Both-faces Hindered Porphyrins. Part 1. Synthesis and Characterization of Basket-handle Porphyrins and Their Iron Complexes

Michel Momenteau,* Joël Mispelter, Bernard Loock, and Emile Bisagni
Institut Curie, Section de Biologie, U. 219 Inserm, Bâtiment 112, Centre Universitaire, 91405 Orsay Cédex, France

The synthesis of the 'both-faces' hindered porphyrins using two different methods is reported. These so-called 'basket-handle' porphyrins (BHP) are derived from 5,10,15,20-tetraphenylporphyrin in which two opposite phenyl groups are bridged by alkylene or arylene-*p*-bisalkylene chains. In addition to the desired compounds [the cross-*trans*-linked isomer (7)], two other isomers were obtained [adjacent-*trans*-linked (8) and adjacent-*cis*-linked (9)]. These were separated by t.l.c. on silica gel and then individually characterized. The structural assignment of the three isomers in the five series studied was based on the ^{1}H n.m.r. spectra of the free bases and of their iron(II) complexes.

Iron(II) porphyrins are known to react with oxygen to form irreversible μ-oxo-iron(III) dimers.[1] In this well-established autoxidation mechanism, which involves several steps, the first and determining one is the attack of a second haem on the dioxygen complex. To inhibit these bimolecular reactions, different approaches have been developed to synthesize compounds in which protection of the dioxygen-binding site is provided by steric hindrance. Such structures must have a similar effect to that of the protein in natural oxygen carriers which forms an hydrophobic pocket around the haem and inhibits the contact necessary for oxidation reactions.

The best known systems developed to prevent such undesirable reactions are 'one-face' hindered iron(II) porphyrins ('picket-fence',[2] 'capped',[3] and 'bridged'[4] porphyrins). These are able to bind oxygen reversibly in the presence of coordinating bases. However, in the absence of the base, these iron(II) complexes have a very short lifetime in organic solvents at room temperature because the μ-oxo-dimer can still be formed on the unprotected side of the haem. Even in the presence of an organic base, the lifetime of the dioxygen species depends largely upon the nature and the concentration of the base.

In a preliminary communication [5] we reported that a much better stability towards oxidation of the haem can be obtained by steric hindrance of both faces of the porphyrin. These new compounds, so called 'basket-handle' porphyrins, are 5,10,15,20-tetraphenylporphyrin derivatives in which the two opposite *meso*-phenyl groups (5,15 and 10,20) are bridged by a convenient chain [structure (7)]. Their iron(II) complexes exhibited a remarkable stability towards oxidation, even at room temperature, because of protection which inhibits completely the dimerization process, but still permits fixation of a nitrogenous base and oxygen on the central metallic ion. The synthesis and characterization of these compounds, which possess alkylene or arylene-*p*-bisalkylene basket-handle bridged chains, and of their iron complexes are now fully described.

Synthesis of the Basket-handle Porphyrins (BHP).—The basket-handle porphyrins (7a—e) are designed to give systematic structural variation of their bridged chains. Thus, (7a), (7b), and (7c) correspond to polymethylene derivatives $(CH_2)_n$ (n = 10 to 12), while (7d), and (7e) have a central phenylene group which is connected to opposite *meso*-phenyl substituents of the porphyrin by two polymethylene chains, $(CH_2)_n$ (n = 3 and 4).

Two different approaches were used to obtain these compounds.

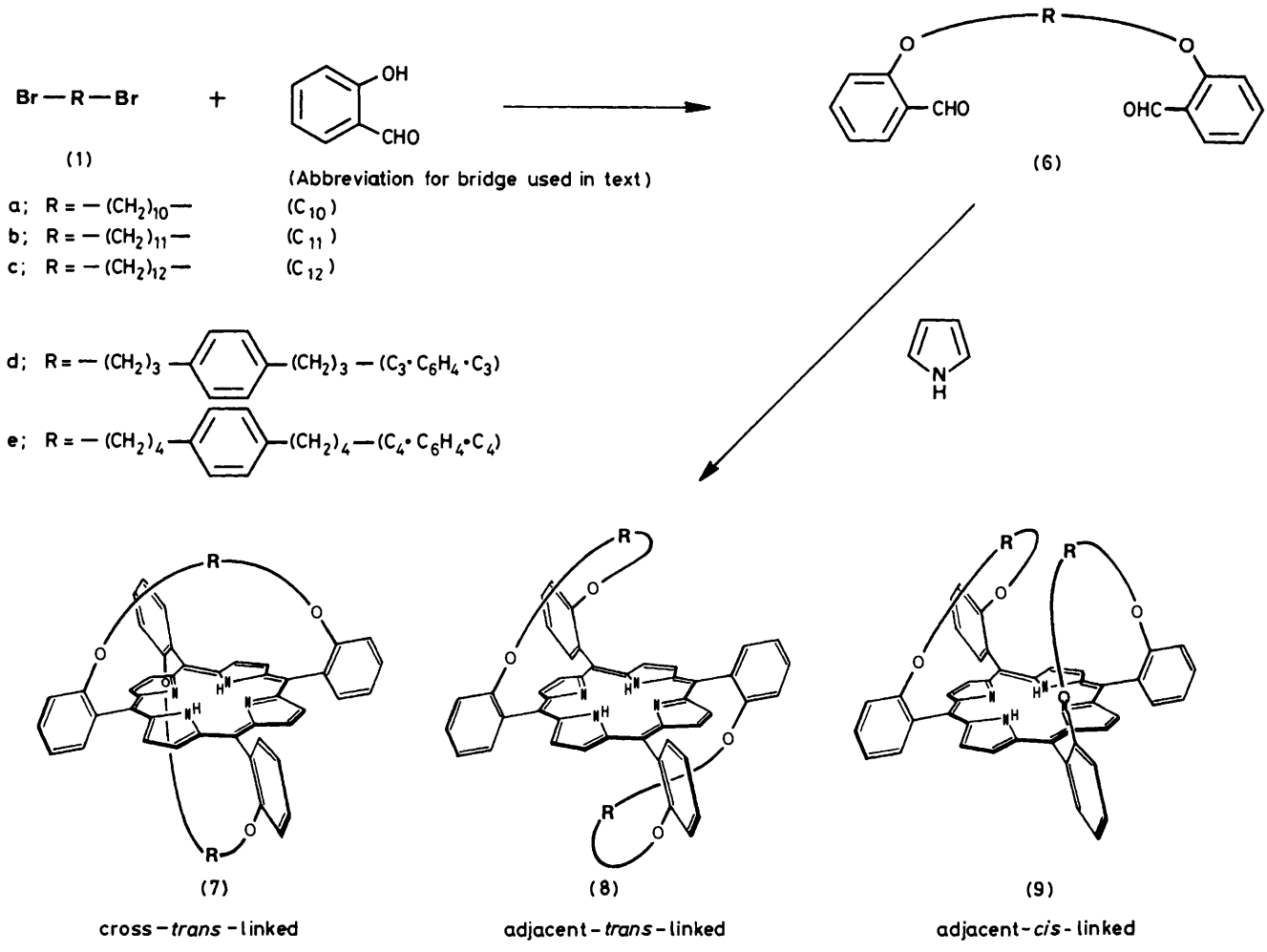
(*a*) One route involves direct acid condensation of the dialdehyde derivatives (6) with pyrrole (Scheme 1). Dialdehydes (6a—e) were obtained by condensation of the sodium salt of salicylaldehyde with commercially available dibromoalkyl derivatives (1a), (1b), and (1c) and with *p*-(dibromoalkyl)benzene derivatives (1d) and (1e). Compound (1d) has already been described; [6] (1e) was obtained from this compound *via* cyanuratic n into the corresponding nitrile (2), subsequent hydrolysis by the usual KOH–H_2O method, esterification, lithium aluminium hydride reduction, and finally bromination with PBr_3, in an overall yield of 69.8%. Several attempts at cyclisation by Treibs and Haberle's method [7] in acetic acid–pyridine were unsuccessful, but the dialdehyde derivatives (6a—d) gave the expected porphyrins *via* condensation with pyrrole by refluxing in propionic acid, the classic method of Adler *et al.*[8]

After the polymeric material had been filtered off and the reaction solvent evaporated to dryness, analytical t.l.c. on silica gel of the residue showed that three different porphyrins were present in each preparation. Chloroform extracts were then chromatographed on a silica-gel column in order to separate the crude porphyrins from residual black tarry compounds which remained on the gel. The three expected isomers were separated by preparative t.l.c. on silica gel (toluene–cyclohexane, 3 : 1 v/v). Pure fractions were finally crystallized from chloroform–methanol as purple crystals. The identification and structural assignments of these isomers were based on their ^{1}H n.m.r. spectra and on their iron complex formation and properties (see below).

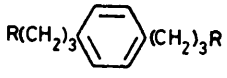
The first band which was the least polar porphyrin was identified as the cross-*trans*-linked isomer (7). Isomers (8) and (9) in which the bridges bind two adjacent *meso*-phenyl groups corresponded to the second and third bands respectively. It should be noted that the undesirable adjacent-*cis*-linked isomers (9), which are one-face hindered porphyrins, were frequently the predominant compounds.

(*b*) In order to obtain the most interesting isomers (cross-*trans*-linked) in higher yields, a second method was investigated.[9] It involved the formation of the basket handles at a later step than the porphyrin-forming condensation (Scheme 2). Thus, the mixture of the four atropisomers (αααα, ααaβ, αβαβ, and ααββ) [10] of 5,10,15,20-tetrakis(*o*-hydroxyphenyl)-porphyrin (11) was used as the starting material. This last compound, however, was obtained in low yield by the standard acid condensation of pyrrole with *o*-salicylaldehyde, because of the difficulty of extracting the porphyrin from the reaction mixture and purifying it further. We then decided to investigate the preparation of compound (11) from 5,10,15,20-tetrakis(*o*-methoxyphenyl)porphyrin (10).

On the condensation of pyrrole with *o*-methoxybenzalde-



Scheme 1



(1d) R = Br
(2) R = CN
(3) R = CO_2H
(4) R = $CO_2C_2H_5$
(5) R = CH_2OH
(1e) R = CH_2Br

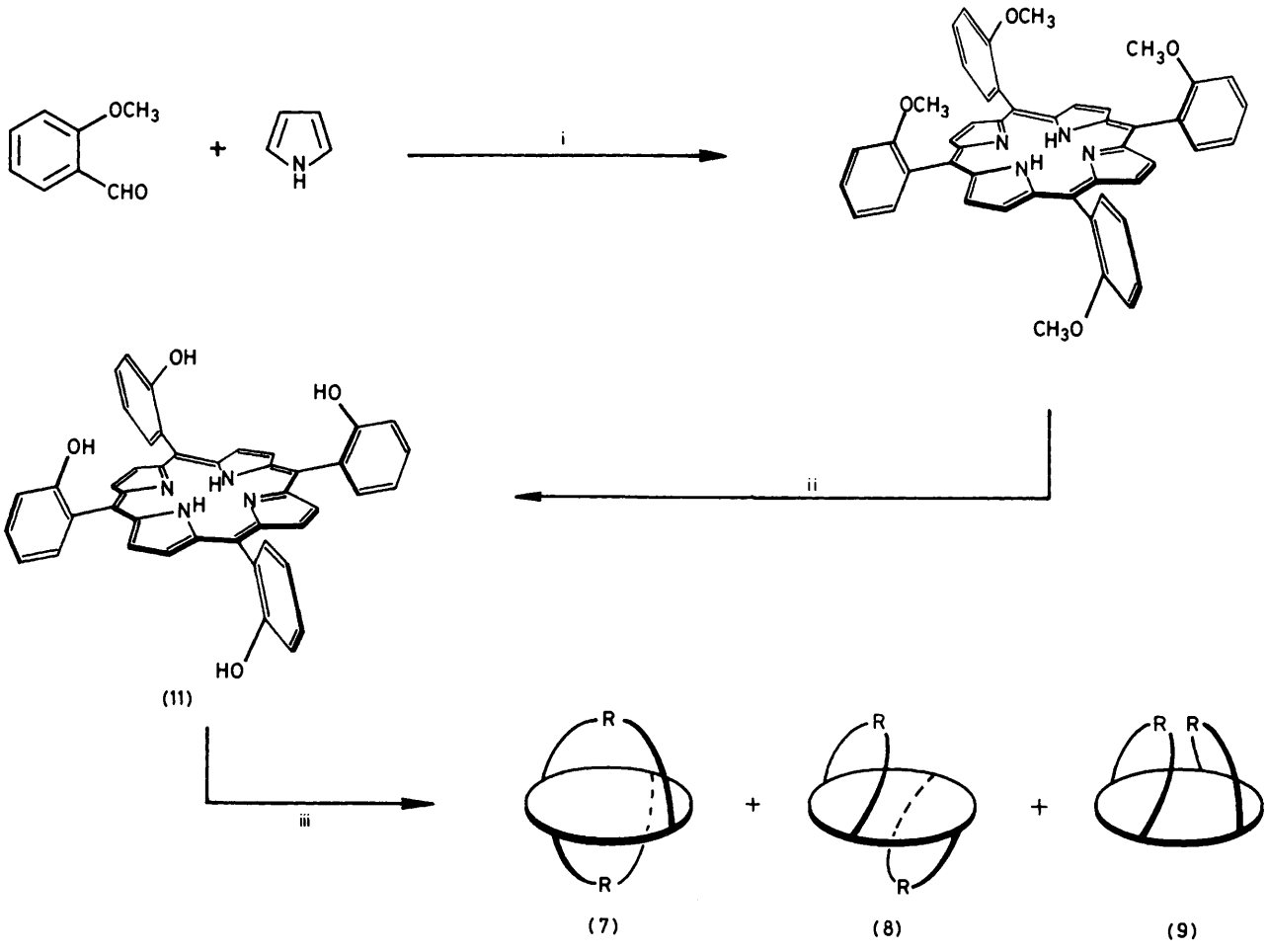
hyde in the presence of an excess of $Zn(OAc)_2 \cdot 2H_2O$, the solid metalloporphyrin precipitated from the cooled propionic acid solution. Chromatography and zinc-complex demetallation under relatively mild conditions gave the corresponding crystallized free base (10) in 10% yield. Demethylation in boiling pyridine hydrochloride afforded the porphyrin (11) in 93% yield with high purity (shown by analytical t.l.c.).

Basket-handle porphyrins were then easily prepared by coupling the dibromo-derivatives (1) with the porphyrin (11) under conditions of high dilution. This condensation was performed in dimethylformamide at 100 °C in the presence of an excess of anhydrous potassium carbonate. After similar work-up to that used in the first method, the three porphyrin isomers (7), (8), and (9) were isolated, but in this case the major product of each reaction was the desired cross-*trans*-linked isomer (7).

Reaction of the both-faces hindered porphyrins (7) and (8) with iron(II) acetate in acetic acid did not give the corresponding iron complexes. A new procedure was used for the direct insertion of iron using anhydrous iron(II) bromide or chloride and pyridine for neutralization of the acid formed. The reaction is slow and must be performed in dimethylformamide under reflux overnight. In contrast the classic metallation of the one-face hindered porphyrins (9) with iron(II) acetate in acetic acid–chloroform was performed successfully. Nearly quantitative yields of chloro-iron(III) complexes were obtained after usual treatment of the solutions, chromatography on silica gel, and crystallization.

The reduction of haemins with aqueous sodium dithionite under anaerobic conditions, in a two-phase system ($C_6H_5CH_3$–H_2O) [11] gave orange compounds. The three reduced isomers are assigned to intermediate spin state four-co-ordinated species [5,12] by electronic absorption and ^1H n.m.r. spectra.

Characterization of the Basket-handle Porphyrins.—Whatever the method of preparation used, three isomers are obtained for the basket-handle porphyrins, depending on which of the *meso*-phenyl rings are linked by the two chains. With two opposite *meso*-phenyl rings (5,15 and 10,20) linked by a chain, it is highly improbable that the second chain can link the remaining two opposite *meso*-phenyl rings on the same side of the porphyrin because of the evident steric considerations. This situation leads therefore to only one cross-*trans*-linked isomer (7). On the other hand, if two adjacent *meso*-phenyl groups (5,10 and 15,20) are bridged, the second chain can link



Scheme 2. *Reagents*: i, $Zn(OAc)_2 \cdot 2H_2O$ then HCl; ii, pyridine–HCl; iii, Br–R–Br(1)

the two adjacent remaining phenyls either on the opposite or on the same side of the porphyrin, leading to the adjacent-*trans*-linked (8) and adjacent-*cis*-linked (9) isomers, respectively.

The electronic spectra of these three isomers differ only slightly, and their identification therefore requires at least an examination of their ^1H n.m.r. spectra; these were recorded for the free-base forms and also for their intermediate spin ($s = 1$) iron(II) complexes [5,12] for which the large spread of the resonances, due principally to the large anisotropic magnetic susceptibility,[12,13] provided confirmation of the structure of these isomers. The ^1H n.m.r. spectra of the three isomers are governed by their symmetry properties. Because of the D_{2d} symmetry of isomer (7), the eight pyrrolic protons are expected to be equivalent. Also, the symmetry planes contain the bridges implying that the two protons of each methylene of the chains must be equivalent. In contrast, isomers (8) and (9) have, respectively, C_{2h} and C_{2v} symmetries implying that the pyrrole proton resonances should appear as two lines each corresponding to four equivalent protons carried by the opposite pyrrole rings. Also, the two protons of each methylene of the bridge could be no longer equivalent except for freely rotating groups. These considerations allow therefore isomer (7) to be distinguished simply from isomers (8) and (9). It was indeed observed that the two protons of the α-methylene groups (Figure) which are well separated from the other methylene resonances in the ^1H n.m.r. spectra of the free bases, are non equivalent, the largest difference being found for $[BHP(C_3 \cdot C_6H_4 \cdot C_3)_2]$ (Table). This non-equivalence was also clearly resolved for all the methylenes in the planar iron(II) paramagnetic complexes of these compounds.[5]

Only one exception was found to these rules, for $[BHP(C_{11})_2]$ for which the pyrrolic protons and α-methylene protons appear equivalent in the n.m.r. spectra of both isomers (7) and (9). In addition, the n.m.r. data cannot separate unambiguously the two isomers (8) and (9). Their respective assignment can be, however, obtained by chemical arguments based on the properties of the iron complexes. First, it has been mentioned in the preceding section that incorporation of iron in the both-faces hindered porphyrins [isomers (7) and (8)] is impossible by the conventional methods, whereas when these are applied to the one-face hindered isomers (9), the corresponding iron complexes are easily obtained. This property of metal incorporation allowed therefore the separation of the two ambiguous isomers for $[BHP(C_{11})_2]$ and of isomers (8) and (9) of all the other porphyrin derivatives. On the other hand, treatment of the iron(III) complexes with sodium hydroxide or reoxidation of a toluene solution of reduced iron(II) porphyrins leads only to a high-spin ferric species for isomers (7) and (8) which are well characterized by their ^1H n.m.r. spectra (^1H pyrrole around 80 p.p.m.[14]), whereas isomer (9) provides a variable mixture of high-spin and μ-oxo-dimeric species characterized by pyrrolic proton resonances at 13.8 p.p.m.[14] Finally, the oxidation time of iron(II) complexes is much longer for the both-faces hindered isomers (7) and (8) than for isomer (9),[5] for which a bimolecular reaction could be involved in the oxidation process.[1]

The ^1H n.m.r. data in the Table show some characteristic

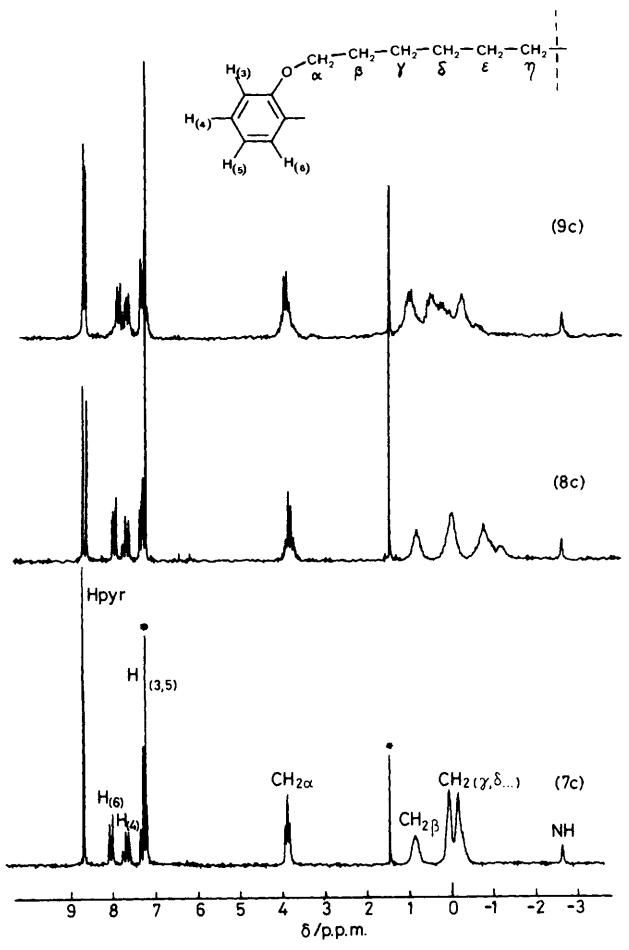


Figure. ^{1}H N.m.r. spectra of the three isomers, cross-*trans*-linked (7c), adjacent-*trans*-linked (8c) and adjacent-*cis*-linked (9c) of bis-dodecamethylene basket-handle porphyrin [BHP(C_{12})$_2$]. The assignment is shown on the Figure

features reflecting the structure of these compounds. Because of the ring current of the porphyrin, all the resonances of the methylene groups, except for the α-groups, and those of the phenylene protons in [BHP(C_3·C_6H_4·C_3)$_2$] and [BHP(C_4·C_6H_4·C_4)$_2$] are significantly shifted to high field relative to the corresponding dialdehyde compounds, indicating that the linking chains are indeed above and below the porphyrin plane. This ring-current shift reaches 3.25 p.p.m. for the phenylene protons of [BHP(C_3·C_6H_4·C_3)$_2$].

We have attempted to use the ring-current model of Abraham *et al.*[15] for a quantitative determination of the stereochemical structure of the chains from the ^{1}H and ^{13}C n.m.r. data. No conclusion can be drawn from these calculations because of the probable presence of a large number of possible conformations for the chains when the porphyrins are in solution. However, for the most interesting cross-*trans*-linked isomer (7) some general features can be drawn.

First, the resonance of 6-H of the *meso*-phenyl ring (Figure) is clearly related to the length of the bridging chains (Table). It is at δ 8.35 and 8.39 for compounds (7a) and (7d) and 8.08 and 8.07 for compounds (7c) and (7e), whereas it is at δ 8.0 and 7.98 for the starting materials (10) and (11). This variation depends only on the carbon-chain length and should be related to the tension imposed on the porphyrin skeleton by the linking chains. This tension effect is also reflected in the position of the resonances for the NH pyrrolic protons, which is largely dependent on the length of the chains. The order of increasing high-field shifts is (7a) < (7b) < (7c) (Table). However the corresponding shifts in the compounds containing the aryl chains (7d) and (7e) are significantly different and are related to the ring current produced by the phenyls above and below the porphyrin ring. The corresponding effect is 0.34 p.p.m. ($\delta_{7a} - \delta_{7d}$) and 0.29 p.p.m. ($\delta_{7c} - \delta_{7e}$) to low field. The direction of this effect indicates that the phenyl rings must be principally perpendicular to the porphyrin plane. Assuming this structure, we caculated from the ring-current shift of the phenyl protons (3.2 p.p.m.), using the model of Abraham *et al.*[15] for 5,10,15,20-tetraphenylporphyrin, that the centre of the phenyl ring is *ca.* 4.9 Å from the porphyrin plane in (7d). Thus, the two phenyl rings contribute to 2 × 0.20 p.p.m. for the NH pyrrolic protons, as calculated by the Johnson and Bovey model,[16] in approximate agreement with experiments.

Such a conformation, but with the phenyl ring elevated by *ca.* 1 Å, is also deduced from both the ^{1}H and ^{13}C n.m.r. data of the square planar iron(II) complex of (7d). In that case, the paramagnetic shift which results from the large anisotropic magnetic susceptibility [12] is one order of magnitude larger than the ring-current shift allowing more precision in the determination of the structure. The paramagnetic shifts observed for the quaternary and other carbons of the phenylene groups, referenced to the diamagnetic dication, are 28.5 and 49.8 p.p.m. respectively at 34 °C. The corresponding phenyl proton shift is 56.2 p.p.m.[12] Using the known magnetic anisotropy for this complex,[12] we found that the centre of the phenyl ring must lie 6 Å (not 3 Å as quoted earlier [12]) from the porphyrin plane, for which the following values for the paramagnetic shifts are calculated: 28.9, 40.5, and 54 p.p.m. (comparable with the observed values). It should be mentioned here that the phenyl ring cannot be parallel to the porphyrin plane as in the case of the free-base porphyrin. In such a structure the two carbon shifts would be equal and the proton shift would be lower than those of the carbons, in complete disagreement with experiment.

This structural behaviour should be considered for an interpretation of the kinetic parameters for the fixation of small axial ligands (O_2, CO, *etc.*) on the pentaco-ordinated iron(II) complexes of porphyrins derived from the cross-*trans*-linked isomers (7). The synthesis and the physicochemical properties of these new compounds will be reported elsewhere.

Experimental

All chemicals used were of reagent grade and were purchased from Aldrich. Dried dimethylformamide was distilled and kept over 4 Å molecular sieve. For t.l.c. separation throughout this work, Merck silica gel 60 (70—230 mesh) and precoated preparative t.l.c. plates (silica gel 60, 2 mm) were used. Optical spectra in the Soret and visible region were recorded using a Varian-Techtron 635 spectrophotometer. Proton n.m.r. spectra of free-base porphyrins and their iron(II) complexes in deuteriochloroform and [$^2H_8$]toluene respectively (C.E.A., France) were measured using a Varian XL-100 spectrometer in the Fourier transform mode using 4 K data points in the frequency domain. Chemical shifts were referenced to internal tetramethylsilane.

1,4-*Bis*(3-*bromopropyl*)*benzene* (1d).—This compound was synthesized and purified according to the published procedure.[6]

1,4-*Bis*(4-*bromobutyl*)*benzene* (1e).—1,4-Bis(4-cyanopropyl)benzene (2) was obtained by cyanuration of the bromo-compound (1d) according to the usual procedure (98%), m.p. 55.5 °C. The corresponding dicarboxylic acid (3) (79%) was obtained by acidic hydrolysis, m.p. 175 °C. The diester (4)

^{1}H N.m.r. spectra of porphyrins in $CDCl_3$ at 34 °C (δ in p.p.m.)

			meso-Phenyl [a]				Phenylene-	Methylene [a]						
		H_{pyr} [a]	6-H	4-H	3-H	5-H	H	α	β	γ	δ	ε	η	NH
TMPP [b] (10)		8.73	8.0	7.75	7.35			8.62	8.58	8.56	(OCH_3)			−2.58
THPP [c] (11)		8.93	7.98	7.75	7.35									−2.71 (v br)
[BHP(C_{10})$_2$]	CT [d] (7a)	8.75	8.35	7.73	7.23	7.43		3.68	0.68	0.5	to	−1.1		−2.45
	AT [e] (8a)	8.74—8.70	7.90	7.71	7.32			3.92	1.00	0.2	to	−0.4		−2.62
	AC [f] (9a)	8.74—8.70	7.91	7.71	7.32			3.92	1.00	0	to	−0.6		−2.58
[BHP(C_{11})$_2$]	CT (7b)	8.73	8.21	7.73	7.3			3.78	0.76	−0.3	−1.0	−0.3	−1.0	−2.55
	AT (8b)	8.73—8.71	7.98	7.72	7.3			3.84	0.93	0	to	−1.4		−2.52
	AC (9b)	8.72	7.99	7.72	7.3			3.97	1.10	0.3	to	−1.4		−2.51
[BHP(C_{12})$_2$]	CT (7c)	8.73	8.08	7.72	7.3			3.91	0.89	0.1	to	−0.2		−2.62
	AT (8c)	8.76—8.66	7.99	7.72	7.34			3.86	0.86	0	to	−1.2		−2.59
	AC (9c)	8.74—8.70	7.89	7.72	7.28			3.94	1.03	0.5	to	−0.5		−2.60
[BHP(C_3·C_6H_4·C_3)$_2$]	CT (7d)	8.78	8.39	7.72	7.17	7.41	3.90	3.49	0.80	1.26				−2.11
	AC (9d)	8.89—8.70	8.01	7.72	7.36		3.89	3.89	1.25					−2.34
								3.44						
[BHP(C_4·C_6H_4·C_4)$_2$]	CT (7e)	8.76	8.07	7.72	7.31		4.06	3.89	0.81	0.41	1.33			−2.33
	AT (8e)	8.74—8.67	8.04	7.71	7.21	7.31	4.10	3.80	1.3	to	0.2			−2.35
	AC (9e)	8.74—8.62	7.86	7.71	7.31		5.0	3.88	1.8	to	0.8			−2.53

[a] The assignment is shown on the Figure. [b] TMPP = 5,10,15,20-tetrakis(*o*-methoxyphenyl)porphyrin. [c] THPP = 5,10,15,20-tetrakis(*o*-hydroxyphenyl)porphyrin. [d] CT = cross-*trans*-linked isomer. [e] AT = adjacent-*trans*-linked isomer. [f] AC = adjacent-*cis*-linked isomer.

obtained from (3) was not isolated. It was converted into the diol (5) by lithium aluminium hydride reduction (89%), m.p. 62 °C. The title compound (89%) was obtained by subsequent bromination with PBr_3, m.p. 39 °C (lit.,[17] m.p. 39.5–40.5 °C).

General Method for the Preparation of the Dialdehyde Derivatives (6).—Salicylaldehyde (16 ml, 0.15 mol) was dissolved in an alcoholic solution of potassium hydroxide (1M; 150 ml) and the dibromo-compound (1) (0.05 mol) was added. The solution was heated under reflux overnight. The mixture was cooled to room temperature and filtered. The filtrate was cooled to 0 °C and the precipitated dialdehyde (6) was collected and recrystallized from ethanol.

1,10-*Bis*(2-*formylphenoxy*)*decane* (6a).—This compound (15.1 g, 79%) had m.p. 67 °C (Found: C, 75.2; H, 8.0. $C_{24}H_{30}O_4$ requires C, 75.36; H, 7.91%); δ($CDCl_3$) 10.5 (d, *J* 0.7 Hz, 2 × ArCHO), 7.84 (q, 2 × H, *o*-H to aldehyde), 7.54 (m, 2 × H, *p*-H to aldehyde), 7.02 (m, 4 × H, *m*-H to aldehyde), 4.09 (t, *J* 6.25 Hz, 2 × ArOC$H_2$$CH_2$), 1.86 (br m, 2 × ArOCH$_2CH_2$$CH_2$), and 1.38 (br, 6 × methylene).

1,11-*Bis*(2-*formylphenoxy*)*undecane* (6b).—This compound (16.5 g, 83.6%) had m.p. 51.5 °C (Found: C, 75.5; H, 8.1. $C_{25}H_{32}O_4$ requires C, 75.73; H, 8.13%); δ ($CDCl_3$) 10.5 (d, *J* 0.6 Hz, 2 × ArCHO), 7.84 (q, 2 × H, *o*-H to aldehyde), 7.53 (m, 2 × H, *p*-H to aldehyde), 7.02 (m, 4 × H, *m*-H to aldehyde), 4.09 (t, *J* 6.25 Hz, 2 × ArOC$H_2$$CH_2$), 1.86 (br m, 2 × ArOCH$_2CH_2$$CH_2$), and 1.35 (br, 7 × methylene).

1,12-*Bis*(2-*formylphenoxy*)*dodecane* (6c).—This compound (17.9 g, 87%) had m.p. 80 °C (Found: C, 75.9; H, 8 4. $C_{26}H_{34}O_4$ requires C, 76.06; H, 8.35%); δ($CDCl_3$) 10.5 (d, *J* 0.6 Hz, 2 × ArCHO), 7.84 (q, 2 × H, *o*-H to aldehyde), 7.54 (m, 2 × H, *p*-H to aldehyde), 7.02 (m, 4 × H *m*-H to aldehyde), 4.09 (t, *J* 6.25 Hz, 2 × ArOC$H_2$$CH_2$), 1.86 (br m, 2 × ArOCH$_2CH_2$$CH_2$), and 1.32 (br, 8 × methylene).

1,4-*Bis*[3-(2-*formylphenoxy*)*propyl*]*benzene* (6d).—This compound (15.7 g, 78.1%) had m.p. 78 °C (Found: C, 77.3; H, 6.55. $C_{26}H_{26}O_4$ requires C, 77.59; H, 6.51%); δ($CDCl_3$) 10.5 (d, *J* 0.6 Hz, 2 × ArCHO), 7.85 (q, 2 × H, *o*-H to aldehyde), 7.53 (m, 2 × H, *p*-H to aldehyde), 7.15 (s, 4 × H, phenylene), 7.00 (m, 4 × H, *m*-H to aldehyde), 4.10 (t, *J* 6.15 Hz, 2 × ArO-C$H_2$$CH_2$), 2.84 (t, *J* 7.5 Hz, 2 × ArOCH$_2$CH$_2$CH_2-Ph), and 2.18 (m, 2 × ArOCH$_2$CH_2CH$_2$-Ph).

1,4-*Bis*[4-(2-*formylphenoxy*)*butyl*]*benzene* (6e).—This compound (18.4 g, 85.4%) had m.p. 87 °C (Found: C, 77.55; H, 7.0. $C_{28}H_{30}O_4$ requires C, 78.11; H, 7.02%); δ($CDCl_3$) 10.5 (d, *J* 0.5 Hz, 2 × ArCHO), 7.84 (m, 2 × H, *o*-H to aldehyde), 7.53 (m, 2 × H, *p*-H to aldehyde), 7.13 (s, 4 × H, phenylene), 7.00 (m, 4 × H, *m*-H to aldehyde), 4.10 (t, 2 × ArOC$H_2$$CH_2$), 2.69 (t, 2 × ArOCH$_2CH_2CH_2CH_2$-Ph), and 1.87 (m 2 × ArOCH$_2$-CH_2CH_2CH$_2$-Ph).

5,10,15,20-*Tetrakis*(o-*methoxyphenyl*)*porphyrin* (10).—A mixture of *o*-methoxybenzaldehyde (136 g, 1 mol) and ZnAc·2H_2O (55 g, 0.25 mol) in propionic acid (6 l) was warmed at 100 °C with vigorous stirring. Pyrrole (67 g, 1 mol) was then added and the resulting mixture was refluxed for 4 h. The solution was allowed to stand for 3 days, and the precipitate was then filtered off, washed with propionic acid and ethanol, and dried. Analytical t.l.c. on silica gel showed evidence of a chlorin compound.

The solid was dissolved in chloroform (400 ml), pyridine (30 ml) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone and the mixture was warmed at 40—50 °C until the absorption band of chlorin (622 nm) disappeared. The reaction mixture was then placed on a 6 × 35-cm silica gel column and eluted with chloroform. The first fraction contained the desired zinc compound. The chloroform eluates, diluted with 1.8 l of the same solvent, were successively washed with concentrated HCl, water and aqueous sodium hydrogen carbonate, dried (Na_2SO_4) and then evaporated to dryness. The free-base porphyrin was recrystallized from dichloromethane–methanol (1 : 1 v/v) to give a purple solid (18 g, 10%) (Found: C, 78.3; H, 5.25; N, 7.15. $C_{48}H_{38}N_4O_4$ requires C, 78.47; H, 5.18; N, 7.63%).

5,10,15,20-*Tetrakis*(*o-hydroxyphenyl*)*porphyrin* (11).—5,10,15,20-Tetrakis(*o*-methoxyphenyl)porphyrin (7.34 g, 10 mmol) was refluxed (220—225 °C) in pyridine hydrochloride (150 g) for 2 h. The mixture was poured into water (2 l) and the porphyrin was extracted with ethyl acetate. The organic solution was washed twice with hydrochloric acid (0.1M) and water and dried (Na_2SO_4). The crystalline compound was obtained by slow evaporation of a solution in dichloromethane–methanol (4 : 1 v/v) (6.42 g, 93%) (Found: C, 77.45; H, 4.25; N, 8.05. $C_{44}H_{30}N_4O_4$ requires C, 77.88; H, 4.42; N, 8.26%).

General Procedure for the Preparation of Basket-handle Porphyrins.—Method 1. The appropriate dialdehyde derivative (6) (30 mmol) and pyrrole (60 mmol) in propionic acid (500 ml) were heated under reflux for 4 h with vigorous stirring. The cooled solution was filtered to remove the polymeric material which was washed with chloroform. The combined filtrates were evaporated to dryness. The residue was dissolved in chloroform and filtered again. The organic solution was washed with water, aqueous sodium hydrogen carbonate and water, then dried (Na_2SO_4). After evaporation the residue was chromatographed on a silica-gel column (4 × 30 cm), equilibrated with toluene. Elution with the same solvent gave a red fraction which was a mixture of three compounds as shown by analytical t.l.c. (silica gel, toluene–cyclohexane 3 : 1 v/v). The following product mixtures were obtained. [BHP(C_{10})$_2$], (7a) + (8a) + (9a) (488 mg, 3.4%); [BHP(C_{11})$_2$], (7b) + (8b) + (9b) (669 mg, 4.55%); [BHP(C_{12})$_2$, (7c) + (8c) + (9c) (492 mg, 3.25%); [BHP(C_3·C_6H_4·C_3)$_2$], (7d) + (8d) + (9d) (130 mg, 0.90%); [BHP(C_4·C_6H_4·C_4)$_2$], (7e) + (8e) + (9e) (827 mg, 5.25%).

Method 2. A solution of the appropriate dibromoalkyl or dibromoaryl derivative (2) (12 mmol) in dry dimethylformamide (50 ml) was added dropwise during 4 h to a mixture of 5,10,15,20-tetrakis(*o*-hydroxyphenyl)porphyrin (11) (2 g, 3 mmol) and an excess of anhydrous potassium carbonate (4.8 g, 35 mmol) in the same solvent (100 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 taken up in chloroform and the organic layer was washed with water (× 3), dried (Na_2SO_4) and then evaporated to dryness. The residue was dissolved in toluene and subjected to column chromatography (silica gel, 4 × 30 cm). Elution with toluene afforded a red fraction which showed three compounds by analytical t.l.c (silica gel, toluene–cyclohexane 3 : 1 v/v). The following products were obtained. [BHP(C_{10})$_2$], (7a) + (8a) + (9a) (1.05 g, 36.8%); [BHP(C_{11})$_2$], (7b) + (8b) + (9b) (1.50 g, 50.4%); [BHP(C_{12})$_2$], (7c) + (8c) + (9c) (1.40 g, 46%); [BHP(C_3·C_6H_4·C_3)$_2$], (7d) + (8d) + (9d) (0.77 g, 25.7%); [BHP(C_4·C_6H_4·C_4)$_2$], (7e) + (8e) + (9e) (1.11 g, 35.2%).

Fractionation of Basket-handle Porphyrins by Preparative T.l.c.—The porphyrin mixtures were submitted to preparative silica gel t.l.c., developing with toluene–cyclohexane. Three bands were obtained and recovered separately. The least polar compound (band 1) was identified by n.m.r. spectroscopy as the cross-*trans*-linked isomer (7) (see text). The second compound was identified as the adjacent-*trans*-isomer (8). The most polar compound which had a low R_F (band 3), was identified as the adjacent-*cis*-linked isomer (9). All the porphyrins were crystallized from chloroform–methanol to give purple crystals. The n.m.r. spectra are described in the Table.

5,10 : 15,20- *and* 5,15 : 10,20-*Bis*[2,2′-(*decamethyleneoxy*)*diphenyl*]*porphyrin* [BHP(C_{10})$_2$].—The three isomers were separated by preparative t.l.c. (silica gel) with toluene–cyclohexane (3 : 1 v/v) (method, yield). α-(5,15) : β-(10,20)-*Porphyrin* (7a). (1, 0.25%; 2, 12.5%) (Found: C, 79.9; H, 6.9; N, 5.2. $C_{64}H_{66}N_4O_4$ requires C, 80.4; H, 7; N, 5.8%); $\lambda_{max.}$ (ε mmol l^{-1}) in toluene 419 (390), 513 (20.1), 546 (6.2), 591 (6.0), and 547 nm (2.8). α-(5,10) : β-(15,20)-*Porphyrin* (8a). (1, 0.3%; 2, trace) (Found: C, 80 2; H, 6.8; N, 5.7. $C_{64}H_{66}N_4O_4$ requires C, 80.4; H, 7; N, 5.8%); $\lambda_{max.}$ (ε mmol l^{-1}) (toluene) 419 (398), 513 (20.4), 546.5 (6.4), 591 (6.1), and 548 nm (2.9). α-(5,10) : α-(15,20)-*Porphyrin* (9a) (1, 2.4%; 2, 7.1%) (Found: C, 79.5; H, 6.9; N, 6.0. $C_{64}H_{66}N_4O_4$ requires C, 80.4; H, 7; N, 5.8%); $\lambda_{max.}$ (ε mmol l^{-1}) (toluene) 419 (366), 513 (19), 546.5 (6.8), 592 (5.6), and 549 nm (3).

5,10 : 15,20- *and* 5,15 : 10.20-*Bis*[2,2′-(*undecamethyleneoxy*)*diphenyl*]*porphyrin* (BHP(C_{11})$_2$].—The three isomers were obtained using the same chromatographic system (method, yield). α-(5,15) : β-(10,20)-*Porphyrin* (7b) (1, 0.20 %; 2, 27.1%) (Found: C, 80.3; H, 7.14; N, 5.6. $C_{66}H_{70}N_4O_4$ requires C, 80.6; H, 7.2; N, 5.7%); $\lambda_{max.}$ (ε mmol l^{-1}) 419 (397), 513 (20), 546 (6.5), 591 (6.5), and 645.5 nm (2.5). α-(5,10) : β-(15,20)-*Porphyrin* (8b) (1, 1.6%; 2, 2.6%) (Found: C, 80.5; H, 7.1; N, 5.7. $C_{66}H_{70}N_4O_4$ requires C, 80.6; H, 7.2; N, 5.7%); $\lambda_{max.}$ (ε mmol l^{-1} 419 (405), 513 (20.5), 546 (6.7), 591 (6.3), and 645.5 nm (2.4). α-(5,10) : α-(15,20)-*Porphyrin* (9b) (1, 2.6%; 2, 4.5%) (Found: C, 80.4; H, 7.1; N, 5.9. $C_{66}H_{70}N_4O_4$ requires 80.6; H, 7.2; N, 5.7%); $\lambda_{max.}$ (ε mmol l^{-1}) 419 (398), 513 (20.1), 546 (6.7), 591 (6.3), and 646 nm (3.0).

5,10 : 15,20- *and* 5,15 : 10.20-*Bis*[2,2′-(*dodecamethyleneoxy*)*diphenyl*]*porphyrin* [BHP(C_{12})$_2$].—Similar chromatography gave the following three isomers (method, yield). α-(5,15) : β-(10,20)-*Porphyrin* (7c) (1, 0.45%; 2, 22%) (Found: C, 79.6; H, 7.2; N, 5.2. $C_{68}H_{74}N_4O_4$ requires C, 80.7; H, 7.4; N, 5.5%); $\lambda_{max.}$ (ε mmol l^{-1}) 419 (409), 513 (20), 546 (6.1), 592 (6.3), and 647 nm (2.2). α-(5,10) : β-(15,20)-*Porphyrin* (8c) (1, 1.7%; 2, 5%) (Found: C, 80.7; H, 7.2; N, 5.7. $C_{68}H_{74}N_4O_4$ requires C, 80.7; H, 7 4; N, 5.5%); $\lambda_{max.}$ (ε mmol l^{-1}) 419 (376), 513 (19.2), 546 (6.6), 593 (6.9), and 648 nm (2.6). α-(5,10) : α-(15,20)-*Porphyrin* (9c) (1, 0.65%; 2, 3%) (Found: C, 80.2; H, 7.3; N, 5.5. $C_{68}H_{74}N_4O_4$ requires C, 80.7; H, 7.4; N, 5.5%); $\lambda_{max.}$ (ε mmol l^{-1}) 419 (365), 513 (17.9), 545 (6.6), 593 (7.5), and 648 nm (2.7).

5,10 : 15,20- *and* 5,15 : 10,20-*Bis*{2,2′-[3,3′-(p-*phenylene*)*dipropoxy*]*diphenyl*}*porphyrin* [BHP(C_3·C_6H_4·C_3)$_2$].—The column chromatography on silica gel of the crude compound (eluting with toluene) gave two bands which were not clearly separated. After evaporation of the two eluates, the residues were separately chromatographed on silica-gel plates (elution with toluene–cyclohexane 2 : 1 v/v). Band 1 contained essentially the cross-*trans*-linked isomer (7d). The most polar compound (trace) was identified as the adjacent-*trans*-linked isomer (8d). T.l.c. of band 2 gave only one major compound corresponding to the adjacent-*cis*-linked isomer (9d). Spectral data were as follows (method, yield). α-(5,15) : β-(10,20)-*Porphyrin* (7d) (1, 0.25%; 2, 23%) (Found: C, 8.0; H, 5.8; N, 5.4. $C_{68}H_{58}N_4O_4$ requires C, 82.1; H, 5.8; N, 5.6%); $\lambda_{max.}$ (ε mmol l^{-1}) 420 (387), 513.5 (18.8), 547 (6.3), 590 (5.8) and 647.5 nm (2.8). α-(5,10) : α-(15,20)-*Porphyrin* (9d) (1, 0.35 %; 2, 0.5%) (Found, C, 81.2; H, 5.9; N, 5.6. $C_{68}H_{58}N_4O_4$ requires C, 82.1; H, 5.8; N, 5.6%); $\lambda_{max.}$ (ε mmol l^{-1}) 419 (383), 512 (19.5), 545 (6.1), 589 (6.0), and 647.5 nm (2.9)

5,10 : 15,20- *and* 5,15 : 10,20-*Bis*{2,2′-[4,4′-(p-*phenylene*)*dibutoxy*]*diphenyl*}*porphyrin* [BHP(C_4·C_6H_4·C_4)$_2$].—After column chromatography on silica gel of the crude compounds, the toluene solution was concentrated, during which time a compound precipitated. The solid was collected and washed with 1,2-dichloroethane. A new precipitate was formed in the filtrate and was filtered off. The combined solid compounds correspond to only one porphyrin isomer, as shown by analytical t.l.c. (toluene–cyclohexane 2 : 1 v/v). Analyses by n.m.r. and other techniques described above showed that this compound corresponds to the adjacent-*trans*-linked isomer (8e). The combined filtrates were evaporated and chromatographed by preparative t.l.c. on silica gel, developing with toluene. Two bands were clearly separated and corresponded to the cross-*trans*-linked (7e) and the adjacent-*cis*-linked (9e) isomers, respectively. Spectral data are as follows (method, yield). α-(5,15) : β-(10,20)-*Porphyrin* (7e) (1, 0.45%; 2, 18.2%) (Found: C, 82.3; H, 6.2; H, 5.1. $C_{72}H_{66}N_4O_4$ requires C, 82.3; H, 6.3; N, 5.3%); $\lambda_{max.}$ (ε mmol l^{-1}) 419.5 (402), 512 (20.0), 546 (6.4), 591 (6.3), and 646 nm (2.9). α-(5,10) : β-(15,20)-*Porphyrin* (8e) (1, 3.15%; 2 9.6%) (Found: C, 82.2; H, 6.3; N, 5.4. $C_{72}H_{66}N_4O_4$ requires C, 82.3; H, 6.3; N, 5.3%); $\lambda_{max.}$ (ε mmol l^{-1}) 419.5 (410), 512 (20.5), 545 (5.9), 590 (5.8), and 646 nm (2.6). α-(5,10) : α-(15,20)-*Porphyrin* (9e) (1, 1%; 2, 1.8%) (Found: C, 81.7; H, 6.3; N, 5.6. $C_{72}H_{66}N_4O_4$ requires C, 82.3; H, 6.3; N, 5.3%); $\lambda_{max.}$ (ε mmol l^{-1}) 418.5 (403), 511.5 (20.2), 545 (6.0), 589.5 (5.9), and 647 nm (2.8).

Chloro-iron(III) *Complexes of Cross*-trans-*linked Isomers.*—A mixture of free-base porphyrin (1 mmol), pyridine (0.2 ml), and iron(II) bromide (5 mmol) in dimethylformamide (25 ml) was refluxed overnight under argon. 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 and then dried (Na_2SO_4). After concentration, the resulting solution was chromatographed on a silica-gel column. Elution with chloroform–methanol (10 : 1 v/v) afforded the iron(III) complex. Crystallization from dichloromethane–methanol containing dry HCl gave crystals of the chloro-iron(III) derivative.

Chloro-iron(III) *Complexes of Adjacent*-trans-*linked Isomers.*—These compounds were prepared and crystallized following the same procedure as the one used for the cross-*trans*-linked isomers.

Chloro-iron(III) *Complexes of Adjacent-cis-Linked Isomers.*—These one-face protected porphyrin complexes were prepared following the usual treatment of porphyrins with iron(II) acetate in acetic acid. The iron(III) complexes were chromatographed on a silica-gel column and eluted with chloroform–methanol (10 : 1 v/v). The eluate was washed with saturated aqueous sodium chloride and dried (Na_2SO_4). Crystallization from dichloromethane–methanol containing dry HCl gave crystals of chloro-iron(III) derivatives.

Iron(II) *Basket-handle Porphyrin Complexes.*—The reduction of chloro-iron(III) basket-handle porphyrins was perform-

ed in a heterogeneous mixture of water and toluene. Distilled water (10 ml) containing sodium dithionite and 10 ml of an organic solution of haemin were vigorously stirred under an atmosphere of argon for 10 min. After separation of the two phases, the organic layer containing the reduced compound was transferred under inert gas into the optical cell or n.m.r. tube *via* an inox tube.

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