Conformational Studies of Macrocyclic Tetrakis-(*gem*-dimethyl)cycloalkanediones

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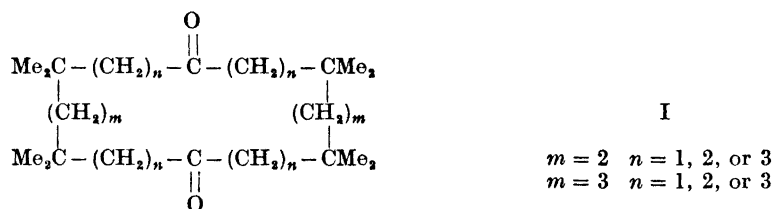
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Diametric cycloalkanediones having four *gem*-dimethyl substi-
tuents have been shown by determination of dipole moments, by
infrared spectroscopy of solid and solution, and by calorimetry of the
melting process, to have the same conformer in solid, melt, and
solution when the ring is 14- and 16-membered, but to be a conformer
mixture in melt and solution when the ring is 18- and 24-membered.
The 20- and 22-membered rings are unclear cases.

The preferred position of a carbonyl group on a diamond-lattice carbon
skeleton of medium or large rings is difficult to establish by studying the
properties of cycloalkanones. When two carbonyl groups are present the result-
ing molecular dipole moment should be informative, particularly if the carbonyl
groups are placed diametrically so that they have to occupy in each conformer
equivalent positions of "rectangular" or "square" ring skeletons.[1]

Two series of macrocyclic diesters having the ester groups situated oppo-
site each other have been studied earlier.[2] However, the orientation of the
dipole moment of the ester group is not defined by symmetry, and the
ambiguity with respect to *cis,trans*-configuration presents difficulties.

Obviously, one cannot expect large carbocyclic rings to be so rigid that
two parallel or antiparallel dipoles far apart, even if they are well-defined
geometrically like the carbonyl group, give a resultant dipole moment corre-
sponding to the exact sum or difference of the group moment. To determine the
magnitude of any deviation, it was of interest first to examine compounds
where the position of the carbonyl groups is more or less given by the presence
of *gem*-dimethyl groups confined to corner positions of rectangular
conformations.[1] The syntheses of such symmetrical 14- to 24-membered
tetrakis (*gem*-dimethyl)cycloalkanediones (I) have been reported recently,[3] and
their physical properties are reported and discussed in this paper.

$$Me_2C - (CH_2)_n - \overset{\overset{\displaystyle O}{\|}}{C} - (CH_2)_n - CMe_2$$

$$(\overset{|}{C}H_2)_m \qquad\qquad (\overset{|}{C}H_2)_m$$

$$Me_2\overset{|}{C} - (CH_2)_n - \underset{\underset{\displaystyle O}{\|}}{C} - (CH_2)_n - \overset{|}{C}Me_2$$

I

$m = 2 \quad n = 1, 2, \text{ or } 3$
$m = 3 \quad n = 1, 2, \text{ or } 3$

In the following paper the properties of unsubstituted symmetrical cycloalkanediones, including also medium rings, will then be described.

DIPOLE MOMENTS

The six tetrakis(*gem*-dimethyl)cycloalkanediones which have been synthesized belong to two series (I, $m = 2$ and I, $m = 3$). In one of these ($m = 2$) the *gem*-dimethyl groups have been so placed as to favour rectangular conformations consisting of parallel chains linked together in both ends by two methylene groups (Fig. 1; 14, 18, and 22 ring atoms). In the other ($m = 3$) the same chains
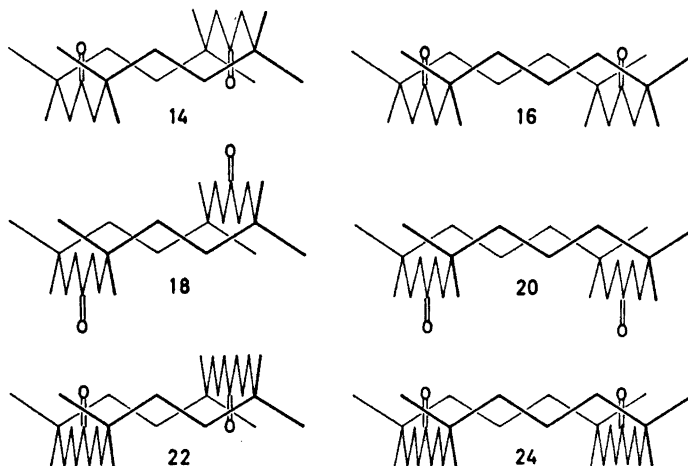

Fig. 1. The most probable conformations of tetrakis(*gem*-dimethyl)cycloalkanediones (I). Numbers indicate ring size.

are linked together in both ends by three methylene groups (Fig. 1; 16, 20, and 24 ring atoms). It is directly seen that if these diamond-lattice conformations are really those present and sufficiently rigid, the former series should have antiparallel dipoles and therefore zero dipole moments, while the latter series should have parallel dipoles and therefore dipole moment values twice that of the carbonyl moment ($2.7 \text{ D} \times 2 = 5.4 \text{ D}$). The observed values (Table 1) are seen definitely to follow such a trend, hence there can be no strong tendency for

Table 1. Properties of tetrakis(*gem*-dimethyl)cycloalkanediones (I).

m,n	Number of ring atoms	M.p. °C	ΔH_m (kcal/mol)	ΔS_m (e.u.)	Dipole moment (Debye)	Infrared spectrum in CS_2-solution as compared to solid
2,1	14	219	5.9	12.2	1.1	identical, sharp bands [a]
3,1	16	150	8.2	19.5	4.4	practically identical, less sharp bands
2,2	18	219	12.1	24.5	1.7	broadened bands and frequency shifts [a]
3,2	20	145	8.8	21.4	4.4	broadened bands, but similar [a]
2,3	22	169	11.4	25.8	2.5	broadened bands, but similar [a]
3,3	24	107	7.8	20.9	—	very broad and different bands

[a] Crystal splitting of *gem.*-dimethyl lines around 1370 cm^{-1} observed.

intramolecular dipole association which would have led to low moments also in the latter series. As ring size increases, both series should converge towards the calculated value for free relative orientation ($2.7\,D \times \sqrt{2} = 3.8\,D$). The rapid convergence seen in the series having antiparallel dipoles may be a consequence either of an increasing number of other stable conformers having a different relative orientation of their carbonyl groups, or simply due to large amplitudes of low-frequency deformation vibrations. More information on this point had to be collected by spectroscopy and calorimetry.

INFRARED SPECTROSCOPY

Since generally a given crystal lattice accepts only one conformation of a molecule, a comparison of the infrared spectrum of the solution with that of the solid should reveal whether new conformations appear. Of the present cyclic diketones only the 14- and 16-membered rings have identical spectra in the solid and in CS_2-solution. Furthermore, the bands are few and sharp, particularly sharp for the 14-membered ring, suggesting that in each case we have to do with a single conformer. It has already been shown [1,4] that only one diamond-lattice conformation can exist for cyclotetradecane and cyclohexadecane and that *gem*-dimethyl substituents can only be accommodated at the four corner positions. There can thus be little doubt that these rings have exclusively the conformations shown in Fig. 1, and that the positions of the carbonyl groups are thereby unambiguously fixed as shown. The deviation of the dipole moments from the extreme values, noticeable already for these ring sizes, is therefore here due to a lack of rigidity.

Our 18-membered cyclic diketone shows a solution spectrum different from the solid spectrum. Certain sharp bands of the crystal have undergone not only marked broadening, but also displacement of frequency, so that several conformers are coexisting in solution. We have shown earlier [4] that four diamond-

lattice conformations are possible for cyclooctadecane and have indicated the positions that may be occupied by a *gem*-dimethyl substituted ring atom. Three of these ring conformations can accept at the same time the four *gem*-dimethyl groups as they are disposed in our diketone, two of them even in more than one way (Fig. 2). Unlike the situation in the hydrocarbon, the criterion of a maximum number of *anti*-bonds may not necessarily be applicable to the diketone to further select the best conformation, since the carbonyl groups might introduce additional features. Not only the conformer a_1 of Fig. 2, corresponding to the exclusive hydrocarbon conformer,[1,5] but also a second conformer a_2 with the same ring skeleton, as well as the four others in Fig. 2, have therefore to
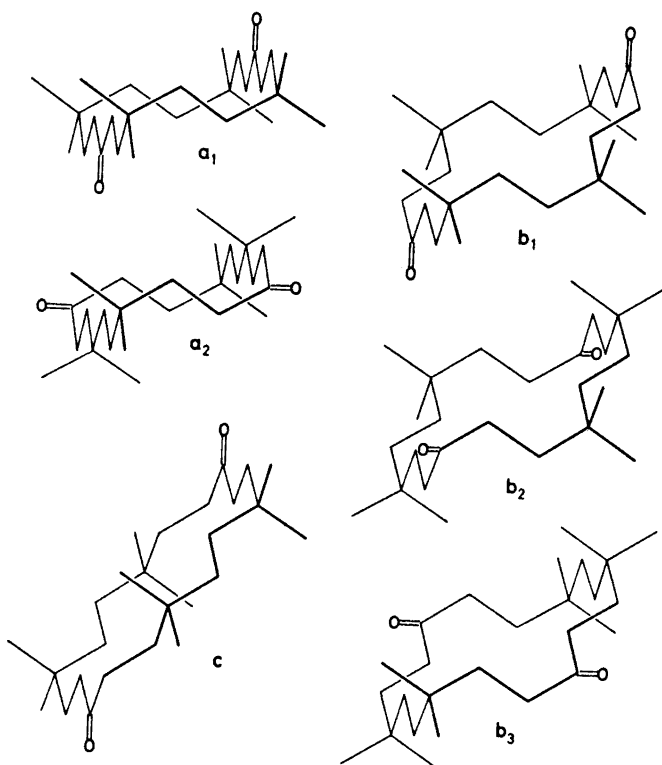

Fig. 2. The six possible diamond-lattice conformations of 4,4,7,7,13,13,16,16-octamethyl-cyclooctadecane-1,10-dione.

be considered, but to decide which of them are present in solution is impossible. As all are centrosymmetric, it seems nevertheless safe to conclude that the observed dipole moment is again due to lack of rigidity rather than to the presence of less symmetrical conformers.

Unexpectedly at first, the larger 20-membered cyclic diketone had a solution spectrum more similar to the solid spectrum, only some bands having

undergone slight broadening. As many as five diamond-lattice conformations can be derived for cycloeicosane, and on each of these ring skeletons the positions that may be occupied by a *gem*-dimethyl substituted ring atom have been indicated.[4] On the other hand, the particular substitution pattern of our diketone fits only one of these ring conformations, and only in the manner shown in Fig. 1. Hence, conformational homogeneity should indeed have been expected. The tendency for this molecule, as well as the corresponding hydrocarbon, to occlude solvent molecules [6] gives extra support for the preferred nature of this open rectangular conformation. Without methyl substituents no such tendency is observed.

The 22-membered cyclic diketone was little soluble in CS_2, but the solution spectrum, again surprisingly, was less different from the solid spectrum than in the case of the related 18-membered diketone. A broad background absorption may represent other possible conformers, whose number is too large to be easily surveyed, but the crystal conformer seems to be dominant.

Finally, the 24-membered cyclic diketone has a solution spectrum more unspecific and different from the solid spectrum than any of the others. The number of possible conformers is again very large and it may not even be certain that the crystal conformer is the open one shown in Fig. 1, since no tendency to occlude solvent molecules was noted.

MELTING PARAMETERS

When the infrared spectrum of the melt (or solution) is found to be identical with that of the solid, it is essential to verify that the solid does not consist of a mixture of conformers. Generally, for macrocyclic compounds, this is encountered only in relatively expanded crystal lattices existing above a solid-solid transition point, below which conformational selection takes place.[1] Such a situation can therefore be revealed by a particularly low entropy of melting, the existence of a solid-solid transition, and spectral simplification (fewer and sharper bands) below the transition temperature.

The data of Table 1 show that the observed entropies of melting are in all cases above the minimum value required for the total melting process of rigid molecules of similar symmetry.[7] No transition points were observed down to $-90°$. The 18- and 22-membered rings have particularly high entropies of melting, and the 24-membered perhaps quite low, when confronted with the conclusions from infrared spectroscopy. It may, however, be dangerous to draw the conclusion from the numerical values that the 18- and 22-membered rings are more complex mixtures in solution than the 20- and 24-membered rings, as the former have also the highest enthalpies of melting. A strong packing may lock the molecules up rigidly in the crystal lattice, thus causing a particularly high entropy gain when they are set free in melt or solution. The reason why the melting enthalpy is particularly small for the 14-membered ring may be steric hindrance to intermolecular carbonyl association due to the proximity of the methyl groups.

EXPERIMENTAL

Determination of dipole moments. Dielectric constants were measured at 20°C in a Weilheim Dipolmeter DM 01 on four different solutions of each compound. Concentrations were in the range of 50 – 200 mg of diketone in about 30 g of benzene. Refractive indices were measured on the same solutions in a Brice-Phoenix Differential Refractometer. Calculation of dipole moments was performed according to Hedestrand,[8] using no correction for atomic polarization.

Infrared spectra. These were recorded in a Perkin-Elmer Grating Infrared Spectrophotometer 457 as KBr pellets and in CS_2 solution.

Calorimetric measurements. A Perkin-Elmer Differential Scanning Calorimeter IB was used down to a temperature of $-90°$.

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