Synthesis and characterization of a chiral nonplanar porphyrin

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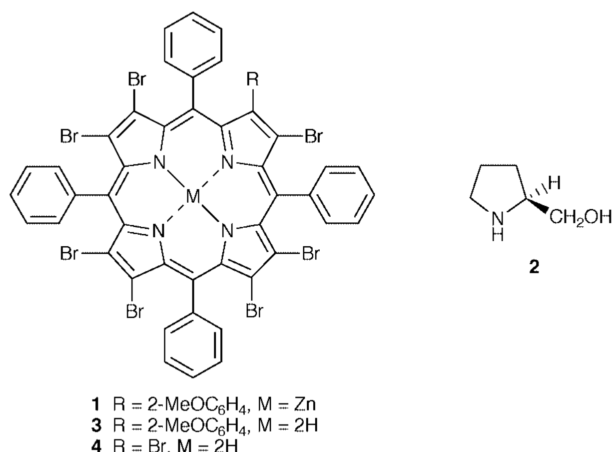
The chiral nonplanar porphyrin zinc(II) 3,7,8,12,13,17,18-heptabromo-2-(2-methoxyphenyl)-5,10,15,20-tetraphenylporphyrin has been synthesized and its properties investigated.

The porphyrin macrocycle provides a versatile platform upon which to build elaborate superstructures, and this feature coupled with a rich and well-developed synthetic chemistry has led to the synthesis of many models of heme protein active sites[1] and numerous porphyrin-based receptor molecules.[2] One characteristic which is not normally considered in the design of porphyrin-based receptors is nonplanarity of the porphyrin macrocycle,[3] although the nonplanar systems that have been investigated (*e.g.* a pyridine sensitive Venus Flytrap[4] and a chirality-memory molecule[5]) have displayed quite unusual properties. Herein, we describe the synthesis and characterization of a new porphyrin-based chiral receptor molecule (**1**)



which exploits some structural features unique to nonplanar porphyrins.

Fig. 1 shows the four structures expected for porphyrin **1**. Structures **A** and **B** (or **C** and **D**) are enantiomers, structures **A** and **C** (or **B** and **D**) are related by rotation of the 2-methoxyphenyl group, and structures **A** and **D** (or **B** and **C**) are related by inversion of the nonplanar porphyrin macrocycle. Porphyrin **1** was calculated[6] to have a very high barrier for rotation of the 2-methoxyphenyl group (>146 kJ mol^{-1}), a low barrier for inversion of the porphyrin macrocycle[7] (*ca.* 40 kJ mol^{-1}), and a strong preference (ΔE = 8 kJ mol^{-1}) for structures **A** and **B** *vs.* structures **C** and **D**. Hence, it should be resolvable into two optically active components consisting primarily of structures **A** or **B**. Porphyrin **1** was designed with the aim of using a cavity formed by the nonplanar macrocycle to orient an axial ligand,[8] such that a hydrogen bond acceptor site (the methoxy group) could interact stereospecifically with hydrogen bond donor sites on the axial ligand. Fig. 2 shows the lowest energy structure calculated for a complex of **1** with (*S*)-2-pyrrolidinemethanol (**2**) which illustrates this ligand orientation effect and the formation of stereospecific hydrogen bonds with one enantiomer of the porphyrin (structure **B**). Note that the nonplanar deformation of the macrocycle serves a dual function as it also moves the methoxy substituent closer to the ligand than would be possible if the porphyrin were planar.

To prepare porphyrin **1**, porphyrin **3** was first synthesized using a Suzuki coupling reaction.[9] In this reaction, porphyrin **4** (1 equiv.), 2-methoxyphenylboronic acid (5 equiv.), Pd[(PPh_3)]$_4$ (0.15 equiv.) and K_2CO_3 (20 equiv.) in toluene under argon were heated at 90–100 °C for two days. MALDI mass spectrometry of the crude product revealed the presence of unreacted **4**, porphyrin **3**, and porphyrins with two or more 2-methoxyphenyl groups. Porphyrin **3** was isolated from this mixture using column chromatography (silica gel eluted with 3:2 $CHCl_3$–hexane) and obtained in 12% yield. The structure of **3** was confirmed by MALDI mass spectrometry and ^{1}H NMR spectroscopy. Zinc was then inserted using the metal acetate method to give **1**.

When porphyrin **1** was subjected to HPLC using a Chiralcel OD column eluted with 89:10:1 hexanes–$CHCl_3$–Pr^{i}OH, two fractions (elution times 12 and 28 min) were obtained. These fractions had identical optical spectra but their CD spectra were mirror images of each other. Leaving each fraction in the eluent and reinjecting it through the HPLC column 24 h after

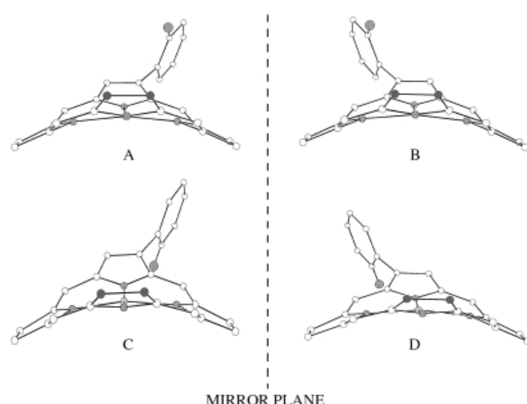


Fig. 1 Representations of the four structures expected for porphyrin **1**.

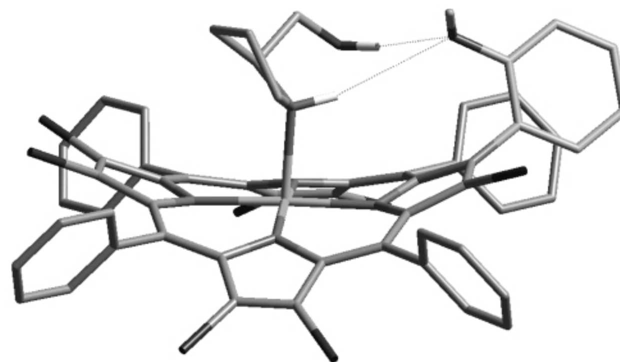


Fig. 2 Minimum energy structure calculated (ref. 6) for the complex of porphyrin **1** with ligand **2**. Porphyrin–ligand hydrogen bonds are indicated by broken lines.

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separation revealed only a trace of racemization, in agreement with the high rotational barrier calculated for the 2-methoxyphenyl group. The isolation of only two HPLC fractions together with ^{1}H NMR studies of **1** confirmed that structures **A** and **D** (or **B** and **C**) were being interconverted by inversion of the porphyrin macrocycle.[7] The ^{1}H NMR spectrum of **1** showed a single broad methoxy signal at 295 K (δ 2.77) which split into two signals at 193 K (δ 2.30, integration 11.5 and δ 3.61, integration 1). As the methoxy signals at δ 2.30 and 3.61 could be assigned to **A** and **B** or **C** and **D** based on the expected ring current shifts of the methoxy protons in these structures, it was clear that the interconversion of **A** and **D** (or **B** and **C**) was rapid at room temperature and that **A** and **B** were significantly favored over **C** and **D**. Both the conformational energy difference (4 kJ mol^{-1} at 193 K) and the activation energy for macrocylic inversion (51 kJ mol^{-1} at the coalescence temperature of 273 K) were in reasonable agreement with the energies obtained from the modelling studies.

Despite repeated attempts we were unable to determine the X-ray structures of the porphyrins in the two HPLC fractions. However, modelling studies suggested that it should be possible to differentiate enantiomers **A** and **B** by their interactions with ligand **2**. In the case of structure **B**, ligand **2** should bind in essentially a single orientation because there is an energy difference of at least 5 kJ mol^{-1} between the minimum energy structure (Fig. 2) and other low energy structures (where the ligand is rotated approximately 180° in the cavity or is bound in either orientation in the cavity on the other face of the porphyrin). For structure **A**, the energy difference between these ligand binding geometries is calculated to be smaller, suggesting that the ligand should bind in multiple orientations. The hydrogen bonding seen in the lowest energy calculated structure of **B** (Fig. 2) is also expected to produce a downfield shift of the ligand NH and OH proton signals that should be absent or less pronounced for structure **A**. NMR spectra of the HPLC fractions dissolved in toluene-d_8 containing approximately 1 equiv. of **2** are shown in Fig. 3. The spectra were measured at 193 K where ligand exchange, ligand rotation, inversion of the porphyrin macrocycle, and rotation of the 2-methoxyphenyl group can all be demonstrated to be slow on the NMR timescale. The ligand proton region of the HPLC fraction with a retention time of 28 min shows only a single downfield-shifted pyrrolidine NH signal (definitively assigned by deuteration with D_2O) and agrees with the spectrum expected for structure **B**. In contrast, the HPLC fraction with a retention time of 12 min displays four NH signals (none of which are shifted downfield) consistent with the spectrum expected for structure **A**. Ligand signals were not seen for **C** and **D** in agreement with the higher energies calculated for these structures.

The results reported here provide further confirmation that nonplanar deformations of the porphyrin macrocycle can be exploited to produce unusual porphyrin-based receptor molecules. The present work also demonstrates the usefulness of molecular modelling techniques in the design and characterization of new porphyrin-based materials.

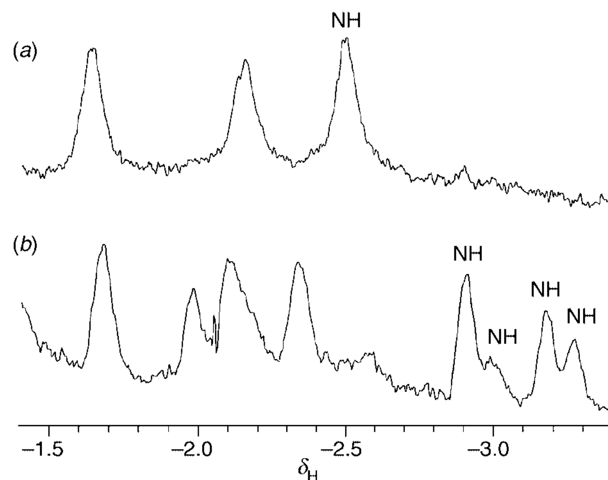

Fig. 3 Part of the ligand proton region from the 300 MHz ^{1}H NMR spectra of the complexes of **1** with ligand **2**: (*a*) fraction of **1** with 28 min HPLC retention time, and (*b*) fraction of **1** with 12 min HPLC retention time.

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Notes and references

1 J. P. Collman, *Inorg. Chem.*, 1997, **36**, 5145.
2 H. Ogoshi, T. Mizutani, T. Hayashi and Y. Kuroda, in *The Porphyrin Handbook*, ed. K. M. Kadish, K. M. Smith and R. Guilard, Academic Press, Burlington, MA, 1999, vol. 6, ch. 46.
3 J. A. Shelnutt, X.-Z. Song, J.-G. Ma, S.-L. Jia, W. Jentzen and C. J. Medforth, *Chem. Soc. Rev.*, 1998, **27**, 31.
4 M. Mazzanti, J.-C. Marchon, M. Shang, W. R. Scheidt, S. Jia and J. A. Shelnutt, *J. Am. Chem. Soc.*, 1997, **119**, 12400.
5 Y. Furusho, T. Kimura, Y. Mizuno and T. Aida, *J. Am. Chem. Soc.*, 1997, **119**, 5267.
6 For details of the force field used in the calculations see: X.-Z. Song, L. Jaquinod, W. Jentzen, D. J. Nurco, S.-L. Jia, R. Khoury, J.-G. Ma, C. J. Medforth, K. M. Smith and J. A. Shelnutt, *Inorg. Chem.*, 1998, **37**, 2009.
7 C. J. Medforth, in *The Porphyrin Handbook*, ed. K. M. Kadish, K. M. Smith and R. Guilard, Academic Press, Burlington, MA, 1999, vol. 5, ch. 35, pp. 70–73.
8 C. J. Medforth, C. M. Muzzi, K. M. Smith, R. J. Abraham, J. D. Hobbs and J. A. Shelnutt, *J. Chem. Soc., Chem. Commun.*, 1994, 1843.
9 K. S. Chan, X. Zhou, B.-S. Luo and T. C. W. Mak, *J. Chem. Soc., Chem. Commun.*, 1994, 271.

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