The Inherent Instability of 1,3-Dioxan and the Conformation of 1,3,7,9-Tetraoxacyclododecane

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Summary The conformation of 1,3,7,9-tetraoxacyclo-dodecane, formed by dimerization of 1,3-dioxan, is shown by n.m.r. spectroscopy to be 'square,' with both 1,3-dioxa-groupings across corners, and to possess a very high conformational barrier (11 kcal/mol).

MOST simple cyclic formals can be converted into polymers and higher cyclic oligomers,[1,2] and the equilibrium thermo-dynamics have been established for the reaction monomer→polymer in the case of 1,3-dioxolan[3] and 1,3-dioxepan.[4] Because of the considerable entropy loss in oligomerizations and polymerizations, quite a large enthalpy lowering is needed to obtain a reasonably high 'ceiling temperature' $(\Delta G^\circ = 0)$.[2] For the above compounds ΔH° is $-5\cdot1$ and $-3\cdot6$ kcal/mol.
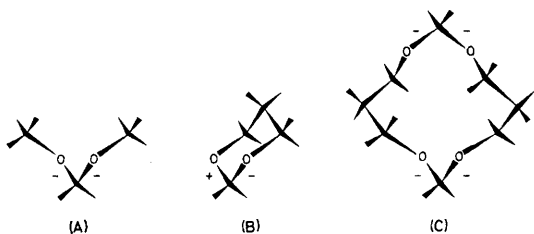

FIGURE 1. The conformations of dimethoxymethane (A), 1,3-dioxan (B), and 1,3,7,9-tetraoxacyclododecane (C). Right- and left-handed *gauche* bonds are indicated by + and − signs.

The six-membered ring, 1,3-dioxan, shows no tendency to polymerize by itself,[2,4] and it might therefore seem natural to consider ring-strain as the driving force in the polymerization of other cyclic formals, and definitely this must be so in the case of medium rings,[1] particularly 1,3-dioxacyclo-octane[5] which gives cyclic dimer and polymers with remarkable ease. For cyclic formals lower than the eight-membered ring, there should, however, exist an additional driving force owing to the impossibility of accommodating the 1,3-dioxa-grouping in its very much preferred +*gauche*,+*gauche* (or− −) conformation (A, Figure 1), observed both in dimethoxymethane,[6] medium rings,[5,7] and large rings, [5,8] as well as in polyoxymethylene.[9]

Although 1,3-dioxan adopts a normal chair conformation, its dioxa-grouping is +*gauche*,−*gauche* (B), and also this ring should therefore possess some instability. In fact, it has been claimed that 1,3-dioxan takes part in copolymeriz-ations,[10] and that at −40° cyclic oligomers are formed.[4] We have repeated the latter experiment and find that the crystalline product is not a mixture of cyclic dimer and trimer as reported,[4] but the pure dimer, m.p. 102°, and that it is formed to some extent at −40° also when the equili-brium is not displaced by crystallization.

This cyclic bis-formal gives evidence of a particularly stable and rigid conformation. Thus, the i.r. spectrum in solution shows very sharp bands and is identical with the spectrum of the solid. The ¹H n.m.r. spectrum at 100 MHz (Figure 2) shows a temperature-dependent O–CH₂–C signal

(δ 3·7), which broadens at −30° and splits into two signals (δ 4·0 and 3·4) below −60° $(T_c = -52°; \Delta G^\ddagger \, ca. \, 11 \, \text{kcal/mol})$, whereas the single line of the O–CH₂–O group (δ 4·53) undergoes no change. The C–CH₂–C signal (δ 1·8) is also
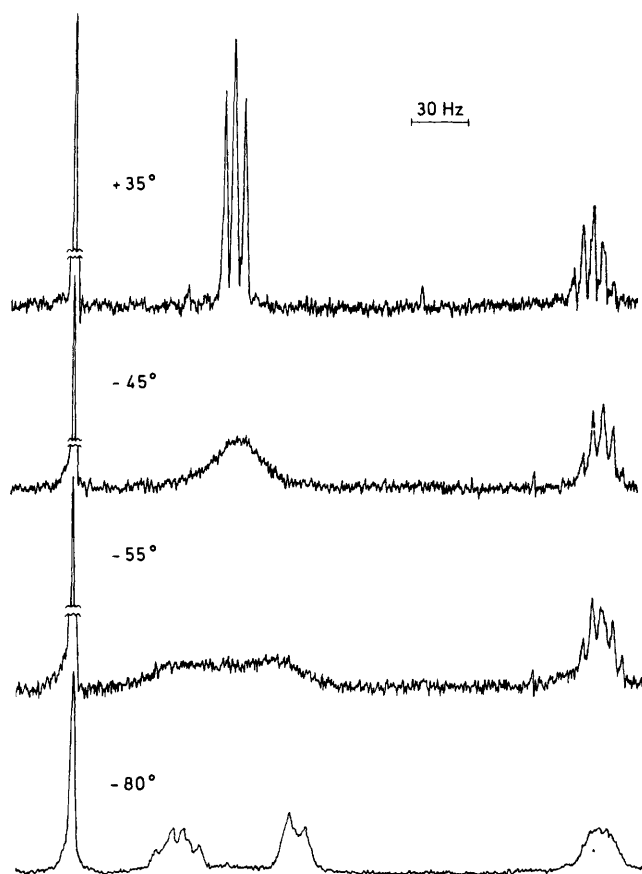

FIGURE 2. ¹H N.m.r. spectra at 100 MHz of 1,3,7,9-tetraoxa-cyclododecane at various temperatures in CHFCl₂ (top curve in CS₂).

unchanged except for a modification of its coupling pattern. Such a molecular symmetry can only correspond to the conformation shown in Figure 1 (C) with a two-fold sym-metry axis passing through each pair of opposite corners, whereby geminal hydrogens on each corner become equivalent.†

This conformation is of the same 'square,' non-diamond-lattice type always encountered so far in 'saturated' 12-membered rings: cyclododecane,[11,12] cyclododecanone,[13] cyclododecane-1,7-dione,[14] and 1,4,7,10-tetraoxacyclodo-decane.[15] The two dioxa-groupings are not only favour-ably placed across opposite corners as in 1,3,8,10-tetra-oxacyclotetradecane[8] and 1,3,9,11-tetraoxacyclohexa-decane,[5] but give the ring an additional stabilization by interacting across the remaining corners with inner O–CH₂–C protons, in the manner found to be favoured in 1,5,9,13-tetraoxacyclohexadecane.[5,15]

† *Added in proof:* The 2,2,8,8-tetramethyl derivative has since been prepared in a similar manner (m.p. 115°). Its n.m.r. spectrum shows an exactly analogous behaviour $(T_c = -5°)$.

The observed conformational barrier is very much higher than in comparable 12-membered rings: 7·3 kcal/mol for cyclododecane,[12] 7·3 kcal/mol for cyclododecanone,[13] and 5·5 and 6·8 kcal/mol for the two processes in 1,4,7,10-tetra-oxacyclododecane.[16] It is inconceivable that replacement of CH_2 by oxygen should raise the absolute energy of any of the barriers on a complete interconversion path,[17] since all have *syn*-eclipsing of one ring bond as the critical interaction.[16,17] The only explanation is therefore that the energy of the conformation is lowered, presumably owing to the favourable $O \cdots CH_2$ interactions. We conclude that there is sufficient conformational strain in 1,3-dioxan to transform it into the cyclic dimer, and that this is so stabilized that the reaction does not proceed to the polymer because of the accompanying further decrease in entropy.

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