# $^1$H N.M.R. Studies of Chiral Porphyrins derived from *meso*-Tetrakis-(2-amino-phenyl) Porphyrins: Simple Proof of the Absence of Racemisation of the Chiral Amino Acid Residues during their Synthesis

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$^1$H N.m.r. studies of bis-strapped chiral porphyrins derived from the *meso*-5,10,15,20-tetrakis(2-aminophenyl) porphyrin show that racemisation does not occur during their synthesis.

In order to imitate the chiral recognition and the asymmetric oxygenation of a substrate by cytochrome P-450,[1] which are probably caused by amino acid residues close to the active site of the iron porphyrin, syntheses of chiral model systems have been reported in the literature: Groves *et al.*[2a] prepared porphyrins with pickets bearing chiral naphthyl moieties, Mansuy *et al.*[2b] and we ourselves[2c] prepared bis-handle porphyrins involving two identical chiral terephthalic handles containing amino acid residues. In order to increase the chiral recognition of substrates in the vicinity of the active site, we synthesised bis-*ansa* porphyrins with one pyridine chiral handle capable of co-ordinating the iron atom (like the gyroscope and bis-strapped porphyrins).[2d,3]

We report here a simple way to ascertain that no racemisation occurred during the synthesis of this new generation of porphyrins, in particular during the insertion of iron into the free porphyrin ($FeCl_2$ or $FeBr_2$ treatment with 2,6-lutidine in refluxing toluene).[4] Inspection of a Corey–Pauling–Koltun (CPK) model of porphyrins (**1**) showed that the β-pyrrolic and the $-CH(CH_3)-$ protons are privileged spectators *vis à vis* the chirality of the handles. The multiplicity of these protons should give structural information about the chiral centres on the four amino acid residues. Thus, for example, the eight β-pyrrolic protons of symmetrical compounds (**1a**) and (**1c**) (Figure 1) should exhibit two sets of four magnetically equivalent nuclei as singlets (H-2, H-3, H-12, H-13 and H-7, H-8, H-17, H-18): in other words, no coupling of the β-pyrrolic protons on the same pyrrole is expected. Of course, if some racemisation occurred, the β-pyrrolic protons of each diastereoisomer would be magnetically non-equivalent and the eight β-pyrrolic protons would then give a multitude of peaks.

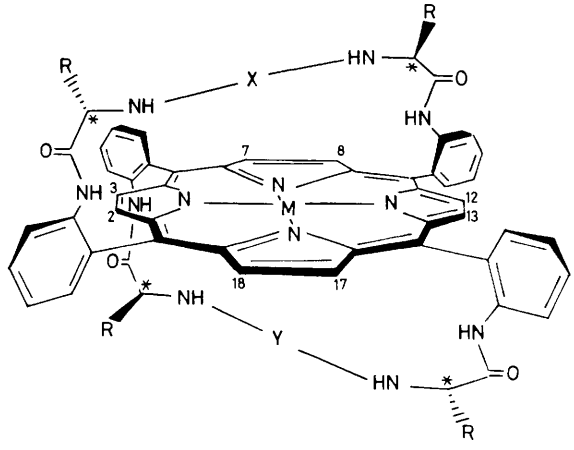


**Figure 1.** R = Me; M = $H_2$. (**1**) **a**, X = Y = $-CO-p-C_6H_4-CO-$; **b**, X = $-CO-p-C_6H_4-CO-$; Y = $-CO-m-C_5H_3N-CO-$[2c]; **c**, X = Y = $-CO-m-C_5H_3N-CO-$; **d**, X = $-CO-CH_2-p-C_6H_4-CH_2CO-$; Y = $-CO-m-C_5H_3N-CO-$[2d]; **e**, X = Y = $H_2$(tetrakis-L-Ala-$NH_2$)[3]; **f**, X = Y = $H_2$(tetrakis-D,L-Ala-$NH_2$).

In order to verify this point, we compared the $^1$H n.m.r. spectrum of the L-alanine derivative (**1e**)† with that of the racemic alanine derivative (**1f**).† As expected, the H-2, H-3, H-12, H-13 and the H-7, H-8, H-17, H-18 pyrrolic protons

† The synthesis of all the compounds will be described in a full paper;[2d] the elemental analysis (C,H,N), mass, $^1$H n.m.r., and u.v.–vis. spectra were in complete agreement with the indicated structures.

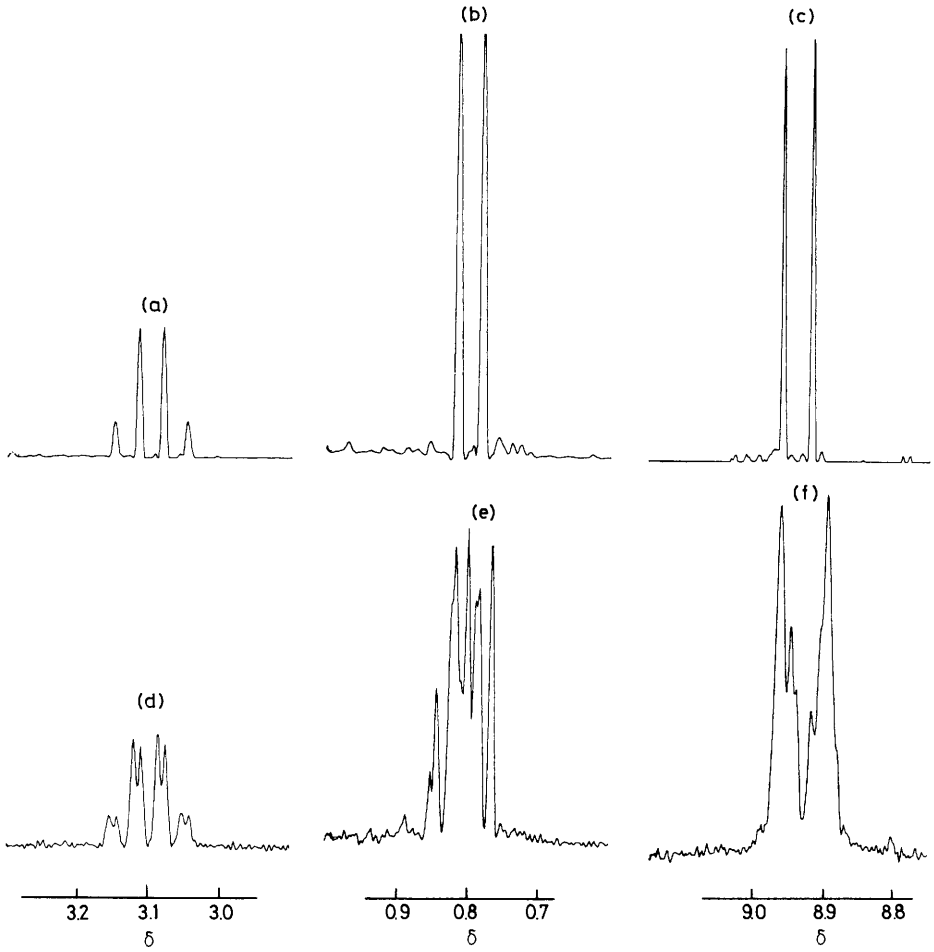


**Figure 2.** Selected $^1$H n.m.r. peaks. (**1e**): -*CH*($CH_3$)- (a); -CH(*$CH_3$*)- (b); β-pyrrolic protons (c); (**1f**): -*CH*($CH_3$)- (d); -CH(*$CH_3$*)- (e); β-pyrrolic protons (f). Gaussian multiplication was performed in both cases with GB = 0.2 and LB = −2 using a 500 MHz BRUKER spectrometer.

gave two resonances‡ as singlets in the first case and two resonances‡ as multiplets in the second case. The same effect has been pointed out for the -CH($CH_3$)- protons of the chiral entities of which resonances are a perfect doublet and quartet in the case of (**1e**) and multiplets in the case of (**1f**) (Figure 2). In the case of the bis-pyridine handle iron(II) porphyrin (**1c**–Fe), we could not detect any side bands or other peaks near the two singlets.‡ The eight β-pyrrolic protons of unsymmetrical compounds (**1b**), (**1d**), (**1b**–FeCO), and (**1d**–FeCO)† are divided into four sets of two magnetically equivalent nuclei (H-2–H-12,H-3–H-13,H-7–H-17,H-8–H18), proving definitively that no racemisation had occurred during their synthesis even in the presence of the nitrogen base 2,6-lutidine in refluxing toluene.[2d]

Analysis of the $^1$H n.m.r. spectrum of a chiral porphyrin is thus sufficient to ascertain that no racemisation had occurred during its synthesis: the ring current of the porphyrin provides a good internal shift reagent capable of distinguishing L–L alanine pairs from D–L alanine pairs. This represents an improvement over the lanthanide induced shift experiments which have been carried out previously using a mixture of (L) and (D) enantiomers of the phenylalanine counterparts of (**1a**).[2d]

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‡ *$^1$H N.m.r. data* for (**1a**): δ 8.65 (s, 4H), 9.03 (s, 4H); (**1b**): δ 8.62 (d, *J* 4.6 Hz, 2H), 8.91 (*J* 4.6 Hz, 2H), 8.93 (d, *J* 4.6 Hz, 2H), 9.03 (d, *J* 4.6 Hz, 2H) (a *J* value of 4.5 Hz has been reported by Baldwin *et al.*[5]); (**1c**): δ 8.91 (s, 4H), 9.00 (s, 4H); (**1d**): δ 8.75 (d, $J_{app.}$ 4.0 Hz, 2H), 8.87 (d, $J_{app.}$ 4.0 Hz, 2H), 8.99 (d, $J_{app.}$ 4.8 Hz, 2H), 9.00 (d, $J_{app}$ 5.1 Hz, 2H); (**1e**): δ 8.91 (s, 4H), 8.95 (s, 4H) (500 MHz $^1$H n.m.r., Pyd5). (**1b**–FeCO): δ 8.59 (*J* 4.7 Hz, 2H), 8.71 (d, *J* 4.7 Hz, 2H), 8.73 (d, *J* 4.7 Hz, 2H), 8.82 (d, *J* 4.7 Hz, 2H); (**1d**–FeCO): δ 8.54 (d, *J* 5.0 Hz, 2H), 8.64 (d, *J* 5.0 Hz, 2H), 8.66 (d, *J* 5.0 Hz, 2H), 8.86 (d, *J* 5.0 Hz, 2H) (500 MHz $^1$H n.m.r., $CDCl_3$/small amount of $CD_3OD$); (**1f**).[2d]

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