

Both-faces Hindered Porphyrins. Part 2.¹ Synthesis and Characterization of internally Five-co-ordinated Iron(II) Basket-handle Porphyrins derived from 5,10,15,20-Tetrakis(*o*-hydroxyphenyl)porphyrin

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Compounds (**9**), so-called ether 'hanging base' porphyrins, derived from 5,10,15,20-tetrakis(*o*-hydroxyphenyl)porphyrin in which one of the faces is hindered by a pyridine-3,5-diylbisalkylene bridge and the other face is protected by an alkylene or an *p*-arylenebisalkylene chain have been synthesized following the concept of the 'basket handle' porphyrins (BHP). From an analysis of the ¹H n.m.r. spectra of their iron(II) derivatives (**20**) at 34 °C, it has been determined that *ca.* 85% were high-spin five-co-ordinated complexes (*s* = 2). Despite the steric hindrance of the distal face, bimolecular associations typical for this class of compounds have been detected except for the most hindered (**20c**). An additional bispyridine 'basket handle' porphyrin (**21**) has been synthesized in order to study the dynamics of the pyridine chain.

During the past decade several five-co-ordinated iron(II) model systems of oxygen-carrier hemoproteins, such as myoglobins and hemoglobins, in which the axial ligand is covalently attached to the porphyrin ring, have been described.²⁻⁸ This covalent attachment of the proximal base allows the co-ordination number of the central metallic ion to be controlled and eliminates the need for an excess of free ligand in solution. Studies of these chelated and tailed compounds have suggested the importance of the *trans* co-ordinating base upon the kinetics and energy of binding of oxygen, and the stabilization of the resulting oxygen complexes. However, in the absence of exogenous base in large excess, several lines of evidence indicate that intramolecular associations are present in solution depending on temperature and concentration.^{5,7}

These last results tempted us to synthesize new compounds, derived from 'basket handle' porphyrins (BHP),¹ in which the proximal ligand is included into one of the two bridges. Such systems should be able to enforce five-co-ordination about the metallic ion. In addition, the sixth co-ordination position is protected by the second bridge which creates a protected 'distal' site, still permitting fixation of a small neutral ligand molecule such as dioxygen or carbon monoxide, and preventing completely the formation of μ -oxo dimeric complexes upon oxygen binding.

Syntheses of double-bridged porphyrins containing pyridine or imidazole incorporated into one of the two bridges have been recently reported by Battersby and his co-workers.⁹ In these compounds, the bridges are built up from the periphery of a symmetrical tetracarboxylic porphyrin. We report herein the synthesis and characterization of compounds, so-called 'hanging base' porphyrins (**9**), in which the pyridine, as the 'proximal' base, is inserted in a chain bridging two opposite *meso*-phenyl substituents of 5,10,15,20-tetraphenylporphyrin. The two other *meso*-phenyl groups are linked by a second bridge of varying length and chemical nature; this determines the varying size of the non-polar cavity of the 'distal' side of the macrocycle. Both chains are linked to the porphyrin *via* ether bonds. The diastereoisomeric nature of these compounds, corresponding to an alternating distribution of the *o*-phenyl substituents between the two faces of the porphyrin ring ($\alpha\beta\alpha\beta$ -atropisomer¹⁰) is designed as cross-*trans*-linked.^{1,11}

In a preliminary communication, we have shown that the iron(II) complexes of these so-called ether-'hanging base' porphyrins exhibit all the magnetic properties of five-co-ordinated species.¹² The synthesis and the results of an extensive n.m.r. study of these complexes are now reported.

Results for the binding of these complexes with gaseous ligands (O₂ and CO) will be described elsewhere.¹³

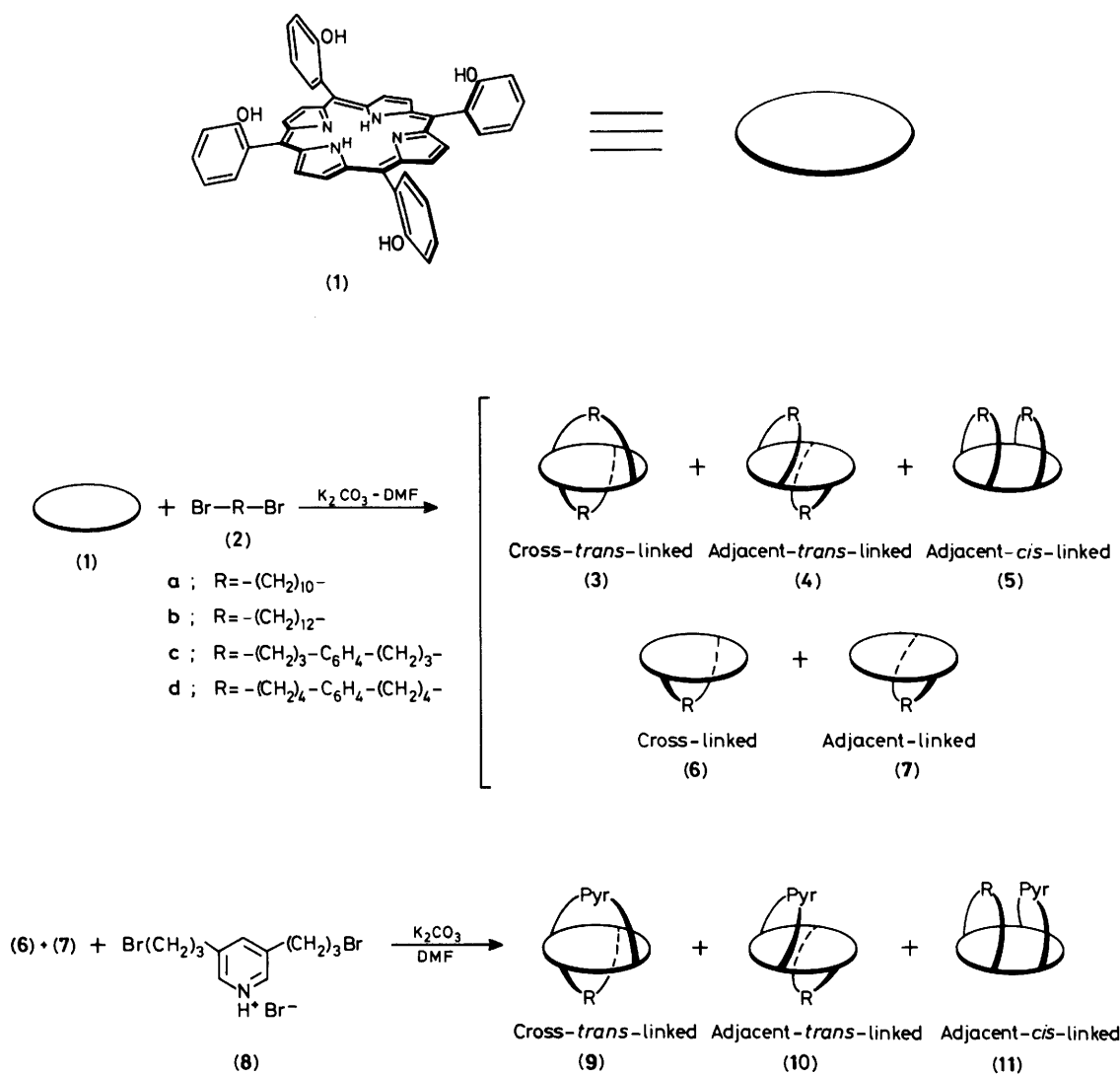
Results and Discussion

Synthesis.—The starting material used for the synthesis of ether 'hanging base' porphyrins was a mixture of the four atropisomers ($\alpha\alpha\alpha\alpha$, $\alpha\alpha\alpha\beta$, $\alpha\alpha\beta\beta$, and $\alpha\beta\alpha\beta$) of 5,10,15,20-tetrakis(*o*-hydroxyphenyl)porphyrin (**1**). They were synthesized in two steps according to the general reaction pathway presented in the Scheme. The first step involved formation of the mono-bridged porphyrins (**6**) and (**7**) following the procedure previously described for the synthesis of symmetrical 'basket handle' porphyrins.¹ Under conditions of high dilution, the coupling of the dibromo derivatives (**2**) with the porphyrin (**1**) in dimethylformamide at 100 °C in the presence of an excess of anhydrous potassium carbonate gave a mixture of mono- and di-bridged porphyrins as evidenced by analytical t.l.c. on silica gel. In order to achieve varying degrees of 'distal' steric hindrance several different bridges were built into the structure, including both simple polymethylene chains (CH₂)_{*n*} (*n* = 10 and 12), and a central phenylene group flanked by two *para*-polymethylene chains (CH₂)_{*n*} (*n* = 3 and 4). After filtration and evaporation of the reaction solvent, the residue was taken up in toluene and chromatographed on a silica-gel column. Initial elution with toluene gave the di-bridged porphyrins (**3**), (**4**), and (**5**). Subsequently elution with chloroform-methanol (100:2.5, v/v) gave the two isomeric monobridged porphyrins (**6**) and (**7**). Starting material (**1**) and polymeric compounds were retained on the top of the column.

Without further purification, compounds (**6**) and (**7**) were treated with a 1.1 equivalent of 3,5-bis(3-bromopropyl)pyridine hydrobromide (**8**) following the same procedure as used in the first step.

The dibromo derivative (**8**) was obtained from pyridine-3,5-dicarboxylic acid (**12**) *via* esterification into the corresponding methyl ester (**13**). Subsequent lithium aluminium hydride reduction and bromination gave 3,5-bis(hydroxymethyl)pyridine (**14**) and 3,5-bis(bromomethyl)pyridine hydrobromide (**15**), respectively, following the methods of Tsuda¹⁴ and Beely.¹⁵ Compound (**15**) was converted into 3,5-bis(3-ethoxycarbonyl-ethyl)pyridine (**16**) by malonic synthesis, and was further reduced by LiAlH₄ into the corresponding diol (**17**).⁹ Bromination gave the dibromo derivative (**8**) needed for the bridging reaction.

These porphyrins were concentrated by chromatography on



(8) $R = (CH_2)_3Br$

(12) $R = CO_2H$

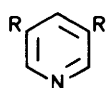
(13) $R = CO_2Me$

(14) $R = CH_2OH$

(15) $R = CH_2Br$

(16) $R = (CH_2)_2CO_2Et$

(17) $R = (CH_2)_3OH$

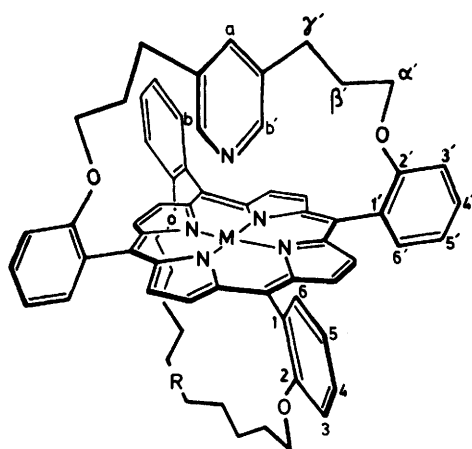


a silica gel column with chloroform-ether (1:1 v/v). It has not been possible to separate the expected cross-*trans*-linked isomer (9) from the two other isomers, adjacent-*trans*-linked (10) and adjacent-*cis*-linked (11), when they were in the free-base form. However, by t.l.c. on silica gel, we succeeded in isolating the desired product (9) as its zinc chelate (18) after treatment of the three-isomer mixture with zinc acetate in chloroform-acetic acid. Demetallation of the three isomers after individual extraction from the main bands, in the presence of trifluoroacetic acid in chloroform, gave the corresponding free-base

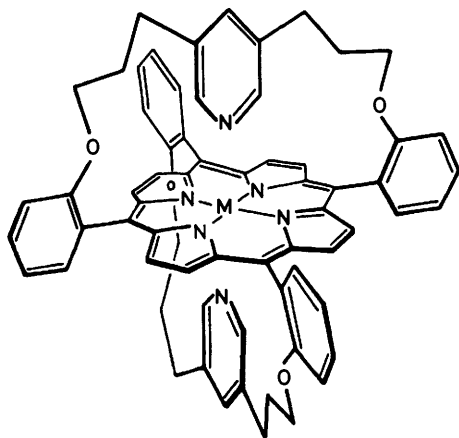
compounds. The identification and structural assignments of these compounds were based on the 1H n.m.r. spectra of the zinc complexes and the free-base forms (see below). The first two bands corresponding to the less-polar zinc compounds were identified as the isomers (10) and (11) in which the bridges bind two adjacent *meso*-phenyl groups. The slower, major fraction was shown to be the expected cross-*trans*-linked isomer (9).

In order to study the dynamics of the pyridine chains,¹³ a basket-handle porphyrin containing two pyridine bridges has been prepared, following a procedure similar to that used for the preparation of symmetrical 'basket handle' porphyrins.¹ The required cross-*trans*-linked isomer (21) was obtained only in poor yield (7.2 %) by reaction between the dibromopyridine derivative (8) and the porphyrin (1). An insoluble material was obtained during work-up of the reaction mixture which was assigned as the adjacent-*trans*-linked isomer. No adjacent-*cis*-linked isomer was, however, recovered.

Anaerobic insertion of iron into (9) and (21) was carried out with iron(II) chloride in dimethylformamide under reflux, the products being chromatographed on silica gel to give a mixture of chloro- and hydroxy-iron(III) porphyrins. The pure hydroxy derivatives (19) were obtained by shaking a toluene solution of iron porphyrins with aqueous potassium carbonate. The



- (9) $M = 2H$
 (10) $M = Zn$
 (19) $M = Fe^{III}OH$
 (20) $M = Fe^{II}$



- (21) $M = 2H$
 (22) $M = Fe^{III}Cl$
 (23) $M = Fe^{II}$

chloroiron(III) complex (22) was prepared by shaking a CH_2Cl_2 solution of iron(III) porphyrin, (21) with saturated aqueous sodium chloride.

Reduction of iron(III) complexes with aqueous sodium dithionite under anaerobic conditions, in a two-phase system (toluene or aqueous benzene)¹⁶ gave the orange iron(II) compounds (20) and (23). They could also be obtained by reduction with zinc amalgam in anhydrous toluene under argon. Their adducts with externally provided ligands (CO , O_2) have been characterized by a variety of physical techniques.¹³ Their electronic spectral characteristics are listed in Table 1 Figure 1.

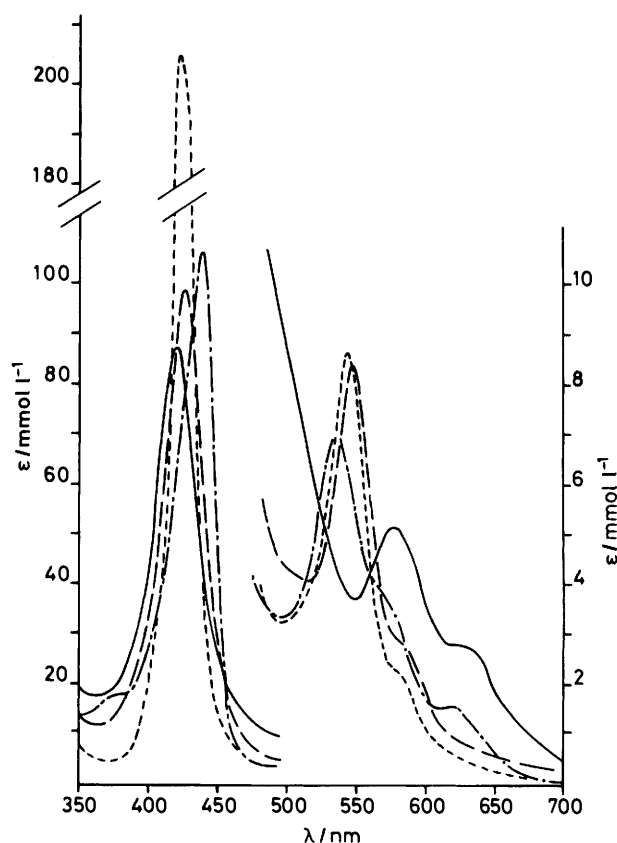


Figure 1. U.v.-visible spectra of the iron complexes of [ether-BHP($C_{12}(C_3Pyr-C_3)$)] (9b) in toluene at 20 °C (—) $Fe^{III}OH^-$; (---) Fe^{II} ; (-·-·-) $Fe^{II}CO$; (— — —) $Fe^{II}O_2$.

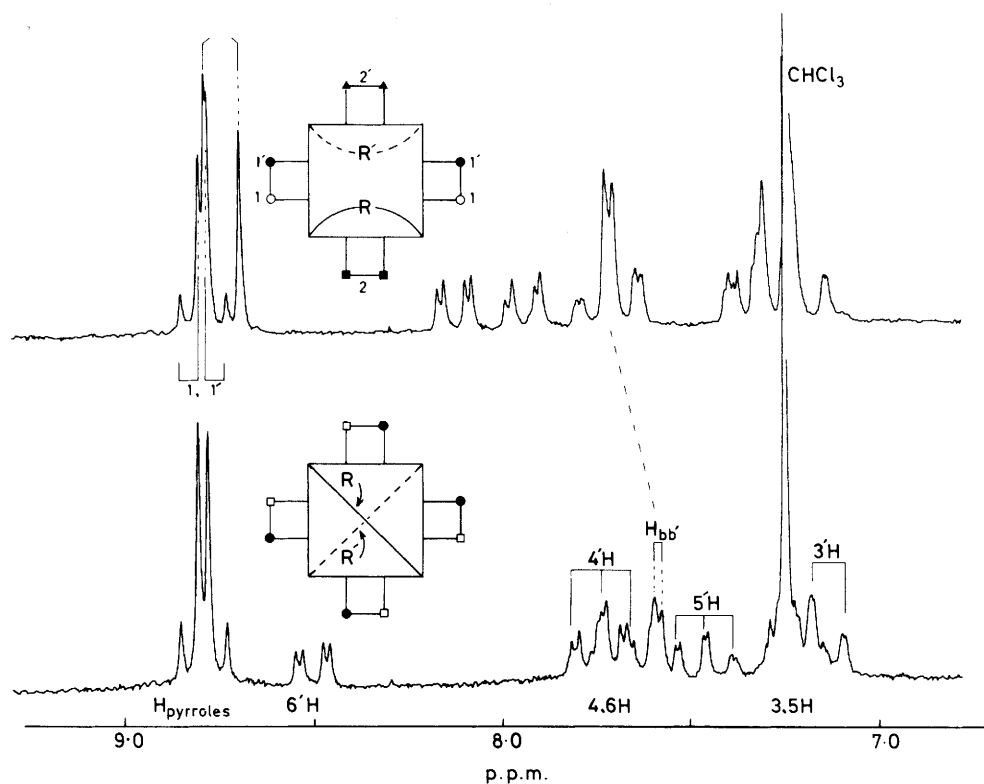
Characterization.—Because of the method of attachment of the 'handles', the products, as the BHP,¹ occur in three isomeric forms. As described in Part 1 of this series,¹ these isomers are designed as cross-*trans*-linked (9) adjacent-*trans*-linked (10), and adjacent-*cis*-linked (11). The cross and adjacent isomers are easily characterized by the n.m.r. spectral characteristics of the pyrrolic protons. The symmetry of the isomers (10) and (11) is such that these resonances appear as three different subspectra (see Figure 2): one AB subspectrum (four protons, J 5 Hz) and two singlets (two protons each). In contrast the pyrrolic proton resonances for isomer (9) appear in all instances as a single AB spectrum, indicating that the effective symmetry of the molecule is C_{2v} .

The chemical shifts of the identified resonances for the free base of isomers (9) are collected in Table 2. The resonances of the *ortho*-phenyl protons 6-H and 6'-H are shifted to lowfield by the porphyrin ring current. The shift of the doublet assigned to the *ortho*-phenyl protons 6'-H is remarkably independent of the nature of the chain lying above the opposite face of the porphyrin ring. In contrast, the chemical shift of 6-H exhibits variations which are very similar to those observed for the symmetrical BHP and which were assigned to tension effects of the chains.¹

The pyridine proton resonances are also easily detected in the n.m.r. spectra. Thus H_a (Scheme 3) appears as a characteristic triplet (J 2.5 Hz) largely shifted to highfield whereas the two equivalent $H_{b,b'}$ protons are assigned by selective decoupling experiments to a doublet appearing in the phenyl protons multiplet (Figure 2). The large shift difference for H_a and $H_{b,b'}$, assigned to the ring-current effect of the porphyrin,¹⁷ shows

Table 1. Absorbance maxima (nm) and molecular extinction coefficients ($l \text{ mmol}^{-1} \text{ cm}^{-1}$) of iron ether 'hanging base' porphyrin complexes, in toluene or dichloromethane

Ether-[BHP(C ₁₀)(C ₃ ·Pyr·C ₃)] ^a	Fe ^{III} -OH ⁻ (19a)	422 (102)	581 (7.6)	631 (3.8)	619 (2.0)
	Fe ^{II} (20a)	439 (121)	536 (7.1)	580 (3.7)	
	Fe ^{II} -CO	425 (225)	545 (8.8)	582 (2.9)	
	Fe ^{II} -O ₂	426 (105)	548.5 (8.5)	585 (3.8)	
Ether-[BHP(C ₁₂)(C ₃ ·Pyr·C ₃)] ^a	Fe ^{III} -OH ⁻ (19b)	421 (92)	579 (7.1)	630 (3.8)	618 (2.9)
	Fe ^{II} (20b)	438 (107)	535 (7.0)	580 (3.5)	
	Fe ^{II} -CO	425 (206)	545 (8.6)	582 (2.8)	
	Fe ^{II} -O ₂	426 (99)	547 (8.4)	584 (3.4)	
Ether-[BHP(C ₃ ·C ₆ H ₄ ·C ₃)(C ₃ ·Pyr·C ₃)] ^a	Fe ^{III} -OH ⁻ (19c)	422 (103)	580 (7.0)	632 (3.8)	619 (2.4)
	Fe ^{II} (20c)	439 (97)	535 (6.1)	580 (3.8)	
	Fe ^{II} -CO	425 (212)	544 (8.6)	582 (2.9)	
	Fe ^{II} -O ₂	426	548	584	
Ether-[BHP(C ₄ ·C ₆ H ₄ ·C ₄)(C ₃ ·Pyr·C ₃)] ^a	Fe ^{III} -OH ⁻ (19d)	422 (99)	578 (7.7)	632 (3.6)	618 (1.7)
	Fe ^{II} (20d)	428 (110)	535 (6.3)	578 (3.3)	
	Fe ^{II} -CO	425 (223)	545 (7.7)	580 (2.6)	
	Fe ^{II} -O ₂	426	548	583	
Ether-[BHP(C ₃ ·Pyr·C ₃) ₂] ^b	Fe ^{III} Cl ⁻ (22)	420 (131)	531 (8.6)		
	Fe ^{II} (23)	425 (181)	533 (18.4)	562 (3.8)	
	Fe ^{II} -CO	427 (234)	546 (10.4)	572 (3.9)	

^a Toluene ^b Dichloromethane**Figure 2.** Lowfield part of the 100 MHz proton n.m.r. spectra of the cross-*trans*-linked isomer (9d) –lower– and of one of adjacent-linked isomer –upper–, recorded in CDCl₃ at 307 K. The diagrams indicate the symmetry of the pyrrolic protons.

that the nitrogen atom of the pyridine points outwards in the free base.

Co-ordination Properties of the Hanging Base.—(a) *Zinc complexes.* The order of the resonances of the pyridinediyl protons in the zinc complexes is reversed, consistent with co-ordination of the pyridine nitrogen to the metal. However, the observed ring current shift for H_a and H_{b,b'} (Table 2) does not agree with that reported by Abraham *et al.*¹⁷ for the co-

ordination of free pyridine to zinc tetraphenylporphin. This suggests that the pyridine molecule exchanges rapidly (on the n.m.r. time scale) between the co-ordinated and the non-co-ordinated sites. Indeed, the chemical shifts of H_a and H_{b,b'} are temperature dependent. They shift respectively by 0.13 p.p.m. to lowfield and by 0.15 p.p.m. to highfield as the temperature is lowered from 307 to 200 K. Even at the lowest temperature, co-ordination is not complete. An estimation of the amount of unligated complex has been obtained assuming that, for this

Table 2. Proton n.m.r. shifts (in p.p.m. from TMS) for the cross-*trans*-linked isomers (CDCl_3 at 307 K). The ring current effect for the covalently linked pyridine protons, referenced from diethyl pyridine-3,5-dipropionate (**16**), is indicated in parentheses for the zinc complexes (**18**). The corresponding ring current shifts for pyridine bonded to zinc tetraphenylporphyrin are: H_a (1.41 p.p.m.) and $H_{b,b'}$ (5.87 p.p.m.).¹⁷ The assignment is shown on the Scheme 3

	H_{pyr}		<i>meso</i> -Phenyl		Pyridinediyl		Methylene		NH
			6-H	6'-H	H_a	$H_{b,b'}$	α	α'	
(9a)	8.84	8.77	7.96	8.58	2.45	7.65	3.71	3.74	-2.16
(18a)	8.83	8.75	8.28	8.70	5.54 (1.82)	2.89 (5.42)	3.63	3.58	
(9b)	8.81	8.76	7.70	8.55	2.21	7.57	3.93	3.74	-2.31
(18b)	8.79	8.73	8.00	8.69	5.49 (1.87)	2.81 (5.50)	3.86	3.58	
(9c)	8.85	8.80	8.07	8.53	2.62	7.71	3.52	3.75	-1.96
(18c)	8.80	8.78	8.43	8.62	5.67 (1.69)	2.96 (5.35)	3.35	3.59	
(9d)	8.84	8.78	7.70	8.52	2.30	7.61	3.88	3.74	-2.17
(18d)	8.81	8.75	8.12	8.67	5.55 (1.81)	2.82 (5.49)	3.83	3.58	
(21)	8.87		8.17		2.96	7.85	3.53		-1.90

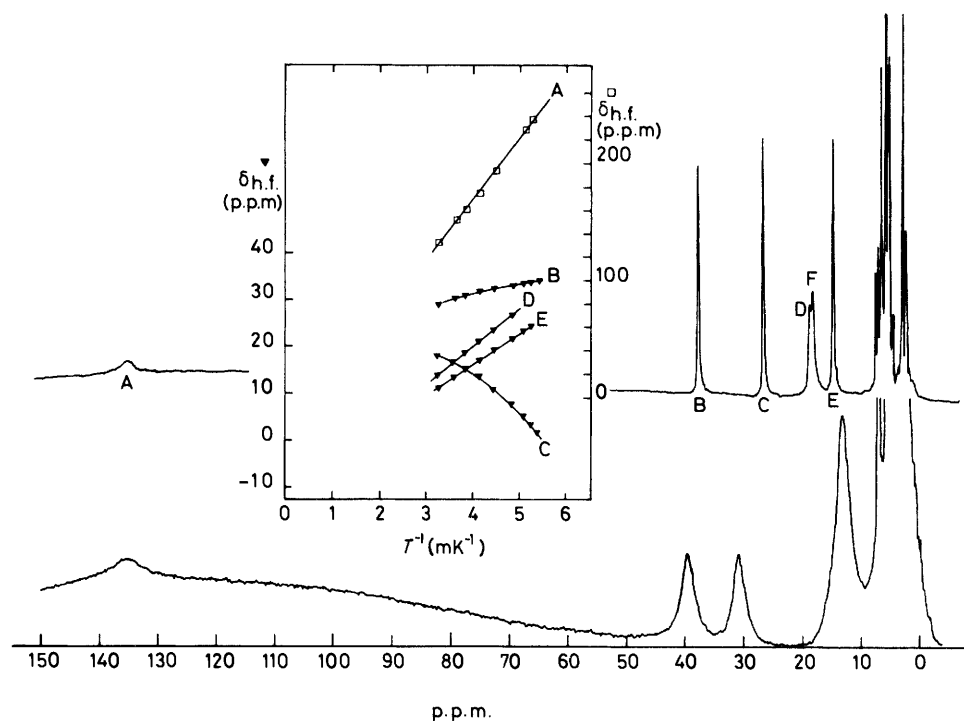


Figure 3. 100 MHz Proton n.m.r. spectra of (**20d**)—lower— and (**20c**)—upper— recorded in $[\text{}^2\text{H}_8]\text{toluene}$ at 307 K. The assignment is as follows: A, (2 H) pyridine protons $H_{b,b'}$; B and C (2×4 H) pyrrolic protons; D, (1 H) pyridine proton H_a ; E, (4 H) phenylene protons and F, (4 H) α -methylene protons bonded to the pyridine. The insert shows the temperature dependence of the isotropic shifts for the resolved resonances for (**20c**) referenced to the zinc complex (**18c**) (Note the different scale for $H_{b,b'}$ to the right).

complex, the shifts of the pyridine protons are identical with those observed for the free base. Then, *ca.* 5% of non co-ordinated zinc complex exists at 307 K in chloroform solution.

(b) *Iron(II) Complexes.*—Typical spectra recorded at 307 K are presented in Figure 3. The assignment is based on integration of the lines, comparison of the spectra for the different models, and sometimes on selective decoupling experiments.¹² Furthermore, this assignment is supported by spin lattice relaxation measurements of the resolved lines for these paramagnetic species (Table 3). At first glance, these spectra are typical of high spin $s = 2$ complexes.^{18,19} The pyrrolic protons are shifted to low-

field in a range (30–40 p.p.m.) lower but consistent with other five-co-ordinated models incorporating a pyridine ligand.⁸ The shifts of the bridging-chain protons remain close to the diamagnetic range (Figure 3) consistent with a moderate pseudo-contact shift contribution.¹⁹ In addition, the pyridine protons $H_{b,b'}$ (Figure 3) are largely shifted to lowfield (135 p.p.m. at 307 K) suggesting that the pyridine is actually co-ordinated to the iron(II). H_a and the methylene group directly bonded to the pyridine are shifted to only 16–22 p.p.m. owing to a decrease of the unpaired spin delocalisation through the direct interaction of the pyridine σ orbitals with the iron d_{z^2} orbital.

The pyrrolic proton resonances for the three complexes (**20a**),

Table 3. Proton n.m.r. data for the iron(II) complexes of the cross-*trans*-linked isomer (20) (C₆D₆ at 307 K). The assignment is shown in the Scheme 3

Compounds	(20a)				(20b)				(20c)				(20d)			
Protons	H _{pyr}				H _{pyr}				H _{pyr}				H _{pyr}			
Shifts/TMS in p.p.m.	40	30	17	138	41	33	22	138	37	26	18.5	135	40	32	16	135
Linewidths in Hz	170	170	200	500	160	160	200	500	12.5	11.5	25	300	150	150	a	500
(concentration, mol l ⁻¹)	(2.7 10 ⁻³)				(3.0 10 ⁻³)				(3.4 10 ⁻³)				(1.5 10 ⁻³)			
T ₁ (ms)	54				56.5				62.2				57			
(standard deviation)	(4)				(2.3)				(0.5)				(0.12)			
1/πT ₁ (Hz)	5.9				5.6				5.1				5.6			

For resonance not resolved at 307 K.

Table 4. Observed and calculated relative shifts (Hz) and linewidths (Hz) of the lowfield pyrrole proton resonance for compound (20d) with and without the corresponding free base (9d) in C₆D₆ solution at 307 K. The calculated data were obtained from the simulated lineshape assuming a two-sites exchange. The parameters used were ν_B - ν_A = 3 190 Hz, λ_B(s = 2) = 12 Hz, λ_A(s = 0) = 1 Hz and ε_A(1/k_{off}) = 103 μs. The proportions P_A and P_B for the two sites were calculated from the resolution of equations (1) to (3) using K₁ = 4.5 and K₂ = K₂' = 254 l mol⁻¹

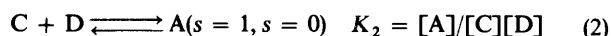
Total concentration of iron(II) porphyrin (10 ⁻³ l mol ⁻¹)	1	1	1	1	1	1	2.5	1.46	0.77	0.38	0.2
P _A (%)	3.4	6.8	10.3	16.9	27.8	44.6	7.5	4.8	2.7	1.4	0.7
Total concentration of free base (10 ⁻³ l mol ⁻¹)	0	0.224	0.465	0.97	2.0	4.2	0	0	0	0	0
Relative shifts:											
observed	0	28	63	168	a	a	59	29	17	7	0
calculated		26	57	131	328	1 142	50	29	13	5	0
Linewidth:											
observed	82	190	320	600	a	a	200	145	95	68	45
calculated	100	197	303	540	1 082	2 340	217	139	82	48	30

a Broadened beyond observation.

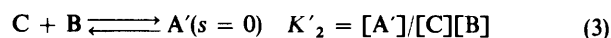
(20b), and (20d) exhibit, however, a large concentration-dependent broadening in contrast with compound (20c), while their T₁ values are very similar (Figure 3 and Table 3). Thus, this broadening is assigned to an intermediate slow-exchange process on the present n.m.r. time scale (Δν_{pyrrole} ≈ 3 000 Hz) owing to the formation of dimeric species; these consist of a bispyridine hemochrome subunit (H_{pyrrole}, δ ≈ 8.8 p.p.m.) and a four-co-ordinated iron(II) (s = 1) subunit (H_{pyrrole}, δ ≈ 5 p.p.m.).^{20,21} On lowering the temperature, the exchange becomes slow and typical resonances for a four-co-ordinated s = 1 species²¹ appear in the range 0 to -90 p.p.m. due to the large pseudocontact through-space interaction.

Thus, despite the covalent binding of the pyridine molecule to the porphyrin and the protection of the free co-ordination site of the metal, these complexes dimerise as for other models,^{5,7} except compound (20c); this is, presumably, owing to the more efficient protection of the short phenylene bridging chain.

Dimerisation can take place only because of the presence in solution of some four-co-ordinated iron(II) monomer in equilibrium with the five-co-ordinated complex, as described by equations (1) and (2) where C (co-ordinated) denotes the five-



co-ordinated species, D (un-co-ordinated) the four-co-ordinated monomer, and A the associated species. Provided K₂ is known, then the proportion [D]/[C] can be estimated, giving information on the efficiency of the covalent linkage to enforce pyridine five-co-ordination. For this reason, the dimerisation has been simulated by titrating the iron(II) complex with the corresponding free base 'hanging base' porphyrin. This is described by equation (3). It may be assumed that K' = K₂.



The titration data given in Table 4 for compound (20d) indicate that the exchange process is intermediate to slow in a manner comparable with that for the dimerisation observed in the absence of free base; this justifies the present approach. As a matter of fact, identical shifts and linewidths for the pyrrolic proton resonances were observed either in 2.5.10⁻³M (P_T) (20d) or in a mixture of 10⁻³M (P'_T) (20d) with 2.24.10⁻⁴M free base (9). Therefore, the proportion of six-co-ordinated species must be the same in both cases. Assuming that this proportion is small (<10%), and by manipulating equations (1)–(3) we obtain equation (4) in which B_T is the concentration of the free base

$$\frac{1}{K_1} \approx \frac{B_T}{P_T - P'_T} \quad (4)$$

added to a total concentration of P'_T iron porphyrin. P_T is the total concentration of iron porphyrin which leads to identical shifts and linewidths solely by the dimerisation process. This estimate is independent of the assumed value of K₂. A rigorous analysis of the three equilibrium equations, has led to the same conclusions. The best fit was determined for K₁ = 4.4 ± 0.9. The error arises from the estimated error for the porphyrin concentrations (±2.10⁻⁴M).

K₂ Was determined from the titration data assuming a two-sites exchange (A, s = 0; B, s = 2) for the pyrrolic protons. The lineshape has been calculated from the known equations²² using a home written program which also calculates the position of the maximum and the linewidth at half-height by iterative procedures. The best fit for both the observed linewidths and shifts gave the dimer lifetime 1/k_{off} = 103 ± 10 s and K₂ = 254 ± 50 l mol⁻¹. As a test of the consistency of this analysis, Table 4 presents the calculated linewidths and relative

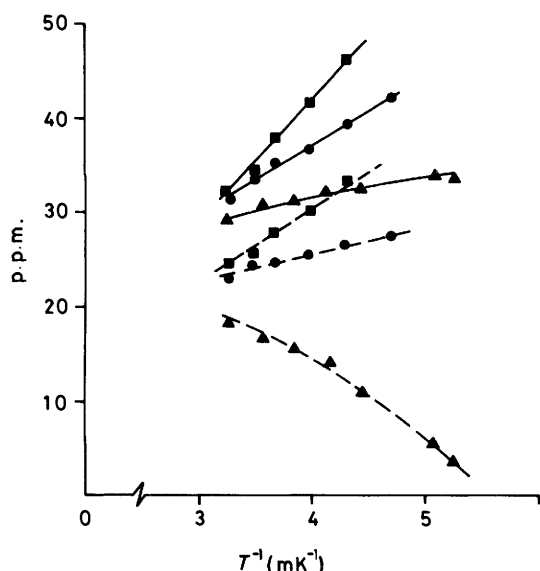


Figure 4. Comparison of the temperature dependence of the isotropic shifts for the two pyrrolic proton resonances for the high spin ($s = 2$) complexes (20c) (▲), (20d) (●), and (20b) (■) recorded in $[^2\text{H}_8]$ -toluene.

shifts with and without added free base showing a reasonable agreement with experiment.

It should be noted that the assumption of a two-sites exchange for the association described by equation (2) is justified by the fact that the pyrrolic proton sites of both partners within species A are nearly identical ($\delta_{s=1} \approx 5$ p.p.m.^{20,21} and $\delta_{s=0} \approx 8.8$ p.p.m.) as compared with the pyrrolic proton site for the dominant species C ($\delta_{s=2} \approx 35$ p.p.m.). Up to now, the exchange process (1) has been assumed to be fast, meaning that C + D in equation (2) can be considered as a unique species in intermediate to slow exchange with A. In fact, the reverse assumption of a slow exchange between C and D does not modify the estimated value of K_1 , but leads to a slightly smaller value for K_2 (200 ± 40 l mol⁻¹). Limits for this exchange time are given by the broadening of the resonances for compound (20c), which is only 7 Hz for the pyrrole and 50 Hz for the pyridine protons respectively (Table 3). Following the two assumptions of fast or slow exchange between C and D, the lifetime of the five-co-ordinated species should be either shorter than 600 ns or longer than 45 ms.

Temperature Dependence of the Isotropic Shifts for the Five-co-ordinated Ferrous Complexes.—The temperature dependence of the well-resolved resonances of the proton n.m.r. spectra of (20c) is shown in the insert of Figure 3. The previously described anomaly of the pyrrolic protons resonances¹² has been confirmed either in dichloromethane as solvent or in dried toluene solution after reduction on amalgam. It has been explained assuming that the electronic ground state is described by at least two electronic levels resulting from the removal of the degeneracy of the 5E level.¹² Another interpretation has been proposed²³ which considers a dynamic effect due to the rotation of the axial base plane around an axis perpendicular to the porphyrin plane. However, the pyrrolic protons resonances of the high-spin species for (20a, c, d) (Figure 4) reveals a clear correlation between the slope of the temperature dependence and the hindrance of the bridging chain. This suggests that the nature of the chain critically modulates the ground electronic states of the present five-co-ordinated iron(II) complexes,

favouring the electronic¹² rather than the dynamic²³ interpretation for the anomalous Curie plot.

Conclusions.—The incorporation of the pyridine base in a chain covalently linked over one face of the porphyrin ring permits the obtention of nearly pure five-co-ordinated iron(II) complexes. However the mode of linkage of the chain leaves sufficient freedom to the pyridine molecule to cause measurable de-co-ordination from the central metal. The proportion of de-co-ordinated molecules in solution at 307 K has been estimated to ca. 5% for the zinc complexes and to 15–20% for the iron(II) complexes. This is just in the ratio of the equilibrium constants for the binding of one free pyridine molecule to the corresponding four-co-ordinated metalloporphyrin, which are respectively 4 800 (ref. 24) and 1 500 (ref. 25) at 298 K in benzene. Furthermore, the protecting chain bridged over the other face of the porphyrin ring does not completely eliminate dimerisation except for (20c).

Experimental

All chemicals used were of reagent grade and purchased from Aldrich. Dried dimethylformamide was distilled and kept over 4 Å molecular sieve. 5,10,15,20-Tetrakis(*o*-hydroxyphenyl)-porphyrin (THPP) (1) was synthesized according to the method previously described.¹ Column chromatography was carried out on silica gel 60 (70–230 mesh) purchased from Merck. For t.l.c. separation throughout this work, Merck precoated preparative t.l.c. plates (silica gel 60, 2 mm) were used. Nitrogen, argon, carbon monoxide, and oxygen were from 'l'Air Liquide'. Element analyses were carried out by the Service Central de Microanalyse du CNRS.

Optical spectra in the Soret and visible region were recorded using a Varian DMS 100 spectrophotometer. ^1H n.m.r. spectra of free-base and zinc porphyrins in deuteriochloroform (CEA, France) were obtained with a Varian XL 100 spectrometer in the Fourier transform mode using 4 K data points in the frequency domain. Chemical shifts in p.p.m. were referenced to internal tetramethylsilane (TMS). $[^2\text{H}_6]$ Benzene and $[^2\text{H}_8]$ -toluene (CEA, France) were used as solvents for recording ^1H n.m.r. spectra of iron(II) compounds. The spin lattice relaxation measurements were performed by the usual inversion-recovery method and a three-parameters nonlinear regression analysis of the intensities of the lines.

3,5-Bis(hydroxymethyl)pyridine (14).—This compound was prepared from dimethylpyridine-3,5-dicarboxylate (13)¹⁴ by lithium aluminium reduction (93%), m.p. 84–85 °C (Found: C, 59.95; H, 6.75; N, 9.6. $\text{C}_7\text{H}_9\text{NO}_2$ requires C, 60.42; H, 6.52; N, 10.07%), $\delta[(\text{CD}_3)_2\text{SO}]$ 4.57 (d, $2 \times \text{CH}_2$), 5.30 (t, J 5.3, $2 \times \text{OH}$), 7.70 (br, *p*-H), and 8.42 (d, J 1.7 Hz, $2 \times \text{o}$ -H).

3,5-Bis(bromomethyl)pyridine Hydrobromide (15).—A mixture of the diol (14) (11 g, 80 mmol) and 66% aqueous hydrobromide acid (150 ml) was kept at 125 °C for 5 h. The solution was cooled and evaporated and the residue dissolved in water (40 ml). Upon cooling of the solution a product was obtained (15.5 g, 56%) the n.m.r. spectral characteristics of which allowed its assignment as the dibromide. It was immediately used without further purification; $\delta(\text{CDCl}_3)$ 4.46 (s, $2 \times \text{CH}_2$), 7.76 (t, J 2.1 Hz, *p*-H), and 8.56 (d, J 2.1 Hz, $2 \times \text{o}$ -H).

3,5-Bis(3-ethoxycarbonyl)pyridine (16).—The title compound was prepared from (15) following the malonate synthesis reported by Battersby *et al.*⁹ and esterification with oxalyl chloride in a mixture of toluene–ethanol (4:1 v/v) under reflux for 2 h (82%), b.p. 184 °C (2 mmHg) (Found: C, 63.7; H, 7.55; N, 5.9. $\text{C}_{15}\text{H}_{21}\text{NO}_4$ requires C, 64.49; H, 7.58; N, 5.01%); $\delta(\text{CDCl}_3)$

1.21 (t, J 7.1 Hz, $2 \times \text{OCH}_2\text{CH}_3$), 2.6 (m, $2 \times \text{CH}_2\text{CH}_2\text{CO}$), 2.9 (m, $2 \times \text{CH}_2\text{CH}_2\text{CO}$), 4.12 (q, J 7.1 Hz, $2 \times \text{OCH}_2\text{CH}_3$), 7.36 (t, J 2.1 Hz, p -H to pyridinediyl), and 8.31 (d, J 2.1 Hz, $2 \times o$ -H to pyridinediyl).

3,5-Bis(3-hydroxypropyl)pyridine (17).—This compound was obtained from (16) by reduction with LiAlH_4 (80%); b.p. 240–245 °C (8 mmHg) [Found: C, 66.7; H, 8.8; N, 7.2. $\text{C}_{11}\text{H}_{17}\text{NO}_2 \cdot 0.2(\text{H}_2\text{O})$ requires C, 66.4; H, 8.8; N, 7.0%]; δ ($^2\text{H}_6$]acetone) 1.88 (m, $2 \times \text{PyrCH}_2\text{CH}_2$), 2.75 (t, J 7.7 Hz, $2 \times \text{PyrCH}_2$), 3.65 (t, J 6.4 Hz, $2 \times \text{PyrCH}_2\text{CH}_2\text{CH}_2$), 4.2 (s, H_2O), 7.6 (t, J 2 Hz, p -H to pyridinediyl), 8.43 (d, J 2 Hz, $2 \times \text{H}$, o -H to pyridinediyl).

3,5-Bis(3-bromopropyl)pyridine Hydrobromide (8).—Bromination of the diol (17) with 60% HBr was accomplished using the method described for the preparation of 3,5-bis(bromomethyl)pyridine hydrobromide (15). After the reaction, the solution was evaporated and dried *in vacuo* to give a solid product. It was purified by recrystallization from acetone to give the title compound (88%) as white crystals, m.p. 131 °C [Found: C, 33; H, 4.0; Br, 59.9; N, 3.6. $\text{C}_{11}\text{H}_{15}\text{NBr}_2 \cdot \text{HBr}$ requires C, 32.9; H, 4.01; Br, 59.6; N, 3.5%]; δ (CD_3OD) 2.29 (q, $2 \times \text{PyrCH}_2\text{CH}_2$), 3.09 (t, J 7.5 Hz, $2 \times \text{PyrCH}_2\text{CH}_2\text{CH}_2$), 3.53 (t, J 6.7 Hz, $2 \times \text{PyrCH}_2$), 8.55 (br m, p -H to pyridinediyl), 8.74 (br m, $2 \times \text{H}$, o -H to pyridinediyl).

General Procedure for the Preparation of Hanging Base Porphyrins.—*First step.* A solution of the appropriate dibromo derivative (2) (4.4 mmol) in dry dimethylformamide (200 ml) was added dropwise during 4 h to a mixture of 5,10,15,20-tetrakis(*o*-hydroxyphenyl)porphyrin (1) (4 mmol) and an excess of anhydrous potassium carbonate (60 mmol) in the same solvent (400 ml) at 100 °C. Nitrogen was bubbled through the solution during the reaction. After the addition was completed stirring was continued for 4 h at the same temperature. The solution was then cooled to room temperature and filtered and the filtrate was evaporated to dryness under reduced pressure. The residue was dissolved in chloroform and the organic layer was washed with water ($\times 3$), dried (Na_2SO_4), and then evaporated. The residue was then subjected to column chromatography (silica gel, $4 \times 25\text{cm}$). Elution with chloroform afforded a red fraction which was identified by analytical t.l.c. as a mixture of three isomers of dibridged 'basket-handle' porphyrins (3), (4), and (5). A more polar fraction, eluted with chloroform-methanol (100:2.5 v/v), was thought to be monobridged porphyrins. The two isomers, cross-linked (6) and adjacent-linked (7), were not separated and used without further purification. Unchanged starting material (1) could be then recovered with acetone-ether (1:1 v/v). The following products were obtained. [Ether-BHP(C_{10}) $_2$],¹ (3a), (4a), and (5a) (0.720 g, 19%); a mixture of 5,15-[2,2'-(decamethyleneoxy)diphenyl]:10,20-bis(*o*-hydroxyphenyl)porphyrin and 5,10-[2,2'-(decamethyleneoxy)diphenyl]:15,20-bis(*o*-hydroxyphenyl)porphyrin, (6a) and (7a) (2.02 g, 62%); and THPP (1) (0.4 g, 15%).

[Ether-BHP(C_{12}) $_2$], (3b), (4b), and (5b) (0.77 g, 19%); a mixture of 5,15-[2,2'-(dodecamethyleneoxy)diphenyl]:10,20-bis(*o*-hydroxyphenyl)porphyrin and 5,10-[2,2'-(dodecamethyleneoxy)diphenyl]:15,20-bis(*o*-hydroxyphenyl)porphyrin, (6b) and (7b) (2.13 g, 63%); and THPP (1) (0.3 g, 11%).

[Ether-BHP($\text{C}_3 \cdot \text{C}_6\text{H}_4 \cdot \text{C}_3$) $_2$], (3c), (4c), and (5c) (0.835 g, 21%); a mixture of 5,15-[2,2'-[3,3'-(*p*-phenylene)dipropoxy]diphenyl]:10,20-bis(*o*-hydroxyphenyl)porphyrin and 5,10-[2,2'-[3,3'-(*p*-phenylene)dipropoxy]diphenyl]:15,20-bis(*o*-hydroxyphenyl)porphyrin, (6c) and (7c) (1.81 g, 54%); and THPP (1) (0.43 g, 16%).

[Ether-BHP($\text{C}_4 \cdot \text{C}_6\text{H}_4 \cdot \text{C}_4$) $_2$], (3d), (4d), and (5d) (0.840 g, 20%); a mixture of 5,15-[2,2'-[4,4'-(*p*-phenylene)dibutoxy]-

diphenyl]:10,20-bis(*o*-hydroxyphenyl)porphyrin and 5,10-[2,2'-[4,4'-(*p*-phenylene)dibutoxy]diphenyl]:15,20-bis(*o*-hydroxyphenyl)porphyrin (6d) and (7d) (2.25 g, 65%); and THPP (1) (0.35 g, 13%).

Second step. 3,5-Bis(3-bromopropyl)pyridine hydrobromide (8) (1.1 equiv.) in dry dimethylformamide (DMF) (125 ml) was added dropwise under nitrogen during 4 h and with vigorous stirring at 100 °C to a solution of monobridged porphyrins (6) and (7) and an excess of anhydrous potassium carbonate in DMF (200 ml). After the addition was complete stirring was continued for 4 h. The reaction mixture was then cooled to room temperature and filtered and the filtrate was evaporated to dryness. The residue was taken up in chloroform and the organic solution was washed with water ($\times 3$), dried (Na_2SO_4), and evaporated to a volume of ca. 20 ml. This concentrated solution was loaded onto a silica-gel column ($3 \times 30\text{cm}$). Elution with chloroform removed some faster-moving impurities. Elution with chloroform-ether (1:1 v/v) gave the 'hanging base' porphyrins (9), (10), and (11). The isomers were not separable either by this method or by preparative t.l.c. on silica gel. The following products were obtained. [Ether-BHP($\text{C}_{10}(\text{C}_3 \cdot \text{Pyr} \cdot \text{C}_3)$)], (9a), (10a), and (11a) (897 mg, 46%). [Ether-BHP($\text{C}_{12}(\text{C}_3 \cdot \text{Pyr} \cdot \text{C}_3)$)], (9b), (10b), and (11b) (622 mg, 31%). [Ether-BHP($\text{C}_3 \cdot \text{C}_6\text{H}_4 \cdot \text{C}_3(\text{C}_3 \cdot \text{Pyr} \cdot \text{C}_3)$)], (9c), (10c), and (11c) (398 mg, 20%). [Ether-BHP($\text{C}_4 \cdot \text{C}_6\text{H}_4 \cdot \text{C}_4(\text{C}_3 \cdot \text{Pyr} \cdot \text{C}_3)$)], (9d), (10d), and (11d) (818 mg, 40%).

Isolation of 'Hanging Base' Porphyrins, Cross-trans-Linked Isomers (9).—In order to separate the three isomers (9), (10), and (11), their zinc complexes were prepared. A mixture of these porphyrins and zinc acetate in chloroform-acetic acid (1:1) was refluxed for ca. 5 min. The reaction mixture was evaporated to dryness and the residue was dissolved in chloroform. The organic solution was successively washed with water and aqueous sodium hydrogen carbonate and then dried (Na_2SO_4). After concentration the resulting metalloporphyrin solution was submitted to preparative silica gel t.l.c. and developed with chloroform-toluene (2:1 v/v). Three bands were obtained. The compounds were individually isolated with chloroform-methanol (100:5 v/v) and characterized by their ^1H n.m.r. spectra.

The two fastest moving bands which, sometimes, could not be clearly separated, corresponded to the adjacent-*trans*-linked and adjacent-*cis*-linked isomers in which the bridges bind two adjacent *meso*-phenyl groups. The slower moving band corresponded to the desired cross-*trans*-linked isomer (18) which was the major product of each reaction. This compound was dissolved in chloroform and stirred with an excess of trifluoroacetic acid for 5 min; the mixture was then washed with water and aqueous potassium carbonate and dried (Na_2SO_4). Evaporation of the solution gave the free-base porphyrin (9) which recrystallized from dichloromethane-methanol as a purple solid. The ^1H n.m.r. spectra of zinc complexes and free-base porphyrins are described in Table 2.

α -5,15-[2,2'-(Decamethyleneoxy)diphenyl]: β -10,20-[2,2'-[3,3'-(pyridine-3,5-diyl)dipropoxy]diphenyl]porphyrin, [ether-BHP($\text{C}_{10}(\text{C}_3 \cdot \text{Pyr} \cdot \text{C}_3)$)], (9a) (234 mg, 12%) (Found: C, 79.0; H, 6.2; N, 7.05. $\text{C}_{65}\text{H}_{61}\text{N}_5\text{O}_4$ requires C, 79.97; H, 6.30; N, 7.17%); λ_{max} (ϵ mmol l^{-1}) in toluene 421 (341), 514.5 (16.5), 548 (6.1), 591 (5.6), and 648 nm (2.4).

α -5,15-[2,2'-(Dodecamethyleneoxy)diphenyl]: β -10,20-[2,2'-[3,3'-(pyridine-3,5-diyl)dipropoxy]diphenyl]porphyrin, [ether-BHP($\text{C}_{12}(\text{C}_3 \cdot \text{Pyr} \cdot \text{C}_3)$)], (9b) (200 mg, 10%) (Found: C, 79.35; H, 6.55; N, 6.95. $\text{C}_{67}\text{H}_{65}\text{N}_5\text{O}_4$ requires C, 80.13; H, 6.52; N, 6.97%); λ_{max} (ϵ mmol l^{-1}) in toluene 420 (330), 514.5 (16.3), 548 (5.5), 591 (5.0), and 648 nm (2.1).

α -5,15-[2,2'-[3,3'-(*p*-Phenylene)dipropoxy]diphenyl]: β -10,20-[2,2'-[3,3'-(pyridine-3,5-diyl)dipropoxy]diphenyl]

porphyrin, [ether-BHP(C₃·C₆H₄·C₃)(C₃·Pyr·C₃)] (**9c**) (190 mg, 9.55%) (Found: C, 80.3; H, 5.6; N, 6.9. C₆₇H₅₇N₅O₄ requires C, 80.78; H, 5.76; N, 7.03%); λ_{\max} . (ε mmol l⁻¹) in toluene 421 (351), 515 (16.9), 549 (6.0), 591 (5.3), and 647.5 nm (2.2).

α-5,15-{2,2'-[4,4'-(*p*-Phenylene)dibutoxy]diphenyl}:β-10,20-{2,2'-[3,3'-(pyridine-3,5-diyl)dipropoxy]diphenyl}-porphyrin, [ether-BHP(C₄·C₆H₄·C₄)(C₃·Pyr·C₃)] (**9d**) (305 mg, 14.9%) (Found: C, 80.25; H, 5.95; N, 6.8. C₆₉H₆₁N₅O₄ requires C, 80.91; H, 6.00; N, 6.84) λ_{\max} . (ε mmol l⁻¹) in toluene 420.5 (359), 514.5 (17.4), 548 (6.0), 590.5 (5.4), and 647 nm (2.4).

α-5,15:β-10,20-Bis{2,2'-[3,3'-(pyridine-3,5-diyl)dipropoxy]diphenyl}porphyrin. [ether-BHP(C₃·Pyr·C₃)₂] (**21**).—A solution of the dibromopyridine derivative (**8**) (2.4 g, 6 mmol) in dry dimethylformamide (100 ml) was added dropwise during 4 h to a mixture of 5,10,15,20-tetrakis(*o*-hydroxyphenyl)porphyrin (**1**) (2.03 g, 3 mmol) and an excess of potassium carbonate (6 g) in the same solvent (300 ml) at 100 °C. After 10 h of stirring under nitrogen at the same temperature, the solution was allowed to cool to ambient temperature. The undissolved material was filtered off and the filtrate was evaporated to dryness under reduced pressure. The residue was dissolved in toluene. A new precipitate was obtained which was filtered off. The filtrate was subjected to column chromatography (silica gel, 3 × 15 cm). Elution with CH₂Cl₂-acetone (1:1 v/v) afforded a red fraction. Purple crystals were obtained from slow evaporation of the eluates. They were filtered off, washed with acetone, and identified as the pure adjacent-*trans*-linked isomer (132 mg). The resulting filtrate was evaporated to dryness and the residue was taken up with acetone. An additional 20 mg of insoluble adjacent-*trans*-linked isomer was again obtained (total yield 5.1%). The acetone solution was evaporated to dryness and the solid was crystallized from CH₂Cl₂-MeOH to eliminate unchanged pyridine derivative. The crystalline red product was dissolved in chloroform and submitted to preparative silica gel t.l.c. with toluene-methanol (100:10 v/v) as developer. The major band was recovered. The solid was recrystallized from CH₂Cl₂-MeOH to give 215 mg (7.2%) of the desired cross-*trans*-linked isomer (**21**) (Found: C, 74.7; H, 5.6; N, 7.8. C₆₆H₅₆N₆O₄·CH₂Cl₂ requires C, 74.4; H, 5.4; N, 7.8%); λ_{\max} . (ε mmol l⁻¹) (CH₂Cl₂) 422 (321.2), 517 (16.4), 552 (7), 592 (5.3), and 648 (2.8).

Hydroxy-iron(III) Complexes of Cross-trans-linked Isomers (**19**).—A solution of free-base porphyrin (**9**) (0.1 mmol) and 2,6-dimethylpyridine (0.1 ml) in dimethylformamide (5 ml) was refluxed under argon. Anhydrous iron(II) chloride (0.5 mmol) in dimethylformamide (5 ml) was added. Insertion of iron was monitored by observation of the disappearance of the absorption band at 648 nm of the free-base porphyrin. The mixture was evaporated to dryness and the residue was dissolved in chloroform. The organic solution was successively washed with water (× 3), HCl (0.1M) and water, then dried (Na₂SO₄). The solution was reduced to a small volume and adsorbed on preparative silica-gel plates. Elution with water saturated ethyl acetate gave a major band. This was extracted with chloroform-methanol (100:10 v/v) and the resulting solution was evaporated to dryness. The metalloporphyrin was dissolved in toluene, vigorously shaken with aqueous sodium carbonate and dried (K₂CO₃). Iron(III) porphyrins were precipitated upon addition of hexane as hydroxy derivatives (**19**).

*Chloroiron(III)-Ether-[BHP(C₃·Pyr·C₃)₂] (**22**)*.—A solution of anhydrous iron(II) chloride (0.4 mmol) in dimethylformamide was added to a mixture of (**21**) (109 mg, 0.1 mmol) and 2,6-dimethylpyridine (0.1 ml) in the same solvent (5 ml). The mixture was refluxed with stirring under argon for 2 h. The solution was allowed to cool to ambient temperature. During

this time a part of iron(II) complex was crystallized. It was filtered off and washed with chloroform. The crystals were dissolved in chloroform-methanol-HCl and the solution then successively washed with water, aqueous sodium hydrogen carbonate, and water and dried (Na₂SO₄). This solution was added to the filtrate and evaporated to dryness. The crude metalloporphyrin was submitted to preparative silica-gel t.l.c. with CH₂Cl₂-MeOH (100:10 v/v) as developer. The major fraction was collected, dissolved in methylene chloride, and the solution washed with a saturated aqueous NaCl, dried (Na₂SO₄), and evaporated to dryness. The resulting solid was recrystallized from CH₂Cl₂-hexane to yield 64 mg (60%) of the chloroiron(III) porphyrin (**21**).

*Iron(II) Complexes of 'Hanging Base' Porphyrins (**20**)(**23**)*.—These compounds were prepared in toluene, benzene, or methylene chloride solution from iron(III) complexes according to the previously described method⁷ or by reduction by zinc amalgam under argon. The electronic absorption and ¹H n.m.r. spectra of iron(III) and iron(II) complexes of cross-*trans*-linked isomers are described in Tables 1 and 2.

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