spectra. As in previous efforts,[21,5] the relatively small contribution of the J coupling is ignored in this study. The possibility also exists that in hydrated samples of polypeptides the bond lengths will be different than the bond lengths obtained from crystalline dipeptides. Structural models of the gramicidin channel show that the alternating L and D amino acids fold into a β-helix in which the Ala_3 amide proton is hydrogen bonded to the carbonyl of Val_8. Therefore, it is anticipated that, like the crystalline dipeptides, the Ala_3 amide proton will be hydrogen bonded. However, crystal packing forces as well as the packing of this polypeptide into a β-helix in a model membrane may result in certain constraints that affect either the bond length directly or the accurate determination of the bond length.

The observations reported here provide for a direct determination of the maximum value for the N-H bond lengths in the gramicidin channel without resorting to crystallization, dehydration, model compounds, or scaling of the dipolar interaction. Furthermore, by assuming that the N-H bond length is 1.024 Å the Ala_3 N-H bond makes an angle with the bilayer normal of less than 10°. The gramicidin channel is typically modeled as a left-handed β-helix. Such a model has the Ala_3 N-H bond orientation tipped by approximately 25° with respect to the bilayer normal. Alternatively, a right-handed β-helix would allow for this experimentally determined N-H bond orientation. Therefore, our results reopen the possibility that the helix is right-handed and not left-handed as generally assumed.

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Cyclodextrin-Sandwiched Porphyrin†

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One of the most characteristic features of hemoproteins is that the porphyrin molecules are usually bound in the hydrophobic pocket formed in the apoprotein structure. Such hydrophobic microencapsulation of porphyrins may significantly affect their properties such as reactivity and substrate interactions.[1] We report here the syntheses of the new type of porphyrins, β-cyclodextrin-sandwiched porphyrin (**I**), which mimics these characteristics of holohemoproteins.

Since considerations of CPK space-filling models of **I** suggested that there may be five possible isomers (**Ia-e**) according to their connection pattern of porphyrin with two cyclodextrins, both of the two coupling reactions of porphyrin with cyclodextrins, diagonal and side coupling, were attempted (Scheme I). The atropisomers of porphyrin, tetrakis(*o*-thioacetoxyphenyl)-porphyrins, prepared from *o*-thioacetoxybenzaldehyde and pyrrole by the method of Lindsey et al.[2] (20% yield), were separated by the preparative HPLC (YMC Co., SIL, benzene/$CHCl_3$ = 90/10), and the coupling reactions of $\alpha\beta\alpha\beta$ and $\alpha\alpha\beta\beta$ atropisomers with A,D-diiodo-β-cyclodextrin[3] were carried out under the basic condition shown in Scheme I. Interestingly, the two types of coupling reactions, diagonal and side coupling reactions, were confirmed by HPLC analyses of the products (YMC Co., ODS-AQ, CH_3CN/H_2O = 14/86 - 17/83 linear gradient) to be completely specific; i.e., two diagonal coupling products and three side coupling products were obtained starting from $\alpha\beta\alpha\beta$ and $\alpha\alpha\beta\beta$ atropisomers of porphyrin, respectively, in the expected statistical yield of each isomer (**Ia/Ib** = 1/1, **Ic/Id/Ie** = 1/2/1 and 10-15% total yield). The FAB mass spectra of these five isomeric products show molecular peaks at 2940 (mw 2940.96 as $C_{128}H_{162}O_{66}N_4S_4$).[4] Further confirmation of structures of **Ia-e** was obtained from analyses of their 400 MHz NMR spectra based on their molecular symmetries. The NMR spectra of **Ia(b)**, **Id**, and **Ie** were shown in Figure 1 as the typical example. Since **Ie** have the C_2 symmetry as shown in Scheme I, two cyclodextrin molecules in **Ie** are expected to be identical. Thus, six C1-H doublets of cyclodextrin containing one overlapped signal were observed at δ 3.9 - δ 5.1 as 14 C1-H protons. On the other hand, 12 C1-H doublets containing two overlapped signals were observed at the same range for **Id** which have no symmetric element. Similar situations were

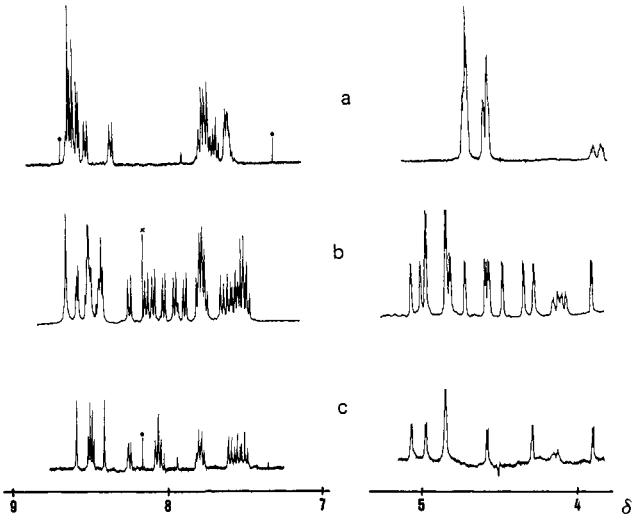
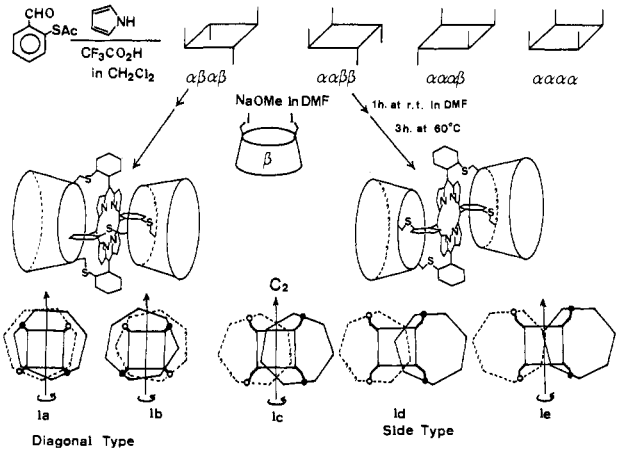


Figure 1. Aromatic and C1 proton regions of 400 MHz ^1H NMR spectra of cyclodextrin-sandwiched porphyrins in 5% D_2O-DMSO-d_6 at 80 °C: (a) isomer **Ia(b)**, (b) isomer **Id** and (c) isomer **Ie**.

Scheme I



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† This paper is dedicated to the late Professor Iwao Tabushi.
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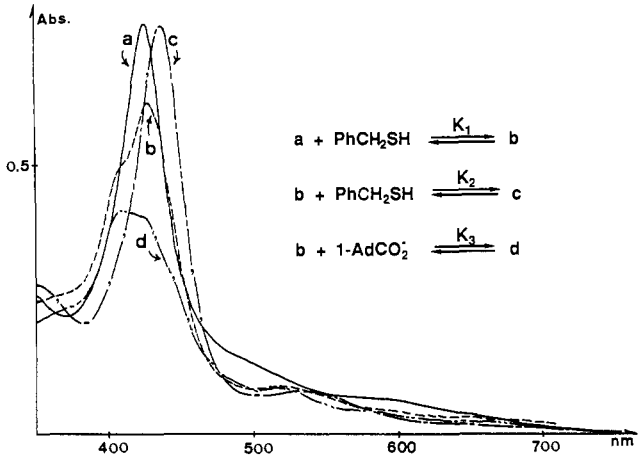

Figure 2. Electronic spectra of the ferric complex of **Ia(b)** in the aqueous phosphate buffer solution (pH = 7.0). (a) **Ia(b)**·Fe(III)·Cl; 6.3×10^{-6} M, (b) (a) + 6.3×10^{-6} M of benzylmercaptane, (c) (a) + 6.0×10^{-5} M of benzylmercaptane, (d) (b) + 6.0×10^{-5} M of 1-adamantanecarboxylate.

observed for an aromatic region where signals of pyrrole and benzene rings appeared;[5] i.e., two types of benzene protons at 3, 4, 5, and 6 positions and four types of pyrrole protons were observed for **Ie**; and, in contrast, all benzene and pyrrole protons appeared separately for **Id** (Figure 1 (parts b and c)). For **Ic**, the reduced signal pattern similar to that for **Ie** was observed because of its C_2 symmetry. In the case of **Ia** and **Ib**, the situations are somewhat different from those of **Ic-e**. Since, in these diagonal coupling products, the C_4 symmetry axis of the tetraphenylporphyrin part and the C_7 symmetry axes of two cyclodextrin parts almost coincide, 14 glucose rings in these compounds exist in the very similar environment. Thus, more heavily overlapped C1-H signals were observed for **Ia** and **Ib** as shown in Figure 1a, though spectra of the aromatic region are still analyzable as that of the molecule with C_2 symmetry. Combining these results of diagonal and side coupling patterns, statistical yields and elution patterns of each isomer in HPLC analyses,[6] and NMR spectra, the structures of present cyclodextrin-sandwiched porphyrins are assigned except **Ia** and **Ib**; i.e., for two diagonal coupling products, it is not determined at the present stage which product is corresponding to **Ia** or **Ib**.

As one of the examples of usefulness of the present cyclodextrin-sandwiched porphyrin that the hemoprotein mimics, the coordination and binding behavior of the Fe(III) complex of **Ia(b)** was preliminarily investigated.[7] The spectroscopic behavior of axial coordination by benzylmercaptane and binding of 1-adamantanecarboxylate in aqueous solution is shown in Figure 2. The titration experiments show the following characteristic behavior of the present Fe(III) complex: (i) tight first coordination by benzylmercaptane ($K_1 > 10^7$ M^{-1}, species b in Figure 2), (ii) second coordination by the mercaptane with the measurable binding constant ($K_2 = (7 \pm 3) \times 10^4$ M^{-1}, species c in Figure 2), (iii) binding of 1-adamantanecarboxylate with the usual binding constant ($K_3 = (7 \pm 1) \times 10^5$ M^{-1}, species d in Figure 2) which suggests that 1-adamantanecarboxylate can be bound more easily than the second benzylmercaptane molecule. The final observation is very interestingly related with the initial substrate binding step of P-450. It is well established for some cytochrome P-450's that the spin state of the ferric heme is largely affected by addition of substrate.[8] Thus, the species generated in step iii which has one mercaptane ligand and one hydrophobic adamantane molecule seems to be a promising model for investigation on these initial reaction steps of P-450.[9]

The more detailed investigations using present cyclodextrin-sandwiched porphyrines as hemoprotein mimics are now underway in our laboratory.

(5) Since the NMR signal of pyrrole protons of **Ic** and **Id** were very broad at 25 °C and sharpened at 80 °C, porphyrin rings of these compounds were expected to suffer significant motional restriction at room temperature.

(6) The order of retention times of these isomers in HPLC analyses is **Ie** > **Id** > **Ic** > **Ib(a)** ≥ **Ia(b)**. This order is determined by the degree of positional deviations of two cyclodextrin molecules relative to the porphyrin ring, which alters the number of exposed C6-OH's, the exposed area of porphyrin surface, and the molecular dimension of **I**.

(7) The Fe(III) and Zn(II) metalation of **I** proceeds normally by using $FeCl_2$ and $Zn(Ac)_2$ in DMF-pyridine or 2,6-lutidine.

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(9) Preliminary results of EPR measurements at 4 K show the generation of the high spin ferric species by addition of 1-adamantanecarboxylate.

Synthesis and Gas-Phase Vibrational Circular Dichroism of (+)-(*S*,*S*)-Cyclopropane-1,2-$^2H_2$

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Synthesis of (+)-(*S*,*S*)-cyclopropane-1,2-$^2H_2$ has been achieved only once, by Berson and Pedersen in 1974.[1] In spite of the evident utility offered by the chiral dideuteriocyclopropanes for fundamental spectroscopic and reactivity studies, they have remained largely a subject for theoretical conjecture rather than of experimental scrutiny. For example, in 1986, Lowe, Segal, and Stephens[2] predicted the vibrational circular dichroism (VCD)[3-7] spectrum of (+)-(*S*,*S*)-cyclopropane-1,2-$^2H_2$, but no VCD data for this exceptionally suitable subject were then or have subsequently been obtained.

We have responded to this situation by developing a new synthetic route to the chiral dideuteriocyclopropanes, preparing both antipodes in optically pure form as well as the racemic species, and securing gas-phase VCD spectra between 3100 and 850 cm^{-1}.

Dimethyl *trans*-cyclopropanedicarboxylate-1,2-$^2H_2$ was hydrolyzed[8] to the enantiomeric acid esters, which were resolved by way of the diastereomeric amides prepared from (-)-(*R*)-2-phenylglycinol.[9] Chromatography provided both diastereomeric ester amides of better than 99% diastereomeric purity. Each amide was hydrolyzed in aqueous H_2SO_4:THF, and the resulting diacids were converted to the corresponding dimethyl esters (96% deuterated at C(1,2) by NMR, >98 ee by $Eu(hfc)_3$ chiral shift reagent analysis, 57% yield from the (±)-d_2-diester). The d_2-diester from the early eluting amide had $[\alpha]_D$ -239° ($CDCl_3$) and thus is of (*R*,*R*) configuration.[10,11] Each chiral d_2-diester was reduced to the corresponding d_2-dialdehyde ($^iBu_2AlH$, -100 °C); the gas

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(11) The (*R*,*R*)-d_0-diester had $[\alpha]_{578}$ -233° (MeOH); lit.[10a] -232°; from the (*S*,*S*)-d_2-amide was secured diester of $[\alpha]_D$ +236 (CCl_4), +239° ($CDCl_3$); lit.[10b] +236° (CCl_4).

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