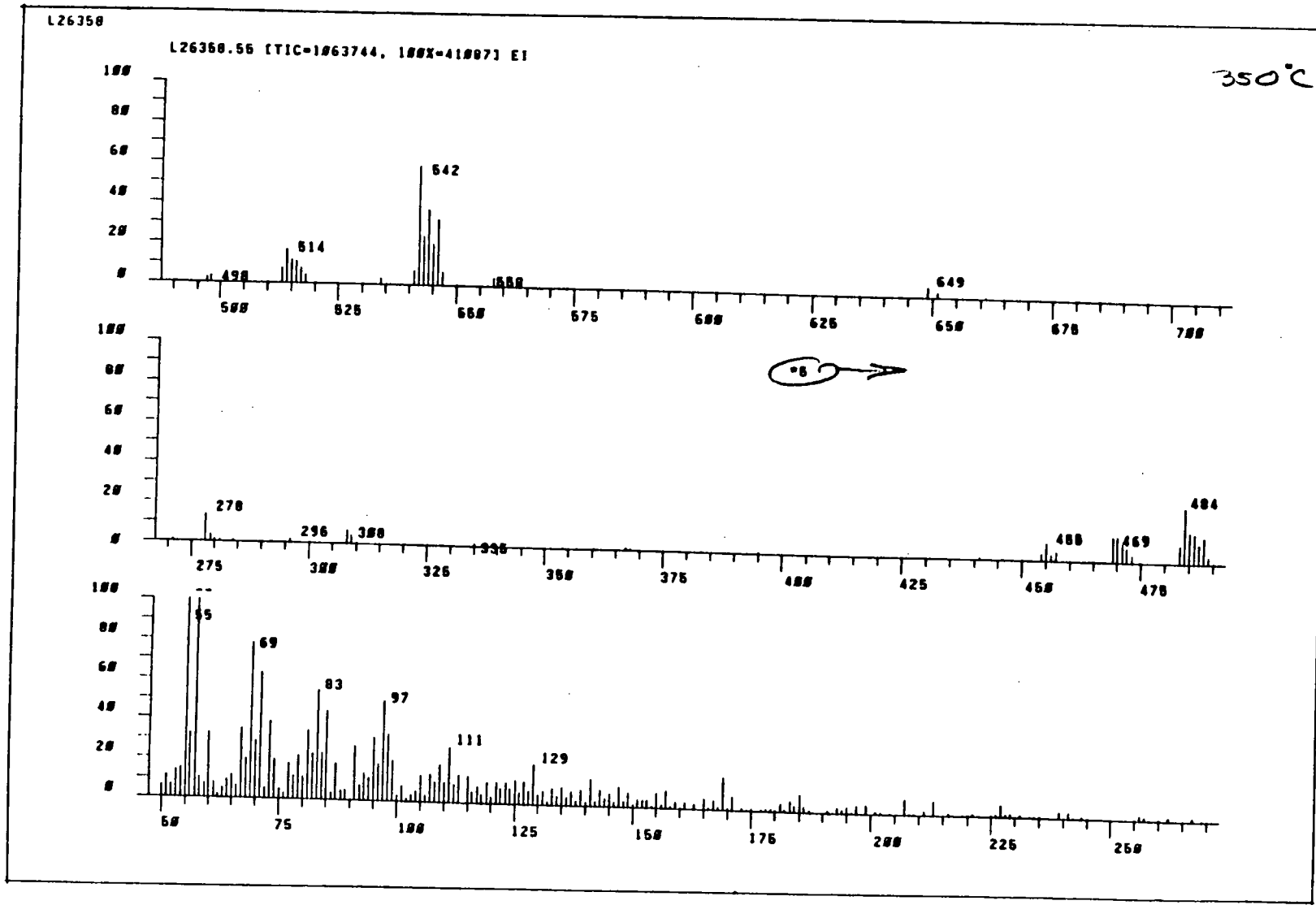


Figure 17: Mass Spectra of 73

4.4 ELECTRONIC ABSORPTION SPECTRA OF THE PENTAPHYRINS AND DERIVATIVES

The visible spectra of porphyrins, metalloporphyrin and their derivatives is a useful and characteristic property. Porphyrins exhibit a characteristic electronic absorption spectrum consisting of one very intense band (ε -$10^4 M^{-1}cm^{-1}$) around 400 nm, known as the "Soret" band and four less intense bands in the region from 500 - 700 nm. The Soret band is observed in all tetrapyrroles in which the nucleus is fully conjugated and is generally regarded as a characteristic of the macrocyclic conjugation. The relative intensities of the four visible bands are sensitive to the nature of the peripheral substituents. Factors which encourage increase in π-electron density of the periphery of the porphyrin nucleus cause shifts to longer wavelength in the absorption bonds[66]. Thus shifts to longer wavelength with increase intensities are found as the electron-attracting power (formyl, carboxylic acid, ester etc.) of the side chain increases.

The pentaphyrins synthesized during the course of this work exhibited very interesting electronic spectra as illustrated ion figures 18-23. The free base pentaphyrin is orange in color but turns green and yellowish-green in methanol and methylene chloride respectively. A drop of TFA into the methylene chloride solution of the pentaphyrin turns it deep green and the yellowish-green color can be obtained again when a drop of triethylamine is added. The pronated pentaphyrin gives a deep blue color.

The most striking feature of the free base (in the presence of triethylamine) and the trication (in the presence of trifluoroacetic acid)

spectra of all the pentaphyrins is their display of exceptionally strong uv-visible absorption. The free base exhibit three bands in the region from 330 to 750 nm with the exception of compound 71 which gives four bands. The trications on the other hand exhibit five bands within the same wavelength. In all cases the Soret band is observed between 450 to 462 nm. The intensities of the absorption bands of compound 75 are noticeably greater than the other pentaphyrins, with the Soret in particular being ten times more intense than the others. Another interesting feature of 75 is the shift to longer wavelength of all the absorption bands compared to the others. The intensities and wavelengths of the absorption bands obtained for pentaphyrin 29 are remarkably different from the reported figures[41]. As what might be causing these differences in wavelengths and intensities of the absorption bands are not easy to predict, more analyses (eg. x-ray studies) are needed before a reasonable conclusion can be drawn.

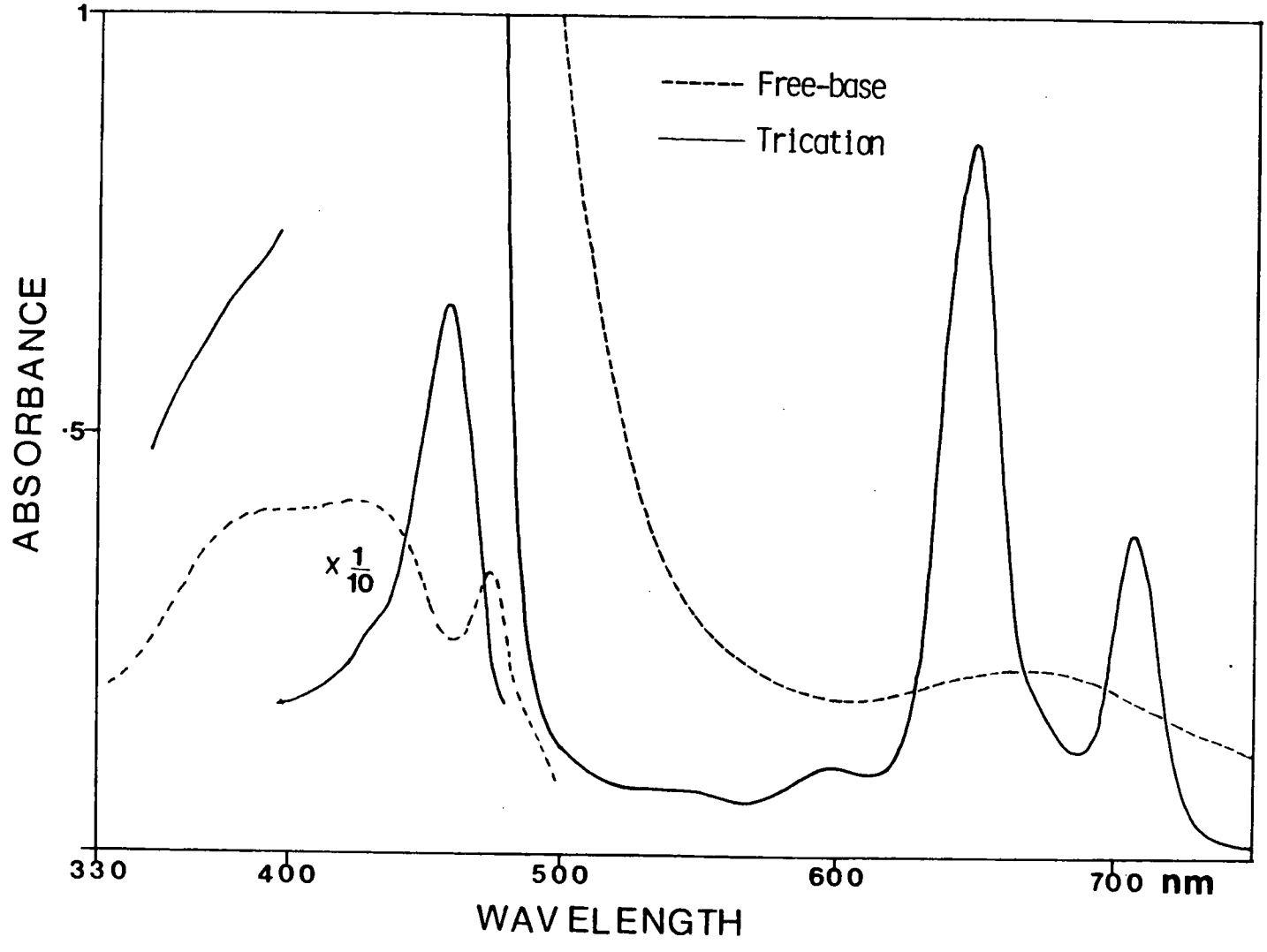


Figure 18: Electronic Absorption Spectra of 71

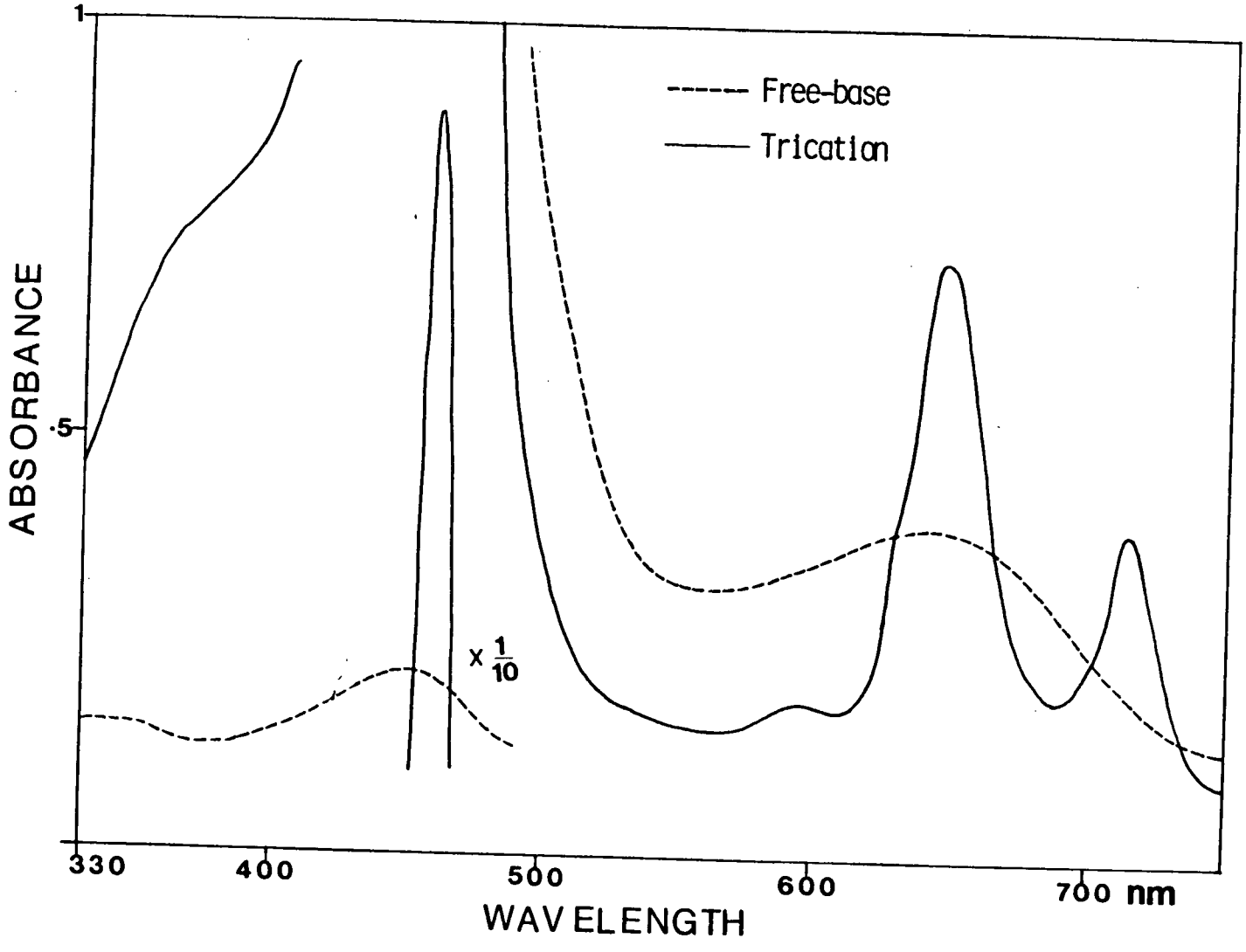


Figure 19: Electronic Absorption Spectra of 74

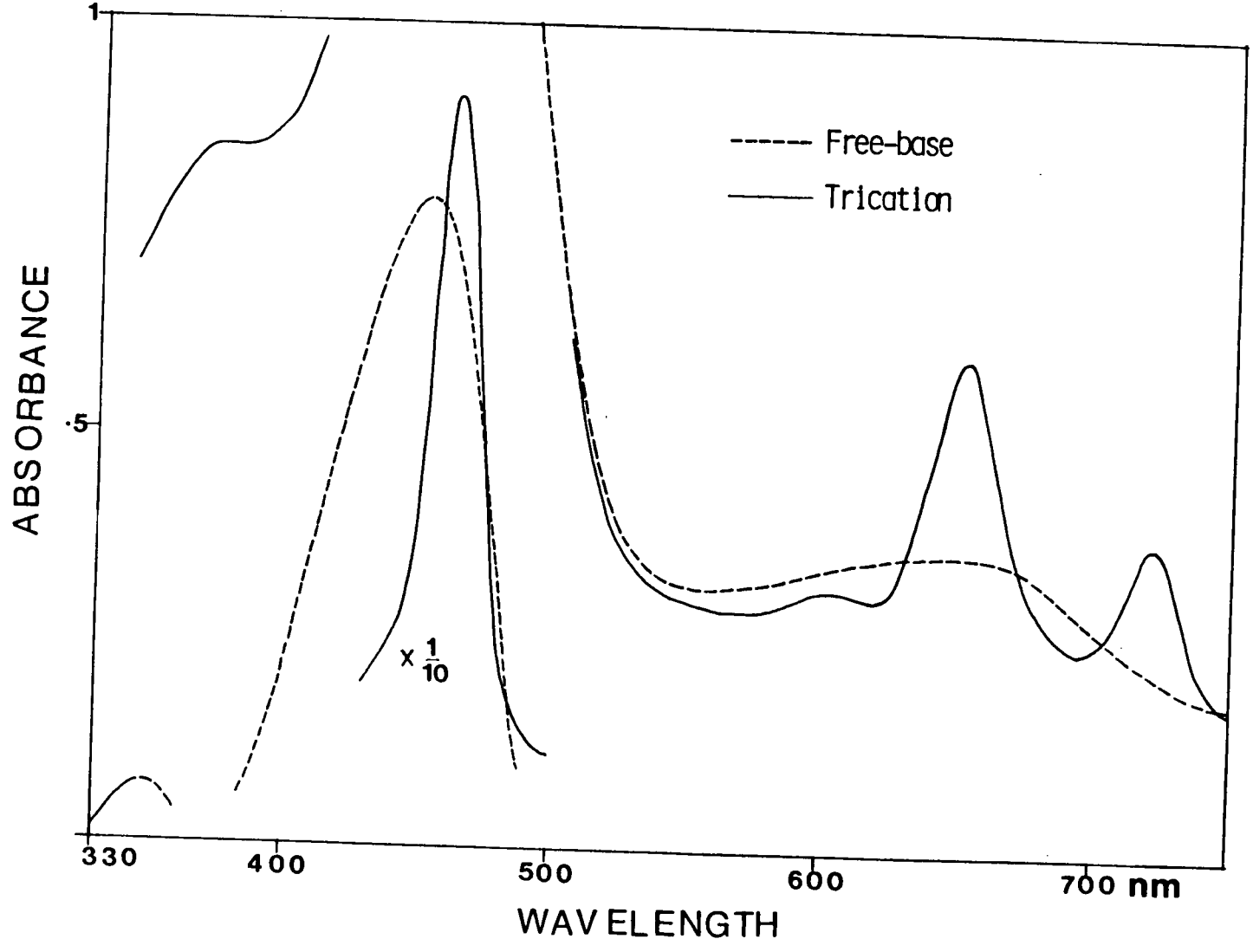


Figure 20: Electronic Absorption Spectra of 75

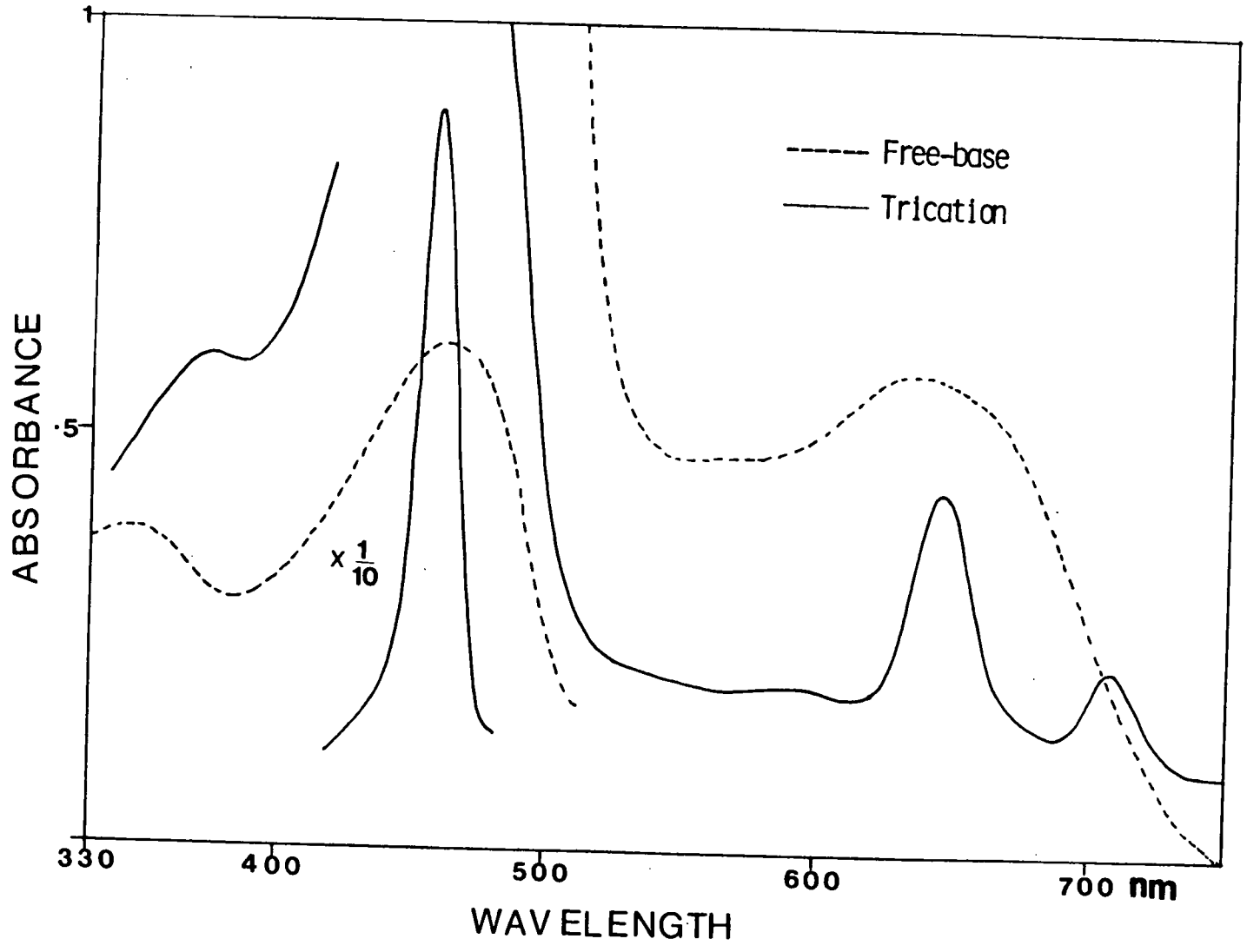


Figure 21: Electronic Absorption Spectra of 29

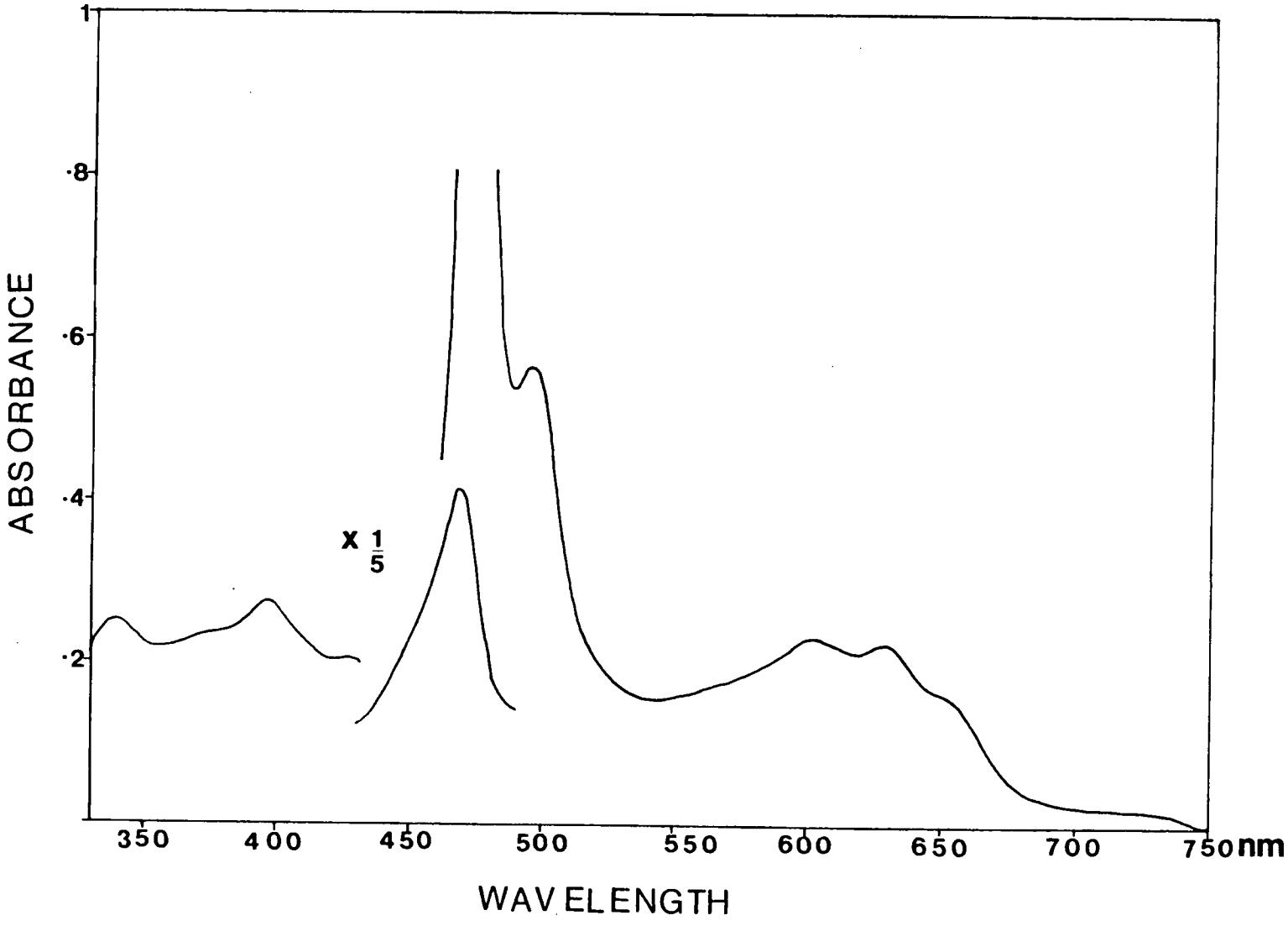


Figure 22: Electronic Absorption Spectra of 72

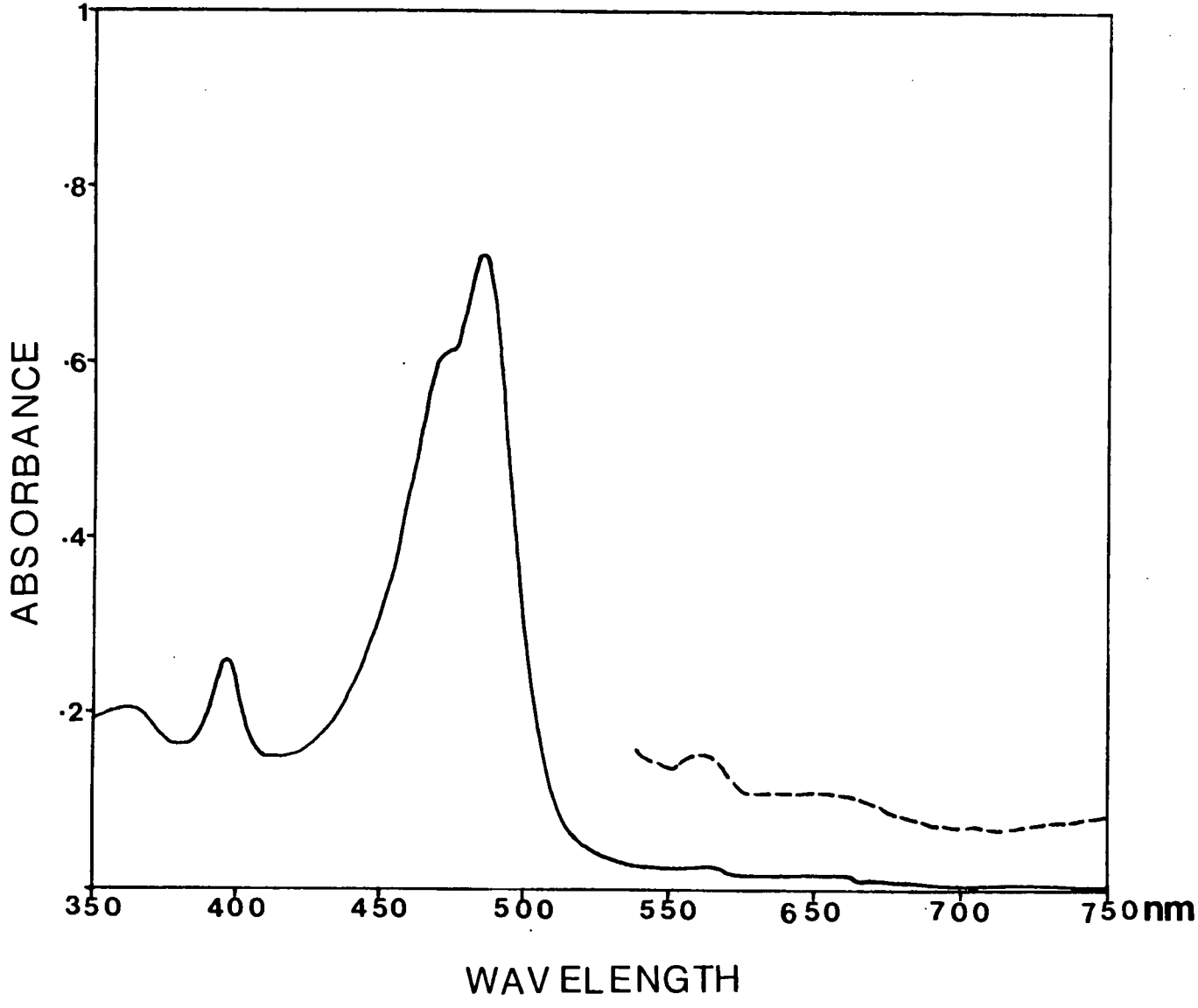
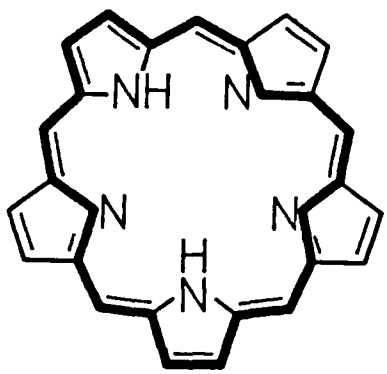


Figure 23: Electronic Absorption Spectra of 73

The spectra of the pentaphyrins discussed so far provide confirmation of their structures and attest to their aromaticity. All the ^1H nmr spectra showed strongly shielded inner N-H protons and the protons at the periphery, meso-protons and β-protons are strongly deshielded. The ability of these macrocycles to sustain a large induce diamagnetic ring current demonstrates the presence of a delocalized aromatic π-system.

The pentaphyrin skeleton 84 contains a total of 28 π-electron, so if all the π-electrons are delocalized, the system would be anti-aromatic (4n + 2 = 28, i.e. n = 6.5) which is not a whole number. A delocalization scheme can be envisaged however, where only 22 π-electrons are delocalized, thus in Huckel's (4n + 2) rule, n = 5. Hence the convincing evidence of the aromaticity of the pentaphyrin provided by the spectra of the compound is in line with theoretic expectation.



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