

The Conformation of 1,4,7,10-Tetraoxacyclododecane and its 1:1 Lithium Salt Complexes

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Infrared spectroscopy and low-temperature ¹H and ¹³C NMR spectroscopy show that both in the free and complexed form this cyclic tetra-ether adopts a "square" conformation with ether oxygen on "side" positions. Dynamic NMR spectroscopy reveals two site exchange processes, the nature of which is discussed in detail.

The medium-ring hydrocarbon cyclododecane is unable to adopt a conformation of diamond-lattice type because of the strong transannular hydrogen interactions that would result. The conformation actually chosen both in the solid¹ and in solution² has been established to be of the "square" type with *D*₄ symmetry shown in Fig. 1. Strain-energy calculations³ also give as a result that this is the lowest-energy conformation for cyclododecane.

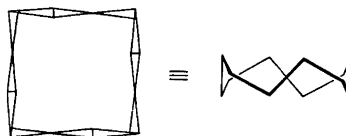


Fig. 1. Two representations of the cyclododecane conformation.

In order to study the conformational effect of replacing in a symmetrical fashion four methylene groups by ether oxygen, we have now studied another 12-membered ring, 1,4,7,10-tetraoxacyclododecane, the tetramer of ethylene oxide.⁴ Since we observed that this tetra-ether forms stable 1:1 cation complexes with lithium salts such as LiSCN, LiBr, LiCl, and LiF, it also became of interest to establish whether the ring-conformation in this complex is the same as, or different from, that of the free ring. Analogous 2:1 complexes are formed with sodium salts; with potassium salts they are much less stable. A

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series of transition metal halides, like CuCl_2 , CoCl_2 , NiCl_2 , and FeCl_2 , also form crystalline 1:1 complexes.

INFRARED SPECTRA

The crystalline lithium bromide complex has a particularly simple infrared spectrum with sharp bands (Fig. 2). The spectrum of the lithium isothiocyanate complex is practically identical except for the additional bands due to the anion. The sodium salt complexes also have very similar spectra. A comparison with the infrared spectra of the ethylene oxide polymer and the potassium bromide complex of the cyclic hexamer, which both have conformationally equivalent monomer units,⁵ strongly suggests a similar situation here. In particular, the presence of only two bands in the $800-1000\text{ cm}^{-1}$ region can be taken as an indication of just one type of $-\text{CH}_2-\text{CH}_2-$ units, and since all experimental data for the polymer point to a strong *gauche*-preference for the

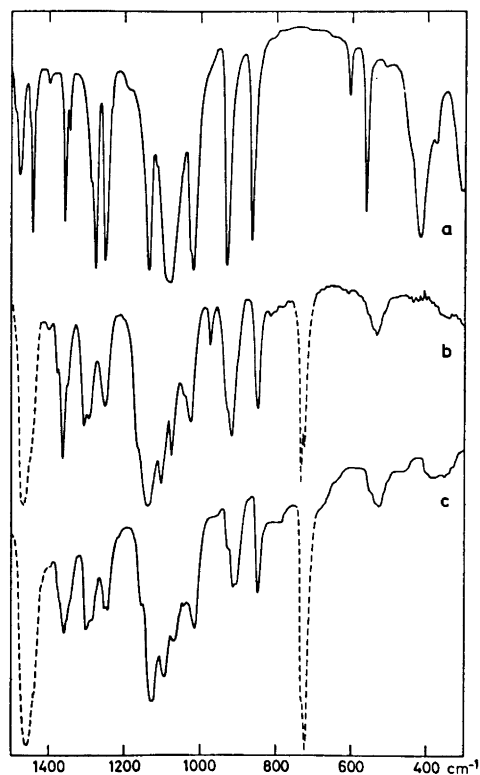


Fig. 2. Infrared spectra of 1,4,7,10-tetraoxacyclododecane as a 1:1 complex with LiBr pressed in KBr (a), alone as liquid at 30° (b) and alone as solid at -60° (c). Absorption bands of the protecting polyethylene film are indicated by dashed curves.

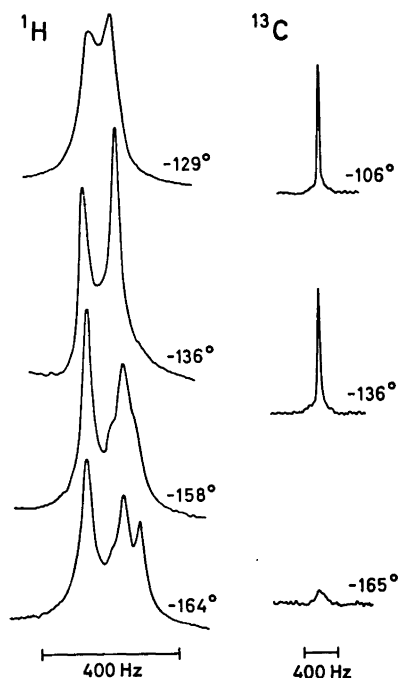


Fig. 3. 251 MHz ^1H and 63.1 MHz ^{13}C NMR spectra of 1,4,7,10-tetraoxacyclododecane in $\text{CHCl}_2\text{F}/\text{CHClF}_2$ (1:2) solution.

CC-bonds and *anti*-preference for the CO-bonds,⁶ there can be little doubt that the tetra-ether ring has the "square" conformation of Fig. 1 with all ether oxygens in "side" positions and not at the "corners". This is obviously also the only way in which all four oxygens can coordinate equally to one and the same Li-cation.*

The uncomplexed tetra-ether melts at 17° and shows sufficient similarity between its infrared spectra in the melt (and solution) and in the crystal (Fig. 2) to suggest that the compound is conformationally homogeneous. It may be more difficult, however, to draw a final conclusion about the identity of this conformation. The infrared spectrum differs somewhat from that of the complex as regards band positions, but not in general character, as the strong band present only in lithium and not in sodium complexes at 420 cm^{-1} can be assigned to LiO stretching. The conformation may therefore be essentially the same in the free ring as in the complex, but less rigid.

MOLECULAR DIPOLE MOMENT

Dipole moment measurements in benzene and in carbon tetrachloride solution gave values of 2.50 and 2.40 D, respectively. This is so far from the value of about 5 D expected for the complexing conformation with all oxygens on

* The crystal structure of the complexes is being determined by Dr. Frank, UCLA.

“side” positions with their dipoles pointing in the same direction, and also so far from the zero value expected if all oxygens are on corner positions, that a variety of alternative “quadrangular” ring conformations were examined as candidates. Those which reproduced the observed molecular dipole moment had, however, a very high calculated energy as the corresponding hydrocarbon,⁷ and too low symmetry to be compatible with the simplicity of the observed infrared spectrum, and had therefore to be rejected.

The use of a measured molecular dipole moment in conformational analysis when several dipoles are present in the molecule may often be hazardous, except when they add up to the maximum possible value or when there is complete cancellation. Intermediate dipole moments may be simulated by vector addition in too many different ways. Also, if the molecule is flexible, a large atomic polarization may increase the apparent value of an intrinsically small molecular moment, while large amplitudes of thermal vibrations may decrease the apparent value of an intrinsically large molecular moment.

In the present tetra-ether, the experimentally determined value is the same as expected if the four ether dipoles were present in separate molecules. Also for the higher cyclic oligomers of ethylene oxide the observed molecular dipole moments⁵ are close to the values expected for free relative orientation of the dipoles. That thermal vibrations have indeed large amplitudes in these polyoxyethylene rings is seen from their broad infrared bands⁵ (Fig. 2) as compared with those of the stiffened complexing molecules. This may be related to the *gauche* preference about the CC-bond; the apparent lack of repulsion between two ether oxygen atoms in 1,4-*gauche* relationship⁶ would be expected to reduce also the energy of adjoining rotational barriers and so create a rather shallow torsional potential.

DYNAMIC NMR SPECTROSCOPY

¹H resonance spectroscopy at 251 MHz shows two processes becoming slow for the uncomplexed tetra-ether (Fig. 3). The single room-temperature line at δ 3.65 has split into two bands at -133° ($T_c \sim -126^\circ$, $\Delta G^\ddagger = 6.8 \pm 0.3$ kcal/mol). At still lower temperature, about -160° , a further splitting takes place; the high-field band gives two new bands, while the low-field band only broadens ($\Delta G^\ddagger = 5.5 \pm 0.3$ kcal/mol). In ¹³C resonance at 63.1 MHz the single room-temperature line at 70.0 ppm (downfield from TMS) on cooling remains a single line after the first process, and only broadens after the second without giving resolved lines. This broadening is not caused by magnetic inhomogeneity because the TMS-signal remains quite sharp. Broadening due to dipole-dipole relaxation can also be ruled out since no further broadening is observed at still lower temperature (-172°). It seems therefore to be due to near coincidence of chemical shifts for different carbon atoms; a similar situation has been encountered for the $-O-CH_2CH_2-O-$ unit in 1,3,6-trioxacyclooctane.⁸

Of the lithium cation complexes, only the one having isothiocyanate as a counter ion was studied by low-temperature spectroscopy. Here also two dynamic processes are revealed by ¹H resonance (Fig. 4). The single-room-temperature line at δ 3.55 is split into two partially overlapping broad bands

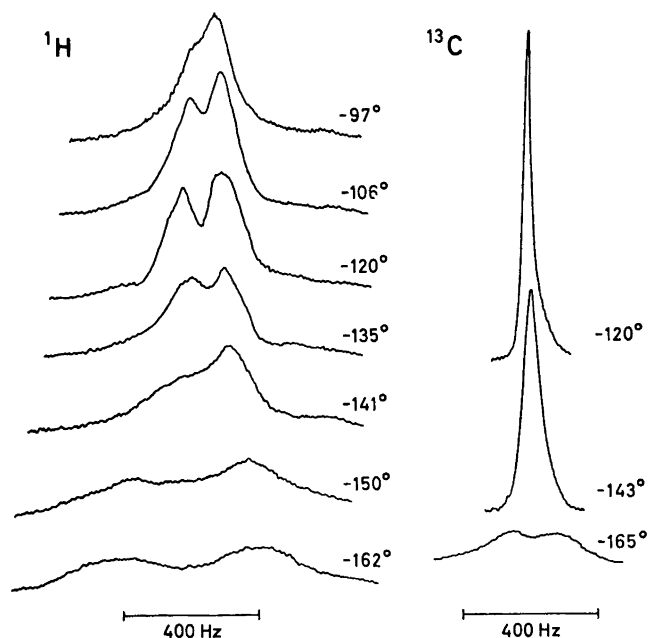


Fig. 4. 251 MHz ^1H and 63.1 MHz ^{13}C NMR spectra of the 1:1 LiNCS complex of 1,4,7,10-tetraoxacyclododecane in $\text{CHCl}_2\text{F}/\text{CHClF}_2$ (1:2) solution.

at -106° ($T_c \sim -96^\circ$, $\Delta G^\ddagger = 8.2 \pm 0.3$ kcal/mol). At -135° a second process starts to become slow, and at -160° two very broad bands are seen, separated by a larger chemical shift than observed for the free ring. In ^{13}C resonance the single room-temperature line at 71.2 ppm on cooling remains single after the first process. After the second process has become slow, two broad bands are now seen ($\Delta G^\ddagger = 5.6 \pm 0.3$ kcal/mol). The tendency for broader signals and larger chemical shift differences in lithium complexes has been observed earlier.⁹

The NMR-spectra obtained at the lowest temperature when both processes are slow are clearly in agreement with the "square" conformation with the oxygen atoms at "side" positions both for the free and the complexed ring. If the oxygen atoms were at corner positions, only a single ^{13}C line and two ^1H bands should have been observed. The presence of two distinct site-exchange processes is also consistent with oxygen atoms at "side" positions as will be shown below.

SITE EXCHANGE PROCESSES

For cyclododecane a ring atom and substituent exchange mechanism has been proposed⁷ which involves the stepwise movement of each corner by one

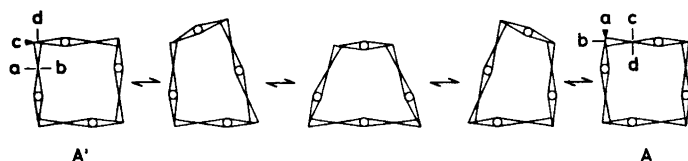


Fig. 5. Proposed one-cycle conformational interconversion path for the low-barrier site-exchange process.

position and passes through higher-energy quadrangular conformations. A complete cycle comprises the passage of four barriers and leads to the enantiomeric "square" conformation with all atoms moved by one step around the ring.

Applying this conformational interconversion mechanism to 1,4,7,10-tetraoxacyclododecane, the stable conformation A can either be transformed in one direction (Fig. 5) through one cycle to its mirror image A', or in the other direction (Fig. 6) through two cycles to an identical conformation A''. In both cases the two types of carbon atoms exchange sites. In the former case (Fig. 5) also the *cis*-related protons of each unit exchange sites ($H_a = H_c$; $H_b = H_d$), while in the latter case (Fig. 6) the *trans*-related protons are exchanged ($H_a = H_d$; $H_b = H_c$). Thus, either of the two paths could in principle represent the low-barrier process since half of the protons would remain different from the other half. The other path would then lead to full exchange and represent the high-barrier process.

A decision can be reached by considering the relative barrier heights. The one-cycle path (Fig. 5) involves passage over four barriers, identical in pairs. Both have been estimated⁷ to be < 14 kcal/mol for cyclododecane, and the kinetically decisive of these determined experimentally to be 7.3 kcal/mol.² If the barrier is defined⁷ as the moment the bond between the old and new corner atom becomes *syn*-eclipsed, all these barriers are seen to involve eclipsing of the CC-bond, so that the critical interaction must be between the adjoining oxygen atoms (Fig. 7a); hence all four barriers must be lower than in the hydrocarbon.

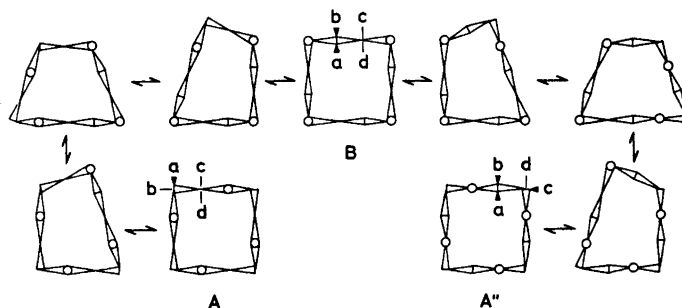


Fig. 6. Proposed two-cycle conformational interconversion path for the high-barrier site-exchange process.

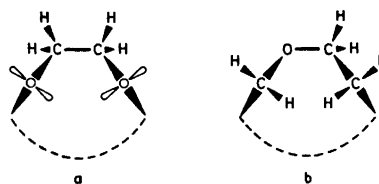


Fig. 7. Critical eclipsed interaction in all barriers on the one-cycle path (a) and on the two-cycle path (b).

On the other hand, the two-cycle path (Fig. 6) involves passage over eight barriers, pairs of which are identical, but these are all seen to involve eclipsing of a CO-bond. The critical interaction is therefore between two methylene groups (Fig. 7b); hence all eight barriers are expected to remain high.

A support for the assignment of path $A \rightleftharpoons A'$ to the low-barrier process and path $A \rightleftharpoons B \rightleftharpoons A''$ to the high-barrier process comes from the observed increase of the higher barrier on complexation with lithium isothiocyanate and the lack of an observed effect on the lower barrier. All along path $A \rightleftharpoons A'$ (Fig. 5) the four ether oxygen atoms point to the same side of the ring, and no real dissociation of the complex is necessary. On the other hand, it is seen that half-way through path $A \rightleftharpoons A''$ (Fig. 6) the intermediate "square" conformation B has got all oxygen atoms at corner positions so that the complex must become completely dissociated and then can only form again if the lithium cation reenters the A'' ring from the opposite side. The activation energy must therefore be increased by an amount corresponding to the stabilization obtained by complexing.

EXPERIMENTAL

1,4,7,10-Tetraoxacyclododecane. This compound was prepared from ethylene oxide in diethyl ether solution using triethylaluminum as a catalyst.⁴ The distilled crude product had to be crystallized from pentane at -20° to remove acyclic material, then dried over P_2O_5 . M.p. 17° .

Lithium salt complexes. The lithium bromide complex was prepared by dissolving equimolar quantities of dry lithium bromide and 1,4,7,10-tetraoxacyclododecane in methanol, evaporating the solution, and drying the solid in vacuum at 100° . (Found: C 36.02; H 6.09; Br 30.37. Calc. for $C_8H_{16}O_4LiBr$: C 36.54; H 6.12; Br 30.38.)

The lithium isothiocyanate complex was also prepared from a solution of equimolar quantities of salt and cyclic tetra-ether in methanol; the complex started to crystallize during concentration in a rotating evaporator and was filtered off. M.p. $240-243^\circ$. (Found: C 45.25; H 6.60. Calc. for $C_8H_{16}O_4LiSCN$: C 45.00; H 6.65.)

The sodium isothiocyanate complex crystallized from a concentrated methanol solution of the components and was filtered off. M.p. $159-163^\circ$. It had a 2:1 stoichiometry and contained methanol as evidenced by OH absorption in the infrared and by analysis (Found: C 45.80; H 7.22. Calc. for $C_{16}H_{32}O_8NaSCN \cdot 2CH_3OH$: C 45.82; H 8.06.)

Infrared spectroscopy. The spectra were recorded in a Perkin-Elmer Grating Infrared Spectrophotometer 457. Liquid films between pressed KBr disks protected by thin polyethylene films were cooled in a RIIC low-temperature cell to obtain the spectrum of crystalline tetra-ether. The lithium and sodium salt complexes could be ground with KBr and pressed into a pellet without any cation exchange taking place.

Dipole moments. Dielectric constants were measured at $25^\circ C$ in a Weilheim Dipolmeter DM 01 on four different solutions in benzene. Refractive indices were measured on the same solutions in a Brice-Phoenix Differential Refractometer. Calculation of dipole moments was performed according to Hedestrand,¹⁰ using no correction for atomic polarization.

NMR spectroscopy. The spectra of $\text{CHCl}_2\text{F}/\text{CHClF}_2$ (1:2) solutions were obtained on a superconducting solenoid NMR spectrometer¹¹ operating at 251 MHz for protons and at 63.1 MHz for ^{13}C . Acquisition and Fourier transform of free induction spectra were carried out with a Data General Nova computer having 12 K 16-bit words, of which 8 K were used for data.¹²

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