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New Type of Cyclodextrin Sandwiched Porphyrin

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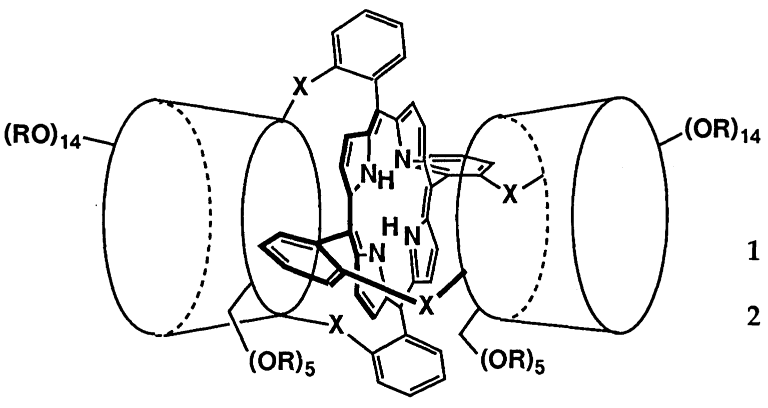
A porphyrin having two molecules of 2,3,6-permethyl-β-cyclodextrin was synthesized. The starting materials employed were the αβαβ atropisomer of meso-tetrakis(o-aminophenyl)porphyrin and the diacidchloride of A,D-dicarboxyl derivative of 2,3,6-permethyl-β-cyclodextrin. As expected the product contained two isomers which were isolated by HPLC.

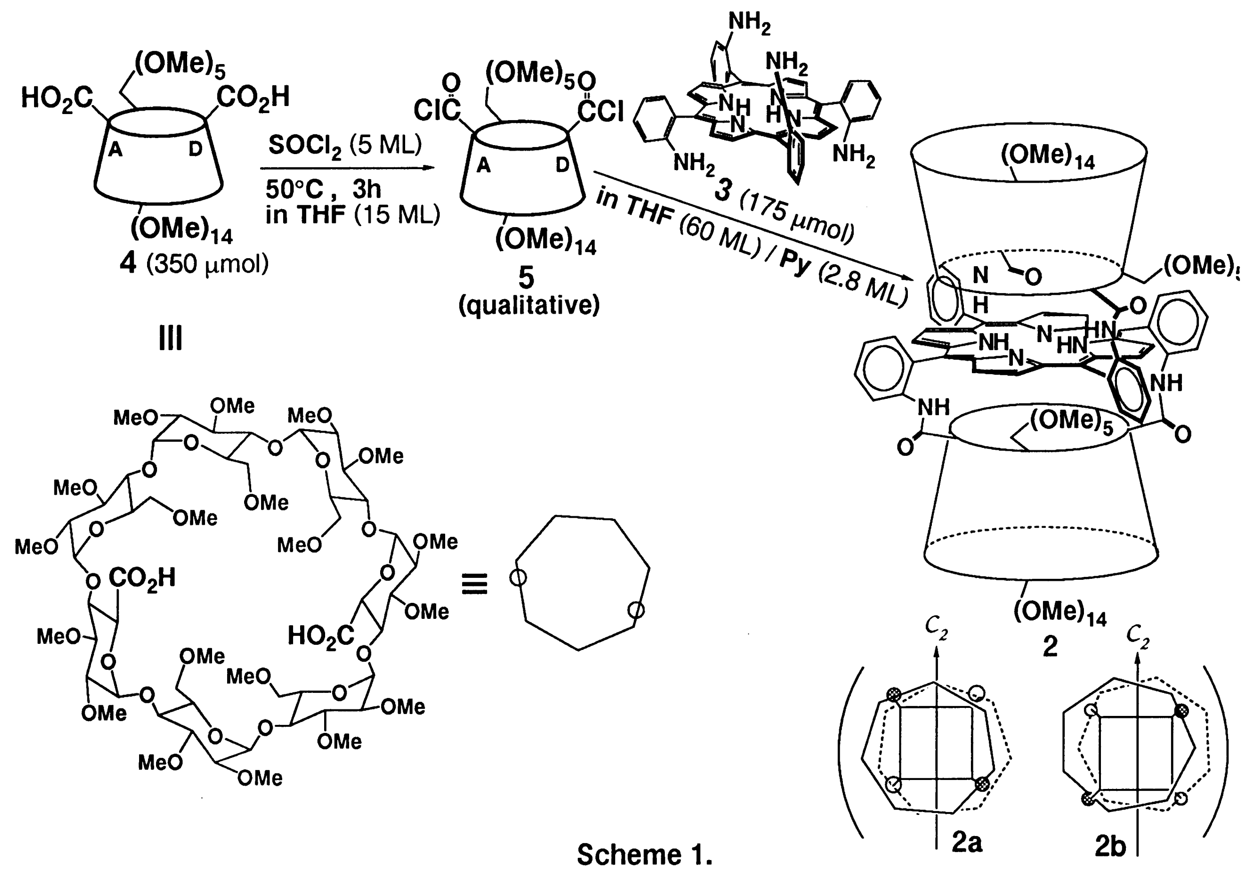
Cyclodextrins and their derivatives exhibit unique and interesting characteristics to provide hydrophobic recognition sites in aqueous solution, which are often conveniently and successfully utilized as (part of) enzyme models.[1] Recently, we have reported cyclodextrin sandwiched porphyrins (1) which mimic hydrophobic environments around porphyrins in hemoproteins by use of a cyclodextrin's cavity.[2] Since it has been shown through these investigations that the cyclodextrin moieties of these molecules may not only control their molecular recognition behavior but also affect the reactivity of the porphyrin in an aqueous solution, it will be very interesting and informative for hemoprotein mimic chemistry to modify characteristics of the cyclodextrin cavity in these molecules.

We wish to report here a synthesis of new cyclodextrin sandwiched porphyrin (2), all hydroxyl groups of which are protected with methyl groups. This new molecule is expected to provide a more aprotic environment around the porphyrin moiety compared with previous one.



1 : R = H , X = - SCH_2 -

2 : R = Me , X = - CONH -



Scheme 1.

The starting materials employed here were the αβαβ atoropisomer of meso-tetrakis(o-aminophenyl)porphyrin (3)[3] and A,D-dicarboxyl derivative of 2,3,6-permethyl-β-cyclodextrin (4).[4] It should be noted that, in contrast with original cyclodextrins, a variety of synthetic reaction is readily applicable to a functionalization of **4** without any protection-deprotection procedures, because of absence of hydroxyl groups on β-cyclodextrin (Scheme 1). Thus, one of the most simplest methods, the reaction of the acid chloride with **3**, was attempted to obtain the target molecule in the present work .

The acid chloride **5** is easily prepared by treatment of **4** with excess of thionyl chloride in THF. After evaporation of the solvent and excess of thionyl chloride, the residual product was used for the next reaction without further purification. The reaction of **3** with **5** in THF-pyridine gave desired product, **2**, in 8% yield which was purified by chromatography on a silica gel column (CH_2Cl_2/CH_3OH = 20/1 - 5/1, linear gradient). The HPLC analysis indicates that, as expected, the product contains the two isomeric compounds, **2a** and **2b** (**2a**/**2b** =1/1), which differ each other only in relative positions of two cyclodextrin moieties (see Scheme 1).[2a] These isomers were isolated by a preparative HPLC column.[5] FAB mass spectra of these products show molecular peaks of m/e 3461.35 which agree with the calculated molecular weight of **2** ($C_{166}H_{234}O_{70}N_8$). The aromatic (δ 7.2 - 9.0) and C1-H (δ 4.2 - 5.2) regions of ^1H NMR spectra of **2a** and **2b** are shown in Fig. 1. Although integration values in ^1H NMR spectra of both products clearly show the existence of one tetraphenylporphyrin and two cyclodextrin moieties,

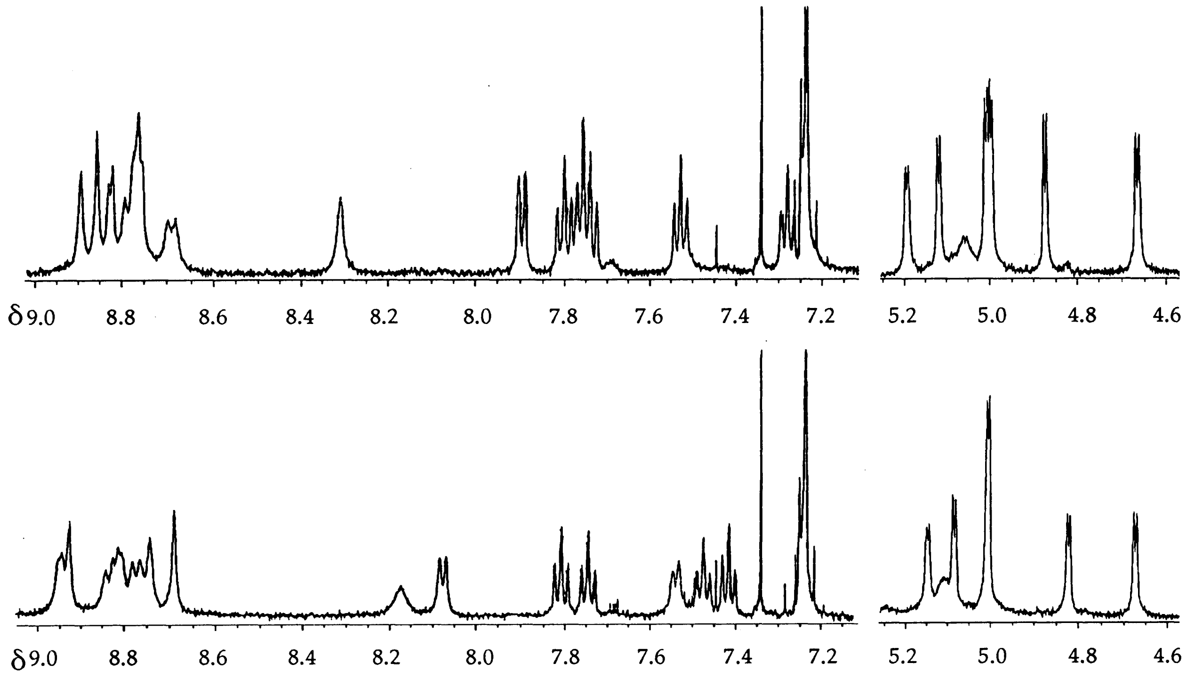


Fig. 1. ^1H NMR spectra (500 MHz) of **2a** and **2b** in d_6-$CDCl_3$ at room temperature. It is not determined at the present stage which product corresponds to **2a** or **2b**.

only seven kinds of glucose C1-H were observed.[6] These observations indicate that two β-cyclodextrin moieties in both products are equivalent and C_2 symmetric axes which are parallel to the porphyrin plane exist as shown in Scheme 1. Another interesting feature of these spectra is that one broad C1-H signal is observed in the spectra of both isomers, at δ 5.06 in upper spectrum of Fig. 1 and δ 5.11 in lower one. Thus, both isomers are expected to have one special glucose ring which may be deformed due to steric crowding between C6-OMe groups and the porphyrin plane. Since, in spite of such steric crowding, the electronic spectrum of 2 is quite similar to that of tetraphenylporphyrin,[5] the structure of the porphyrin ring in 2 seems to keep the usual porphyrin structure.

Finally, we preliminarily compared the photochemical characteristics of 2 with those of 1. Fluorescence lifetimes of 1, 2 and related porphyrins are summarized in Table 1. The

Table 1. Fluorescence Lifetimes (ns) of Porphyrin Derivatives[a]

Porphyrin	TPP[b]	$TPP_{SO_3^-}$[c]	TPP_{SMe}[d]	1[e]	2	2
Solvent	Benzene	H_2O	$CHCl_3$	H_2O	H_2O	$CHCl_3$
	12.4	10.8	3.5	3.2	13.9	14.2

a) The life time data were obtained at room temperature on Hamamatsu Pico-second Fluorescence Lifetime Measuring System type C4780 equipped with a N_2 laser pumped dye laser (cumalin 500), LN120C1, PRA LASER INC. b) Tetraphenylporphyrin. O. Ohno, Y. Kaizu, and H. Kobayashi, *J. Chem. Phys.*, 82, 1779 (1985) c) meso-tetrakis(o-sulfonate)porphyrin. d) meso-tetrakis-(o-thiomethyl)porphyrin. e) Ref. 2e.

fluorescence lifetimes of TPP types of porphyrins are usually longer than 10 ns. However, we found in the previous work that the lifetime of **1** is only 3.2 ns.2e) The results shown in Table 1 reveal very interesting differences between fluorescence lifetimes of these porphyrins, i.e., in contrast to the abnormally short fluorescence lifetime of **1**, that of **2** is quite normal in a organic solvent and an aqueous solution(13.9 ns). Since the lifetime of porphyrin seems to be insensitive toward the polarity of solvents ($\tau_{2\ \mathrm{in}\ H_2O} \cong \tau_{2\ \mathrm{in}\ CHCl_3}$ and $\tau_{TPPSO_3^-\ \mathrm{in}\ H_2O} \cong \tau_{TPP\ \mathrm{in}\ CHCl_3}$),7) the observed difference is not due to the microscopic polarity around the porphyrin chromophores in these compounds. Thus, observed difference of the lifetimes between **1** and **2** may be ascribed to substituent effects on the meso-phenyl groups which have thioether linkages in **1** and amide ones in **2** respectively. The results are supported by the shorter fluorescence lifetime of TPP_{SMe} (see Table 1). Since these observations are interesting in relation to the mechanism and the efficiency of the intra-complex electron transfer between these porphyrins and quinones,2e) further photochemical investigations for these functionalized porphyrins are now underway in our laboratory.

In conclusion, we have presented new types of cyclodextrin sandwiched porphyrins which can be prepared by the simple method using acid chloride derivative of 2,3,6-permethyl-β-cyclodextrin. It should be noted that **2** thus obtained is soluble in not only wide range of organic solvents such as hexane, chloroform, and methanol but also water at the concentration of the order of 10^{-5} M where electronic and fluorescence spectra are measurable.

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5) Two isomers, **2a** and **2b**, were separated on the HPLC column (YMC AQ313-S5 120A ODS column, MeOH/H_2O = 92 / 8). Similar formation of isomers was observed in previous work, see ref. 2a. Electronic spectra of both isomers are practically same, i.e., λ_{max} (log ε) in H_2O : 421 (5.41), 514 (4.11), 546 (3.32), 588 (3.66), 642 (3.01).

6) These protons give more sharp doublet signals in CD_3OD at 60 °C.

7) For other examples of solvent dependency of fluorescence lifetimes of porphyrins, see T. H. Tran-Thi, J. F. Lipskier, P. Maillard, M. Momenteau, J.-M. Lopez-Castillo, and J.-P. JAy-Gerin, *J. Phys. Chem.*, **96**, 1073 (1992) ; P. F. Heells, B. J. Parsons, G. O. Phillips, E. J. Land, and A. J. Swallow, *ibid.*, **86**, 5169 (1986).

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