Introduction of Chirality to the Remote, Open Face of a Metalloporphyrin through Coordination to the Metal of a Specially Designed Pendant Arm

Akihisa Hamazawa, Toshihiro Yano, Takanori Nishioka, Isamu Kinoshita,* Kiyoshi Isobe, Shigenobu Yano,†
L. James Wright,†† and Terrence J. Collins†††
Department of Material Science, Graduate School of Science, Osaka City University, 3-3-138, Sugimoto, Sumiyoshi-ku, Osaka 558-8585
†*Division of Material Science, Graduate School of Human Culture, Nara Women's University, Kitauoyanishimachi, Nara 630-8506*
††*Department of Chemistry, The University of Auckland, Private Bag 92019, Auckland 1020, N. Z.*
†††*Department of Chemistry, Carnegie Mellon University, 4400, Fifth Av., Pittsburgh, PA 15213-2683, U. S. A.*

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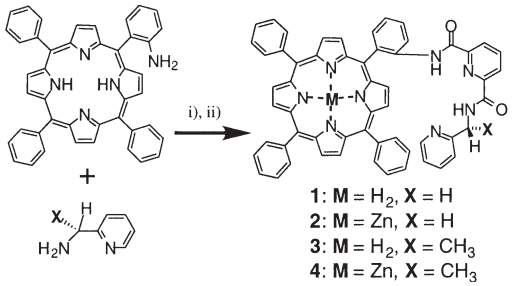
Chirality has been introduced to a metalloporphyrin by a new approach that involves coordination to the metal of a pendant arm, with the preferred conformation adopted by the resulting chelate ring causing the *meso*-phenyl group to which the arm is attached to twist and thereby introduce chirality to the remote, open face of the metalloporphyrin.

The study of chiral porphyrins and metalloporphyrins has developed into an important area of scientific endeavour. Interest in these compounds is stimulated by the diverse relevance they have in medicine,[1] enantioselective catalysis,[2] chiral recognition,[3] chirogenesis[4] and even chiral sensing and memory.[5] Chirality has been introduced into porphyrins using several different strategies. The most common approach involves the attachment of chiral units either to preformed porphyrins or to the aldehyde and pyrroles employed in the porphyrin-forming stage.[2g] An alternative approach involves the introduction of achiral substituents to the porphyrin core in such a way that chirality is generated. For example, intrinsically chiral porphyrins have been formed by the introduction of selectively substituted, achiral *meso*-aryl groups,[6] or by the addition of achiral straps, either between the ortho-positions of adjacent *meso*-phenyl substituents[7] or opposite β-pyrrolic positions.[8]

In this paper we describe the induction of chirality into a metalloporphyrin by a new approach that involves coordination to the metal of a specially designed pendant arm that is covalently attached to the ortho-position of one of the *meso*-phenyl groups. The conformation adopted by the chelated pendant arm causes the attached *meso*-phenyl ring to twist with respect to the porphyrin plane, and this twist imparts chirality to the remote, open face of the metalloporphyrin.

The achiral porphyrin **1** was prepared by treatment of 5-(2-aminopheny)-10,15,20-triphenylporphyrin with 2,6-pyridinedicarbonyl dichloride and 2-(aminomethyl)pyridine as shown in Scheme 1. Metallation of **1** with $Zn(OAc)_2 \cdot 2H_2O$ affords the zinc porphyrin **2** and the structure of **2** was determined by X-ray crystallography.[9] The terminal pyridine of the pendant arm is axially coordinated to the zinc atom ($Zn–N_{pyridine} = 2.234(4)$ Å) and the Zn(II) ion deviates 0.366(2) Å from the $4N_{pyrrole}$ plane toward the axial pyridine. The 2,6-diamidepyridine group, with hydrogen bonds between the amide nitrogen atom and the central pyridine nitrogen atom, is rigidly planar. The chelate ring gains flexibility through rotations about the bonds to the phenyl group and the methylene carbon atom. In order to accommodate coordination of the terminal pyridine nitrogen atom to zinc, the



Scheme 1. Syntheses of **1**–**4**. i) 2,6-pyridinedicarbonyl dichloride, NEt_3, THF. ii) $Zn(OAc)_2 \cdot 2H_2O$, $CHCl_3$, MeOH.

chelate ring adopts a conformation that is chiral and the unit cell contains a pair of enantiomers related by an inversion centre. In the enantiomer depicted in Figure 1, the coordinated arm has M helicity and the diastereotopic nature of the methylene hydrogen atoms can be clearly seen, with one C–H bond lying parallel to the porphyrin ring and the other directed towards the porphryin ring. One significant feature associated with the chelate ring is that the ortho-substituted *meso*-phenyl group is rotated by 22.5° from the perpendicular to the average plane through the porphyrin ring. The rotation of this one phenyl group introduces chirality to the open porphyrin face remote from the chelate ring.

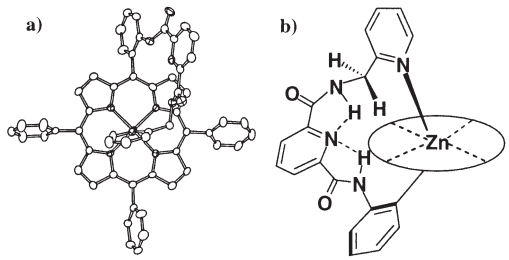


Figure 1. a) ORTEP drawing of the M helical isomer of **2**. b) Schematic presentation of pendant arm of **2**. One of the methylene protons lies parrallel to the porphyrin ring, and the other points directly towards the porphyrin ring.

Studies of **2** by variable temperature, solution ^1H NMR spectroscopy show that the CH_2 protons undergo an equilibration process at higher temperatures that is rapid on the ^1H NMR time-scale. Thus, at 293 K the two CH_2 protons of **2** are observed as a broad singlet at 0.5 ppm. As the temperature is lowered to 243 K this signal practically disappears, and at 193 K, the signal for the CH_2 group reappears as two sharp signals at 2.84 ppm and −2.26 ppm (see Figure 2). The large difference in the chemical shift observed between the signals at low temperature is

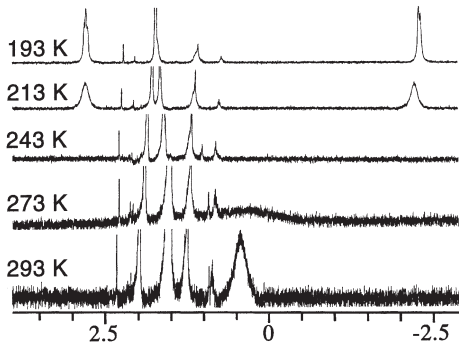


Figure 2. Variable-temperature ^{1}H NMR spectra (400 MHz) of a solution of **2** in CD_2Cl_2 between 193 and 293 K.

consistent with the two CH_2 protons being located in very different environments, as was found in the solid-state structure. The coalescence of these signals as the temperature rises is interpreted as resulting from a rapid interchange between the two enantiomers of **2** through a simple conformational change of the chelate ring. From the difference in chemical shifts of the diastereotopic methylene protons at low temperature and the coalescence temperature of 243 K, $\Delta G^{\ddagger}$ for this dynamic process was estimated as 10.2 kJ mol^{-1}.[10]

If (*R*)-1-(2-pyridyl)ethylamine[11] is used instead of 2-(aminomethyl)pyridine in the synthesis of the pendant arm porphyrin (see Scheme 1) compound **3** is produced. Compound **3** is an analogue of **1** in which one of the methylene hydrogen atoms has been replaced with a methyl group. Metallation of **3** with $Zn(OAc)_2{\cdot}2H_2O$ produces **4**, which is the corresponding analogue of **2**. ^{1}H NMR data for **4** indicate that the terminal pyridine of the pendant arm is coordinated to zinc in the same manner as it is in **2**. The resonances of the two amide protons, which are strongly influenced by the porphyrin ring current, are observed at 4.55 and 10.72 ppm. The corresponding resonances in **2** appear at 4.16 and 11.2 ppm. Only one sharp signal is observed in each case for the CH (−1.67 ppm) and CH_3 (0.36 ppm) protons of the $CHCH_3$ group over the entire temperature range investigated (193–293 K). This indicates that the chelate ring in **4** is conformationally locked and only one enantiomer is formed. The data is most consistent with this enantiomer being the one that has the methylene proton pointing in towards the porphyrin ring.

Figure 3 shows the circular dichroism spectra of **3** and **4**. A significant Cotton effect appears around the Soret band of **4**, but this is not observed for **3**. The difference between the CD spectra for **3** and **4** indicates the presence of chirality for **4** but not for **3**,

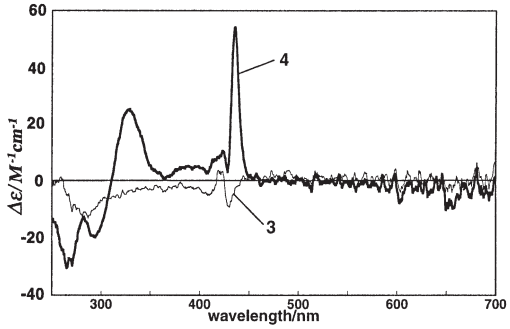


Figure 3. Circular dichroism spectra of solutions of **3** and **4** in CH_2Cl_2.

and that the origin of the chirality must therefore be mainly caused by the coordination of the side arm.

In conclusion, we report here a new approach to the synthesis of chiral metalloporphyrins. In **2**, a specially designed pendant arm, which is covalently attached to the ortho-position of a *meso*-phenyl group, coordinates to the metal. The arm has limited flexibility and the chirality arises from the conformation adopted by the chelate ring and the associated twisting of the attached *meso*-phenyl ring with respect to the porphyrin plane. The two enantiomers of **2** rapidly interconvert at 293 K. As they do this, the helicity of the coordinated arm and the direction of tilt of the *meso*-phenyl ring changes. When one of the hydrogens of the methylene group is replaced by methyl, as in metalloporphyrin **4**, the chelate ring is locked into one conformation and only one enantiomer is observed. Importantly, the imposed, controlled rotation of the *meso*-phenyl group with respect to the porphyrin plane introduces chirality to the remote, open face of the porphyrin. In principle this feature could be utilized in the design of chiral, synthetic enzymes, such as those modelled on the heme-containing cytochromes P_{450}.

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9 Crystal data for **2**: $C_{57}H_{38}N_8O_2Zn$, $M_r = 932.36$, purple blocks, monoclinic, space group $P2_1/c$ (no. 14), $a = 11.742(6)$ Å, $b = 17.379(7)$ Å, $c = 22.29(1)$ Å, $\beta = 99.267(9)^\circ$, $V = 4489(3)$ Å^3, $Z = 4$, $F(000) = 1928.00$, $D_{calcd} = 1.379$ g cm^{-3}, μ(Mo Kα) = 6.03 cm^{-1}. Crystal dimensions: $0.30 \times 0.10 \times 0.40$ mm^3. A total of 33819 reflections was collected, 9885 unique ($R_{int} = 0.117$). The structure was solved by direct method (SIR92), and developed through subsequet cycles of least squares refinement and difference Fourier synthesis, final $R1 = 0.068$ and $R_w = 0.190$ for 5330 reflections ($I > 2\sigma(I)$) with a GOF of 0.98. Data were measured on a Rigaku/MSC mercury CCD diffractometer with graphite monochromaized Mo Kα ($\lambda = 0.71070$ Å) radiation at 153 K.

10 The ^{1}H NMR behavior of the CH_2 protons does not change with addition of up to 10 equivalent of CD_3CN. The chemical shift of the 6th position of the coordinated pyridine stays in the same field from 193–293 K indicating the same coordination for these temperature regions.

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