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ON THE CONFORMATION OF 6-KETONONANOLIDE AND 1,4-CYCLOHEXANEDIONE IN SOLUTION BY DIPOLE MOMENT STUDIES[1]

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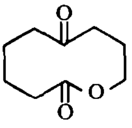
Abstract—The dipole moments of 6-ketononanolide (**1**) and its 2,4,7 and 8-Me derivatives (**2–5**) are found to be 1·8 – 1·9 ± 0·2 D. Utilizing the known solid-state geometry of **1**, a dipole moment of 1·6 D is calculated by the INDO quantum mechanical method. Thus the conformation of **1** in solution does not differ much from its solid-state conformation which is diamond-lattice derived with the CO groups 174° apart and in "Type III" positions. However, the IR spectrum of **1** in solution shows differences from that in the solid state (Nujol or KBr).

The dipole moment of 1,4-cyclohexanedione (**10**) is calculated to be 1·2 D for the experimental 156° twist boat conformation (found in the solid-state). This is in excellent agreement with the experimental value found by several groups. 1,6-Cyclodecanedione (**6**), however, is found to have an experimental dipole moment of 0·7 D, as contrasted with a calculated value of 0 D for 180° opposed carbonyls.

6-Ketononanolide (**1**)[5] is a 10-membered ring system whose conformation should be diamond-lattice derived with the CO groups and the ring O atom all in "Type III" positions (*i.e.* **i**).[6] The solid-state conformation of **1** was indeed found to be **i**.[7] It was of interest to determine if the dipole moment of **1** in solution is consistent with this geometry and to find the possible effects caused by placing Me substituents at various positions on the ring. This is in relation to anticipated studies on the next higher diamond-lattice derived 14-membered ketolactone system found in the erythromycin antibiotics. Erythromycin, oleandomycin, and other 14-membered ring macrolides have similar diamond-lattice derived conformations in solution and in the solid phase.[8]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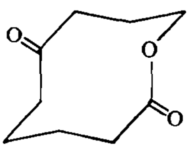
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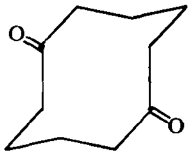
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It seemed worthwhile to determine whether the dipolemoments of **1** and of 1,6-cyclodecanedione (**6**)[9] in solution were consistent with their solid phase conformations.

RESULTS AND DISCUSSION

Experimental dipole moment determination. Table 1 lists the dipole moments obtained for **1**, its 2,4,7 and 8-Me derivatives (**2–5**), 1,6-cyclodecanedione (**6**) and several cycloalkanones. The values obtained for cyclohexanone (**7**), cyclodecanone (**8**) and cyclododecanone (**9**) are in good agreement with previously reported values,[10,11] thus lending confidence to our experimental method. The dipole moment of **6** is found to be 0·7 D. The dipole moments of **1–5** fall within the narrow range of 1·8–1·9 D. Because of errors inherent in the approximate method used to calculated the dipole moments[12a] and the use of the change of refractive index with concentration in estimating the induced polarization,[12b] the estimated error in the experimental dipole moments is ± 0·2 D except for **6** where it is ±0·1 D.

Calculation of dipole moments. When the solid-state geometry is known, the dipole moment of a molecule (for that geometry) can be calculated either by vectorial addition of group moments[13] or by a quantum mechanical treatment such as the INDO method.[14] If there is a change in the conformation of a molecule in solution, this can result in a change of dipole moment. The method provides no information about different conformations with the same dipole moment.

For 1,6-cyclodecanedione (**6**), the equilibrium solid-state geometry has no dipole moment because of the symmetry of the system. This is also true for the conformation believed to exist in solution.[15a,b] Internal vibrational distortions from the equilibrium geometry are expected to cause only a small moment to result. The observed moment for **6** is consistent with incomplete cancellation of atomic polarization and/or the presence of a small amount of a more polar form.

The theoretical dipole moment of **1** is difficult to determine accurately by vectorial addition of group moments since the relative orientation of the ketone and lactone moments are not known. Assuming group

Table 1. Calculated and experimental dipole moments

Compound	Dipole Moment, Calcd (D)	Dipole Moment, Obsvd (D)
Acetone	2·9[a]	2·9[b]
Cyclohexanone	2·9[a]	3·1(20°, benzene or cyclohexane) 3·1[c]
Cyclodecanone		2·6 (25°, benzene) 2·75[d]
Cyclododecanone		2·7 (25°, benzene) 2·75[d]
6-Ketononanolide (**1**)	1·6[a]	1·8[e]
2-Methyl-6-ketononanolide		1·8[e]
4-Methyl-6-ketononanolide		1·9[e]
7-Methyl-6-ketononanolide		1·85[e]
8-Methyl-6-ketononanolide		1·8[e]
1,6-Cyclodecanedione (**6**)	0·0[f]	0·7 (25°, *p*-xylene)
1,4-Cyclohexanedione (**10**)		1·2[g]
Chair form (**iii**)	0·0[a]	
180° twist boat (**iv**)	0·0[a]	
156° twist boat (**ii**)	1·2[a]	
2,5-boat form (**vi**)	2·2[a]	
1,4-boat form (**v**)	4·6[a]	

[a] By the INDO method-this work. [b] See ref. 17. [c] See ref. 10. [d] See ref. 11. [e] At 25° in benzene solution. [f] By vectorial addition of group moments [g] See ref. 21a, 23 and 24.

moments of *ca* 2·0 D for an *s-trans* lactone[16] and 2·9 D for a ketone,[17] the minimum moment for the molecule is *ca* 0·9 D.* Actually since the angle between the carbonyls is only 174° (*via* X-ray determination[7]) and assuming that the vector of the lactone group is directed *ca* 40° off the carbonyl towards the alkyl C-O, an approximate dipole moment of 1·8 D can be calculated.

The INDO method, which gives good values for dipole moments,[19] gives 1·6 D for **1** using the X-ray data of Dunitz.[7] It is concluded that there is little if any conformation change for **1** in solution. Furthermore the dipole moments of **2**–**5** suggest that these molecules have similar conformations (or mixtures of conformations) to **1** in solution. Table 1 lists the dipole moments of acetone, cyclohexanone (**7**) and several conformations of 1,4-cyclohexanedione (**10**) as calculated by the INDO method. The latter system deserves further comment.

The X-ray structure of **10** has been determined by two groups.[20,21] The conformation found is a distorted twist-boat **ii** with an angle between the carbonyls of *ca* 155°. The usual methods for dipole moment determination give a value of 1·2–1·3 D for **10** in solution.[20a,22,23] The INDO method, using solid state geometry of Mossel and Romers,[20b] gives a value of 1·2 D. A study by Aihara, however, had claimed that the true moment of **10** may be no larger than 0·43 D and that the larger "apparent moment" is due to the residual induced atomic polarization which is not properly cancelled by the refractive index in this case.[24] Furthermore, arguments have been presented for a nonpolar structure (**iii** or **iv**) in the gas phase.[25] A recent electron diffraction study on gaseous **10** reveals a twist-boat structure with an angle between the CO groups of 143·8 ± 8·7°.[26] Thus a twist-boat conformation exists in both the solid and gas phases. Assuming the 1·20 experimental moment of **10** to be valid, our INDO result suggests that a twist-boat conformation is also found in solution. This agreement of experimental and calculated moments is not enough to prove this point and the possibility that the observed moment of **10** is due to other causes must be admitted. It is relevant that an attempted NMR study of **10** could not separate out conformers down to −160°, suggesting a barrier of less than 5 kcal/mole between conformers.[27] Although Allinger[15c] does not report data on the 156° twist boat, he does calculate that the 180° D_2 twist-boat (**iv**) is of slightly lower energy than chair form (**iii**).

Infrared data. The IR spectra of **1** in carbon tetrachloride (or benzene) when compared to that in potassium bromide or nujol show several differences in band intensity and band position. The 15 cm^{-1} shift to lower energy CO absorption noted in comparing solution and solid-state spectra is in the normal range.[28] While the data suggests that some conformation change might be present, it does not prove it.[29]

The solid-state conformation of **1** has a short ketone CO-ester alkyl oxygen transannular distance (2·83 A°).[7] It was anticipated that this might lead to ketone CO group absorption at lower energy. However, cyclodecanone absorbs at *ca* 1700 cm^{-1} (in CCl_4) while the ketone of **1** absorbs at the *higher* energy value of 1709 cm^{-1}. Similarly,

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*For the use of bond moments and a coordinate system[18] in calculating the dipole moment of **1** see: R. Rapp, Ph.D. Thesis, Lehigh University, 1967. The method is limited in this case by the problems inherent in using bond moments for a lactone group. It is more useful for simpler groups.

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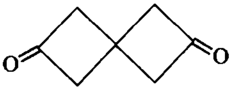

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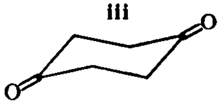

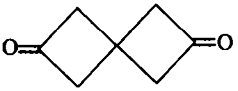

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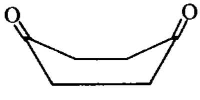

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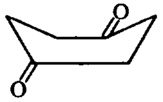

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the ketone of 7-ketoundecanolide (11)[5b] absorbs at the higher value of 1712 cm^{-1} in comparison to 1706 cm^{-1} for cyclododecanone.* The absence of transannular ether oxygen interaction with a ketone group in an 8-membered ring has been noted.[30]

EXPERIMENTAL†

Ketolactones **1**–**5** were previously described.[5]

1,6-Cyclodecanedione (**6**). Oxidation of a mixture of 1,9- and 9,10-octalin[31]‡ with performic acid, according to Dev,[32] gave crude 9,10-decalindiol (34%): m.p. 90–95° (from acetone-water) lit.[32] 95–96°. Treatment of the diol with lead tetraacetate in dry benzene[32] gave **6** (59%): m.p. 99·5–100·5° [lit.[32] m.p. 100°]; IR (CCl_4) 2980, 1712, 1450, 1420, 1370, 1350, 1260, 1185, 1145, 1110, 1040, 980w, 910w, cm^{-1}. (Found: C, 71·40; H, 9·30. Calcd for $C_{10}H_{16}O_2$: C, 71·40; H, 9·59%).

Infrared studies. The IR spectrum of **1** (CCl_4) had: 1732, 1709, 1437, 1367, 1342, 1332, 1282, 1272, 1242, 1229, 1177, 1162, 1142, 1072, 1052, 1025, 994, 967, 929 and 900 cm^{-1}. In KBr(1%) it had: 1709, 1694, 1442, 1384, 1357, 1332, 1292, 1269, 1247, 1227, 1170, 1137, 1082, 1049, 1029, 997, 962, 937, 899, 804 and 794 cm^{-1}.

Dipole moment measurements. Dipole moment measurements were performed with a Kahlsico Dipolmeter Type DM-01. The instrument operates at a frequency of *ca* 2·0 MHz with a measuring sensitivity of $\Delta E/E = 4 \times 10^{-5}$. The measuring cell and an Abbe refractometer were kept at 25·0 ± 0·1° *via* a constant temp bath. The cell was calibrated with benzene and cyclohexane at 20°. The dipole moments were determined by measuring the dielectric constant and refractive index of a series of solns of decreasing solute concentration. The dipole moments were then calculated according to Guggenheim[12a] using the following equation. The symbols are defined as follows: N_L is Avogardo's number, K is the Boltzmann constant, M_2 is the molecular weight of the solute, ϵ_1 is the dielectric constant of the solvent, d_1 is the solvent density, a_ϵ is the rate of change of the dielectric constant of the soln with concentration, and a_n is the rate of change with concentration of the difference in the square of the refractive index of the pure solvent and the square of the refractive index of the soln.

$$\mu^2 = \frac{27KT}{4\pi N_L} \cdot \frac{M_2}{d_1(\epsilon_1 + 2)^2} \cdot (a_\epsilon - a_n)$$

Values of ϵ_1 = 2·0228 (cyclohexane, 20°), 2·2727 (benzene, 25°)[33] and d_1 = 0·7791 (cyclohexane, 20°), 0·87370 (benzene, 25°)[34] were used.[1b]

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*These comparisons were done on 3–5% CH_2Cl_2 solutions.

†Solvents were dried by distillation from phosphorus pentoxide, calcium hydride, or lithium aluminum hydride. Infrared spectra were recorded on Beckman IR-8, IR-10 and Perkin Elmer 257 spectrophotomers.

‡Attempted isomerism of the 3:1 mixture of 9,10- and 1,9-octalin with *p*-toluenesulfonic acid and other acids under various conditions did not change the ratio. (G. Gonis, Ph.D. thesis, Lehigh University, 1964).

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