Both-faces Hindered Porphyrins. Part 5.[1] Synthesis and Characterization of Iron(III) Basket Handle Porphyrins having Multiple Secondary Amide Groups inserted in the Superstructures

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The synthesis of basket handle porphyrins in a cross-*trans* configuration (**27**) and (**28**) derived from 5,10,15,20-tetrakis(*o*-aminophenyl)porphyrin, and their hydroxy-iron(III) complexes, in which one of the faces is hindered by a bridge substituted by one or two amino-acids (L-phenylalanine or L-valine) and with the other face protected by a hanging-imidazole chain is described. The synthetic methodology for these compounds allows the preparation of other superstructured porphyrins containing several amino acids in the handles; this gives an increasing number of secondary amide groups in the vicinity of the metallic centre. Structural assignments for the various compounds were made on the basis of the ^{1}H n.m.r. spectra of the free bases. The optical purity of the compounds was established by g.l.c. on a chiral phase. Absorption spectra of hydroxy-iron(III) derivatives of hanging imidazole basket handle porphyrins display an unusual pattern consistent with the presence of water partially co-ordinated to the metallic ion and stabilized in the distal cavity by a hydrogen bond formed between water proton(s) and the carbonyl group of the 'peptide' bond.

For some time now, our laboratory has been describing the synthesis of several both-faces hindered porphyrins, the so-called basket handle porphyrins (BHPs), in which handles are linked onto the *ortho* position of the opposite phenyl rings of 5,10,15,20-tetraphenylporphyrin (cross-*trans* isomer)[2] by ether or amide linkages (e-BHP or a-BHP). Iron complexes of these superstructured porphyrins have mainly been elaborated in order to mimic the microenvironment of the prosthetic groups of oxygen carrier hemoproteins. In this case, the two handles are of a different nature. A nitrogen base (imidazole or pyridine) hangs on one of the two chains so as to provide axial co-ordination to the central iron(II).[3,4] Thus these compounds reversibly bind dioxygen at room temperature without auto-oxidation of the iron(II).[5]

However, equilibrium and kinetic constants of dioxygen binding show that the presence of ether linkages and secondary amide linkages on the distal side produces remarkable micro-environmental effects on the reactivity of the central metal. Of particular relevance in this connection is the contribution of amide linkages to strong stabilization of the oxygenated complexes by polar interactions (as hydrogen bonds or dipole-dipole interactions).[6]

As a contribution to these studies, the number of secondary amide groups in the bridging chains was increased in order to see if the affinity of the iron for O_2 binding would be reinforced. This can be achieved by the insertion of amino acids into the distal handle. Substituted porphyrins bearing amino acids have recently been reported in connection with elucidating the effects of both the degree of steric hindrance and of chiral centres upon the asymmetric and selective oxidation reactions of some organic substrates modeling cytochromes P_{450} activity.[7-10]

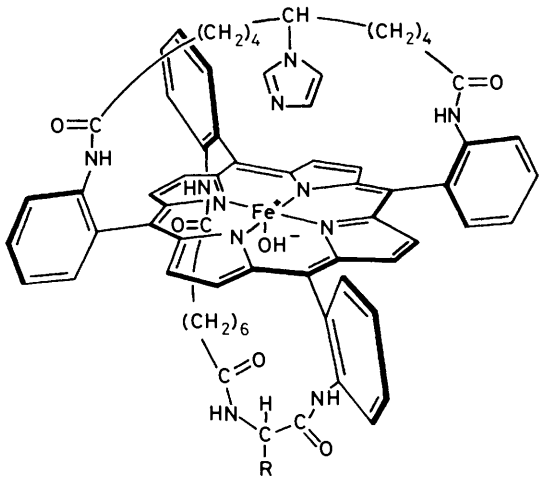
Besides the fact that the NHCO increases the local solvation, such molecules are attractive systems because the relative rigidity of the handle provides strong distal steric hindrance, the main structural feature, it appears, in the discrimination of CO ligation relative to O_2 in hemoproteins.[12-14]

Here we report the synthesis of the first hanging-base basket handle porphyrins (**27**) and (**28**) in which there is an unsymmetrical environment on the two sides of the porphyrin plane: a 'proximal' imidazole hangs on one of the two handles, whilst one or two amino acid residues (L-phenylalanine or L-valine) are inserted into the second and directly linked to the *meso* phenyl groups *via* amide functions. Thus, the design of these compounds allows control both of the cavity size and its polarity on the distal side of the macrocycle as well as five-co-ordination of the metal ion in iron(II) complexes necessary to the formation of stable dioxygen complexes.

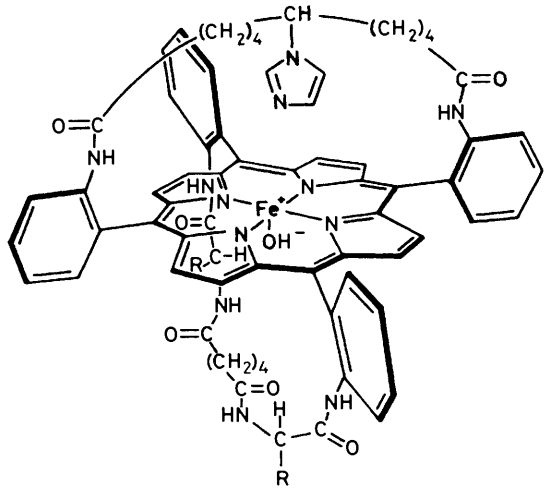
Several intermediate derivatives have been used for the preparation of BHPs in which a variable number of amino acids is included in the superstructure. With such compounds containing 5,6 or 8 NHCO groups, it has been possible to investigate the effects of the polarity created by the additional amide groups on the redox reactivity of their iron complexes, in comparison to simple a-BHP.[15] Their synthesis is also described.

Synthesis

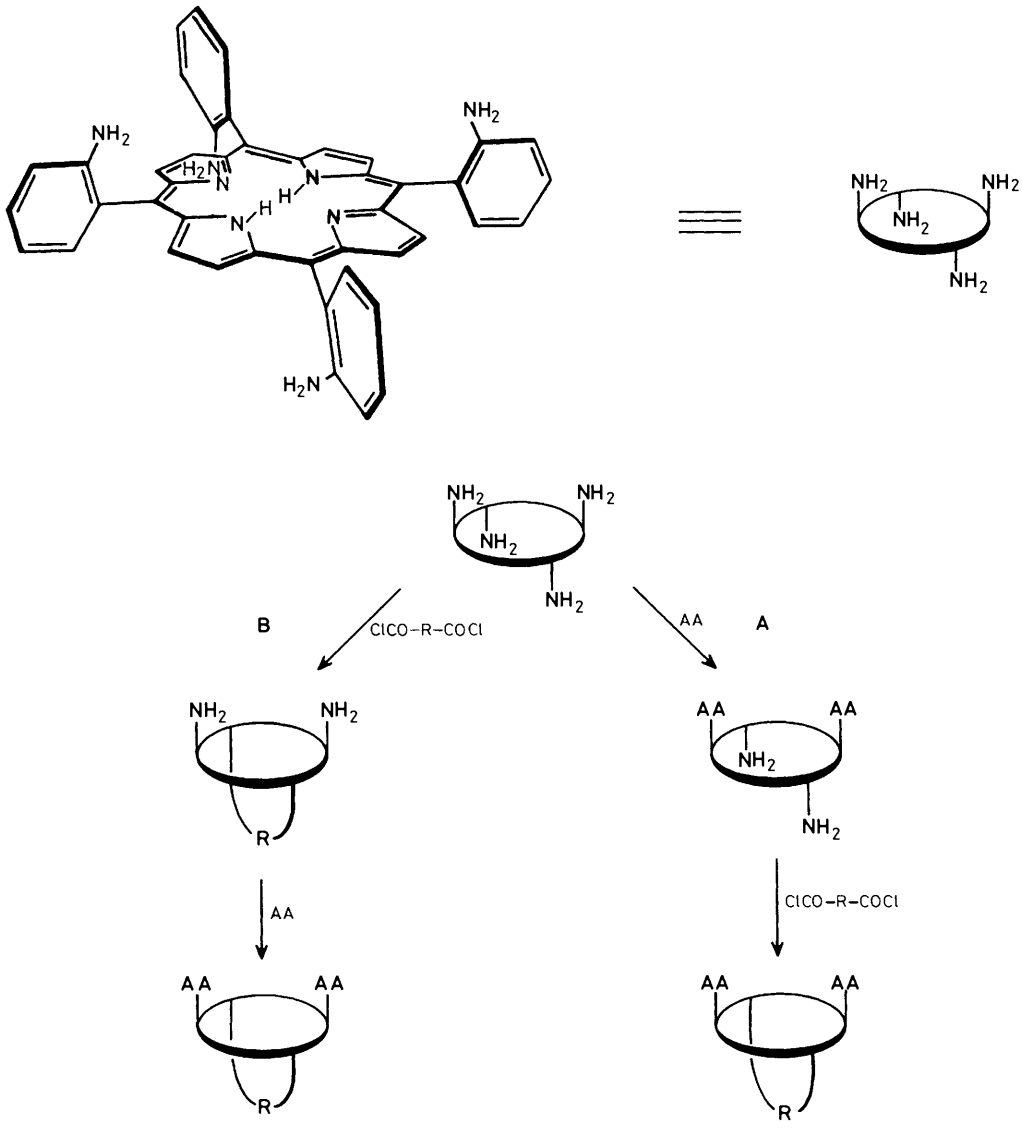
The porphyrins (**27**) and (**28**) can be synthesized following two different strategies both starting from α,β,α,β-5,10,15,20-tetra(*o*-aminophenyl)porphyrin (**1**) (Scheme 1). In route A an N-protectected amino acid is linked to the two α,α amino groups of the porphyrin followed by bridging of the two β,β amino groups by a convenient chain. Path B involves preparation of the single face hindered porphyrin prior to coupling with an N-protected amino acid on the opposite face. In the event, the former synthetic route appeared ineffectual (Scheme 2) in that preparation of the α,α-di (N-protected amino acid) porphyrin (**3**) required a large excess of N-protected amino acid. Typical coupling reactions were, therefore, carried out using the classical mixed anhydride procedure of peptide synthesis.[16] Thus, we accomplished amide bond formation between a porphyrin and an L-amino acid in dry tetrahydrofuran in the presence of triethylamine at room temperature after activation of the carboxylated group of the latter with isobutyl chloroformate as reagent in the same solvent at −15 °C. This method allowed the chiral integrity of the amino acids to be maintained during the coupling reaction. We chose t-butoxycarbonyl (BOC) hereafter as protecting group for L-phenylalanine and L-valine



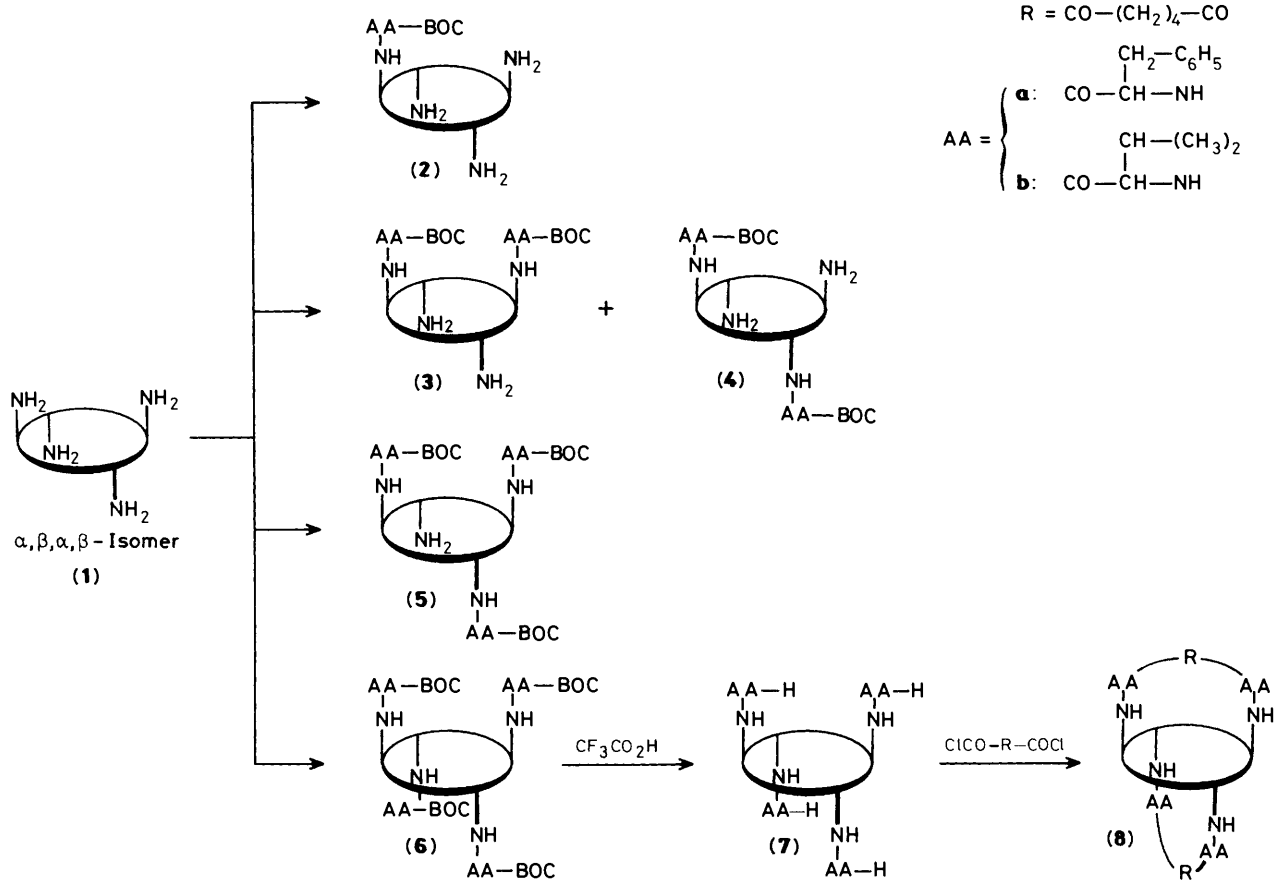
(27) • $Fe^{III}OH$



(28) • $Fe^{III}OH$



Scheme 1.



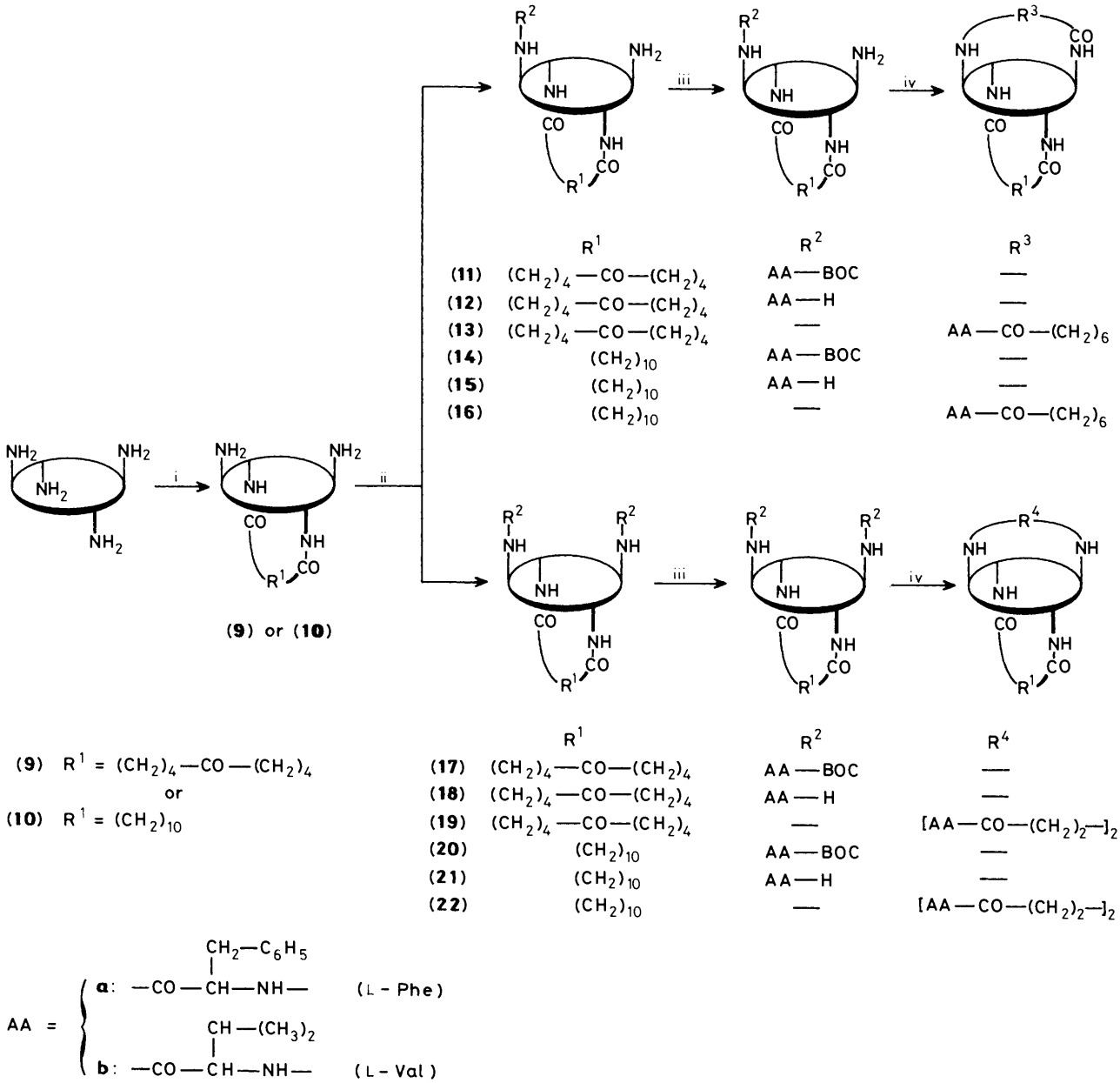
Scheme 2.

by analogy with the methodology developed earlier for this kind of synthesis.[8] Furthermore, an easier deprotection of the amino acids by treatment with strong acids in organic solvent proceed essentially without racemization.

Analytical t.l.c. on silica gel of the reaction mixture showed that several compounds were formed corresponding to mono-(**2**), di-(**3**) and (**4**), tri-(**5**), and tetra-(**6**) amino acid derivatives which are increasingly polar. Despite extensive efforts, and whatever the nature of the amino acids, α,α-(**3**) and α,β-(**4**) diamino-acid species proved to be chromatographically inseparable in our hands. However, compound (**6**) was a key intermediate for the preparation of symmetric BHPs in which eight amido groups are present. Compound (**6**) was obtained using 5 equiv. of N-BOC-L-phenylalanine or N-BOC-L-valine. After 3 days, the reaction was stopped and the desired compounds (**6a**) and (**6b**) were recovered by high performance liquid chromatography (h.p.l.c.) on silica gel in 33 and 15% yield respectively. It was then treated with trifluoroacetic acid in methylene dichloride at room temperature to yield quantitatively, after neutralization and crystallization, the corresponding unprotected compound (**7**).[17] Without further purification, (**7**) was coupled with 2 equiv. of adipoyl chloride in dry THF under conditions of high dilution to give the handle compound (**8**) in 60% yield.

This method was less applicable for the functionalized precursors (**13**) and (**19**) of the hanging-imidazole BHPs (**27**) and (**28**) from (**2**) and (**3**). Thus, compounds in which one or two amino acids were inserted in only one handle were synthesized *via* route B by the construction of a mono bridged porphyrin as a first step (Scheme 3). The mono handle porphyrin (**9**) was prepared by treatment of the porphyrin (**1**) with the 5-oxononane-1,9-dicarbonyl chloride according to the method described in the preceding paper of this series.[1] As described above, treatment of compound (**9**) with a large excess of BOC-L-amino acid afforded compounds (**11**) and (**17**) which were separately recovered by h.p.l.c. on silica gel and identified on the basis of their ^{1}H n.m.r. spectra. The relative yields of these compounds is very sensitive both to the quantity of activated amino acid used and to the time of reaction. In all cases the reactions were monitored by analytical t.l.c. When 2.5 equiv. of amino acid (by amino groups) were used, the mono amino acid derivative was preferentially formed even after several days. In contrast, use of 5—10 equiv. of amino acid and a 3-day reaction period gave a mixture of mono and diamino acid derivatives in the ratio *ca.* 2:3. These species were then converted into unprotected amino acid porphyrin derivatives which upon subsequent cyclization with suberoyl chloride or adipoyl chloride under the same conditions used for the preparation of compound (**8**) afforded the functionalized unsymmetrical BHPs (**13**) and (**19**) in 35—70% yield after chromatography and crystallization.

Hanging imidazole porphyrins bearing amino acids in their superstructures were prepared by adaptation of the chemistry previously used to synthesize analogous compounds.[1] The porphyrins (**13**) and (**19**) were quantitatively converted into the hydroxy derivatives (**23**) and (**24**) by $NaBH_4$ reduction. Subsequent bromination with CBr_4–Ph_3P gave (**25**) and (**26**) in good yields. Finally, a coupling reaction with a large excess of



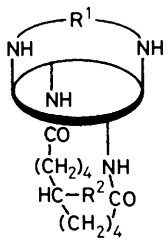
Scheme 3. *Reagents:* i, ClCO-R^1-COCl, THF, Et_3N; ii, activated AA-BOC, THF; iii, CF_3CO_2H; iv, ClCO-R^3-COCl or ClCO-R^4-COCl, THF, Et_3N

imidazole in dimethylformamide at 100 °C for 3 days furnished the desired compounds (**27**) and (**28**) in 30—55% yield after h.p.l.c. on silica gel and crystallization (Scheme 4).

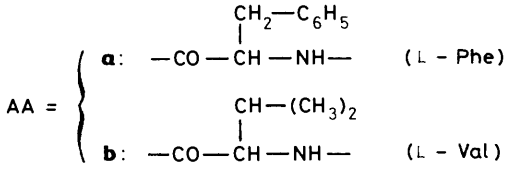
The synthetic route B appeared suitable for the preparation of unsymmetrical BHPs and was chosen for the synthesis of compounds (**16**) and (**22**) bearing one or two amino acids in one handle, the second face of the macrocycle ring being bridged by a pure polymethylene chain. Treatment of compound (**1**) with dodecanedicarbonyl chloride gave the single-face hindered porphyrin (**10**). Coupling reactions of activated N-protected amino acids with this latter compound were similar to those used for previous functionalized porphyrins (**11**) and (**17**) and gave compounds (**14**) and (**20**) which were separated by h.p.l.c. Deprotected amino acid porphyrins (**15**) and (**21**) were obtained in quantitative yield by acid treatment. Porphyrins (**16**) and (**22**) bearing 5 and 6 amide groups respectively in their superstructures were obtained by cyclization with appropriated diacid chlorides in 55—80% yield.

Anaerobic insertion of iron into compounds (**8**), (**16**), (**22**), (**27**), and (**28**) was carried out with iron(II) bromide in refluxing dimethylformamide until the 630 nm absorption band disappeared,[4] the products being chromatographed on silica gel to give a mixture of bromo- and hydroxy-iron(III) porphyrins. Pure hydroxy derivatives were obtained by shaking a methylene dichloride solution of iron porphyrin with aqueous potassium carbonate.

Characterization of Compounds.—^{1}H *N.m.r.* ^{1}H N.m.r. spectra recorded at 100 and at 400 MHz were used for the characterization of the synthesized compounds and of the conformation of the handles; their main chemical shifts are listed in Table 1. Assignments of the resonances to individual



	R^1	R^2
(23)	—AA—CO—$(CH_2)_6$—CO—	—O—H
(24)	—[AA—CO—$(CH_2)_2$—]$_2$	—O—H
(25)	—AA—CO—$(CH_2)_6$—CO—	—Br
(26)	—[AA—CO—$(CH_2)_2$—]$_2$	—Br
(27)	—AA—CO—$(CH_2)_6$—CO—	
(28)	—[AA—CO—$(CH_2)_2$—]$_2$	



protons are based on integration and selective homonuclear decoupling experiments. These spectra are very similar to those of amide BHPs in a cross-*trans* configuration[4] for which the ^1H chemical shifts may be regarded as dominated by the porphyrin ring current (Figure 1).

In the spectra of the symmetric compounds (**8a**) and (**8b**) bearing two identical handles, the eight pyrrolic protons appear as two singlets. They are expected to be inequivalent due to the asymmetry induced by the amino acid chiral centres. The most important feature is that the resonance of these protons in other porphyrin spectra appear as two AB patterns indicating an effective dissymetry of the molecules. All these compounds possess multiple signals in the ranges 8.9 to 7.5 and 0.4 to −2.5 p.p.m. corresponding to the *meso*-phenyl protons and the methylene protons of the handles respectively. Their chemical shifts are close to those in amide BHPs[4] and are not reported in Table 1. In addition, all spectra display a single resonance near −2.7 p.p.m. corresponding to the two pyrrolic NH protons. This value is nearly identical with that in both-face hindered porphyrins indicating that no significant deformation of the porphyrin ring is induced by the amino acid chain(s).[18]

Amide group protons linking the handles to the macrocycle are easily assigned by deuterium exchange in the presence of D_2O. By comparison with the amido-BHP previously synthesized,[4] the resonance set at higher field (near 6.7 p.p.m.) was assigned to the amide groups of the polymethylene chain whereas the second ones (near 8 p.p.m.) correspond to the phenyl NH protons of the amide group linking the amino acids to the porphyrin handle. In the case of the symmetrical BHP (**8**) bearing four amino acids, a single resonance at 8 p.p.m. is observed for these protons. Furthermore, the latter resonances are always more downfield shifted in the porphyrins bearing phenylalanine residues than in those bearing valine residues. Table 1 shows that the chemical shifts of these protons in compounds bearing N-t-BOC amino acids (**20**) appear at *ca.* 7.3 p.p.m. and are upfield shifted by 1.5 p.p.m. in comparison with the same protons in unprotected amino acid porphyrins (**21**). This suggests a large difference in the conformation of the 'pickets' which present some degree of freedom along the phenyl-nitrogen bond in the latter compounds. That the resonance set of NH *amide* protons bearing the amino acid residues appears at low field could be due to a specific hydrogen interaction of these protons with the carbonyl group of the second amide series, the so called 'peptide' bond (Figure 2), rather than to a particular conformation of the substituted handle. This is supported by the chemical shift of the NH protons of the amide group linking the polymethylenic part of the substituted handle to the macrocycle in compounds (**16**) and (**27**) which bear only one amino acid; this is always comparable with that in the second handle affected only by the ring current of the porphyrin.

Such an intramolecular hydrogen bond requires an outer position for the NH *peptide* protons. The resonances for these, found at 4 and 4.5 p.p.m. for the phenylalanine and valine compounds respectively, are shifted by 0.8—0.9 p.p.m. to low field as compared with the same protons in the free but protected amino acid taken as reference. Using a Drieding molecular model, we have estimated the position of the amide groups assuming that their protons point outwards from the porphyrin centre (Figure 2). In this configuration, the NH *peptide* protons are located in a region for which the ring current effect induces a downfield shift of *ca.* 0.7 p.p.m.[19] Comparison of the observed and calculated shift values shows good agreement with this, both confirming an outer orientation of these protons and, consequently, a reverse orientation for the carbonyl groups. There is also qualitative evidence for interaction of the NH amide with the carbonyl group of the 'peptide' bond. As mentioned above, amidic protons are easily assigned by deuterium exchange and this exchange always appears faster for the amidic protons linked to the polymethylenic fragment of the handles than for amidic protons linking the amino acid to the phenyl group.

The protons relative to the chiral carbon of unprotected amino acid 'picket' porphyrins (**7**) and the BHPs (**8**), (**13**), (**16**), (**19**), and (**22**) appear in the range 3.5—4.4 p.p.m. depending on the chemical nature of the amino acid inserted in the chains. In contrast, an unusual upfield shift (δ 2.5) of these protons is observed in porphyrins bearing N-t-BOC amino-acid as pickets. This could be due to a larger ring-current effect from the porphyrin and suggests that they point towards the centre of the porphyrin ring in the latter compounds. An inverse configuration must be present in the other porphyrins.

Consistent with these configurations is the significant upfield chemical shift of the substituent chain protons on the chiral carbon compared to the free amino acids. This is particularly important for the methyl group of the valine and the phenyl group of the phenylalanine residues. The two methyl groups of the former are inequivalent and each well separated resonance appears as a doublet. This is clear evidence for a hampered rotation of the isopropyl group of the valine residue by steric strains as shown by Drieding molecular models. The two methyl groups are thus affected differently by the porphyrin ring current. In contrast, the phenyl group of the phenylalanine seems to be rotating freely. Indeed the corresponding *ortho* and *meta* protons appear as a simple resonance respectively.

Finally, imidazole protons of compounds (**27**) and (**28**) appear as three well separated signals at 4.5, 5.5, and 6 p.p.m. Their relatively high-field chemical shifts are ascribed to the ring current effect of the macrocycle on the heterocycle ring located in the cavity formed by the substituted handle. However, in the case of the mono amino acid BHP (**27**) each of these peaks is split into two signals. This splitting must find its origin in the dissymmetry of the chain inserting one amino acid on the other

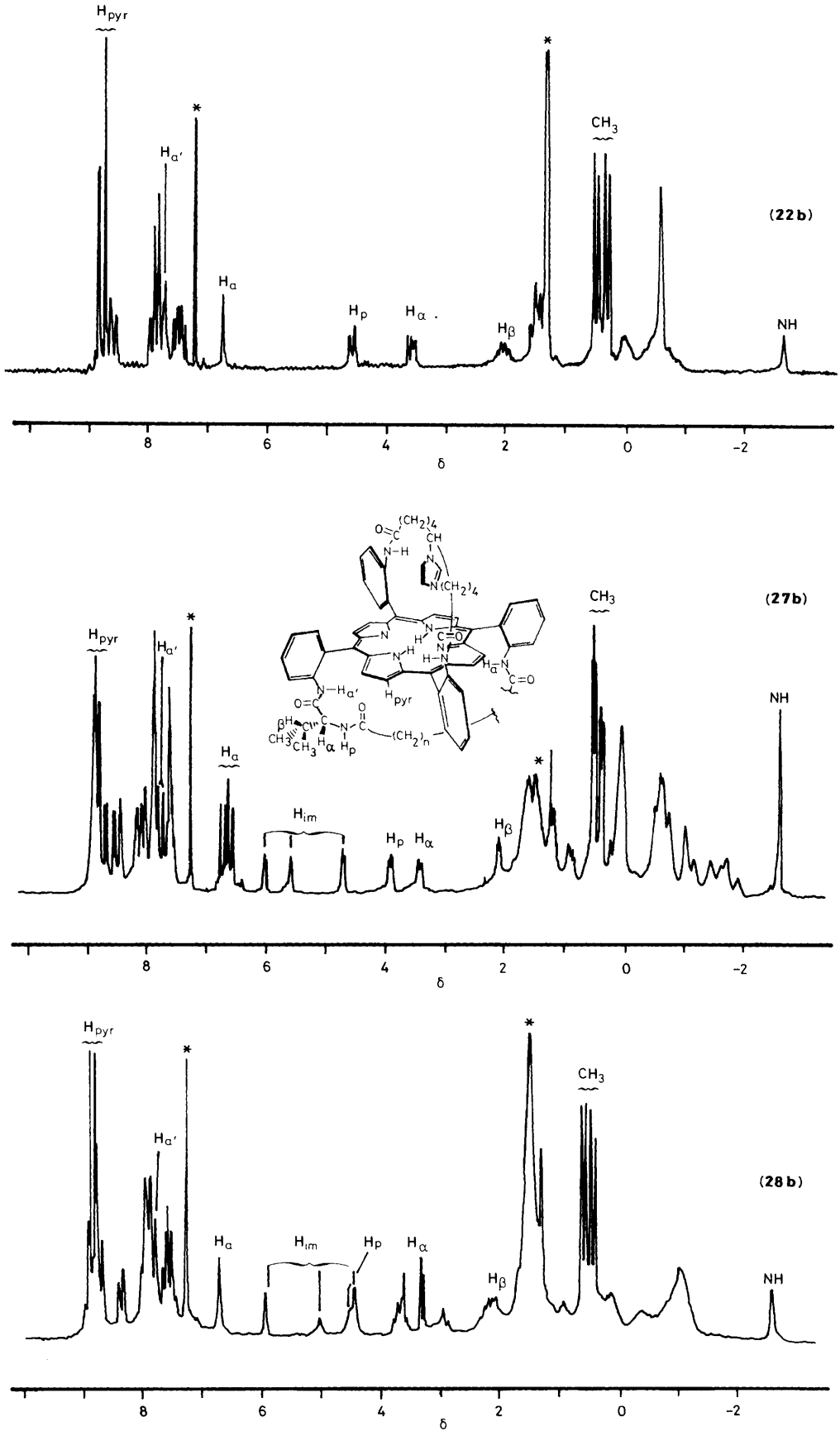


Figure 1. ^{1}H N.m.r. spectra of BHPs bearing valine in $CDCl_3$. The assignments are shown in the Figure. The asterisks denote solvent impurities

Table 1. Selected ^{1}H n.m.r. shifts (in p.p.m.) for the free bases of the BHPs recorded in $CDCl_3$ at 307 K

				Amino acid						
				Phenylalanine		Valine				
Compounds	Hpyr	NH amide	CH	CH_2	C_6H_5	CH	CH_3	NH peptide	NHpyr	BOC
(**20a**)	8.73	7.45	3.44	2.41	6.62			4.15	−2.60	0.58
		6.86			6.42					0.49
(**20b**)	8.80	7.15	2.91			1.18	0.06*	4.40	−2.59	0.84
		6.84					−0.01*			
(**21a**)	8.73	9.22	2.02	2.97	6.81			1(NH_2)	−2.62	
		6.81		2.77	6.49					
(**21b**)	8.82	9.06	3.58			1.83	0.39 (d)	?	−2.60	
		6.81					0.21 (d)			
(**8a**)	8.89	8.55	4.34	2.99	7.10			3.87	−2.76	
	8.74				6.95					
(**8b**)	8.90	8.00	3.72			2.16	0.56 (d)	4.52	−2.70	
	8.74						0.54 (d)			
										H_{Im}
(**27a**)	8.87	8.67	4.00	2.98 (m)	7.02			3.90	−2.64	6.00†
	8.84	6.72			6.76			3.80		5.51*
		6.64								4.66†
		6.57								
(**27b**)	8.89	7.75	3.48			2.14	0.57 (d)*	3.89	−2.57	6.01†
	8.86	6.70					0.44 (d)			5.59*
	8.80	6.60								4.68†
(**28a**)	8.85	7.42	4.19	2.90(m)	7.07			4.39	−2.64	5.89
		7.34			6.89					4.37
		6.83								4.15
		6.79								
(**28b**)	8.90	7.85	3.67			2.08	0.45 (d)	4.40	−2.60	5.93
	8.82	6.72					0.25 (d)			5.03
										4.50
(**16a**)	8.84	8.05	3.69	2.80	6.99			4.00	−2.70	
	8.80	6.96			6.71					
		6.67								
(**16b**)	8.87	7.69	3.51			2.10	0.53 (d)	3.80	−2.64	
	8.84	6.80					0.39 (d)			
	8.78	6.72								
(**22a**)	8.82	8.45	4.23	2.90 (m)	7.09			4.11	−2.71	
		6.78			6.89					
(**22b**)	8.85	7.70	3.55			2.05	0.43 (d)	4.74	−2.75	
	8.75	6.75					0.23 (d)			

* Broad signal. † Two signals.

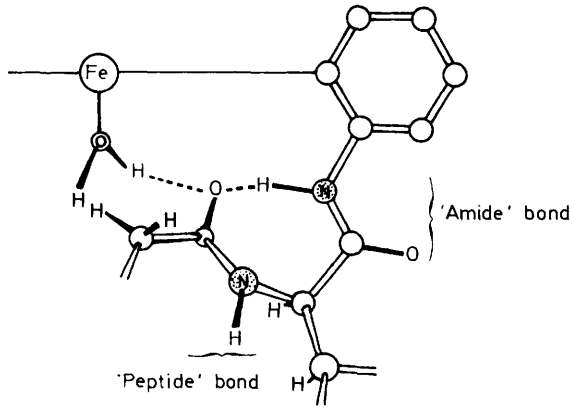


Figure 2. Suggested conformation of the handles bearing amino acids showing the intramolecular hydrogen bonding between NH *amide* proton and CO *peptide* oxygen, and the intermolecular hydrogen bonding to co-ordinated water molecule and CO *peptide* oxygen

side of the porphyrin ring.[1] In the same way, the dissymmetry of the imidazole handle induces a slight splitting of some proton resonances on the second handle.

Optical Purity.—The n.m.r. spectra of all porphyrins containing one, two, or four amino acids appear as a limited number of well defined sharp signals indicating that these compounds have a well-defined configuration at the chiral centre. This suggests that no racemization has occurred during the synthesis.

In order to ensure that the initial chirality of the asymmetric carbon had not been lost during the synthesis we measured the optical purity of compound (**22a**) by inserting L-phenylalanine. Among different methods, the use of a chiral lanthanoid shift reagent for the determination of optical purity shows considerable advantages. For example, this method has been applied to a BHP bearing L-phenylalanine by Mansuy *et al.* using europium complexes.[8] However, an analysis of the effects of paramagnetic reagents on the ^{1}H n.m.r. signals of the porphyrin requires the synthesis of the D-enantiomeric analogue. Thus,

Table 2. Absorbance maxima (nm) and molecular extinction coefficients (l $mmol^{-1}$ cm^{-1}) of hydroxy-iron(III) BHP complexes in toluene

Compounds				
(**8a**) $Fe^{III}OH^-$	417 (83)		581 (10)	627sh
(**8b**) $Fe^{III}OH^-$	416 (72)		578 (8)	627sh
(**16a**) $Fe^{III}OH^-$	419 (94)		575(9)	627sh
(**16b**) $Fe^{III}OH^-$	420 (100)		577 (8.6)	627sh
(**22a**) $Fe^{III}OH^-$	419 (94)		577 (9)	626sh
(**22b**) $Fe^{III}OH^-$	416 (92)		576 (10)	627sh
(**27a**) $Fe^{III}OH^-$	423 (98.9)	548 (8.7)	594 (4.3)	638 (2.7)
(**27b**) $Fe^{III}OH^-$	422 (94.8)	545.5 (8.7)	594 (4.1)	636 (2.7)
(**28a**) $Fe^{III}OH^-$	422 (119), 431 (115)	543.5 (10.3)	590 (3.7)	632 (1.9)
(**28b**) $Fe^{III}OH^-$	423 (106.4), 427 (101.8)	544.(7.9)	592 (5.6)	632.5 (2.6)

we decided to use another method in which the optical purity is measured on derivatized phenylalanine obtained by acid degradation of compound (**22a**) by gas chromatographic analysis on a chiral phase.[20,21] A comparison of derivatized phenylalanine with authentic L- and D-phenylalanine derivatives as reference showed an optical purity higher than 97%. This result clearly shows that compound (**22a**) is a pure enantiomer consistent with a complete absence of racemization during the synthesis and corroborates the n.m.r. results.

Electronic absorption spectra.—Neutral free-base porphyrins bearing amino acids are soluble in non-polar organic solvants. Their electronic spectra are very similar to those of amide BHPs with a Soret band at 420 nm and four less intense *Q* bands at 514, 546, 587, and 645 nm.[4]

Amide linked cross-*trans* BHP structures give an efficient protection of the $Fe^{III}OH$ complexes against formation of μ-oxo dimers.[22] Table 2 shows the absorbance maxima and molecular extinction coefficients of these complexes in the Soret and visible regions. In toluene or methylene dichloride solution, the electronic spectra of complexes in which an imidazole is hung to one of the two handles and two amino acids are inserted in the second ones [compounds (**28**)] are quite distinct from those without the heterocyclic ring. Their spectra show a splitting of the Soret band into two bands at 422 and 430 nm while the visible region is not readily distinguished from that of hanging-imidazole BHPs.[4] Furthermore, the additional band at 430 nm is very sensitive to the temperature. When the temperature decreases, the absorption band at 430 nm increases whereas the typical band of hydroxy species at 422 nm decreases. The reverse behaviour prevails at high temperature. These thermal processes have never been observed with the $Fe^{III}OH$ complexes of amide BHPs previously described[4] and are consistent with the existence of two species differently co-ordinated in equilibrium.

Such behaviour is observed at lower temperature for the iron complex of porphyrins (**27**) with one amino acid inserted in one chain. A shoulder at 430 nm appears reversibly at −30 °C, in agreement with the formation of the second species.

Such a change in the electronic spectrum of the $Fe^{III}OH$ complex of (**28a**) occurs upon addition of 1-methylimidazole, with the formation of a six-co-ordinated bis(imidazole) adduct the absorption maximum of which is at 427 nm. Among the potential ligands in the sixth position of co-ordination in the absence of added 1-methylimidazole, water appears as a good candidate. When solid iron(III) complexes dried *in vacuo* (0.1 mmHg at 50 °C for 3 h) are dissolved in strictly anhydrous methylene dichloride, their electronic absorption spectra in the Soret region are identical with those obtained with simple hydroxy-iron(III) BHPs. Addition of water to these solutions results in the formation of a new species with an absorption maximum at 430 nm. This confirms the co-ordination of the ferric ion by the oxygen atom of one water molecule which could be stabilized in the cavity by hydrogen bonding(s) to the carbonyl group(s) of the peptide linkage (Figure 2). Further support for the presence of co-ordinated water comes from electrochemical studies of these compounds.[23]

Conclusion.—In this paper, we describe the synthesis and the characterization of BHPs in which amino acids [L-phenylalanine or L-valine] are inserted in the handles in order to increase the number of secondary amide groups in the micro-environment of the central reacting centre. The present strategy may be easily applicable to the preparation of superstructured porphyrins with other amino acids included in the basket handles. In particular, use of amino acids having ionisable carboxylic or basic side chains may allow the synthesis of water-soluble compounds.[24] Some effects of the degree of polarity created by the presence of secondary amide groups have been investigated by the electrochemical behaviour of their iron derivatives.[15] With asymmetrical iron(II) compounds in which a proximal imidazole is hung into one handle whereas the second handle incorporates amino acids, both solvation and steric hindrance effects on the distal cavity have been evaluated by comparison with compounds previously described.[6] A forthcoming paper will report their magnetic and electrochemical properties and their affinities for oxygen and carbon monoxide.[23]

Experimental

All chemicals used were of reagent grade and were purchased from Aldrich and Jansen Chimica. *N*-t-Butyloxycarbonyl-L-phenylalanine (*N*-t-BOC-Phe) and *N*-t-butyloxycarbonyl L-valine (*N*-t-BOC-Val) were purchased from Senn Chemicals. Dry tetrahydrofuran (THF) was obtained by distillation from benzophenone–sodium and used immediately. Merck silica gel 60 (40—60 μm) or 60H (15 μm) was used for column chromatography. Pure porphyrins were obtained by preparative high pressure liquid chromatography (h.p.l.c.) with a Jobin Yvon apparatus. Merck pre-coated preparative plates (silica gel 60, 2 mm) were used for t.l.c. Elemental analyses were carried out by the Service Central de Microanalyse du CNRS.

^1H N.m.r. spectra were obtained in the indicated deuteriated solvents with a Varian XL-100 or a Bruker AM-400 instruments. Optical spectra in the Soret and visible regions were recorded using a Varian DMS-100 spectrometer.

General Method for the Preparation of Amino Acid Porphyrins.—Isobutyl chloroformate (22 mmol) was added to a solution of *N*-t-BOC-L-amino acid (20 mmol) and triethylamine (3.2 ml) in dry THF (50 ml) cooled to −15 °C. After 30 min, α,β,α,β-5,10,15,20-tetrakis(*o*-aminophenyl)porphyrin[4] (1 mmol) and triethylamine (3.2 ml) in dry THF (100 ml) were added. The resulting solution was stirred for 3 days at room temperature when analytical t.l.c. showed that five compounds were present. The mixture was evaporated to dryness under reduced pressure and the solid residue was dissolved in methylene dichloride and the solution washed with water (×3) and aqueous hydrogen carbonate, dried (Na_2SO_4), and evaporated. The residue, dissolved in chloroform, was chromatographed on a silica gel column (4 × 4 cm) when methylene dichloride–ether (20:1, v/v) eluted five red fractions; these were recovered separately and identified from their ^1H n.m.r. spectra. The first fraction was unchanged starting material (**1**) and the second the mono amino acid porphyrin (**2**). The third fraction corresponded to a mixture of two isomers of diamino acid porphyrins (**3**) and (**4**).

Compound (**5**) bearing three amino acids was obtained as the fourth fraction. The last red fraction, the fully substituted porphyrin (**6**) was crystallized from methylene dichloride–hexane.

α,β,α,β-5,10,15,20-Tetrakis[*o*-(N-t-butoxycarbonyl-L-phenylalaninamido)phenyl]porphyrin (**6a**) (550 mg, 33%); α,β,α,β-5,10,15,20-*tetrakis*[o-(N-*t*-*butoxycarbonyl*-L-*valinamido*)-*phenyl*]*porphyrin* (**6b**) (220 mg, 15%) (Found: C, 66.8; H, 7.0; N, 11.0. $C_{84}H_{102}N_{12}O_{12}\cdot 2H_2O$ requires C, 66.9; H, 7.0; N, 11.2%).

α,β,α,β-5,10,15,20-Tetrakis[*o*-(L-phenylalaninamidophenyl)]-porphyrin (**7a**). Compound (**6a**) (165 mg, 0.1 mmol) was dissolved in a mixture of methylene dichloride (10 ml) and trifluoroacetic acid (10 ml) and the resulting green solution was stirred for 1 h at room temperature; it was then evaporated to dryness. The residue was taken up in ethyl acetate and the solution washed with dilute aqueous ammonia and water (× 2), dried (Na_2SO_4), and evaporated to afford the title compound (**7a**); this crystallized from ethyl acetate–hexane as a purple solid (120 mg, 96%). α,β,α,β-5,10,15,20-*Tetra*[o-(L-*valinamido*)-*phenyl*]*porphyrin* (**7b**) (20 mg, 70%) was obtained by similar deprotection of (**6b**).

α-5,10:β-15,20-*Bis*{o,o′-[(*hexanediamido*)*di*-L-*phenylalaninamido*]*diphenyl*}*porphyrin* (**8a**). A solution of adipoyl chloride (36 mg, 0.20 mmol) in dry THF (2 ml) was added dropwise to a mixture of compound (**7a**) (60 mg, 0.04 mmol) and triethylamine (400 μl) in the same solvent (100 ml) under argon. After addition was complete, stirring was continued for 1 h and the solution was evaporated to dryness under reduced pressure. The residue was dissolved in methylene dichloride and the solution washed with water (× 3), dried (Na_2SO_4), and concentrated. T.l.c. on silica gel plates [toluene–acetone (2:1, v/v)] gave two bands, the major of which (R_F 0.41) afforded (**8a**) which was crystallized from methylene dichloride–hexane (40 mg, 57%) (Found: C, 73.5; H, 5.5; N, 11.2. $C_{92}H_{76}N_{12}O_8\cdot H_2O$ requires C, 73.9; H, 5.3; N, 11.2%); $\lambda_{max.}$(ε/mmol l^{-1}) (CH_2Cl_2) 423 (377), 517 (18.4), 549 (4.2), 589 (6.0), and 645 nm (1.8).

α-5,10:β-15,20-*Bis*{o,o′-[(*hexanediamido*)*di*(L-*valinamido*)]-*diphenyl*}*porphyrin* (**8b**). This compound was obtained from (**7b**) (20 mg, 0.19 mmol) and adipoyl chloride (13.6 mg, 0.07 mmol) by the previous procedure (10 mg, 45%) (Found: C, 69.8; H, 6.2; N, 14.1. $C_{70}H_{74}N_{12}O_6\cdot H_2O$ requires C, 70.2; H, 6.4; N, 14.0%); $\lambda_{max.}$(ε/mmol l^{-1}) (CH_2Cl_2) 422 (370), 517 (18), 547 (3.6), 588 (6.0), and 644 nm (1.9).

General Procedures for the Preparation of One Amino Acid Mono BHPs (**11**) *and* (**14**).—α-5,15-[*o,o′*-(6-Oxoundecanediamido)diphenyl]-β,β-10,20-(bis(*o*-aminophenyl)porphyrin (**9**)[1] or α-5,15-[*o,o′*-dodecanediamido)diphenyl]-β,β-10,20-bis(*o*-aminophenyl)porphyrin (**10**)[4] (0.2 mmol) and triethylamine (210 μl) in dry THF (50 ml) was added dropwise to a mixture of *N*-t-BOC-L-amino acid (1 mmol), triethylamine (210 μl), and isobutyl chloroformate (1.5 mmol) in dry THF (20 ml) at −15 °C for 0.5 h. After complete addition the reaction mixture was stirred for 3 days at room temperature. The solvent was then evaporated and the residue dissolved in methylene dichloride. The solution was washed with water, aqueous sodium hydrogen carbonate (1%), and 0.1M aqueous HCl, dried (Na_2SO_4), and evaporated to give a purple solid. Preparative h.p.l.c. on a silica gel column (2 × 35 cm) with methylene dichloride–ether (10:1, v v) as eluant gave three fractions. The first fraction was characterized as the starting material (**9**) (30 %) whilst the major second band contained the desired mono amino acid derivative which was crystallized from methylene dichloride–hexane. The diamino acid porphyrin was obtained in the final more-polar fraction.

α-5,15-[o,o′-(6-*Oxoundecanediamido*)*diphenyl*]:β-10-[o-(*t*-*butoxycarbonyl*-L-*phenylalaninamido*)*phenyl*]-β-20-(o-*aminophenyl*)*porphyrin* (**11a**). This compound was obtained from (**9**) and *N*-t-BOC-L-phenylalanine (143 mg, 64%) (Found: C, 73.7; H, 5.9; N, 11.0. $C_{69}H_{65}N_9O_6$ requires C, 74.2; H, 5.9; N, 11.3%).

α-5,1 5-[o,o′-(6-*Oxoundecanediamido*)*diphenyl*]:β-10-[o-(*t*-*butoxycarbonyl*-L-*valinamido*)*phenyl*]-β-20-(o-*aminophenyl*)-*porphyrin* (**11b**). This compound was prepared according to the general procedure using compound (**9**) and *N*-t-BOC-L-valine (96 mg, 45%) (Found: C, 72.3; H, 6.2; N, 11.5. $C_{65}H_{65}N_9O_6$ requires C, 73.1; H, 6.1; N, 11.8).

α-5,15-[o,o′-(*Dodecanediamido*)*diphenyl*]:β-10-[o-(*t*-*butoxycarbonyl*-L-*phenylalaninamido*)*phenyl*]-β-20-(o-*aminophenyl*)-*porphyrin* (**14a**). This compound was prepared from (**10**) and *N*-t-BOC-L-phenylalanine (110 mg, 50%) (Found: C, 73.2; H 6.3; N, 10.6. $C_{70}H_{69}N_9O_5\cdot 2H_2O$ requires C, 73.0; H, 6.4; N, 10.9%).

α-5,15-[o,o′-(*Dodecanediamido*)*diphenyl*]:β-10-[o-(*t*-*butoxycarbonyl*-L-*valinamido*)*phenyl*]-β-20-(o-*aminophenyl*)*porphyrin* (**14b**). This compound was prepared from (**10**) and *N*-t-BOC-L-valine (100 mg, 45%) (Found: C, 70.6; H, 6.7; N, 11.1. $C_{66}H_{69}N_9O_5\cdot H_2O$ requires C, 70.9; H, 6.4; N, 11.3%).

General Procedure for the Preparation of the Two Amino Acids Mono BHPs (**17**) *and* (**20**).—The foregoing general procedure was used. The mono BHPs (**9**) and (**10**) (0.2 mmol) were each treated with *N*-t-BOC-L-phenylalanine (530 mg, 2 mmol) or with *N*-t-BOC-L-valine (868 mg, 4 mmol). Preparative h.p.l.c. gave two bands. The less polar compound corresponding to the mono amino acid was obtained in 10% yield. The major second fraction was the expected porphyrin which was crystallized from methylene dichloride–hexane. Even after several attempts at purification this latter compound always contained a small quantity of activated *N*-protected amino acid which could be eliminated during the next chemical step.

α-5,15-[o,o′-(6-*Oxoundecanediamido*]*diphenyl*]:β,β-10,20-*bis*[o-(*t*-*butoxycarbonyl*-L-*phenylalaninamido*)*phenyl*]-*porphyrin* (**17a**). This compound was obtained from (**9**) (191 mg, 70%).

α-5,15-[o,o′-(6-*Oxoundecanediamido*)*diphenyl*]:β,β-10,20-*bis*[o-(*t*-*butoxycarbonyl*-L-*valinamido*)*phenyl*]*porphyrin* (**17b**). This compound was prepared according to the general procedure using compound (**9**) (116 mg, 45%).

α-5,15-[o,o′-(*Dodecanediamido*)*diphenyl*]:β,β-10,20-*bis*[o-(*t*-*butoxycarbonyl*-L-*phenylalaninamido*)*phenyl*]*porphyrin* (**20a**). The foregoing procedure was used in the preparation of the title compound from (**10**) (141 mg, 63%).

α-5,15-[o,o′-(*Dodecanediamido*)*diphenyl*]:β,β-10,20-*bis*[o-(*t*-*butoxycarbonyl*-L-*valinamido*)*phenyl*]*porphyrin* (**20b**). This compound was prepared from the previous procedure using compound (**10**) (156 mg, 70%).

α-5,15-[o,o′-(6-*Oxoundecanediamido*)*diphenyl*]:β-10-[o-(L-*phenylalaninamido*)*phenyl*]-β-20-(o-*aminophenyl*)*porphyrin* (**12a**). This compound was obtained by treatment of (**11a**) with trifluoroacetic acid following the method described above for the preparation of (**7a**). It was crystallized from methylene dichloride–hexane (98%) (Found: C, 74.8; H, 5.8; N, 12.1. $C_{64}H_{57}N_9O_4\cdot H_2O$ requires C, 74.3; H, 5.8; N, 12.2%).

α-5,15-[o,o′-(6-*Oxoundecanediamido*)*diphenyl*]:β-10-[o-(L-*valinamido*)*phenyl*]-β-20-(o-*aminophenyl*)*porphyrin* (**12b**). This compound was prepared according to the procedure described for the preparation of (**7a**) using compound (**11b**) (98%) (Found: C, 73.3; H, 6.1; N, 12.3. $C_{60}H_{57}N_9O_4\cdot H_2O$ requires C, 73.1; H, 6.0; N, 12.8%).

α-5,15-[o,o′-(*Dodecanediamido*)*diphenyl*]:β-10-[o-(L-*phenylalaninamido*)*phenyl*]-β-20-(2-*aminophenyl*)*porphyrin* (**15a**). This compound was prepared by treatment of (**14a**) with trifluoroacetic acid and crystallized from methylene dichloride–hexane (99%) (Found: C, 73.6; H, 5.5; N, 11.8. $C_{65}H_{61}N_9O_3\cdot 2H_2O$ requires C, 74.2; H, 6.2; N, 11.9%).

α-5,15-[o,o′(*Dodecanediamido*)*diphenyl*]:β-10-[o-(L-*valinamido*)*phenyl*]-β-20-(o-*aminophenyl*)*porphyrin* (**15b**). This compound was prepared by treatment of (**14b**) following the previous procedure and crystallized from methylene dichloride–hexane (97%) (Found: C, 74.0; H, 6.2; N, 12.3. $C_{61}H_{61}N_9O_3 \cdot H_2O$ requires C, 74.3; H, 6.4; N, 12.8%).

α-5,15-[o,o′-(6-*Oxoundecanediamido*]*diphenyl*]:β,β-10,20-*bis*[o-(L-*phenylalaninamido*)*phenyl*]*porphyrin* (**18a**). This compound was prepared from (**17a**) according to the procedure described for the preparation of (**12a**). After reaction, the organic phase was washed with water in order to eliminate the free unprotected amino acid which was present in the starting material. The title compound was crystallized from ethyl acetate–hexane (98%) (Found: C, 74.1; H, 5.8; N, 11.8. $C_{73}H_{66}N_{10}O_5 \cdot H_2O$ requires C, 74.2; H, 5.8; N, 11.9%).

α-5,15-[o,o′-(6-*Oxoundecanediamido*)*diphenyl*]:β,β-10,20-*bis*-[o-(L-*valinamido*)*phenyl*]*porphyrin* (**18b**). Compound (**17b**) was treated following the procedure used for the preparation of (**18a**). The title compound was crystallized from ethyl acetate–hexane (94%) (Found: C, 72.7; H, 6.2; N, 12.9. $C_{65}H_{56}N_{10}O_5 \cdot H_2O$ requires C, 72.6; H, 5.4; N, 13.0%).

α-5,15-[o,o′-(*Dodecanediamido*)*diphenyl*]:β,β-10,20-*bis*[o-(L-*phenylalaninamido*)*phenyl*]*porphyrin* (**21a**) The previous procedure was used in the preparation of the title compound from (**20a**). It was crystallized from ethyl acetate–hexane (95%) (Found: C, 74.1; H, 6.0; N, 10.9. $C_{74}H_{70}N_{10}O_4 \cdot 2H_2O$ requires C, 74.1; H, 6.2; N, 11.7%).

α-5,15-[o,o′-(*Dodecanediamido*)*diphenyl*]:β,β-10,20-*bis*[o-(L-*valinamido*)*phenyl*]*porphyrin* (**21b**). This compound was obtained from (**20b**) following the previous procedure and crystallized from methylene dichloride–hexane (95%) (Found: C, 72.6; H, 6.6; N, 12.0. $C_{66}H_{60}N_{10}O_4 \cdot 2H_2O$ requires C, 72.5; H, 5.9; N, 12.8%).

General Procedure for the Preparation of BHPs bearing One or Two Amino Acids.—A solution of the appropriate diacid chloride (0.2 mmol) in dry THF (2 ml) was added dropwise during 1 h to a mixture of single-face hindered porphyrins (**12**), (**15**), (**18**), and (**21**) (0.1 mmol) and triethylamine (0.5 mmol) in the same solvent (200 ml) under argon. After complete addition stirring was continued for 1 h. Solvent was then removed on a rotary evaporator and the residue was dissolved in methylene dichloride. The solution was washed with water (×2), aqueous hydrogen carbonate, and water and dried (Na_2SO_4). The porphyrins were then chromatographed on silica gel plates.

α-5,15-[o,o′-(6-*Oxoundecanediamido*)*diphenyl*]:β-10,20-{[o,o′-(*octanediamido*)(L-*phenylalaninamido*)]*diphenyl*}-*porphyrin* (**13a**). This compound was obtained from (**12a**) and suberoyl chloride, and purified by t.l.c. using methylene dichloride–acetone (3:1, v/v) as eluant (92 mg, 79%) (Found: C, 74.9; H, 6.0; N, 11.0. $C_{72}H_{67}N_9O_6$ requires C, 74.9; H, 5.9; N, 10.9%).

α-5,15-[o,o′-(6-*Oxoundecanediamido*)*diphenyl*]:β-10,20-{o,o′-[(*octanediamido*)(L-*valinamido*)]*diphenyl*}*porphyrin* (**13b**). This compound was obtained using (**12b**) by the previous procedure and purified by t.l.c. with toluene–acetone (2:1, v/v) (60 mg, 54%) (Found: C, 73.1; H, 6.2; N, 11.0. $C_{68}H_{67}N_9O_6$ requires C, 73.8; H, 6.1; N, 11.4%).

α-5,15-[o,o′-(6-*Oxoundecanediamido*)*diphenyl*]:β-10,20-{o,o′-[(*hexanediamido*)*di*(L-*phenylalaninamido*)]*diphenyl*}*porphyrin* (**19a**). This compound was prepared in an analogous manner to that described above using (**18a**) as starting material and adipoyl chloride. It was purified by t.l.c. with toluene–acetone (1:1, v/v) (90 mg, 71%) (Found: C, 72.9; H, 5.5; N, 10.8. $C_{79}H_{72}N_{10}O_7 \cdot H_2O$ requires C, 73.5; H, 5.8; N, 10.8%).

α-5,15-[o,o′-(6-*Oxoundecanediamido*)*diphenyl*]:β-10,20-{o,o′-[(*hexanediamido*)*di*(L-*valinamido*)]*diphenyl*}*porphyrin* (**19b**). This compound was obtained according to the procedure described above using (**18b**) and purified by t.l.c. with toluene–acetone (1:1, v/v) (41 mg, 35%) (Found: C, 70.6; H, 5.6; N, 11.5. $C_{71}H_{62}N_{10}O_7 \cdot 2H_2O$ requires C, 70.9; H, 5.5; N, 11.6%).

α-5,15-[o,o′-(*Dodecanediamido*)*diphenyl*]:β-10,20-{o,o′-[(*octanediamido*)-(L-*phenylalaninamido*)]*diphenyl*}*porphyrin* (**16a**). This compound was obtained from single-face hindered porphyrin (**15a**) and suberoyl chloride and purified by t.l.c. with methylene dichloride–ether (2:1, v/v). Crystallization from methylene dichloride–hexane afforded (**16a**) (64 mg, 55%) (Found: C, 70.0; H, 5.9; N, 9.0. $C_{73}H_{71}N_9O_5 \cdot 2H_2O$ requires C, 73.6; H, 6.3; N, 10.6%); $\lambda_{max.}$(ε/mmol l^{-1}) (CH_2Cl_2) 421 (279, 514.5 (18.7), 547 (4.6), 588 (5.8), and 645 nm (1.8).

α-5,15-[o,o′-(*Dodecanediamido*)*diphenyl*]:β-10,20-{o,o′-[(*octanediamido*)-(L-*valinamido*)]*diphenyl*}*porphyrin* (**16b**). Coupling of the porphyrin (**15b**) with suberoyl chloride gave the desired compound which was purified by t.l.c. with methylene dichloride–ether (2:1, v/v) and crystallized from methylene dichloride–hexane (55 mg, 50%) (Found: C, 71.5; H, 6.4; N, 11.8. $C_{72}H_{66}N_{10}O_6 \cdot 2H_2O$ requires C, 71.9; H, 5.9; N, 11.6%); $\lambda_{max.}$(ε/mmol l^{-1}) (CH_2Cl_2) 420 (301), 514 (16), 547 (4.4), 588 (5.0), and 646 nm (2.9).

α-5,15-[o,o′-(*Dodecanediamido*)*diphenyl*]:β-10,20-{o,o′-[(*hexanediamido*)*di*(L-*phenylalaninamido*)]*diphenyl*}*porphyrin* (**22a**). Adipoyl chloride and the porphyrin (**21a**) were used for the preparation of this compound which was purified by t.l.c. with methylene dichloride–acetone (5:1, v/v) and then crystallized from methylene dichloride–hexane (104 mg, 82%) (Found: C, 73.6; H, 6.1; N, 10.4. $C_{80}H_{76}N_{10}O_6 \cdot 2H_2O$ requires C, 73.4; H, 6.2; N, 10.7%); $\lambda_{max.}$(ε/mmol l^{-1}) (CH_2Cl_2) 421 (341), 515 (19), 547 (5.0), 589 (6.0), and 653 nm (5.0).

α-5,15-[o,o′-(*Dodecanediamido*)*diphenyl*]:β-10,20-{o,o′-[(*hexanediamido*)*di*(L-*valinamido*)]*diphenyl*}*porphyrin* (**22b**). This compound, obtained from (**21b**) and adipoyl chloride, was purified by t.l.c. with methylene dichloride–acetone (2:1, v/v) and crystallized from methylene dichloride–hexane (76 mg, 65%) (Found: C, 71.5; H, 6.4; N, 11.8. $C_{72}H_{66}N_{10}O_6 \cdot 2H_2O$ requires C, 71.9; H, 5.9; N, 11.6%); $\lambda_{max.}$(ε/mmol l^{-1}) (CH_2Cl_2) 421 (348), 515 (19), 546 (4.5), 588 (6.0), and 653 nm (3.5).

α,5,15-[o,o′-(6-*Hydroxyundecanediamido*)*diphenyl*]:β-10,20-{o,o′-[(*octanediamido*)-(L-*phenylalaninamido*)*diphenyl*]}-*porphyrin* (**23a**). Compound (**13a**) (300 mg, 0.26 mmol) in methanol (75 ml) was reduced by treatment with an excess of sodium borohydride (23 mg, 0.5 mmol) After complete reaction [monitored by analytical t.l.c. on silica gel using methylene dichloride–acetone (2:1, v/v) as eluant] the solution was treated with water and dilute sulphuric acid. The porphyrin was extracted with methylene dichloride and the extract washed with water and aqueous hydrogen carbonate, dried (Na_2SO_4), and then directly crystallized from methylene dichloride–hexane (290 mg, 96.5%) (Found: C, 73.9; H, 6.0; N, 10.9. $C_{72}H_{69}N_9O_6 \cdot H_2O$ requires C, 73.6; H, 6.1; N, 10.7%).

α-5,15-[o,o′-(6-*Hydroxyundecanediamido*)*diphenyl*]:β-10,20-{o,o′-[(*octanediamido*)-(L-*valinamido*)*diphenyl*]}*porphyrin* (**23b**). Reduction of the ketone oxoporphyrin (**13b**) (290 mg, 0.25 mmol) was accomplished using the foregoing method used for the preparation of (**23a**) (222 mg, 77%) (Found: C, 72.5; H, 6.2; N, 10.9. $C_{68}H_{69}N_9O_6 \cdot H_2O$ requires C, 72.5; H, 6.3; N, 11.2%).

α-5,15-[o,o′-(6-*Hydroxyundecanediamido*)*diphenyl*]:β-10,20-{o,o′-[(*hexanediamido*)*di*(L-*phenylalaninamido*)]*diphenyl*}-*porphyrin* (**24a**). This was obtained from (**19a**) (330 mg, 0.26 mmol) according to the procedure described for the preparation of (**23a**) (288 mg, 87%) (Found: C, 73.0; H, 5.9; N, 10.8. $C_{79}H_{74}N_{10}O_7 \cdot H_2O$ requires C, 73.3; H, 5.9; N, 10.8%).

α-5,15-[o,o′-(6-*Hydroxyundecanediamido*)*diphenyl*]:β-10,20-{o,o′-[(*hexanediamido*)*di*(L-*valinamido*)*diphenyl*]}*porphyrin* (**24b**). This compound was prepared from (**19b**) as starting material (304 mg, 0.26 mmol) in an analogous manner to that

described above for the preparation of (**23a**) (255 mg, 84%) (Found: C, 70.6; H, 5.6; N, 11.5. $C_{71}H_{62}N_{10}O_7 \cdot 2H_2O$ requires C, 70.9; H, 5.5; N, 11.6%).

α-5,15-[o,o′-(6-*Bromoundecanediamido*)*diphenyl*]:β-10,20-{o,o′-[(*octanediamido*)-(L-*phenylalaninamido*)*diphenyl*]}-*porphyrin* (**25a**). To a mixture of (**23a**) (100 mg, 0.09 mmol) pyridine (65 μl), and carbon tetrabromide (220 mg, 0.69 mmol) in dry THF (7.5 ml) was added triphenylphosphine (100 mg). The reaction was monitored by t.l.c. on analytical silica gel plates [toluene–acetone (2:1, v/v)]. The reaction mixture was evaporated to dryness and the residue was dissolved in methylene dichloride containing a trace of pyridine. The solution was then washed with water (× 3) and dried (Na_2SO_4). The crude product was washed with hexane to remove the triphenylphosphine oxide and crystallized from toluene–hexane (1:1, v/v) (95 mg, 90%) (Found: C, 71.2; H, 5.6; N, 10.4. $C_{72}H_{68}BrN_9O_5$ requires C, 70.9; H, 5.6; N, 10.3%).

α-5,15-[o,o′-(6-*Bromoundecanediamido*)*diphenyl*]:β-10,20-{o,o′-[(*octanediamido*)-(L-*valinamido*)]*diphenyl*}*porphyrin* (**25b**). This compound (95 mg, 90%) was obtained by the previous method from (**23b**) (100 mg, 0.09 mmol) (Found: C, 70.4; H, 6.0; N, 10.4. $C_{68}H_{68}BrN_9O_5$ requires C, 69.7; H, 5.8; N, 10.8%).

α-5,15-[o,o′-(6-*Bromoundecanediamido*)*diphenyl*]:β-10,20-{o,o′-[(*hexanediamido*)*di*(L-*phenylalaninamido*)]*diphenyl*}-*porphyrin* (**26a**). In the same manner as for (**25a**), the title compound was prepared using (**24a**) (100 mg, 0.08 mmol) as starting material (88 mg, 84%).

α-5,15-[o,o′-(6-*Bromoundecanediamido*)*diphenyl*]:β-10,20-{o,o′-[(*hexanediamido*)*di*(L-*valinamido*)]*diphenyl*}*porphyrin* (**26b**). This compound was prepared in an analogous manner to that described above for the preparation of (**25a**) using (**24b**) (100 mg, 0.085 mmol) as starting material (89 mg, 84%).

α-5,15-[o,o′-(6-*Imidazol-1-ylundecanediamido*)*diphenyl*]:β-10,20-{o,o′-[(*octanediamido*)-(L-*phenylalaninamido*)*diphenyl*]}-*porphyrin* (**27a**). A solution of the porphyrin (**25a**) (160 mg, 0.13 mmol) and imidazole (500 mg, 7.7 mmol) in dimethylformamide (25 ml) was heated and stirred at 100 °C for 3 days. The solvent was evaporated under reduced pressure and the residue taken up in methylene dichloride. The organic phase was washed with water (× 3), dried (Na_2SO_4), and concentrated. The resulting solution was chromatographed on silica gel plates. A first elution with methylene dichloride–acetone (1:1, v/v) gave a first fraction which was identified as an ethylenic derivative[1] obtained by dehydrobromination. A second fraction was recovered from a second elution with methylene dichloride–methanol (10:1, v/v) corresponding to the title compound which was crystallized from methylene dichloride–hexane (60 mg, 40%) (Found: C, 72.7; H, 5.8; N, 12.8. $C_{75}H_{71}N_{11}O_5 \cdot 2H_2O$ requires C, 72.5; H, 5.8; N, 12.6%); $\lambda_{max.}$(ε/mmol l^{-1}) ($CHCl_3$) 420 (304), 514 (17), 545 (4.8), 588 (5.4), and 645 nm (2.9).

α-5,15-[o,o′-(6-*Imidazol-1-ylundecanediamido*)*diphenyl*]:β-10,20-{o,o′-[(*octanediamido*)-(L-*valinamido*)]*diphenyl*}-*porphyrin* (**27b**). This compound was obtained from (**25b**) (40 mg, 0.03 mmol) by the previous coupling reaction with imidazole (0.4 g) in DMF (5 ml) (20 mg, 51%) (Found: C, 72.7; H, 5.8; N, 12.6. $C_{75}H_{71}N_{11}O_5 \cdot 2H_2O$ requires C, 72.5; H, 6.1; N, 12.4%); $\lambda_{max.}$(ε/mmol l^{-1}) ($CHCl_3$) 421 (365), 514 (17.7), 545.5 (4.9), 587.5 (5.6), and 649 nm (1.5).

α-5,15-[o,o′-(6-*Imidazole*-1-*ylundecanediamido*)*diphenyl*]:β-10,20-{o,o′-[(*hexanediamido*)*di*(L-*phenylalaninamido*)]-*diphenyl*}*porphyrin* (**28a**). An analogous reaction to that described above for the preparation of (**27a**) was used from (**26a**) (30 mg, 0.025 mmol) to give the title compound (15 mg, 50%) (Found: C, 73.0; H, 5.9; N, 10.8. $C_{82}H_{76}N_{12}O_6 \cdot H_2O$ requires C, 73.3; H, 5.8; N, 12.5%); $\lambda_{max.}$(ε/mmol l^{-1}) ($CHCl_3$) 421 (305), 515 (16.6), 548 (4.3), 587.5 (5.4), and 643 nm (1.9).

α-5,15-[o,o′-(6-*Imidazole*-1-*ylundecanediamido*)*diphenyl*]:β-10,20-{o,o′-[(*hexanediamido*)*di*(L-*valinamido*)]*diphenyl*}-*porphyrin* (**28b**). This compound was obtained from (**26b**) (140 mg, 0.1 mmol) by the previous coupling reaction used for the preparation of (**27a**) (65 mg, 47%) (Found: C, 68.1; H, 6.1; N, 12.9. $C_{74}H_{66}N_{12}O_6 \cdot 4H_2O$ requires C, 68.8; H, 5.8; N, 13.0%); $\lambda_{max.}$(ε/mmol l^{-1}) ($CHCl_3$) 420 (323), 514.5 (17.6), 546 (4.5), 586 (5.8), and 643 nm (2.0).

Hydroxy-iron(III) *Complexes of BHPs.*—Iron complexes were synthesized in dimethylformamide using anhydrous iron(II) bromide and purified by chromatography on a silica gel column with methylene dichloride–methanol (10:1, v/v). Hydroxy-iron(III) derivatives were generated by shaking a methylene dichloride solution of metalloporphyrins with aqueous sodium carbonate.

Analysis of Optical Purity.—Gas chromatography was performed on an Erba Science apparatus equipped with a 50-m fused silica capillary column coated with XE-60-(*S*)-Val-(*S*)-α-phenylethylamide (Chrompack) at 135 °C. Compound (**22a**) (1 mg) was treated as follows in a one-pot procedure. After being heated in 6M HCl at 110 °C for 24 h the solution was evaporated to dryness and the residue was treated with a mixture of isopropyl alcohol–HCl 6% (4 ml) at 100 °C for 1 h. After evaporation of the solvents, the solid residue was redissolved in methylene dichloride and treated with trifluoroacetic anhydride (0.2 ml) at room temperature for 1 h. Subsequent evaporation gave the *N*-trifluoroacetyl-amino acid isopropyl ester which was taken up in acetone and submitted to g.l.c. analysis.

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