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THE PROTON MAGNETIC RESONANCE SPECTRA OF PORPHYRINS—VII[1]

SYNTHESIS AND NMR STUDIES OF THALLIUM(III) COPROPORPHYRIN CHELATES

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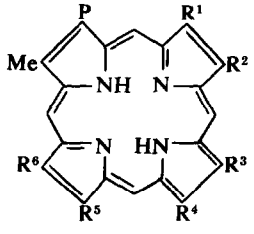
Abstract—The four coproporphyrin "type-isomers" have been synthesized as their tetramethyl esters (1) through modifications of existing procedures. When treated with thallium(III) trifluoroacetate, these porphyrins furnish the corresponding aquo porphinatothallium(III) hydroxides (2) after ligand exchange induced by chromatography on deactivated alumina.

The proton NMR spectra of the chloroform solutions of thallium(III) coproporphyrins show a pronounced concentration dependence, all resonances moving to low field upon dilution; the spectra of the type-III and -IV isomers show additional fine structure in solution. Both the *meso*- and β-Me protons show thallium-proton spin couplings. These results are interpreted in terms of a monomer-dimer equilibrium. In the dimers of the type-I and -II chelates, the rings lie directly one above another, whereas with the type-III and -IV complexes, steric repulsions of the propionate side-chains cause lateral displacement of one molecule in the dimer relative to the other, resulting in the observed fine structure in the spectra. The inter-porphyrin distances and lateral displacements are calculated on this basis and are compared with the corresponding dimers of the parent coproporphyrins, with which there are considerable similarities.

Proton magnetic resonance spectra of metalloporphyrins and porphyrins have received considerable attention in recent years.[1-5] The NMR spectra of mesoporporphyrin-IX dimethyl ester and its nickel chelate showed[2] an appreciable concentration dependence, all resonances shifting downfield upon dilution. At high concentrations the β-methyl and *meso*-proton resonances showed fine structure which disappeared when diluted. These results were interpreted[2] on the basis of a monomer-dimer equilibrium. In the dimer, the porphyrin rings were shown to be stacked into layers and separated by a distance of 10·0 Å in mesoporphyrin and 7·9 Å in the chelate. In Part IV[5] of this series, the NMR spectra of coproporphyrins-I, -II, -III, and -IV (tetramethyl esters) were investigated as a function of concentration in chloroform solution. The spectra showed a pronounced concentration dependence, with all resonances moving to low field upon dilution. The spectra of coproporphyrin-III (1c) and coproporphyrin-IV (1d) showed additional structure in concentrated solutions. A satisfactory quantitative interpretation of these results was given in terms of a monomer-dimer equilibrium. In the dimer, the porphyrin rings were calculated to be separated by about 8 Å.

Preliminary reports of the synthesis[6] and NMR spectra[6,7] of thallium(III) porphyrin chelates have appeared. The thallium atom (ionic radius 0·95 Å) is presumed to be out of the plane of the porphyrin ring, though the visible absorption spectra appear to indicate[8] no major distortion of the macrocyclic ring. The thallium-proton spin coupling constants for the *meso*- and β-Me protons were determined[6,7] to be 45·0 and 8·2 Hz respectively. It was of interest to us to investigate the effects that the thallium(III) atom and its ligands might have upon the chemical shifts and fine structure present in the free coproporphyrins.



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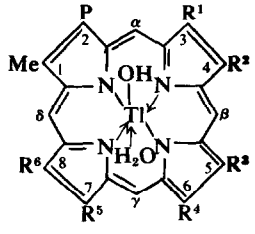

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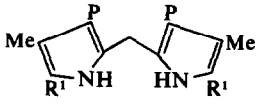
	R^1	R^2	R^3	R^4	R^5	R^6
a	Me	P	Me	P	Me	P
b	P	Me	Me	P	P	Me
c	Me	P	Me	P	P	Me
d	Me	P	P	Me	P	Me

P = $CH_2CH_2CO_2Me$

Syntheses of coproporphyrins and their thallium-(III) *chelates*

Coproporphyrin-I tetramethyl ester (**1a**) was prepared by the recently reported[9] modification of Fischer's pyrromethene synthesis, whilst the type-IV isomer (**1d**) was prepared from pyrromethenes following Fischer's original route.[10]

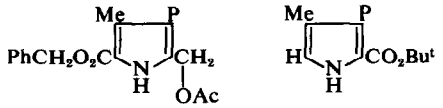
The synthesis of coproporphyrin-II tetramethyl ester (**1b**) was accomplished through a variation[11] of the MacDonald procedure.[12] Thus, the pyrromethane dicarboxylic acid (**3a**) was condensed with the diformylpyrromethane (**3b**) in methanol/methylene chloride in the presence of toluene *p*-sulphonic acid. After aerial oxidation and chromatography, a 45% yield of coporporphyrin-II tetramethyl ester (**1b**) was obtained.



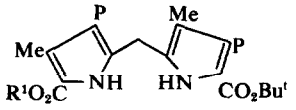
3

a: $R^1 = CO_2H$
b: $R^1 = CHO$

A similar route to the biologically significant coproporphyrin-III tetramethyl ester (**1c**) was employed. Condensation of the α-free pyrrole (**4**) with the acetoxymethylpyrrole (**5**) in methanol in the presence of toluene *p*-sulphonic acid[13] gave a high yield of the unsymmetrically substituted pyrromethane (**6a**). The pyrromethane (**6b**) bearing 5- and 5'-t-butyl esters would have been a more logical target, but we have in the past[e.g.11] experienced considerable difficulty in the crystallization and purification of pyrromethanes bearing two t-butyl ester functions. Catalytic hydrogenation over palladized charcoal gave the corresponding carboxylic acid (**6c**) which was treated with cold trifluoroacetic acid to furnish the 5,5'-unsubstituted pyrromethane (**7**). This substance was condensed with the diformylpyrromethane (**3b**) as described earlier, and gave coproporphyrin-III tetramethyl ester in 41% yield.



5 **4**



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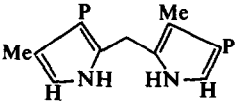
a: $R^1 = CH_2Ph$
b: $R^1 = Bu^t$
c: $R^1 = H$

All of the coproporphyrins were identified with authentic samples prepared earlier[14] and their NMR spectra were identical to those reported in Part IV.[5]

Treatment of the appropriate coproporphyrin isomer with one equivalent of thallium(III) trifluoroacetate in methylene chloride and tetrahydrofuran, followed by chromatography on deactivated alumina gave the thallium chelates (**2**). The chromatographic work-up served both to purify the product and also to replace the trifluoroacetate ligand, which is initially present in the complex, with hydroxyl.



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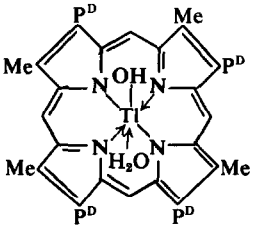

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$P^D = CH_2CH_2CO_2CD_3$

The extreme complexity of the β-Me region of the thallium coproporphyrin-III tetramethyl ester (**2c**) NMR spectrum necessitated the removal of the resonances associated with the methyl esters of the propionic side-chains. This was accomplished by treatment of the tetramethyl ester (**1c**) with 5% sulphuric acid in d_4-methanol. Insertion of thallium in the normal way gave the coproporphyrin-III chelate (**8**).

RESULTS

The complete results from the dilution studies are given in Table 1. It can be seen that dilution of the thallium(III) coproporphyrins causes all of the resonances to move to low field, the shifts being largest for the *meso*-protons and least for the Me groups of the propionic esters. In comparison with the free coproporphyrins, the shifts of the thallium-(III) chelates are to lower field.

In the complexes (**2a**) and (**2b**), the β-Me protons appear as doublets due to J_{Tl-H} coupling (Table 2). The *meso*-protons in **2a** appear as a doublet (Fig 1a) and in **2b** they are seen as two sets of doublets, reflecting the two equivalent sets of *meso*-protons (α,γ and β,δ) expected on symmetry grounds. Neither **2a** nor **2b** exhibit any additional fine structure in concentrated solutions. However, **2c** and **2d** do possess fine structure which disappears upon dilution. In **2c** the *meso*-protons appear as two sets of 1:1:2 triplets and the β-Me protons as two sets of 1:2:1 triplets (Fig 1b). In **2d** the *meso*-protons are observed as a doublet of 1:2:1 triplets and the β-Me protons as two sets of doublets. The differences in the J_{Tl-H} *meso*-couplings reflect the

Table 1. Proton chemical shifts (δ, ppm) of thallium(III) coproporphyrins as a function of concentration (moles/litre) in chloroform

Thallium(III) *coproporphyrin*-I (**2a**)

Conc.	β-Methyl	*meso*-	Methoxyl	Methylene *1*	Methylene *2*	$CHCl_3$
0·026	3·659	10·279	3·653	4·44	3·300	7·234
0·045	3·655	10·221	3·654	4·40	3·271	7·214
0·051	3·653	10·202	3·644	4·39	3·273	7·210
0·056	3·643	10·188	3·641	4·38	3·270	7·211
0·068	3·637	10·172	3·641	4·37	3·264	7·202
0·082	3·620	10·145	3·640	4·37	3·256	7·197
0·102	3·590	10·112	3·640	4·36	3·230	7·178

Thallium(III) *coproporphyrin*-II (**2b**):

Conc.	β-Methyl	*meso*- α,γ	*meso*- β,δ	Methoxyl	Methylene *1*	Methylene *2*	$CHCl_3$
0·037	3·662	10·255	10·230	3·638	4·42	3·316	7·224
0·047	3·652	10·232	10·205	3·630	4·42	3·293	7·219
0·063	3·622	10·184	10·155	3·631	4·44	3·286	7·200
0·072	3·615	10·166	10·136	3·626	4·36	3·269	7·193
0·094	3·586	10·126	10·092	3·626	4·32	3·259	7·181
0·125	3·562	10·082	10·046	3·615	4·32	3·243	7·165

Thallium(III) *coproporphyrin*-III (Deuteriated derivative, **8**):

Conc.	Methyl 5	Methyl 3,8	Methyl 1	*meso*- γ	*meso*- β	*meso*- α,δ	Methoxyl* *1*	Methoxyl* *2*	Methoxyl* *3*	Methylene *1*	Methylene *2*	$CHCl_3$
0·060	3·650	3·616	3·597	10·230	10·188	10·166	3·651	3·637	3·620	4·42	3·310	7·212
0·079	3·641	3·597	3·563	10·201	10·159	10·120	3·640	3·626	3·610	4·40	3·305	7·203
0·089	3·623	3·572	3·537	10·178	10·136	10·088	3·628	3·613	3·596	4·40	3·293	7·192
0·124	3·591	3·533	3·467	10·125	10·083	10·012	3·626	3·610	3·595	4·37	3·263	7·170
0·153	3·566	3·493	3·443	10·086	10·044	9·957	3·621	3·602	3·588	4·37	3·239	7·147

*Shifts for the non-deuteriated sample (**2c**) at concentrations 0·02, 0·04, 0·053, 0·106, and 0·201.

Thallium(III) *Coproporphyrin*-IV (**2d**):

Conc.	Methyl 6,7	Methyl 1,4	*meso*- α	*meso*- β,δ	*meso*- γ	Methoxyl	Methylene *1*	Methylene *2*	$CHCl_3$
0·031	3·676	3·646	10·306	10·267	10·267	3·640	4·42	3·311	7·224
0·050	3·655	3·623	10·281	10·219	10·199	3·632	4·38	3·294	7·217
0·070	3·632	3·573	10·247	10·167	10·129	3·631	4·37	3·281	7·201
0·100	3·605	3·516	10·208	10·107	10·048	3·630	4·33	3·263	7·182
0·135	3·573	3·460	10·166	10·049	9·972	3·631	4·32	3·243	7·154

different symmetry elements of the individual thallium(III) coproporphyrins (**2**), (Table 2).

We will show that the concentration dependence of the porphyrin NMR spectra can be attributed to a monomer-dimer equilibrium. In the dimer, the porphyrin rings are stacked one upon another. In such complexes, the magnetic effects of the ring current in one component of the dimer will shield the protons of the other. It follows, therefore, that dilution of the solution will cause dissociation of the complex and a concomitant shift of the resonances to low field.

(a) *Reference compound shifts.* Determination of the shifts due to solute association must be carried out with care, since both tetramethylsilane and chloroform are shifted in solution. The situation is precisely analogous to that for the parent coproporphyrins (**1**) in that it is only necessary to estimate that part of the total porphyrin shift which is due to the association of the porphyrin molecules. This value can be obtained, as in reference 5, by subtraction of the chloroform concentration shift ($\delta_c - \delta_\infty$) at the particular concentration from the observed

Table 2. Coupling constants (Hz) of thallium(III) coproporphyrins

Thallium(III) coproporphyrin	β-Methyl			*meso*-		
I (**2a**)		8·4			45·5	
II (**2b**)		8·3		44·9		45·3
III (**2c**)	8·3	8·1	8·1	44·9	45·0	45·3
IV (**2d**)	8·0		8·2	44·8	45·1	45·4

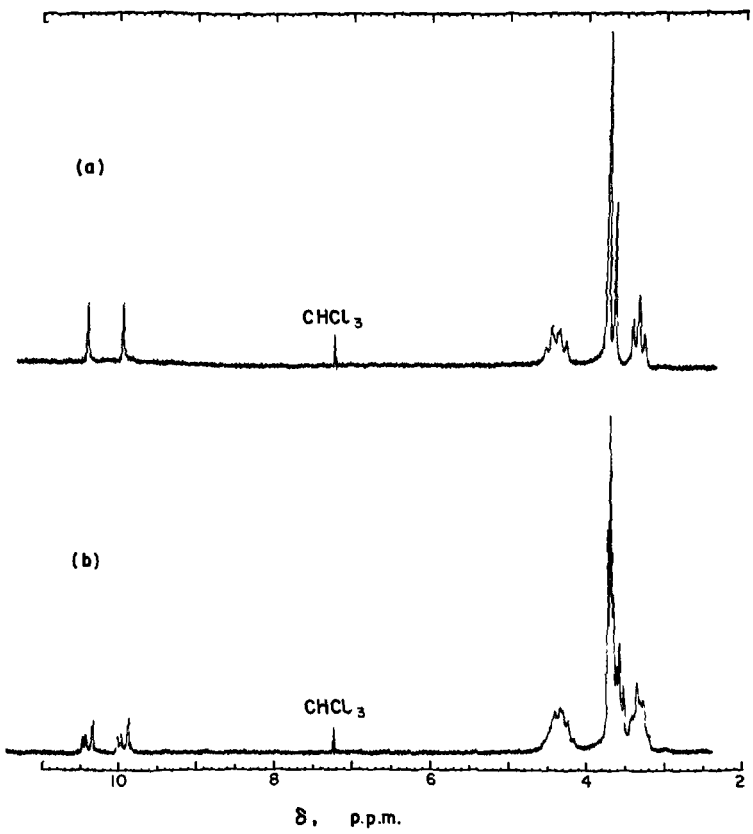

Fig 1. NMR spectra (HA 100), in $CDCl_3$ solution, of: (a) Thallium(III) coproporphyrin-I tetramethyl ester (2a) (*ca* 0·1 M), (b) Thallium(III) coproporphyrin-III tetramethyl ester (2c) (*ca* 0·15 M).

porphyrin shift. From these values, plots similar to those shown in Fig 1 of reference 5 were obtained.

(b) *Porphyrin concentration shifts.* Assuming that the porphyrin molecules are undergoing a monomer-dimer equilibrium, the observed chemical shift (δ_{obsd}) of the porphyrin in solution is given[5] by:

$$\delta_{obsd} = \delta_1 + (\delta_2 - \delta_1)\frac{[\sqrt{(1+8aK)}-1]^2}{8aK}$$

where K is the equilibrium constant, a is the total molar porphyrin concentration, and δ_1 and δ_2 are the monomer and dimer shifts respectively. The three unknowns (δ_1, δ_2 and K) were determined from a least squares computer program. A value for the equilibrium constant of 4·1 l/mole gave a good fit for all of the thallium(III) coproporphyrins (2). The corresponding monomer and dimer shifts are shown in Table 3.

Table 3. Extrapolated monomer and dimer shifts (δ, ppm) of thallium(III) coproporphyrins

Thallium(III) coproporphyrin	*meso*-Protons*			β-Methyl protons*		
I (2a)		10·365(0·6)			3·737(0·2)	
	α,γ		β,δ			
II (2b)	10·040(0·6)		10·387(0·6)		3·734(0·2)	
	γ	β	α,δ	5	3,8	1
III (2c)	10·048(0·5)	10·364(0·5)	10·458(0·9)	3·726(0·1)	3·755(0·4)	3·784(0·6)
	α	β,δ	γ	6,7		1,4
IV (2d)	10·388(0·3)	10·411(0·7)	10·471(1·0)	3·712(0·1)		3·799(0·6)

*Infinite dilution shifts, with high field shifts in dimer compared with monomer in parentheses.

The chemical shifts of the coproporphyrin-I chelate (**2a**) at various temperature are shown in Table 4. It is apparent that lowering of the temperature causes the resonances to shift to higher field, indicating an increase in the amount of association. The equilibrium constant is given[5] by:

$$K = \frac{(\delta - \delta_1)/2(\delta_2 - \delta_1)}{[1 - (\delta - \delta_1)/(\delta_2 - \delta_1)]^2}$$

where K is now normalized to unit concentration (i.e., $a = 1$). The least squares plot of log K against the reciprocal of the temperature gave values for ΔH and ΔS of $-4{\cdot}9 \pm 0{\cdot}2$ Kcal/mole and $-17{\cdot}1 \pm 2{\cdot}5$ e.u. respectively.

Table 4. Chemical shifts (δ, ppm) of thallium(III) coproporphyrin-I tetramethyl ester (**2a**) at a concentration of 0·066 M as a function of temperature

T (°K)	*meso*-	β-Methyl
279	1007·2	358·5
251	1004·6	356·8
226	995·6	353·5
215	990·6	353·4

The magnitude of the shielding of a proton on one ring by the ring current of a second ring can be calculated from existing theory.[15–17] The Tables of Johnson and Bovey[16] or Haigh and Mallion[17] give the shielding values at a series of points around a benzene ring in terms of ring radius. These values can be adjusted[3] for the porphyrin ring current by multiplying by 0·88, thereby accounting for both the larger ring current and radius. Using the monomer-dimer shifts ($\delta_2 - \delta_1$) from Table 3 it is possible to calculate the dimer shifts for **2a** and **2b** for various inter-porphyrin distances; the best fit is obtained for a separation of 8·5 Å using Johnson and Bovey's Tables and of 5·6 Å using the more recent Haigh and Mallion Tables. The calculated high field shifts were 0·6 and 0·4 ppm for the *meso*- and β-Me protons, in agreement with the extrapolated values of Table 3. For both **2c** and **2d** the values were 8·1 Å (J. and B.) and 5·3 Å (H. and M.). The decreased separation in these latter porphyrins increases the steric interference of the propionate side-chains. This necessitates a displacement of the two rings, and results in the observed fine structure.

(c) *The fine structure of thallium*(III) *coproporphyrin*-III (**2c**) *and* -IV (**2d**). The assignments of the *meso*-proton resonances in chloroform have been made by analogy with those reported[5] for the free coproporphyrins and are presented in Table 1. At high concentrations the *meso*- and β-Me resonances show fine structure not due to spin–spin couplings. This structure disappears in dilute solution and must therefore be due to the nature of the complex.

The pattern observed in **2c** consists of two sets of 1:1:2 triplets for the *meso*-protons and 1:2:1 triplets for the β-Me protons.* The two sets of peaks observed are due to coupling with the thallium atom. This pattern of fine structure approximates to the case in which there is a displacement along the x or y axis, as shown in Fig A of Part IV.[5] In **2d** the observed fine structure (i.e. 1:2:1 for *meso*-protons; doublet for β-Me protons) is as expected for displacement along the diagonal.

For thallium(III) coproporphyrin-III (**2c**), a displacement of 1·8 Å in the $+y$ direction gives a good fit. The calculated shifts (in ppm) for the *meso*- and β-Me protons are 0·3(γ), 0·3(β), 0·7(α,δ), 0·1(5), 0·5(3,8), and 0·6(1). These can be compared with the corresponding extrapolated values in Table 3. With the type-IV isomer (**2d**), a displacement of 1·0 Å along the diagonal gives a good fit; the calculated values for the *meso*- and β-Me protons are 0·1(α), 0·4(β,δ), 0·7(γ), 0·1(6,7) and 0·6(1,4). Again, the appropriate extrapolated values are presented in Table 3.

DISCUSSION

The preceeding sections have shown how the dilution shifts of the porphyrin NMR spectra can be interpreted quantitatively on the basis of a monomer-dimer equilibrium in which the two porphyrin molecules stack one above the other. It is interesting to note that the inter-porphyrin distance can vary by *ca* 3 Å depending upon which shielding values are used in the calculation. Consequently, the significance of these calculations should be judged with extreme caution.

The inter-ring separations are surprisingly similar to those calculated in Part IV[5] for the free coproporphyrins (**1**). In fact, the extrapolated dimer chemical shifts (Table 3) for the *meso*- and β-Me protons of thallium coproporphyrins-I (**2a**) and -II (**2b**) are identical to those found for the parent coproporphyrins-I (**1a**) and -II (**1b**). With the thallium atom out of the porphyrin ring plane and the space consuming axial ligands being present, one might have expected that the ring separation might have been greater than in the metal-free cases. However, there is ample opportunity for intermolecular H-bonding which would decrease the separation. An examination of the shifts of the OH proton would have been expected to clarify this point, but this resonance was not observed. Only very broad and concentration dependent O—H stretching bands were observed in the solution IR spectra of these complexes.[8] This effect (termed[18]

*Due to interference from the methyl esters of the propionate side-chains in the NMR spectra of **2c** it was necessary to carry out the dilution studies, in this particular case, using the deuteriated derivative **8**.

"ligand uncertainty") has also been noted[18] with other metal chelates in the porphyrin series. The possibility exists that the associated porphyrins are stacked with the displaced thallium atoms on the outer faces of the aggregate. In such a case, the dimer separation might be expected to be more similar to the free coproporphyrins (1); an association of this type would eliminate the possibility of the existence of aggregates larger than dimers.

The equilibrium constant of 4·1 litre/mol for thallium(III) coproporphyrin-I (2a) is similar to that determined for coproporphyrin-III (1c) (3·55 litre/mol). The thermodynamic parameters, ΔH and ΔS calculated for thallium coproporphyrin-I (2a) are −4·9 Kcal/mole and −17·2 e.u. respectively. These differ from the values found for coproporphyrin-III (1c) (−1·2 Kcal/mole and −5·4 e.u.); this indicates a greater tendency for association to occur in the thallium complex.

The chemical shifts of the thallium complexes (2) were unchanged by the addition of small amounts of methanol and pyridine to the chloroform solutions. This is in complete contrast to the chlorophylls,[19] (which have magnesium as the central metal), and zinc porphyrins,[20] with which small amounts of such reagents resulted in dissociation of the dimers into monomers. This latter effect is a specific interaction between the CO group of certain side-chains and the metal atom. In the thallium complexes (2), the axial coordination sites of the metal are occupied and therefore are incapable of additional coordination which might lead to the specific interaction mentioned above. The thallium aggregates are assumed to be formed from an electrostatic interaction between the porphyrin rings. This has been observed in the parent coproporphyrins (1)[5] and in nickel mesoporphyrin.[2] The thallium porphyrins differ from the nickel complex in that the nickel porphyrin does have additional coordination sites available for adduct formation. The investigation of the nickel mesoporphyrin adduct formation is extensively documented;[1] in this case the metalloporphyrin is paramagnetic and the large shifts observed by the addition of extra ligands completely obscured the smaller, non-specific shifts.

EXPERIMENTAL

M.ps were measured on a microscopic hot-stage and are uncorrected. All chromatographic separations were carried out using Merck neutral alumina (Brockmann Grade III). Thallium trifluoroacetate was prepared from thallic oxide (B.D.H.) as described by Taylor *et al.*;[21] the material was thoroughly dried of trifluoroacetic acid and used as a fine white powder. Mass spectra were measured on an A.E.I. MS12 Spectrometer using a direct insertion probe with the source temp at about 220°. Visible absorption spectra were measured in CH_2Cl_2 soln using a Unicam SP 800 Spectrophotometer.

NMR spectra were obtained using a Varian HA100 spectrometer at about 35°. Solns of the four thallium(III) coproporphyrin esters (2) were prepared in $CDCl_3$, with TMS as internal reference. The chemical shifts were measured by the usual side-band method and are estimated to be accurate to ±0·003 ppm (except for the methylene protons, ±0·02 ppm). The coupling constants are accurate to ±0·2 Hz. Because of interference from other resonances in the spectrum, the *meso*- and β-methyl J_{Tl-H} couplings in thallium coproporphyrin-III (2c) were measured using the deuteriated sample (8); the PMR spectra of all of the porphyrins are reported in Table 1. Typical high concentration spectra are shown in the Fig.

The PMR spectra of thallium coproporphyrin-I tetramethyl ester (2a) at a concentration of 0·066 M was recorded at a series of temps in the range 6° to −58° using a Varian V-4343 variable temp controller; the temp is estimated to be accurate to within ±2°. These results are recorded in Table 4.

t-Butyl 3-(2-*methoxycarbonylethyl*)-4-*methylpyrrole*-2-*carboxylate* (4). t-Butyl 5-iodo-3-(2-methoxycarbonylethyl)-4-methylpyrrole-2-carboxylate[22] (14·4 g) in MeOH (300 ml) containing sodium acetate trihydrate (14 g) was hydrogenated at atmospheric pressure and room temp over Adams catalyst (H_2 uptake, 820 ml). The catalyst was removed by filtration through a bed of celite and the filtrate was evaporated on a rotary evaporator until the total bulk was about 100 ml. This was poured into water (200 ml) and the product was extracted with several quantities of CH_2Cl_2, which was dried (Na_2SO_4) and evaporated to dryness. The resultant pale orange oil was put under high vacuum, whereupon it crystallized (9·8 g; 100%), m.p. 63–64°. (Found: C, 63·2; H, 8·0; N, 5·3. $C_{14}H_{21}NO_4$ requires: C, 62·9; H, 7·9; N, 5·2%); NMR spectrum (in $CDCl_3$) δ, 9·5 NH broad; 6·63, (1H, d, $J = 3$ Hz), α-H; 3·67, (3H,s), OCH_3; 3·2–2·3, (4H,m) CH_2CH_2; 2·03, (3H,s), β-CH_3; 1·48, (9H,s), $C(CH_3)_3$.

Benzyl 5′-*t-butyloxycarbonyl*-3,4′-*di*(2-*methoxycarbonylethyl*)-3′,4-*dimethylpyrromethane*-5-*carboxylate* (6a). Benzyl 2-acetoxymethyl-3-(2-methoxycarbonylethyl)-4-methylpyrrole-5-carboxylate[23] (2·1 g) was suspended in MeOH (30 ml) containing t-butyl 3-(2-methoxycarbonylethyl)-4-methylpyrrole-2-carboxylate (1·5 g) and toluene *p*-sulphonic acid hydrate (60 mg) and heated with stirring under N_2 during 4 hr. 10% $NaHCO_3$ aq (3 ml) was added slowly and the product separated by filtration. Recrystallization from hot MeOH gave the required *pyrromethane* (2·05 g; 64%) m.p. 150–153°. (Found: C, 66·2; H, 7·2; N, 5·0. $C_{32}H_{40}N_2O_8$ requires: C, 66·2; H, 6·9; N, 4·8%); NMR spectrum (in $CDCl_3$) δ, 9·0 (2NH, broad); 7·31, (5H,s), C_6H_5; 5·24, (2H,s), $PhCH_2$; 3·87, (2H,s), CH_2; 3·64, (6H,s), $2 \times OCH_3$; 3·1–2·3, (8H,m), CH_2CH_2; 2·27, (3H,s), β-CH_3; 1·98, (3H,s), β-CH_3; 1·40, (9H,s), $C(CH_3)_3$.

Coproporphyrin-II *tetramethyl ester* (1b). 5,5′-Diformyl-3,3′-di(2-methoxycarbonylethyl)-4,4′-dimethylpyrromethane[24] (1·0 g) was suspended in a soln of 3,3′-di-(2-methoxycarbonylethyl)-4,4′-dimethylpyrromethane-5,5′-dicarboxylic acid (1·19 g) in CH_2Cl_2 (1 l), and with strict exclusion of light, toluene *p*-sulphonic acid hydrate (2·57 g) in MeOH (43 ml) was added. The mixture was stirred during 24 hr in the dark and then treated with a saturated soln of zinc acetate in MeOH (43 ml) and stirred for a further 3 hr. The mixture was washed with water, $NaHCO_3$ aq and then water again, dried (Na_2SO_4) and evaporated to dryness. The residue was set aside overnight in the dark in 5% v/v H_2SO_4 in MeOH and then poured into CH_2Cl_2 and water. The organic phase was washed with $NaHCO_3$ aq and then water, dried (Na_2SO_4) and

evaporated to dryness. The residue was chromatographed, eluting with CH_2Cl_2. After evaporation of the porphyrin eluates, the product was crystallized from CH_2Cl_2/MeOH (800 mg; 45%), m.p. 289–291° (Lit.[25] 286–289°). The NMR spectrum of this material was in accord with that in the literature,[5] and a mixed m.p. with authentic material showed no depression.

Coproporphyrin-III *tetramethyl ester* (**1c**), (with Mr. J. A. S. Cavaleiro). Benzyl 5'-t-butyloxycarbonyl-3,4'-di-(2-methoxycarbonylethyl)-3',4-dimethylpyrromethane-5-carboxylate (456 mg) in THF (100 ml) and Et_3N (2 drops) was hydrogenated at room temp and atm pressure over Pd-C (46 mg of 10%) until H_2 uptake was complete (*ca* 1 hr). The catalyst was removed by filtration through celite and the filtrate evaporated to dryness. The residue was dissolved in trifluoroacetic acid (25 ml) and kept under N_2 during 45 min before evaporation of the trifluoroacetic acid. CH_2Cl_2 and water were added and the organic phase was separated and washed with $NaHCO_3$ aq and then water, before being dried (Na_2SO_4) and made up to a total volume of 150 ml with further CH_2Cl_2. This soln was added to a darkened flask containing 5,5'-diformyl-3,3'-di(2-methoxycarbonylethyl)-4,4'-dimethylpyrromethane[24] (250 mg) in CH_2Cl_2 (100 ml) and then treated with a soln of toluene *p*-sulphonic acid hydrate (900 mg) in MeOH (12·5 ml). After stirring during 6 hr in the dark, the soln was treated with a saturated soln of zinc acetate in MeOH (12·5 ml) and then set aside overnight. The reaction was worked-up as described above and gave the required porphyrin (180 mg; 41%) m.p. 150–153, remelting at 179–180°. (Lit.[14] 150–155, 179–182°). The product was shown to be identical with a sample of authentic material,[14] by mixed m.p., which showed no depression.

Aquo 2,4,6,8-*tetra*(2-*methoxycarbonylethyl*)-1,3,5,7-*tetramethylporphinatothallium*(III) *hydroxide*, ["*thallium*-(III) *coproporphyrin*-I *tetramethyl ester* (OH,H_2O)"] (**2a**). Coproporphyrin-I tetramethyl ester (500 mg) in CH_2Cl_2 (50 ml) was treated with a soln of thallium(III) trifluoroacetate (400 mg) in THF (20 ml). After being allowed to stand during 5 min the mixture was poured into water and extracted twice with CH_2Cl_2, which was dried (Na_2SO_4) and evaporated to dryness. The residue was chromatographed, eluting initially with chloroform containing 2% EtOH (to facilitate ligand exchange on the alumina) and thereafter with CH_2Cl_2. The porphyrin eluates were evaporated to dryness and the required *thallium chelate* was crystallized from CH_2Cl_2/MeOH (703 mg; 99%), m.p. 242–245°. (Found: C, 50·7; H, 4·85; N, 5·9. $C_{40}H_{47}N_4O_{10}Tl$ requires: C, 50·7; H, 5·0; N, 5·9%); λ_{max} ($\epsilon_{max} \times 10^{-3}$) in CH_2Cl_2: 417 (350), 544 (18·8), 582 (12·4); mass spectrum *m/e*(%),* 948(7), 946(3) P^+; 913(2), 911(1) P^+—OH, H_2O; 710(100) [P^+—OH, H_2O, Tl / H_2].

The following compounds were prepared in an analogous manner:

Aquo 2,3,6,7-*tetra*(2-*methoxycarbonylethyl*)-1,4,5,8-*tetramethylporphinatothallium*(III) *hydroxide*, ["*thallium*-(III) *coproporphyrin*-II *tetramethyl ester* (OH, H_2O)"] (**2b**), m.p. 155–158°. (Found: C, 50·6; H, 4·9; N, 6·1. $C_{40}H_{47}N_4O_{10}Tl$ requires: C, 50·7; H, 5·0; N, 5·9%); λ_{max} ($\epsilon_{max} \times 10^{-3}$): 417 (362), 544 (18·9), 582 (12·1); mass spectrum, *m/e*(%),* 948(9), 946(4); 913(3), 911(1), 710(100).

Aquo 2,4,6,7-*tetra*(2-*methoxycarbonylethyl*)-1,3,5,8-*tetramethylporphinatothallium*(III) *hydroxide*, ["*thallium*-(III) *coproporphyrin*-III *tetramethyl ester* (OH, H_2O)"] (**2c**), m.p. 182–183°. (Found: C, 50·8; H, 4·7; N, 5·8. $C_{40}H_{47}N_4O_{10}Tl$ requires: C, 50·7; H, 5·0; N, 5·9%); λ_{max} ($\epsilon_{max} \times 10^{-3}$): 417 (393), 544 (19·5), 582 (12·7); mass spectrum, *m/e*(%),* 948(6), 946(2); 913(2), 911(1); 710(100).

Aquo 2,3,5,8-*tetra*(2-*methoxycarbonylethyl*)-1,4,6,7-*tetramethylporphinatothallium*(III) *hydroxide*, ["*thallium*-(III) *coproporphyrin*-IV *tetramethyl ester* (OH, H_2O)"] (**2d**), m.p. 206–208°. (Found: C, 50·7; H, 4·8; N, 5·9. $C_{40}H_{47}N_4O_{10}Tl$ requires: C, 50·7; H, 5·0; N, 5·9%); λ_{max} ($\epsilon_{max} \times 10^{-3}$), 417 (381), 544 (19·4), 582 (13·1); mass spectrum, *m/e*(%),* 948(6), 946(2); 913(2), 911(1); 710(100).

Aquo 2,4,6,7-*tetra*(2-*deuteriomethoxycarbonylethyl*)-1,3,5,8-*tetramethylporphinatothallium* (III) *hydroxide*, ["*thallium*(III) *coproporphyrin*-III *tetradeuteriomethyl ester* (OH, H_2O)"] (**8**). Coproporphyrin-III tetramethyl ester (75 mg) was dissolved in CH_2Cl_2 (1 ml) and treated with d_4-methanol (1 ml) and conc H_2SO_4 (0·03 ml) and left overnight in the dark. The soln was poured into NaOAc aq and extracted with CH_2Cl_2 which was washed with water and dried (Na_2SO_4). The soln was evaporated to dryness (75 mg) and then treated with thallium trifluoroacetate as described earlier. The product showed no evidence of methyl ester resonances in its NMR spectrum, m.p. 181–183°, mass spectrum, *m/e*(%),* 960(2), 958(1); 925(1), 923(0·5); 722(100); 721(10); 720(8); 719(9).

*Only those peaks which assist in characterization are reported; the mass spectra of thallium(III) porphyrin chelates show certain anomalies which will be reported in detail elsewhere.

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