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^{1}H NMR Characterization of the Hydrogen-Bond Network in the Water Complex of Resorcinol-Dodecanal Cyclotetramer[1)]

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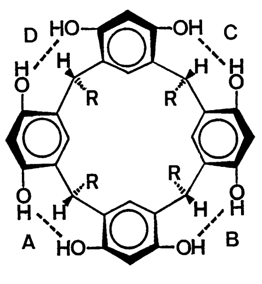
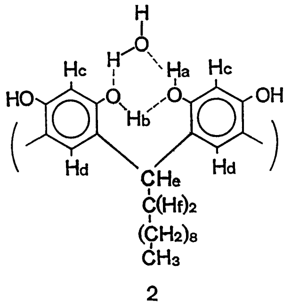
Synopsis. ^{1}H NMR spectroscopy on the water complex of resorcinol-dodecanal cyclotetramer indicates that a bound water molecule and a pair of OH groups on adjacent benzene rings of the macrocycle are strongly NOE correlated, but the proton exchange in the resulting hydrogen-bond network is very slow.

We have recently shown that the resorcinol-dodecanal cyclotetramer **1** as a lipophilic polar host forms complexes with water, glycerol, and sugars such as ribose as guests via hydrogen-bond formation in nonpolar organic media.[2)] The significance of a pair of hydrogen bonded OH groups on adjacent benzene rings of the macrocycle (A, B, C, and D in structure **1**) as the essential binding site with the guest was also suggested.[2b)] In order to get a deeper insight into the hydrogen-bond network, we studied on the correlation and exchange of the OH protons of the water complex of **1**. We now report that the hydrogen-bond network involved is rather rigid and the proton exchange therin is very slow.



1 ; R = $(CH_2)_{10}CH_3$



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Results and Discussion

As has already been reported,[2b)] the tetrahydrate complex of **1** ($1\cdot4H_2O$, 0.01 M, 1 M=mol dm^{-3}) in $CDCl_3$ shows distinct signals for bound water at δ=2.93 and two types of the OH protons of **1** at δ=9.65 (H_b) and 9.38 (H_a), referring to structure **2**. Addition of D_2O to this solution resulted in facile H_2O-D_2O exchange. The H–D exchange between the OH protons (H_a and H_b) and D_2O in the resulting D_2O complex ($1\cdot4D_2O$), however, was very slow and was not complete even after 12 h.[3)] This slowness was in marked contrast to a rapid H–D exchange between phenol and added D_2O in $CDCl_3$ under otherwise identical conditions.

The slow proton exchange could also be shown by variable temperature ^{1}H NMR studies. Figure 1 shows the OH proton resonances for the tetrahydrate complex (0.01 M) in $(CDCl_2)_2$ at various temperatures. The signals for a pair of OH groups of **1** (H_a and H_b, especially the former) as well as that for bound water undergo significant line broadening at higher temperatures, but no averaging of these due to exchange takes place even at 100 °C.[4)] Further information about the hydrogen-bond network was available from the NOE measurements,[5)] actually done on the dihydrate complex.

The dihydrate complex of **1**[2b)] ($1\cdot2H_2O$, 0.01 M) in $CDCl_3$ shows the OH proton resonances at δ=9.60 (H_b), 9.28 (H_a), and 3.89 (H_2O), referring to structure **2**. They were found to be strongly correlated with each other via NOE, as revealed by the two-dimensional NOE spectroscopy as well as individual NOE measurements. In addition, the aromatic proton H_c (but not H_d) and the benzylic proton H_e were NOE correlated with bound H_2O. Significant NOE's were also observed among H_a and H_b, H_c, and H_e and among H_d, H_e, and H_f. The results are shown in Table 1,[6)] where negative NOE's observed indicate reduction in the absorption intensities.[7)]

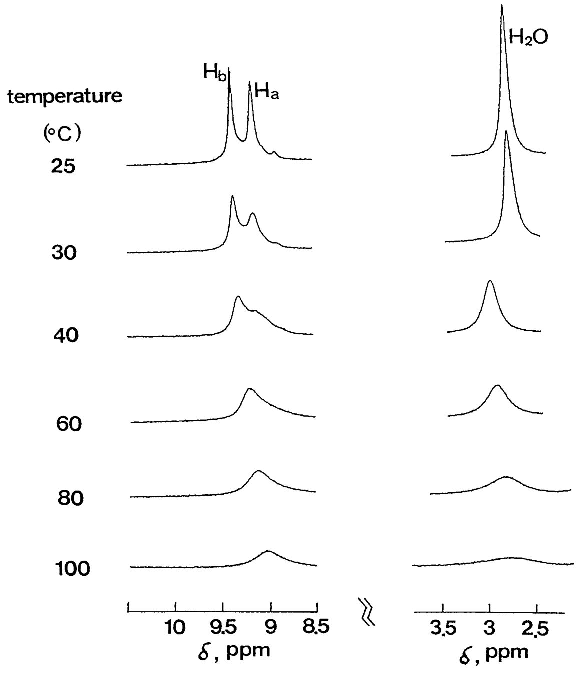
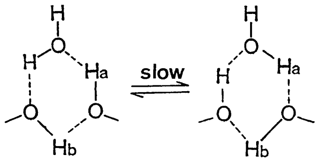


Fig. 1. Portions of the ^{1}H NMR spectra for the OH proton resonances of the tetrahydrate complex of **1** ($1\cdot4H_2O$) in $(CDCl_2)_2$ at various temperatures (°C).

Table 1. NOE for Complex $1 \cdot 2H_2O$ in $CDCl_3$ at Room Temperature

Nucleus irradiated (δ/ppm)	NOE observed (%) at						
	H_2O	H_a	H_b	H_c	H_d	H_e	H_f
H_2O (3.89)		−28.7	−20.4	−24.8	0	−11.5	0
H_a (9.28)	−30.7		−37.7	−42.1	0	−32.5	0
H_b (9.60)	−18.3	−30.8		−42.5	0	−30.8	0
H_c (6.10)	−16.5	−23.7	−32.3		0	−14.4	0
H_d (7.20)	0	0	0	0		−7.0	−18.7
H_e (4.28)	−19.5	−17.0	−17.0	−12.0	>-3		−5.6
H_f (2.21)	0	0	0	0	−50.8	−20.0	

Examination of CPK molecular models of **1** indicates that (1) the two OH groups on adjacent benzene rings are very close to each other (O–O distance being approximately 2.2 Å) so that formation of a six-membered hydrogen-bond network upon binding of a molecule of H_2O is possible and (2) H_e is very close to the OH groups, which are, as a consequence, surrounded by two H_c's and H_e. The observed NOE correlation of the H_2O protons with H_a and H_b, H_c, and H_e thus provides rather direct evidence for the hydrogen-bonding fixation of H_2O with the OH pair, as schematically shown in **2**. The resulting multiple hydrogen-bond network seems to be so rigid that the proton exchange between even H_a and bound water (Eq 1) is surprisingly slow. The exchange between H_b and bound water is even slower, and this fact may be taken as evidence that the four benzene rings of **1** are linked firmly via hydrogen bonds.



(1)

Experimental

Preparation and NMR spectra of di- and tetrahydrate complexes of **1** have been described:[2b] Mp 225—227 °C (decomp) for the tetrahydrate and 248—250 °C (decomp) for the dihydrate. The IR spectra of both complexes in $CHCl_3$ were similar to each other and showed a strong and broad absorption at 3600—2400 cm^{-1} with a maximum at 3250 cm^{-1} for the hydrogen-bonded OH groups of **1** and bound water molecules. ^{1}H NMR spectra were recorded on a JEOL GX-270 spectrometer with tetramethylsilane as an internal standard. The JEOL PLXUS (version 1.5) program was used to obtain NOE spectra. The H_2O–D_2O exchange was carried out by adding two drops of D_2O to a $CDCl_3$ solution of $1 \cdot 4H_2O$ (0.01 M) followed by occasional swirling of the mixture.

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3) Disappearance of the OH protons due to exchange was also very slow even in a homogeneous solution in CD_3OD.

4) At 130 °C was observed an extensively broad absorption ranging from δ=9.5 to 1.5 (OH, 16H).[2b]

5) NOE (Nuclear Overhauser Effect) is a kind of correlation spectroscopy for two nuclei in close vicinity, where irradiation of one nucleus results in either enhancement or reduction of the absorption intensity of the other, depending on the correlation time and hence molecular weight of the system.

6) Comparison of absolute reduction values between different NOE experiments is not warrented because decoupler power levels are not constant.

7) The proton exchange in the hydrogen-bond network is very slow as shown and is certainly much slower than the proton relaxation. Thus, the reduction in the intensities of H_a and H_b upon irradiation of H_2O or vice versa can not be due to proton exchange.