Induced Circular Dichroism of Atropisomeric Porphyrins by Combined Amino Acid Residues

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L-Amino acids combined with the atropisomeric porphyrins, *meso*-tetra(*o*-aminophenyl)porphyrin and *meso*-tetra(*o*-carboxyphenyl)porphyrin, induced circular dichroism at the Soret band of porphyrins to an extent which depended on conformation.

By a variety of modifications, atropisomeric *meso*-tetra(*o*-aminophenyl)porphyrins have been employed for studies on haem protein models,[1] electron-transfer functions[2] and molecular recognition.[3] Complex molecular structures have been constructed,[4] and further developments in this area should be achieved by utilizing the secondary structure of polypeptides. In particular, a hybrid of an atropisomer and a peptide with appropriate sequence seems to have potential in the design of sophisticated artificial proteins.

In the first steps in this approach, protected amino acid derivatives need to be effectively combined with an atropisomeric porphyrin and the fundamental spectral properties determined. Accordingly, we coupled *tert*-butoxycarbonyl (Boc)-L-Ala-OH to each atropisomer of *meso*-tetra(*o*-aminophenyl)porphyrin[1] and H-L-Ala-OEt to that of *meso*-tetra(*o*-carboxyphenyl)porphyrin[5] respectively (Fig. 1). Boc-L-1-naphthylalanine and naphthoyl-L-alanine moieties were also combined with the α,α,β,β-isomer of *meso*-tetra(*o*-amino-

phenyl)porphyrin (Fig. 1). These porphyrin compounds were subjected to various spectral analyses including absorption, fluorescence, circular dichroism (CD) and ^{1}H NMR studies.†

The absorption and CD spectra of the porphyrin derivatives **1a–f** and **2a** in methanol in the visible and UV region are shown in Fig. 2. Induced CD curves with different profiles were observed for the Soret band with the molar ellipticities [θ] varying in the range 2–8 × 10^4 deg cm^2 dmol^{-1} at the corresponding negative Cotton effect. The highly symmetrical α,α,α,α,- and α,β,α,β-isomers **1a** and **1b** showed a positive peak at 426 nm and negative peak at 416 nm, though the λ_{max} of the Soret band was 421 nm, near the mid-point of the two CD peaks. These split CD patterns seem to be related to the regularly arranged chiral moieties on the porphyrin ring. The splitting intensity of the induced CD of **1b** is greater than that of **1a**, which may be attributed to the smaller steric hindrance in **1b** as explained by the illustration in Fig. 3. This explanation

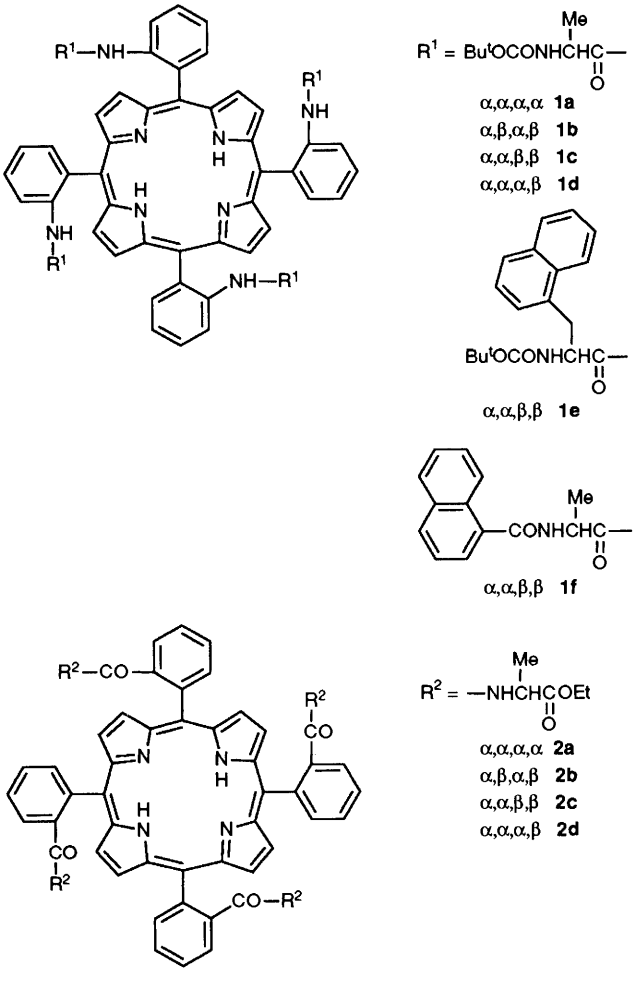

Fig. 1 Atropisomeric porphyrin derivatives combined with amino acids. Brief synthetic details: Boc-L-Ala-OH was activated as the symmetrical anhydride with dicyclohexylcarbodiimide (DCC), and then the anhydride (2.0 equiv.) was treated with each isomer of *meso*-tetra(*o*-aminophenyl)porphyrin to give **1a–d**; 74–87%, field-desorption mass spectrum (FD-MS): *m/z* 1359 (M^+). Compound **1e** was synthesized by the same method: 79%, after deprotection of the Boc groups, FD-MS, *m/z* 1463 (M^+). After removal of the Boc groups in **1c** with trifluoroacetic acid, naphthoic acid was coupled with DCC in the presence of 1-hydroxybenzotriazole (HOBt) to give **1f**: 86%, FD-MS, *m/z* 1575 (M^+). Each isomer of *meso*-tetra(*o*-carboxyphenyl)porphyrin was condensed with H-L-Ala-OEt (1.5 equiv.) with DCC–HOBt to afford **2a–d**: 65–82%, FD–MS, *m/z* 1186 (M^+).

† All the porphyrin–amino acid derivatives showed a similar fluorescence spectrum in methanol (λ_{exc} 420 nm, λ_{em} 600, 650 and 700 nm).

is supported by the very high chemical shift of the L-Ala side chain methyl group of **1b** (δ −0.124 ppm); that of **1a** was δ 0.087 ppm.‡ The more the arrangement of the methyl group placed it over the porphyrin ring, the greater the observed higher-field. Therefore, the more crowded arrangement of the four amino acid residues in **1a** on the same side of the porphyrin ring might disturb their overlap on the porphyrin moiety, and as a result give weaker ellipticity. The α,α,β,β-isomer **1c** gave an unusual induced CD, which had the greatest negative trough among the atropisomers **1a–d** at 421 nm and shoulders at 412 and 400 nm. This may be due to the irregular arrangement in conformation caused by the interaction of two

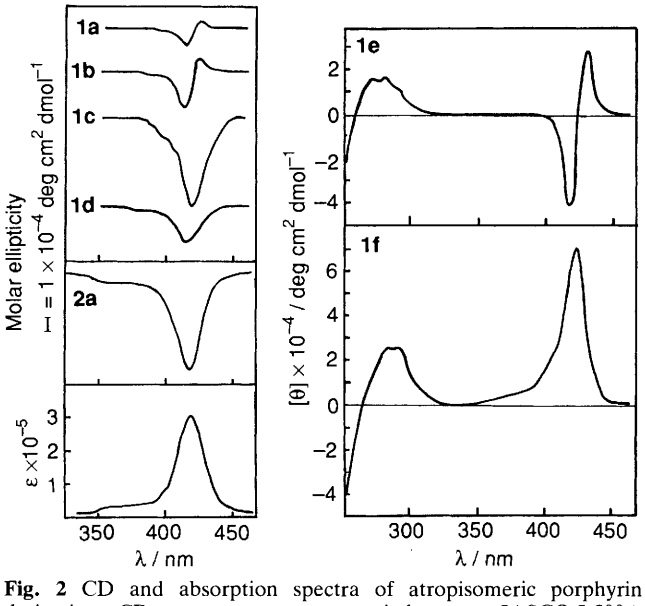

Fig. 2 CD and absorption spectra of atropisomeric porphyrin derivatives. CD measurements were carried out on a JASCO J-500A spectropolarimeter at concentrations in the range 5.0–5.9 × 10^{-5} mol dm^{-3} with a 1.0 mm light-path cell. Compounds **2b–d** showed similar induced CD to **2a** (**2a**, [θ] −82 000; **2b**, −68 000; **2c**, −41 000; **2d**, −61 000 deg cm^2 dmol^{-1}). The absorption spectrum shown is that of **1a**. The L-Ala-OEt derivatives of *meso*-tetra(*p*-carboxyphenyl)-porphyrin showed a weaker induced CD at the Soret band ([θ] + 18 000 deg cm^2 dmol^{-1}) than that of the *o*-isomer. The D-Ala-OEt derivative of α,α,α,α-*meso*-tetra(*o*-carboxyphenyl)porphyrin showed an induced CD of positive sign with similar intensity ([θ] + 81 000 deg cm^2 dmol^{-1}) to that of **2a**.

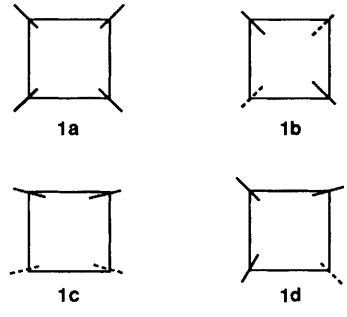

Fig. 3 Illustration of the conformational interactions between the porphyrin ring and amino acid residues in various atropisomeric porphyrin derivatives. The square represents the porphyrin ring. The solid and broken bars denote the L-Ala unit above and below the porphyrin ring, respectively. The location of the bar shows the extent of overlap with the ring. The angle of the bar to the ring denotes the extent of the interaction.

‡ ^{1}H NMR spectra were recorded in $(CD_3)_2SO$ at 20 °C on a JEOL JNM GX-400 spectrometer. The porphyrin–amino acid derivatives **1a**, **1b**, **2a** and **2b** showed simple spectra, while those of **1c**, **1d**, **2c** and **2d** were complicated. The details of the NMR studies will be reported elsewhere.

neighbouring amino acid residues as illustrated in Fig. 3. The asymmetric isomer **1d** showed a simple negative Cotton effect for the whole Soret band region. The fine structure of the CD is too complicated for resolution by the instrument used.

The other series of porphyrin derivatives **2a–d** all gave featureless induced CD in the Soret band region (Fig. 2). In both series, the tetraphenylporphyrin moiety is separated from the chiral centre by an amide group, although in opposite directions. The effect of the direction of the amide bond on the overlapping of the amino acid residues on the porphyrin ring was further examined by ^{1}H NMR measurements. The chemical shifts of the L-Ala side chain methyl groups in **2a** and **2b** were at δ 0.519 and 0.516 ppm,‡ respectively, at much lower magnetic field than those of **1a** and **1b**. The methyl groups in **2** interact only shallowly with the porphyrin ring. Therefore, the amino acid residues retain flexibility so that they can adopt a looser orientation with respect to each other and as a result induce a featureless CD.

For further investigation of the induced CD of porphyrin compounds, the derivatives **1e** and **1f** were additionally prepared. Their CD spectra in the Soret band region are shown in Fig. 2. Compound **1e** showed a very sharply split CD pattern (positive peak at 427 nm and negative peak at 417 nm), probably because the bulky naphthalene rings in the side chains of the chiral amino acid increased its conformational regularity. In contrast, the more remote achiral naphthoyl groups of **1f**, which would be in a looser orientation, led to a featureless CD pattern. These facts suggest that spatial arrangement must be taken into account in the design of porphyrin–peptide hybrids.

In conclusion, atropisomeric porphyrin derivatives are useful in allowing different arrangements of amino acids on the porphyrin ring, and the preferred conformations can be distinguished by spectroscopic analyses (CD and NMR). Fine-tuning of such designs with polypeptides may produce specially functionalized artificial proteins.

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