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SYNTHETIC ROUTES TO SINGLY AND DOUBLY BRIDGED PORPHYRINS

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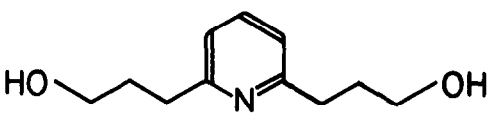
Summary: Routes are outlined for synthesis of porphyrins having a bridge across one face of the macrocycle and a second bridge across the other or a tail delivering a ligand to it.

A successful line of research on the relationship between structure and function for the active sites of haem proteins has been based on the synthesis of simpler model systems designed to mimic some of the properties of the natural materials.[1] In this connection, our aim has been to synthesise porphyrins



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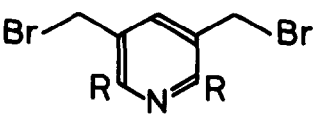
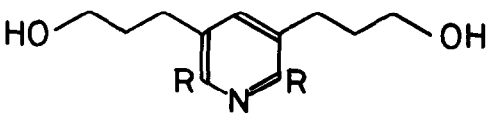


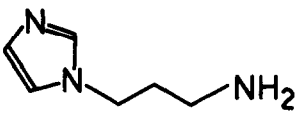
(5) R = H

(6) R = Me



(3) R = H

(4) R = Me



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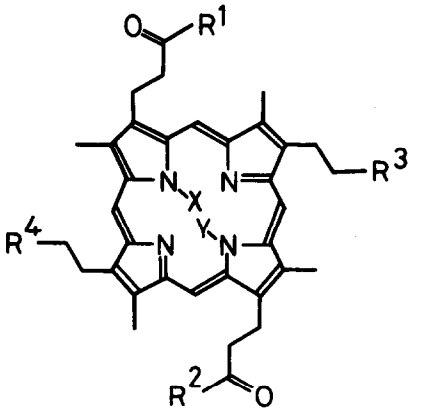
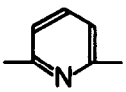
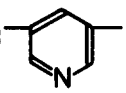
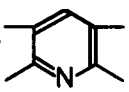
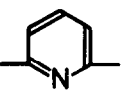
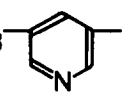
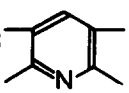
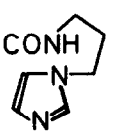
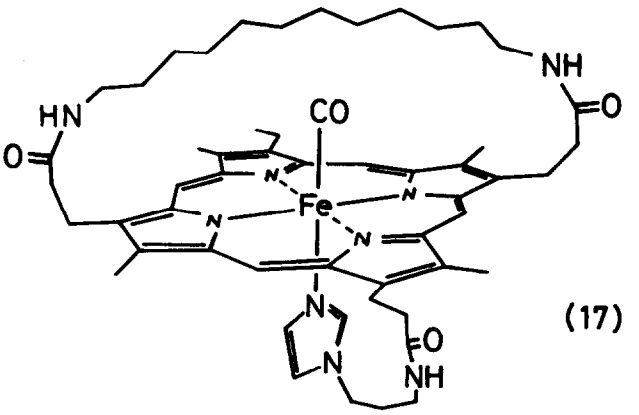


	R^1	R^2	R^3	R^4	X	Y
(1)	OH	OH	H	H	H	H
(7)	$O(CH_2)_3$  $(CH_2)_3O$		H	H	H	H
(8)	$O(CH_2)_3$  $(CH_2)_3O$		H	H	H	H
(9)	$O(CH_2)_3$  $(CH_2)_3O$		H	H	H	H
(10)	$O(CH_2)_3$  $(CH_2)_3O$		H	H	$-Fe^{III}(Cl)-$	
(11)	$O(CH_2)_3$  $(CH_2)_3O$		H	H	$-Fe^{III}(Cl)-$	
(12)	$O(CH_2)_3$  $(CH_2)_3O$		H	H	$-Fe^{III}(Cl)-$	
(13)	OH	OH	CO_2Et	H	H	H
(14)	$NH-(CH_2)_{12}-NH$		CO_2Et	H	H	H
(15)	$NH-(CH_2)_{12}-NH$			H	H	H
(18)	OH	OH	CO_2Et	CO_2Et	H	H
(19)	$NH-(CH_2)_{12}-NH$		$CONH(CH_2)_{12}NH$	CO	H	H

carrying a variety of bridges which have been built out from the periphery and span the macrocycle (e.g. 17). The examples now outlined allow control of the stoichiometry and nature of ligation for a metal ion held at the heart of the macrocycle; in addition, the bulk and rigidity of the bridge have been varied.

The required starting materials were the porphyrins (1), (3) and (18) and synthesis of the latter two involved experimental modification of the a,c-biladiene route[2] to preserve the differentation (by ester protection) of the attached propanoic acid residues. Treatment of the bis acid chloride from porphyrin (1) with the pyridine diol (2) gave (7, 13.5%); iron insertion then yielded the model (10). Similarly, the pyridine diols (3) and (4) gave the bridged porphyrins (8) and (9); (8) was prepared last under the best conditions in 38% yield. Metal insertion into (8) and (9) gave the Fe(III) complexes (11) and (12).

The diol (2) was obtained from the bis anion of 2,6-dimethylpyridine (using butyl lithium) and ethylene oxide, whilst (3) and (4) were prepared by a malonate synthesis from (5)[3] and (6), followed by reduction.



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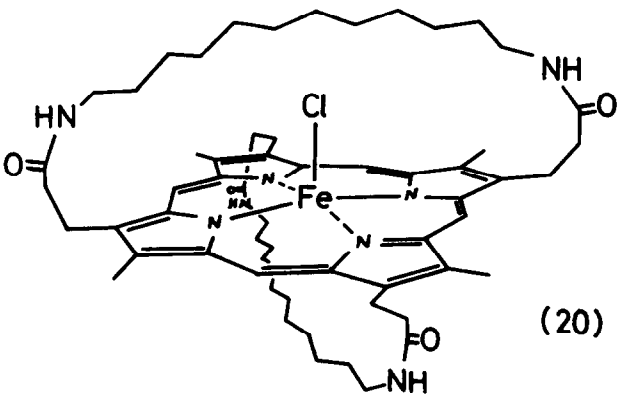

(20)

A bridged porphyrin with a covalently attached ligand (15) was prepared by reacting the bis acid chloride, derived from (13), with dodecane-1,12-diamine[4] to form (14) in 38% yield. Acidic hydrolysis cleaved the ester without affecting the amide links (82% yield) and the acid, after activation as the acid chloride, was reacted with the amine[5] (16) to attach the imidazole "tail",

forming (15). Iron insertion and reduction to Fe(II) afforded the model (17) for the active site of myoglobin, illustrated here as its stable complex with carbon monoxide which showed the expected spectroscopic properties[6].

The differentially protected tetracarboxylic porphyrin (18) was used for an analogous sequential construction of bridges across each face of the porphyrin to give the novel system (19) and the corresponding Fe(III) complex (20).

The foregoing methods allow attachment of a bridge across one face of a porphyrin and either a tail to present an imidazole ligand to the other face or a second bridge which can positively deliver a pyridine ligand. The properties of the foregoing model systems and those of related macrocycles are under investigation.

Acknowledgement

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