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STUDY ON 5,15-DIALKYLPORPHYRINS INTERCONVERSION BETWEEN TWO CONFORMERS IN SOLUTION

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ABSTRACT

Novel structural features of 5,15-dialkylporphyrins in solution are described. The ^{1}H-NMR spectra of these compounds showed broad signals at room temperature, which split into two sets of signals at lower temperatures. This unusual phenomenon was ascribed to a dynamic interconversion between two distorted structures. The 5,15-dialkylporphyrin has a distorted ring due to the steric hindrance between the 5(or 15)-alkyl group and the 3,7(or 13,17)-alkyl groups and, depending on the position of the 5,15-alkyl groups relative to the average ring plane, can exist in two conformations; syn (where the two alkyl groups are on the same side of the ring plane) and anti (on the opposite sides). Preliminary kinetic study of this interconversion using the NMR line shape analyses is also reported.

INTRODUCTION

The *meso*-substituted porphyrins seem to constitute an especially unique group among a wide variety of porphyrin compounds. Woodward, in the course of his brilliant study of the total synthesis of chlorophyll, pointed out the proximity (about 3 Å) of the *meso*-position and the neighboring β-pyrrolic positions in a porphyrin ring.[1] Such proximity should cause the severe steric crowding between the 5-(*meso*-)alkyl substituent and the 3,7-(β-pyrrolic-)alkyl substituents in a 5-substituted-2,3,7,8,12,13,17,18-octaalkylporphyrin. Then it is likely that such a porphyrin should tend to distort itself in order to relax the severe steric hindrance. Indeed, the studies on 5,15-dimethyl-2,3,7,8,12,13,17,18-octaethylporphyrin[2] indicated that this porphyrin should suffer some distortion of the porphyrin macrocycle. The X-ray analysis of the crystal of μ-oxo-bis((5, 15-dimethyl-octaethylporphinato) iron (III)) dimer confirmed the 'ruffled' conformation of the porphinato core.[3] The NMR spectra of *meso*-substituted porphyrins were reported and explained in terms of ring folding and decrease of the porphyrin ring current.[4,5] Thus it is now widely accepted that ring distortion is taking place in the *meso*-substituted-octaalkylporphyrins.

We wish to report here a novel feature of 5,15-dialkylporphyrins. They not only have distorted ring systems, but can also exist in two different conformations in solution. Moreover, dynamic interconversion between these two conformers could be observed by NMR spectroscopy. The rates of interconversion were estimated by the NMR line shape analyses, and preliminary kinetic results are also reported.

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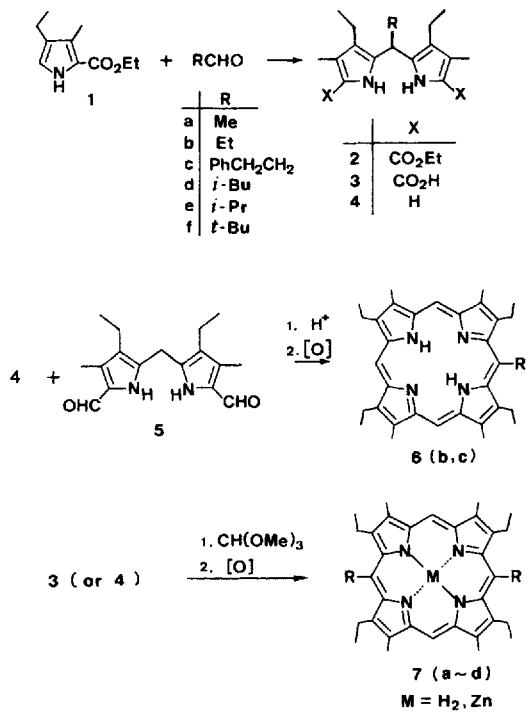
SYNTHESIS

The synthetic routes to the 5-alkylporphyrins and 5,15-dialkylporphyrins are summarized in Scheme 1. The 5,15-dialkylporphyrins were prepared by condensation of the 1,1-bis(5-carboxyl-3-ethyl-4-methylpyrrol-2-yl)alkane (*meso*-alkyl-dipyrromethane-dicarboxylic acid, **3**) with trimethylorthoformate.[6] The 5-alkylporphyrins were prepared by coupling of the 1,1-bis(3-ethyl-4-methylpyrrol-2-yl)alkane (*meso*-alkyl-α-free-dipyrromethane, **4**) with diformyl-dipyrromethane (**5**).[7]



Scheme 1. Syntheses of 5-alkyl- and 5,15-dialkylporphyrins

^{1}H-NMR SPECTRA

The ^{1}H-NMR spectra of the 3,5,7,13,15,17-hexaethyl-2,8,12,18-tetramethylporphyrin (**7b**, M=H_2) showed very broad signals at room temperature. The signals became somewhat sharper when measured at 45°C, while at −30°C they split into two sets of signals. This unusual phenomenon can be explained in terms of ring flapping as follows.

It has been pointed out that in the case of *meso*-substituted porphyrins, the steric hindrance between the *meso*-(5-)substituent and the adjacent β-pyrrolic substituents (3,7-substituents) is quite severe,[1] and in order to relax this steric hindrance, the porphyrin ring is folded at the *meso*-position in such a way that the *meso*-position is above the (average) porphyrin ring plane and the adjacent pyrrole rings are below the plane. Such folding will bring the *meso*-substituent above the ring plane and the β-pyrrolic substituents below the ring plane, thus the steric hindrance is reduced. Now, let us consider the case of the 5,15-

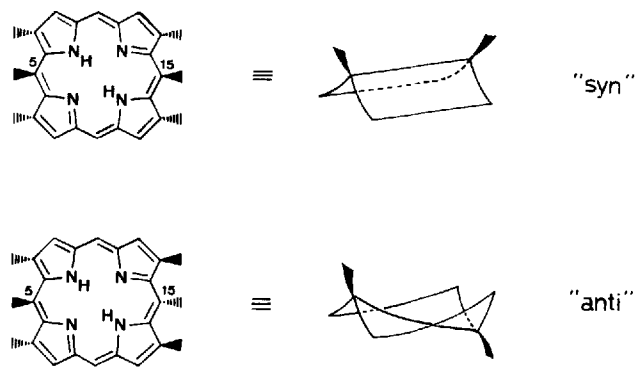


Figure 1. Two possible conformations of 5,15-dialkylporphyrins. Above: the 'syn' conformation. Below: the 'anti' conformation

dialkylporphyrins: the Corey–Pauling–Koltun molecular model study of these compounds revealed that there should be two manners in the ring folding, as shown in Figure 1. First: the 5-position and 15-position are both above the average porphyrin ring plane and the four pyrrole rings are all below the plane. The resulting conformation has a 'roof-like' porphyrin ring. This conformation has both 5- and 15-alkyl groups in the same side (above) of the average ring plane, and therefore we can call it a 'syn' conformation. Second: the 5-position is above the plane and the two pyrrole rings adjacent are below, but the 15-position is below the plane and the remaining two pyrrole rings above. The resulting conformation has a rather 'twisted' porphyrin ring, and has the 5- and 15-alkyl groups in the opposite side of the average ring plane. This conformation, therefore, can be called an 'anti' conformation. These two conformers have not only different orientations of two *meso*-substituents, but also different ring geometries. As the different ring geometries cause different ring currents, it is expected that the NMR spectra of these conformers should differ significantly. Now, if the two conformers can interconvert in solution, and if the rate of this interconversion is appropriate, the NMR spectrum is expected to be broad at room temperature, to become sharper as the temperature rises (because the rate of interconversion rises and the average resonance should be observed), and to split at low temperature into two sets of signals, each set corresponding to each conformer. This is exactly what was observed.

The above-described hypothesis of two interconverting conformers requires that the 5-monoalkylporphyrins do not show any broadening phenomena, because in this case only one conformer is possible. This was indeed the case. The NMR spectra of 5-ethylporphyrin and 5-(2-phenyl)ethyl-porphyrin showed sharp signals at room temperature and did not show any broadening or splitting in the temperature range of −30 °C to 20 °C. (Only the methylene protons of the 3,7-ethyl groups gave a broadened signal at room temperature, which split into two sets of signals at low temperature. This is apparently due to the restricted rotation because of the steric hindrance with the 5-alkyl group).

The central NH resonances showed systematic change as the number of the *meso*-substituents increased. The larger the number of the *meso*-substituents became, the more the NH protons showed reduced upfield shift; i.e. −3·7 ppm for etioporphyrin (3,7,13,17-tetraethyl-2,8,12,18-tetramethylporphyrin) and octaethylporphyrin (OEP), −2·8 and −2·9 for 5-monoethylporphyrin (lowered symmetry causing two unequivalent NH protons), and −1·6

Table 1. Variable temperature ^{1}H-NMR data of the free base 5,15-Diethylporphyrin (**7b**, M=H_2) and its zinc complex (**7b**, M=Zn)

Compds.	Free base			Zinc complex		
Temp.(°C)	50	−40		50	−40	
		(A)	(B)		(A)	(B)
meso-H	10·02 s	10·11s	10·08s	9·87s	9·97s	9·85s
meso-CH_2CH_3	5.01 q	4·99m		5·05q	4·99m	
β-CH_2CH_3	4·01 q	4.04m	3.94m	4·04q		4·0 m
CH_3	3·59 s	3·62s	3·61s	3·54s	3·58s	3·52s
mesoCH_2CH_3	(1·8)br	1·95t	(1·8)	1·33br	1·75t	1·14t
β-CH_2CH_3	1.80 t	1·80t	1·76t	1·86t	1·77t	1·87t
NH	−1.55 br	−1·82br		—	—	—

for 5,15-diethylporphyrin. This change indicates that the ring current of the porphyrin π-system should be reduced as an alkyl group is introduced into the *meso*-position.[5,8]

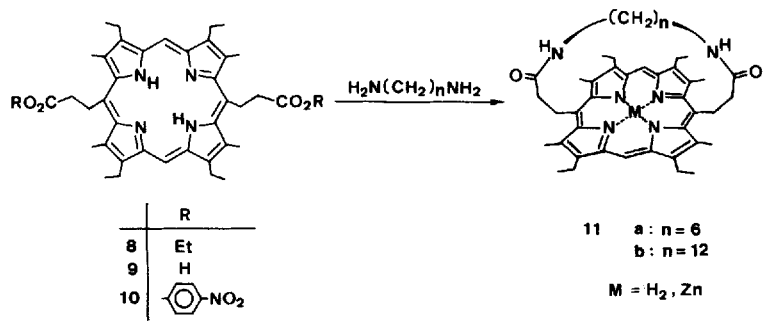
Table 1 summarizes the change in the NMR spectra of 5,15-diethylporphyrins (free base and zinc complex). At low temperature two sets of signals were observed. Each component should be assigned to each of the two conformers. Here the two components are named A and B, A being the minor component and B the major one. The ratio B/A for porphyrins **7b**, **7c** and **7d**, as well as **8** and **11b** (see Scheme 2), were obtained from the integral ratio of the NMR spectra, and are shown in Table 2. The values were obtained at −40 °C, expect for the zinc complex of **8** and **11b** (at −20 °C).

Table 2. The ratio (B/A) of the two conformers of 5.15-dialkylporphyrins

Compds.	**7b**	**7c**	**7d**	**8**	**11b**
Free base	1·2	1·6	5·0	1·0	4·0
Zinc complex	3·3	7·6	>30	3·4	>10

It cannot be assigned definitely which component (A or B) corresponds to which conformer (syn or anti). However, the fact that the observed ratio of B/A increased significantly in the zinc complex suggests that B might be the syn conformer, because the severe nonplanarity of the porphyrin ring in the anti conformation should put the four inner nitrogen atoms more apart than in the syn conformer, probably making the anti-zinc complex more unstable than the syn-zinc complex.

If the interconversion between the two conformers were prohibited by some intramolecular steric factor, the NMR spectra would give sharp signals at any temperature. We made two attempts on this basis. One is to 'link' the two *meso*-alkyl substituents; that is, preparation of 5,15-'strapped'-porphyrins (**11**). The syntheses of these compounds are shown in Scheme 2. As can be easily recognized, these porphyrins cannot form the anti conformation if the bridge is sufficiently short.



	R
8	Et
9	H
10	-C6H4-NO2

11 a: n = 6
b: n = 12

Scheme 2. Syntheses of 5,15-'strapped'-porphyrins

Two of these porphyrins, **11a** and **11b**, were prepared and their NMR spectra were measured. The NMR spectra of **11a** indeed showed sharp signals at room temperature. No broadening or splitting was observed when the temperature was lowered down to −40 °C. The signals due to the diamine bridge protons moved significantly as the temperature was lowered, suggesting some conformational change (not syn–anti type) was taking place. The NMR spectra of the zinc complex of **11a** showed similar trends.

The NMR spectra of **11b** was so complicated that the complete assignment of all the signals is not yet achieved. Two signals were observed in the region of *meso*-protons (A: 10·02 ppm, B: 9·94 ppm), indicating that **11b** is a mixture of two components. These two signals did not merge in the temperature range of −40 °C to 40 °C, which suggests that interconversion between the two components, if any, should be too slow for NMR time scale. Attempts to separate these two components by column chromatography were unsuccessful. The ratio of the two components, B/A, was 4·0, and showed no significant change in the observed temperature range. The zinc complex of **11b** also seems to be a mixture of two components, B/A being 10 (at −20 °C). In the case of **11b**, the longer bridge seems to allow formation of the anti conformer. The larger B/A values compared with the 'parent' 5,15-dialkyl compound, diester porphyrin (**8**, see Table 2), are consistent with the instability of the anti conformer of **11b** due to the strain of the bridge, if we similarly assume that B is the syn conformer.

Another attempt to 'fix' the two conformers is to introduce very bulky groups to the 5,15-positions. It was expected that these bulky *meso*-substituents should prohibit the interconversion between syn and anti conformers, and enable isolation of each component. The attempted syntheses of 5,15-di-*tert*-butylporphyrin and of 5,15-di-*iso*-propylporphyrin, however, were both unsuccessful. When the 1,1-bis(5-carboxyl-3-ethyl-4-methylpyrrol-2-yl)-2,2-dimethyl-propane (**3f**) was treated with trimethyl orthoformate, no desired porphyrin was obtained, but 5,15-di-*t*-butyl-5,15-dihydroporphyrin was obtained instead.[9] Attempts to oxidize this material into the corresponding porphyrin were unsuccessful. The *iso*-propyl group could not be introduced, either. It seems that the desired porphyrins are extremely unstable because of the severe steric hindrance itself.

Now let us return to the simple 5,15-dialkylporphyrins. The rate of interconversion between the two conformers can be estimated by the line shape analysis of the NMR spectra.[10] The *meso*-proton resonances were utilized, because they always showed singlet signals and thus allowed simpler treatment. Line widths and chemical shifts of the individual resonances (in the absence of exchange process) were estimated from the spectra at low temperatures. The ratio B/A was given as an integral ratio at low temperatures. As this ratio did not seem to change

Table 3. Rates of interconversion at 23 °C between the two conformers

Compds.	Free base			Zinc complex	
	7b	**7c**	**7d**	**7b**	**7c**
rate (s^{-1})	180	80	6	850	270

significantly with temperature, the values at lower temperatures were assumed as valid for higher temperatures. Comparison of the measured spectra with the simulated ones was made and the rate constant k was obtained for each temperature (k is defined as the rate constant of the process A to B, not B to A). In the higher temperature range, where the exchange process was fast, the rate constants were estimated from the observed line widths.[11]

The rate constants obtained at 23 °C are listed in Table 3, for compounds **7b**, **7c** (where M=H_2 and Zn), and **7d** (M=H_2). In the case of 5,15-dimethylporphyrin (**7a**), interconversion between the two conformers was too fast for NMR time scale, and no broadening phenomenon was observed in the temperature range down to −40 °C. The data for **7d** zinc complex have been omitted, since in this case the signals of the minor component were so weak that no reliable treatment was possible.

Table 3 discloses two general tendencies. (1) As the size of the *meso*-substituent increases, the rate of interconversion falls rapidly. (2) The rate of interconversion increases significantly in the zinc complexes. The latter may be somewhat surprising, if we consider the central metal atom will 'fix' the ring geometry through the strong coordination. Alternatively, it is likely that the zinc complex has a less distorted porphyrin ring because zinc requires the square-planar coordination.

The Eyring plots of the rate constants at various temperatures gave fairly good straight lines for all of the five compounds listed in Table 3. The resulting activation parameters are shown in Table 4. The activation enthalpies ranged from 57 to 62 kJ/mol. The activation entropies were so sensitive to the errors of the rate constants that precise discussions are impossible at present. However, the essentially constant activation enthalpies require that the rate of interconversion should be controlled mainly by the entropy factor. This is quite reasonable, if we consider a transition state with a 'planar' ring conformation.

The initial (and final) state in the interconversion process is either the syn- or the anti-conformer, in which the *meso*-alkyl groups win considerable freedom of movement because of the reduced steric hindrance by the ring folding. In the transition state the porphyrin ring should be (at least partially) planar, in order to allow 'flipping' of the *meso*-alkyl group. Such a planar conformation should have the *meso*-alkyl groups with

Table 4. Activation parameters of interconversion

Compds.	Free base			Zinc complex	
	7b	**7c**	**7d**	**7b**	**7c**
ΔH (kJ/mol)	+62	+56	+58	+62	+57
ΔS (J/K/mol)	+9	−18	−35	+23	−6
ΔG_{298K} (kJ/mol)	+60	+61	+68	+56	+58

reduced freedom, causing a decrease in entropy, as well as higher energy because of the strain. The energy (enthalpy) factor is mainly ascribed to the overcrowding of the CH_2 groups directly attached to the *meso*-position and the neighboring β-pyrrolic positions. As all the compounds listed in Table 4 have primary alkyl groups at the *meso*-positions, the energy factor is expected to be of the same magnitude. Thus the rate of interconversion could be controlled mainly by the entropy factor ('A larger group is reluctant to move').

Now it is confirmed that 5,15-dialkylporphyrins have two distorted conformations which can interconvert in solution. We expect that this novel feature can be utilized to control the physicochemical properties of porphyrin compounds in modeling certain biological systems (such as cooperativity of hemoglobin).

EXPERIMENTAL SECTION

Melting points were measured on a Yanagimoto micro melting point apparatus and are uncorrected. Infrared spectra were recorded on a JASCO IRA-1 spectrometer. Ultraviolet and visible spectra were measured with a Shimadzu UV-3000 spectrometer. 400MHz ^{1}H-NMR spectra were recorded on a JEOL GX-400, and chemical shifts (δ) are reported in parts per million relative to an internal standard of tetramethylsilane. Variable temperature NMR measurement was performed with a JEOL NM-GVT3 temperature control unit, which was precalibrated with methanol.[12] Elemental analyses were performed at the Microanalytical Laboratory of Kyoto University. Preparative separations were usually performed by flash column chromatography on silica gel (Merck, Kieselgel 60H, Art.7736).

Solvents were used as commercially obtained unless otherwise stated. All aliphatic aldehydes and trimethyl orthoformate were distilled before use. Water-free trichloroacetic acid was prepared by azeotropic distillation and recrystallization from benzene solution, and used as methylene chloride solution (3·8 to 4 M). Methylene chloride, where described as 'dry', was dried over calcium chloride and refluxed over P_2O_5 and distilled (under nitrogen).

Preparation of 'dipyrromethanes'

1,1-Bis(5-ethoxycarbonyl-3-ethyl-4-methylpyrrol-2-yl)ethane (**2a**). Ethyl 4-ethyl-3-methylpyrrole-2-carboxylate[13] (**1**, 1·1g, 6·1mmol) was dissolved in ethanol (10ml), acetaldehyde (0.6g, 14·2mmol) was added, followed by 4 drops of concentrated HCl, and the mixture was heated under reflux for 2 hours (under N_2). The reaction mixture was cooled, diluted with aqueous Na_2CO_3 solution, and extracted with CH_2Cl_2. The CH_2Cl_2 layer was washed with water, dried over Na_2SO_4, and evaporated. The residual solid was washed with hexane, and recrystallized from ethanol. Yield: 1·1g (2·8mmol, 93%). m.p. 122 °C. NMR ($CDCl_3$) : 8·72 (br, 2H, NH), 4·31 (q, 1H, $C\underline{H}CH_3$), 4·27 (q, 4H, $OC\underline{H}_2CH_3$), 2·34 (q, 4H, $C\underline{H}_2CH_3$), 2·25 (s, 6H, $C\underline{H}_3$), 1·59 (d, 3H, $CHC\underline{H}_3$), 1·31 (t, 6H, $OCH_2C\underline{H}_3$), 0·95 (t, 6H, $CH_2C\underline{H}_3$). Analyses calculated for $C_{22}H_{32}O_4N_2$: C, 68·01; H, 8·30; N, 7·21. Found: C, 67·74; H, 8·43; N, 6·95.

1,1-Bis(5-ethoxycarbonyl-3-ethyl-4-methylpyrrol-2-yl)propane (**2b**). The pyrrole **1** (5·2g, 28·7mmol) was dissolved in benzene (100ml) and brought to reflux under N_2. Catalytic amount of *p*-toluenesulfonic acid was added followed by propionaldehyde (3·3g, 57 mmol), and reflux was continued for 3 hours. The reaction mixture was cooled, washed with aqueous $NaHCO_3$ and water, dried over Na_2SO_4, and evaporated. The residual solid was washed with hexane, and recrystallized from ethanol. Yield: 4·2g (10.5mmol, 73%). m.p. 146 °C. NMR ($CDCl_3$) : 9·00 (br, 2H, NH), 4·25 (q, 4H, $OC\underline{H}_2CH_3$), 4·02 (t, 1H, $C\underline{H}CH_2CH_3$), 2·39 (q, 4H,

$C\underline{H}_2CH_3$), 2·24 (s, 6H, $C\underline{H}_3$), 2·00 (quintet, 2H, $CHC\underline{H}_2CH_3$), 1·29 (t, 6H, $OCH_2C\underline{H}_3$), 0·97 (t, 6H, $CH_2C\underline{H}_3$), 0·91 (t, 3H, $CHCH_2C\underline{H}_3$). Analyses calculated for $C_{23}H_{34}O_4N_2$: C, 68·63; H, 8·51; N, 6·96. Found: C, 68·54; H, 8·67; N, 6·66.

1,1-Bis(5-ethoxycarbonyl-3-ethyl-4-methylpyrrol-2-yl)-3-phenylpropane (**2c**). This was prepared from **1** (1·1g, 6mmol) and 3-phenylpropionaldehyde (0·46g, 3·3mmol) by the same method as **2b** (see above). Yield: 1·2g (2·6mmol, 86%). m.p. 124 °C. NMR ($CDCl_3$) : 9·43 (br, 2H, N$\underline{H}$), 7·1–7·4 (5H, Ph), 4·19 (q, 4H, $OC\underline{H}_2CH_3$), 4·15 (t, 1H, $C\underline{H}CH_2CH_2Ph$), 2·56 (t, 2H, $C\underline{H}_2Ph$), 2·35 (m, 6H, $C\underline{H}_2CH_2Ph$ and $C\underline{H}_2CH_3$), 2·25 (s, 6H, $C\underline{H}_3$), 1·21 (t, 6H, $OCH_2C\underline{H}_3$), 0·94 (t, 6H, $CH_2C\underline{H}_3$). Analyses calculated for $C_{29}H_{38}O_4N_2$: C, 72·77; H, 8·00; N, 5·85. Found: C, 72·88; H, 8·15; N, 5·66.

1,1-Bis(5-ethoxycarbonyl-3-ethyl-4-methylpyrrol-2-yl)-3-methylbutane (**2d**). This was prepared from **1** (3·6g, 20mmol) and 3-methylbutyraldehyde (1·4g, 16mmol) by the same method as **2b** (see above). Yield: 3·2g (7·5mmol, 75%). m.p. 120 °C. NMR ($CDCl_3$) : 8·99 (br, 2H, N$\underline{H}$), 4·26 (q, 4H, $OC\underline{H}_2CH_3$), 4·23 (t, 1H, $C\underline{H}CH_2CH(CH_3)_2$), 2·39 (q, 4H, $C\underline{H}_2CH_3$), 2·24 (s, 6H, $C\underline{H}_3$), 1·83 (t, 2H, $CHC\underline{H}_2CH$), 1·45 (m, 1H, $C\underline{H}(CH_3)_2$), 1·30 (t, 6H, $OCH_2C\underline{H}_3$), 0·98 (t, 6H, $CH_2C\underline{H}_3$), 0·90 (d, 6H, $CH(C\underline{H}_3)_2$). Analyses calculated for $C_{25}H_{38}O_4N_2$: C, 69·74; H, 8·89; N, 6·51. Found: C, 69·72; H, 9·17; N, 6·33.

1,1-Bis(5-ethoxycarbonyl-3-ethyl-4-methylpyrrol-2-yl)-2-methylpropane (**2e**). This was prepared from **1** (3·6g, 20mmol) and 2-methylpropionaldehyde (1·4g, 20mmol) by the same method as **2b** (see above). Yield: 2·4g (5·9mmol, 59%). m.p. 176 °C. NMR ($CDCl_3$) : 10·19 (br, 2H, N$\underline{H}$), 4·18 (m, 4H, $OC\underline{H}_2CH_3$), 3·73 (d, 1H, $C\underline{H}CH(CH_3)_2$), 2·73 (m, 1H, $C\underline{H}(CH_3)_2$), 2·47 (q, 4H, $C\underline{H}_2CH_3$), 2·26 (s, 6H, $C\underline{H}_3$), 1·17 (t, 6H, $OCH_2C\underline{H}_3$), 1·05 (t, 6H, $CH_2C\underline{H}_3$), 0·85 (d, 6H, $CH(C\underline{H}_3)_2$). Analyses calculated for $C_{24}H_{36}O_4N_2$: C, 69·20; H, 8·71; N, 6·72. Found: C, 69·22; H, 8·94; N, 6·61.

1,1-Bis(5-ethoxycarbonyl-3-ethyl-4-methylpyrrol-2-yl)-2,2-dimethylpropane (**2f**). This was prepared from **1** (3·6g, 20mmol) and 2,2-dimethylpropionaldehyde (1·0g, 12mmol) by the same method as described above. In this case, complete conversion could not be achieved after 36 hours, so the resulting mixture (**2f** and the pyrrole **1**) was separated by flash column chromatography (hexane/diethyl ether = 95/5 (v/v) to elute residual pyrrole, and benzene/methanol to elute **2f**). The fraction containing **2f** was evaporated, checked by NMR spectroscopy and used without further purification. Yield: 1·3 g (3mmol, 30%). NMR ($CDCl_3$) : 9·46 (br, 2H, N$\underline{H}$), 4·30 (q, 4H, $OC\underline{H}_2CH_3$), 4.03 (s, 1H, $C\underline{H}C(CH_3)_3$), 2·43 (m, 4H, $C\underline{H}_2CH_3$), 2·23 (s, 6H, $C\underline{H}_3$), 1·34 (t, 6H, $OCH_2C\underline{H}_3$), 1.031 (s, 9H, $C(C\underline{H}_3)_3$), 1·026 (t, 6H, $CH_2C\underline{H}_3$).

1,1-Bis(5-carboxyl-3-ethyl-4-methylpyrrol-2-yl)-ethane (**3a**). The diester **2a** (2g, 5·1mmol) was dissolved in 40ml of ethanol. Aqueous sodium hydroxide (8ml of 10% solution) was added, and the mixture was heated under reflux overnight (under N_2). Ethanol was distilled off at ambient pressure. The residual viscous solution was ice-cooled, diluted with 15ml of water, and acidified with dilute HCl. The pale-yellow precipitate was collected by filtration, washed thoroughly with water, and dried in vacuo. The resulting diacid was rather unstable, especially sensitive to acids, and it is recommended that it be used immediately after preparation. The compounds **3b**, **3c**, **3d**, **3e**, and **3f**, were prepared in the same manner as **3a**.

1,1-Bis(3-ethyl-4-methylpyrrol-2-yl)ethane (**4a**). The diacid **3a** (see above) was dissolved in 20ml of 2-aminoethanol and the resulting solution was heated under reflux for 5 hours (under N_2). The mixture was poured into 200g of ice water, and extracted with benzene. The benzene layer was washed with water, dried over sodium sulfate, and evaporated. The residual dark-brown oil was found by NMR spectroscopy to be a crude product. This oil could be used

for preparation of porphyrins without further purification. The compounds **4b**, **4c**, **4d**, **4e** and **4f** were prepared in the same manner as **4a**.

Synthesis of 5,15-dialkylporphyrins

3,5,7,13,15,17-Hexaethyl-2,8,12,18-tetramethylporphyrin (**7b**). The diacid **3b** (prepared from 2·2g = 5·5mmol of diester **2b**) was dissolved in dry dichloromethane (400ml). Dry trichloroacetic acid (70mmol) was added, followed by trimethyl orthoformate (5·3g, 50mmol), and the mixture was brought to reflux (dark, under N_2). After 40 hours 1,4-benzoquinone (600mg) was added, and reflux was continued for 3 hours. The reaction mixture was cooled, washed with aqueous Na_2CO_3 and water, dried over Na_2SO_4, and evaporated. After most of the solvent was removed, ethanol was added, and evaporation was continued. The product crystallized during evaporation, and this was collected by filtration and washed thoroughly with ethanol. This crude material was purified by flash column chromatography ($CHCl_3$ as eluent) and recrystallization from CH_2Cl_2/MeOH. Yield: 269mg (0·5mmol, 18%). m.p. 270–275 °C. UV–vis (toluene): λ_{max}/nm = 413, 513, 547, 584. As for NMR data, see text.

The starting material **3b** should be completely dried. Careless use of wet material led to a complex reaction without producing any desired porphyrin. The α-free dipyrromethane **4b** could be used in place of **3b**. In this case the reaction conditions seemed less critical.

The zinc complex of **7b** was prepared by the ordinary method; the free-base porphyrin **7b** was dissolved in chloroform, methanolic solution of zinc acetate (large excess) was added, and the mixture was refluxed until no free-base porphyrin was detected by thin-layer chromatography. The resulting zinc complex was purified by flash column chromatography followed by recrystallization from CH_2Cl_2/hexane. The zinc complexes of other porphyrins were prepared in the similar manner.

The other 5,15-dialkyporphyrins, **7a**, **7c** and **7d** were prepared in the same manner as **7b**. Compound data of these porphyrins are listed in the following.

Porphyrin **7a**: m.p. >300 °C. UV–vis (toluene): λ_{max}/nm = 412, 513, 548, 588, 648. NMR ($CDCl_3$): 9·95 (s, 2H, *meso*-H), 4·49 (s, 6H, *meso*-CH_3), 4·01 (q, 8H, CH_2CH_3), 3·55 (s, 12H, CH_3), 1·76 (t, 12H, CH_2CH_3), −1·79 (br, 2H, NH).

Porphyrin **7c**: m.p. 250–253 °C. UV–vis (toluene): λ_{max}/nm = 414, 514, 549, 585, 637(sh). NMR ($CDCl_3$, 45 °C): 10·03 (s, 2H, *meso*-H), 7·2–7·4 (10H, Ph), 5·3 (m, 4H, CH_2CH_2Ph), 4·04 (br, 8H, CH_2CH_3), 3.58 (s, 12H, CH_3), 3·3 (very broad, CH_2Ph), 1·77 (t, 12H, CH_2CH_3), −1·48 (s, 2H, NH).

Porphyrin **7d**: m.p. 280–283 °C. UV–vis (toluene): λ_{max}/nm = 412, 513, 548, 588, 648. NMR ($CDCl_3$). Two sets of signals were observed at 20 °C. A: 10·00 (s, 2H, *meso*-H), 4·83 (d, 4H, $CH_2CH(CH_3)_2$), 3·97 (q, 8H, CH_2CH_3), 3.55 (s, 12H, CH_3), 2·30 (m, 2H, $CH(CH_3)_2$), 1·72 (t, 12H, CH_2CH_3), 0·66 (d, 12H, $CH(CH_3)_2$), −1·75 (br, 2H, NH). B: 9·84 (s), 4·75 (d), 3·95 (q), 3·50 (s), 1·88 (m), 1·81 (t), 0·50 (d), −1·47 (br). B was the major component with B/A = 5·0.

Synthesis of 5-alkylporphyrins

3,5,7,13,17-Pentaethyl-2,8,12,18-tetramethylporphyrin (**6b**). Bis(3-ethyl-5-formyl-4-methyl-pyrrol-2-yl)methane[14] (**5**, 860mg, 3mmol) was dissolved in 240ml of methanol. To this clear solution 2·4g of *p*-toluenesulfonic acid was added, followed immediately by **4b** (3mmol). The

resulting mixture was stirred for 2 days, being protected from light. The reaction mixture was poured into water and extracted with CH_2Cl_2, washed with aqueous Na_2CO_3 and water, dried, and evaporated. The porphyrin **6b** was purified by flash column chromatography (CH_2Cl_2 as eluent). Yield: 290mg (0·57mmol, 19%). m.p. 266–269 °C. UV-vis (toluene): λ_{max}/nm = 406, 503, 536, 576, 629. NMR ($CDCl_3$): 10·05 (s, 2H, 10- and 20-H), 9·78 (s, 1H, 15-H), 5·13 (q, 2H, *meso*-CH_2CH_3), 4·03 and 4·01 (m+q, 8H, CH_2CH_3), 3·62 and 3·69 (s+s, 12H, CH_3), 1·82 (t+t, 12H, CH_2CH_3), 1·73 (t, 3H, *meso*-CH_2CH_3), −2·83 and −2·91 (s+s, 2H, NH).

3,7,13,17-Tetraethyl-2,8,12,18-tetramethyl-5-(2-phenyl)ethylporphyrin (**6c**). This porphyrin was prepared by the similar method as **6b** (see above). m.p. 225–228 °C. UV–vis (toluene): λ_{max}/nm = 408, 506, 548, 579, 629. NMR ($CDCl_3$) : 10·06 (s, 2H, 10- and 20-H), 9·80 (s, 1H, 15-H), 7·24–7·43 (5H,Ph), 5·42 (m, 2H, CH_2CH_2Ph), 4·08 (br. 4H, 3- and 7-CH_2CH_3), 4·01 (q, 4H, 13- and 17-CH_2CH_3), 3·61 and 3·59 (s+s, 12H, CH_3), 3·23 (m, 2H, CH_2Ph), 1·84 (t, 6H, 13- and 17-CH_2CH_3), 1·79 (t, 6H, 3- and 7-CH_2CH_3), −2·80 and −2·87 (s+s, 2H, NH).

Synthesis of 5,15-'Strapped'-Porphyrins

2,8,12,18-Tetraethyl-3,7,13,17-tetramethyl-5,15-bis(2-((4-nitrophenyl)oxycarbonyl)ethyl) porphyrin (**10**). The porphyrin-5, 15-dipropionic acid (**9**, 172mg, 0·276mmol) was dissolved in 75ml of pyridine (The diacid **9** was obtained by acid hydrolysis of the diester porphyrin **8**[6] followed by recrystallization from methanol/pyridine). 4-Nitrophenol (460mg, 3·3mmol), 2-chloro-1-methylpyridinium iodide (565mg, 2·2mmol) and triethylamine (445mg, 4·4mmol) were added, and the resulting mixture was heated at 70 °C for 16 hours (under N_2). After the reaction mixture was cooled, the crystalline product was collected by filtration and washed with pyridine. Yield : 150mg (0·173mmol, 63%). m.p. >300 °C. IR (KBr pellet) : $\nu/(cm^{-1})$ = 1760 (C=O); 1520, 1340 (NO_2); 1120 (Ar—O).

5,15-(4, 11-Diaza-3, 12-dioxotetradecan-1, 14-diyl)-2,8,12,18-tetraethyl-3,7,13,17-tetramethylporphyrin (**11a**). The 4-nitrophenyl ester **10** (60mg, 0·069mmol) was suspended in 75 ml of pyridine, and heated to 70 °C. To this mixture 1,6-hexanediamine (8·1mg, 0·069mmol; dissolved in small amount of pyridine) was added in four portions during 3 hours. After the addition was completed, heating was continued for 14 hours. The reaction mixture was cooled, and the solvent was evaporated. The residue was dissolved in CH_2Cl_2/methanol (v/v = 5/1), passed through an alumina short column, and evaporated again. The residual mixture was separated by flash column chromatography ($CHCl_3$/methanol = 100/1 (v/v)). The first porphyrinic fraction was the strapped-porphyrin **11a**. Yield: 26·8mg (0·038mmol, 55%). m.p. 280–285 °C. UV–vis (toluene): λ_{max}/nm = 413, 513, 551, 584, 636(sh). IR (KBr pellet): $\nu/(cm^{-1})$ = 2850 (N—H) and 1620 (C=O). NMR ($CDCl_3$) : 9·99 (s, 2H, *meso*-H), 5·54 (m, 4H, $CH_2CH_2C(O)$), 4·04 (m, 8H, CH_2CH_3), 3·61 (s, 12H, CH_3), 2·79 (m, 4H, $CH_2CH_2C(O)$), 2·62 (t, 2H, amide-NH), 1·78 (t, 12H, CH_2CH_3), 1·72 (q, 4H, $NHCH_2$), −1·6 (br, 2H, central-NH), −1·63 (t, 4H, $NHCH_2$ CH_2CH_2), −1·78 (quintet, 4H; $NHCH_2CH_2$).

5.15-(4, 17-Diaza-3,18-dioxoeicosan-1,20-diyl)-2,8,12,18-tetraethyl-3,7,13,17-tetramethylporphyrin (**11b**). This porphyrin was prepared from the 4-nitrophenyl ester **10** (60mg, 0·069mmol) and 1,12-dodecanediamine (14mg, 0·069mmol) by the similar method as **11a**. Yield: 29·2mg (0·037mmol, 54%). m.p. 195–200 °C. UV-vis (toluene): λ_{max}/nm = 413, 513, 550, 585, 637(sh). IR (KBr pellet): $\nu/(cm^{-1})$ = 2860 (N—H) and 1630 (C=O).

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