

Dynamics of Molecular Cavities of Macrocyclic Polyethers and of the Corresponding Guanidinium Perchlorate Complexes; a Carbon-13 N.M.R. T_1 Relaxation Time Study

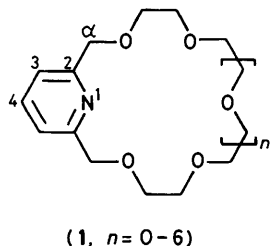
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Carbon-13 T_1 relaxation time measurements show that the structures of 2,6-pyrido crown ethers (**1**, $n = 0-6$) with ring sizes varying from 15 to 33 ring atoms and of two corresponding 'encapsulated' guanidinium perchlorate complexes in solution correspond to the structures in the solid state.

For the design of macrocyclic host molecules that bind selectively guest species, the *principle of optimal complementary binding sites*¹ serves as a major guideline. In this approach Corey-Pauling-Koltun (CPK) molecular models are a useful tool since they mimic accurately the dimensions of the macrocyclic polyether cavity. From *X*-ray studies of several

crystalline 18-membered macrocyclic polyethers it is known that the molecular cavity is partly filled by methylene hydrogen atoms of the macrocycle.² This implies that the host molecule has to undergo energetically unfavourable conformational changes prior to the favourable binding of the guest. Therefore, Cram *et al.*³ designed a class of highly structured



ligands, the (hemi)spherands, in which almost no conformational reorganization is needed in the complexation process. As a consequence these ligands exhibit very strong and selective binding properties.

Hitherto virtually all the information about conformations of crown ethers and their corresponding complexes with charged and neutral molecules is limited to macrocycles having 12–18 ring atoms. In a systematic approach to design urea-binding ligands,⁴ we are investigating a number of crown ethers that possess large, flexible polyether macrorings (24–33 ring atoms) in combination with rigid pyrido,⁵ benzo,⁶ and xyleno moieties.⁷ X-Ray studies of the crystalline 2,6-pyrido-24-crown-8 (**1**, $n = 3$) surprisingly showed that the pyrido moiety is completely encapsulated in the polyether cavity of the molecule.⁵ However, in the guanidinium perchlorate complexes of 27- and 30-membered macrocycles the guest cation is encapsulated in the cavity. Obviously, unfolding of the ligand is required before encapsulation of the guest can occur.

In the solid state crystal packing effects may well determine the structure. Therefore we decided to study the dynamics of the conformation in solution of a series of crown ethers with different ring sizes using carbon-13 spin-lattice relaxation time (¹³C- T_1) measurements in order to compare structural information with solid state X-ray data.⁵ In principle, T_1 studies⁸ may provide information about rapid molecular motion on a time scale far shorter than the normal n.m.r. time scale.

Hitherto ¹³C- T_1 data have only been used to study the dynamics of complexation of salts by macrocycles with ring sizes of 12–21 ring atoms,⁹ but to the best of our knowledge the conformational dynamics of uncomplexed crown ethers as a function of the ring size have not been studied.

In this contribution we present the results of a ¹³C- T_1 study† of a series of 2,6-pyrido crown ethers (**1**, $n = 0-6$) with ring sizes varying from 15 to 33 atoms. The observed T_1 values for the discrete carbon atoms are presented in Figure 1.

In general the T_1 values show the same tendency, viz. that with an increasing number of ring atoms T_1 decreases. If it is assumed that extreme narrowing conditions are fulfilled,⁸ this effect can be attributed to more effective dipole-dipole (DD) relaxation originating from a decreased molecular mobility of

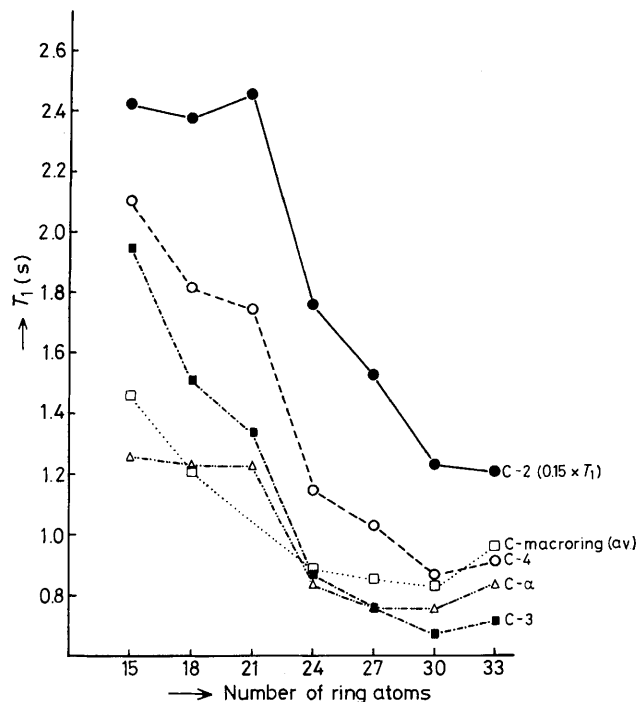


Figure 1. T_1 (s) values of 2,6-pyrido crown ethers (**1**, $n = 0-6$) (CDCl_3 , 20 °C). In order to facilitate visual comparison, for the quaternary C-2 atoms the values given are $0.15 \times T_1$. The averaged T_1 value is given for the macroring atoms.

the larger macrocycles. This is consistent with observations for 15-crown-5 and 18-crown-6.^{9c} All the nuclear Overhauser enhancement (n.O.e.) factors observed for the quaternary C-2 carbons (Figure 1) are between 1.8 and 2.0. This shows that the spin-rotation relaxation is dominated by a constant DD relaxation.

The most remarkable observation in the series of experiments was the large discontinuity found in the T_1 value between the cycles having 21 and 24 ring atoms. Combining CPK models with X-ray crystallographic studies shows that the observed decrease of T_1 coincides with a ring size where the macrocyclic polyether chain is able to encapsulate the pyrido moiety of the crown ether. Since we have studied the pyrido crown ethers in a homologous series, it is very likely that other parameters influencing the T_1 values change gradually. Therefore, the discontinuity in the T_1 data between 21 and 24 ring atoms has to be explained in terms of specific internal conformational reorganization, probably combined with an abruptly changed solvation of the ligand. This means that the cavity is filled by the rapidly rotating pyrido nucleus part of the time.

Support for this interpretation was obtained from T_1 measurements of the corresponding guanidinium perchlorate complexes. The average T_1 values of the macroring atoms, which may reflect most directly the freezing of the crown ether conformation upon complexation, decrease to 0.50 and 0.59 s for the 27- and 30-membered ligand, respectively. Previously we have shown that these crown ethers form encapsulated (1:1) complexes with guanidinium perchlorate.⁵

We found that the T_1 values for the C-3 atoms of the free and complexed pyrido ligands studied are somewhat larger than the T_1 values for the C-4 atoms. This indicates the presence of anisotropic motion, probably caused by preferential rotations of the molecule around the C_2 -symmetry axis. This phenomenon has been observed previously for pyridine

† The ¹³C relaxation n.m.r. spectra were recorded at 293 ± 2 K on an N.M.C. 1280 spectrometer operating at a frequency of 50.31 MHz. 0.2–0.3 M Crown ether solutions in CDCl_3 were used, which were carefully degassed before every measurement. In the case of the guanidinium perchlorate complexes the samples were prepared from the CDCl_3 layers of extraction experiments. Dissociation of the complexes was not observed. Relaxation time measurements were accomplished using the inversion-recovery pulse sequence (TIIR), 48 accumulations, with pulse delay times of 140 s. All determinations were carried out at least twice; estimated standard deviation: $\pm 10\%$. Nuclear Overhauser enhancement (n.O.e.) factors were measured by comparative methods using the ALNOE pulse sequence. The n.O.e. values for all resonances, the C-2 resonance excepted, are in the range 2.7–3.0, showing that the relaxation proceeds by the dipole-dipole mechanism.

in methanol solutions,¹⁰ where strong hydrogen bonds between the nitrogen atom and the solvent are present.

In order to evaluate the effect of the rigid aromatic moiety on the conformation in crown ethers of type (1) we have also determined the T_1 values of the corresponding 2-bromo-1,3-xylene-30-crown-10. We found an average T_1 value of 0.85 s for the macroring atoms which indicates a similar intramolecular encapsulation of the aromatic functionality. In 30-membered benzo and dibenzo crown ethers these internal rotations are not observed as is illustrated by the average T_1 values obtained for the macroring atoms, 1.20 and 1.05^{9a} s respectively. The values are essentially the same and, therefore, may be compared with the T_1 values of the ring atoms in the smaller pyrido crown ethers. These observations are in line with CPK models that show that rotations around the catecholic C–O–C bonds are sterically hindered by the *ortho* protons of the aromatic ring and the OCH₂-protons.

The correspondence between the results obtained from X-ray analysis and the T_1 relaxation time studies indicates a direct relation between the conformations of crown ethers in the solid state and in solution.

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