184. *The Conformation of Hexamethylcyclohexane*-1,3,5-*trione.*

By Johannes Dale.

The low dipole moment (1·03 D) of hexamethylcyclohexane-1,3,5-trione suggests a twisted flexible boat conformation rather than a flattened chair. This is supported by the infrared spectra of this trione and its perdeuterated analogue. The ease with which ketonic cyclohexane derivatives adopt non-chair conformations is due not only to interaction between axial substituents in the chair, and the high entropy of boat forms, but also to the small rotational barrier in C–C bonds adjacent to carbonyl groups.

In a normal chair-conformation (IIIa) of hexamethylcyclohexane-1,3,5-trione the three axial methyl groups would come much too close and create a serious strain, considering that already one single 1,3-diaxial methyl–methyl interaction represents[1] an instability of 3·7 kcal./mole. It was of interest to find out whether the molecule avoids this situation by simple flattening of the ring or by taking up some (flexible) boat conformation (III b and c). The dipole moment would seem capable of yielding information, as the three ketone groups point to the same side in a flattened chair, but not in the flexible forms.

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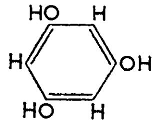
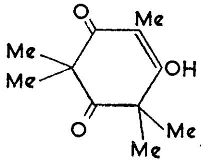
[1] Allinger and Miller, *J. Amer. Chem. Soc.*, 1961, **83**, 2145.

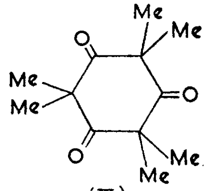
The strain in this compound manifests itself already in its synthesis by methylation of phloroglucinol with methyl iodide (or bromide). Thus, the early observation [2,3] that the first five methyl groups enter rapidly under gentle conditions was confirmed; no intermediate less alkylated products were isolated, and the last methyl group could only be introduced by using very long reaction times. It was also confirmed that *O*-alkylation can be largely avoided by using alkali hydroxide in water [3] instead of sodium methoxide in methyl alcohol; the stronger base potassium t-butoxide in t-butyl alcohol presented no advantage. We find now that in aqueous alkali above 130°, in an autoclave, the hexamethyl derivative is obtained readily in such a good yield that the recent alternative method of cyclic trimerization of dimethylketen [4] may hardly present the advantage claimed for it.



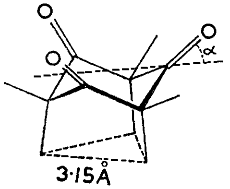
(I)



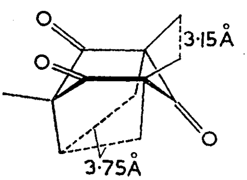
(II)



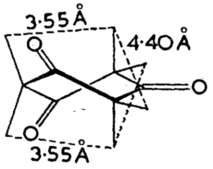
(III)



(IIIa)



(IIIb)



(IIIc)

For the pentamethyl derivative, the enol structure (II), suggested in 1890,[2] could be confirmed both by ultraviolet ($\lambda_{max.}$ 260 mμ, ε 12,700) and infrared spectroscopy. In this structure five carbon atoms of the ring tend to remain coplanar, and there are no interacting methyl groups, whereas the hexamethylated triketone will be expected to approach a non-planar form and encounter the difficulties already discussed. That this is the reason for the sluggishness of the last methylation step is also borne out by the reported [5] formation of mainly the mono-*O*-penta-*C*-alkylated isomer when the larger ethyl group is used, since *O*-alkylation does not require the ring to become bent. In fact, we find this to be the only neutral product formed when the ethylation is carried out in water, and its structure could be unequivocally confirmed by infrared and ultraviolet spectroscopy (see Experimental section).

The dipole moment of hexamethylcyclohexane-1,3,5-trione, measured in benzene solution at 25°, was 1·15 D, or 1·03 D after correction for the atomic polarization. In a cyclohexane chair form (IIIa) with tetrahedral angles, the angle (α) between the C=O bond and a plane through carbon atoms 1, 3, and 5 is 35°, which with a group moment of 2·8 D,[6] gives a calculated moment as high as 4·9 D. The actual wider CCC angle at the carbonyl group is seen on Dreiding models [7] to flatten the ring ($\alpha = 27°$) which leads to a calculated dipole moment of 3·8 D; at the same time the distance between axial methyl-carbons is

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[2] Spitzer, *Monatsh.*, 1890, **11**, 104.

[3] Herzig and Erthal, *Monatsh.*, 1910, **31**, 827.

[4] Pregaglia, Mazzanti, and Binaghi, *Makromol. Chem.*, 1961, **48**, 234.

[5] Herzig and Zeisel, *Monatsh.*, 1888, **9**, 217; Herzig and Erthal, *ibid.*, 1911, **32**, 491.

[6] Smyth, " Dielectric Behavior and Structure," McGraw-Hill, New York, 1955, p. 290.

[7] Dreiding, *Helv. Chim. Acta*, 1959, **42**, 1339.

increased from 2·55 to 3·15 Å. To arrive at the observed dipole moment, the angle α would have to be only 7°, which corresponds to a degree of flattening and a methyl–methyl distance in excess of what is really needed (about 3·4 Å)[8]; hence, already on this basis a flattened chair becomes improbable. For a classical boat form (IIIb) the calculated moment is 1·1 D, but this conformation is hardly better than a chair as it has two-eclipsed ring bonds and, on Dreiding models, one pair of methyl groups as close as 3·15 Å.

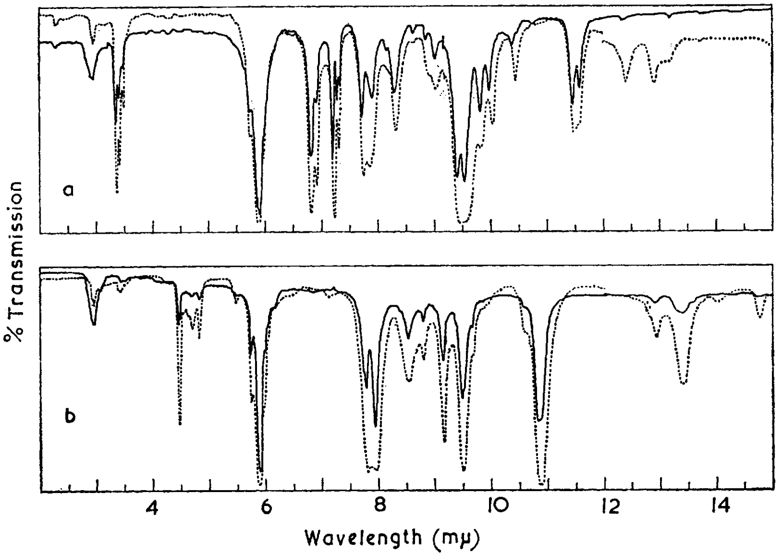

FIG. 1. Infrared spectra of (a) normal and (b) perdeuterated hexamethylcyclohexane-1,3,5-trione. Full line: solid in a KBr disc; broken line: solution in CCl_4 (2—12μ) and CS_2 (12—15μ).

On the other hand, the twisted boat of symmetry C_2 (IIIc) has its two shortest methyl–methyl distances at 3·55 Å, but the calculated moment is nearly zero. The only logical conclusion is that in benzene solution one has to do with a mixture of flexible, mainly twisted, boat forms with a small admixture of the chair form to increase the average moment.

Support for this comes from a comparison of the infrared spectra of the solid and for solutions (Fig. 1); there is a marked broadening of several bands and appearance of new bands in solution. It was not *a priori* excluded that the unique conformation believed to be present in the solid could be the flattened chair, as the predominance of flexible boat forms in solution might very well be due wholly to the favourable entropy [9] if the enthalpy difference is small. It was hoped that the number of skeletal vibration bands observed in the infrared might give a clue to the conformation present in the solid, as the trigonal axis of the chair would cause some degeneracies and slightly stricter selection rules. As an aid in the assignment of the bands, the fully deuterated (99%D) hexamethylcyclohexane-1,3,5-trione was prepared by alkylation of phloroglucinol with trideuteromethyl iodide or bromide. Its infrared spectrum (Fig. 1) allowed us to sort out the vibrations of the methyl groups and led to the suggested partial assignments given in the Table. These have been based on a critical comparison with deuteration shifts in compounds containing single

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[8] Braude and Sondheimer, *J.*, 1955, 3754.

[9] Allinger and Freiberg, *J. Amer. Chem. Soc.*, 1960, **82**, 2393.

Infrared bands of hexamethylcyclohexane-1,3,5-trione (A) and the perdeutero-derivative (B) (in cm.$^{-1}$).

Assignment	A (solid)	A (solution)	B (solid)	B (solution)	Isotopic factor
CH stretch.	2980, 2935, 2865	2970, 2925, 2865	2240, 2130, 2070	2240, 2130, 2075	1·33, 1·38, 1·39
C=O stretch.	1695	1700	1693	1698	
CH_3 as. def.	1470, 1445	1470, 1445	1090	1090	1·35
CH_3 sym. def.	1390, 1371, 1364	1383, 1370	1053, (1049)	1053	1·32
Ring stretch.[a]	1297, 1264	1287, 1270	1284, 1258	1280, 1257	
Me–C–Me as. stretch (B_1) [b]	1204	1200	1172	1172	1·03
CH_3 rock (A_2) [b]	1128, 1110	(1119), 1106	(945?)	(945?)	1·19
CH_3 rock (A_1) [b]	1061, 1049	1057, (1041)	924, 919	920	1·15
Ring stretch [a, c]	1019, 1002	1015, 995	(1010)	(1010)	
Me–C–Me sym. stretch (A_1) [b]	962	955	(945?)	(945?)	1·02
CH_3 rock (B_1) [b]	873, 862	870, (864)	745	745	1·17
CH_3 rock (B_2) [b]	(810)	805	—	715	1·13

[a] Degenerate in chair. [b] Refers to local symmetry. [c] Or overtone in Fermi resonance with CH_3 rock (A_1).

methyl groups, such as the methyl halides,[10] methyl cyanide,[11] acetyl chloride,[12] and toluene; [13] and geminal dimethyl groups, such as propane.[14] The exocyclic C–C stretching would be expected to be more influenced by deuteration than the ring stretching, and this leaves as ring-stretching modes the bands at the astonishingly high frequencies of almost 1300 cm.$^{-1}$. In comparable compounds the highest C–C stretching lies much lower, for example at 1030 cm.$^{-1}$ for cyclohexane [15] and at 1070 cm.$^{-1}$ for acetone.[16] Not all skeletal vibrations could be assigned rigorously so that conclusions about the ring shape on this basis could not be drawn. However, the quite general occurrence of doublet bands suggest both the removal of degeneracies in the ring and the non-equivalence of the geminal dimethyl groups, assuming that these vibrate independently from each other. In either case the chair form must then be excluded.

The preference for non-chair conformations in the present case might quite plausibly be ascribed to the strong interaction between the axial methyl groups in the chair form. It is very likely, however, that another major contributing factor is the very small rotational barrier in C–C single bonds adjoining a carbonyl group (0·78 kcal./mole in acetone [17]), as compared with the barrier in ordinary C–C bonds (2·7—3·0 kcal./mole in ethane [18]). The flexible forms, which must necessarily have some partially eclipsed [*] bonds, therefore have their inherent Pitzer strain reduced to a minimum compared with that of the cyclohexane boat,[9,19] and in the chair–boat equilibrium the large entropy of the boat form will begin to dominate over the diminished enthalpy difference. It is interesting to note that among the 6 (or 7) cases found in the literature of established (twisted) boat conformations of noncondensed cyclohexane derivatives 5 (or 6) are ketones. Thus, whereas one axial di-t-butyl group in a hypothetical chair-conformation of a hydrocarbon ring (*trans*-1,3-di-t-butylcyclohexane [9]) is needed to force it into a boat form, it is sufficient in a cyclohexanone

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[*] In a bond adjoining a carbonyl group " eclipsed " is here defined with respect to the two bent substituent bonds from oxygen making up the double bond on a formally tetrahedral carbon atom. The observed stable conformation next to a carbonyl group [18, 20] then becomes " staggered." Calculations of relative stabilities of chair and boat forms in cyclohexanone and cyclohexane-1,4-dione based on the wrong assumption that this orientation is associated with strain,[19] have therefore no sense.

[10] King, Mills, and Crawford, *J. Chem. Phys.*, 1957, **27**, 455.
[11] Milligan and Jacox, *J. Mol. Spectroscopy*, 1962, **8**, 126.
[12] Overend, Nyquist, Evans, and Potts, *Spectrochim. Acta*, 1961, **17**, 1205.
[13] Fuson, Garrigou-Lagrange, and Josien, *Spectrochim. Acta*, 1960, **16**, 106.
[14] McMurry and Thornton, *J. Chem. Phys.*, 1951, **19**, 1014.
[15] Beckett, Pitzer, and Spitzer, *J. Amer. Chem. Soc.*, 1947, **69**, 2488.
[16] Schumann and Aston, *J. Chem. Phys.*, 1938, **6**, 485.
[17] Swalen and Costain, *J. Chem. Phys.*, 1959, **31**, 1562.
[18] Wilson, *Proc. Nat. Acad. Sci. U.S.A.*, 1957, **43**, 816.
[19] Allinger, *J. Amer. Chem. Soc.*, 1959, **81**, 5727.
[20] Pitzer and Donath, *J. Amer. Chem. Soc.*, 1959, **81**, 3213.

ring with one axial methyl group in the 3-position [21] (although a t-butyl group is needed when the axial substituent would have been in the 2-position [22]). Two axial methyl groups placed in the 3- and 5-positions, as in 3,3,5,5-tetramethylcyclohexanone derivatives, give rise to anomalies which have been interpreted [23] as a " reflex effect," but the possibility of a boat conformation has not been ruled out; in the corresponding 6-oxa-derivatives the presence of twisted boat conformations has been demonstrated,[23] and it is not easy to see how this structural change could make much difference, the rotational barrier in ether-like C–O bonds being as high as in C–C bonds (2·72 kcal./mole in dimethyl ether [24]). When the ring carries two (non-conjugated and non-enolized) oxo-groups, four of the ring bonds have their rotational barrier reduced, and not only have both isomers of 2,5-di-t-butylcyclohexane-1,4-dione been shown to occupy most probably non-chair conformations,[25] but also cyclohexane-1,4-dione itself.[26,27] In the latter case the particular twisted boat found in the crystal lattice has a calculated dipole moment close to that observed in solution,[28] but this must be a coincidence and can hardly be taken as a proof of a unique rigid conformation. In fact, we find that the infrared spectra (Fig. 2) of the solid and the solution are markedly different, in spite of earlier statements to the contrary.[27] Of particular importance is the CH_2-scissoring region ($\sim$1400 cm.$^{-1}$) where the solid shows several discrete resolved bands indicating a twisted boat conformation (in the chair as well as in the classical boat all 4 CH_2-groups are identical), whereas in solution one broad unresolved band indicates a complex mixture. If, as it thus seems likely, the preponderance of boat-forms is really due only to the favourable entropy, and not to a higher enthalpy of the chair, the dipole moment should diminish as the temperature is lowered. In the solid more efficient packing and dipole association might of course favour one particular form, and it is interesting that in the crystalline addition compound with mercuric chloride,[29] cyclohexane-1,4-dione has a twisted conformation different from that of the pure compound.

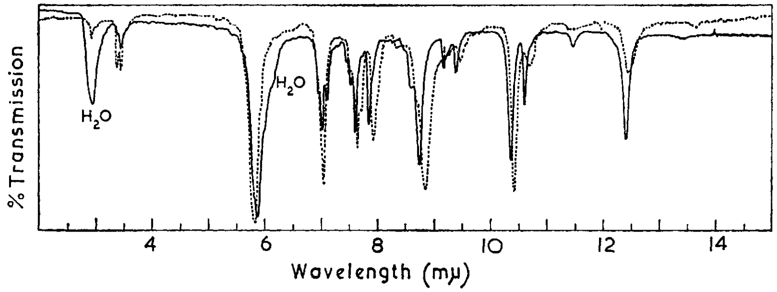

FIG. 2. Infrared spectrum of cyclohexane-1,4-dione. Full line: solid in KBr; broken line: solution in CCl_4 and CS_2.

EXPERIMENTAL

2,2,4,4,6,6-*Hexamethylcyclohexane*-1,3,5-*trione* (III).—In a 1-l. autoclave phloroglucinol dihydrate (100 g.) and sodium hydroxide (150 g.) were dissolved in water (300 ml.). When the solution had become clear and cool, methyl iodide (630 g.) was added, and the autoclave was heated at 130° for 24 hr. After cooling, two layers formed. The aqueous lower layer was separated, made alkaline, and extracted with petroleum; the extracts were added to the upper layer and the solvents distilled off. The trione (80·3 g., 62%) crystallized directly and, after

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[21] Djerassi, Warawa, Berdahl, and Eisenbraun, *J. Amer. Chem. Soc.*, 1961, **83**, 3334.
[22] Allinger and Blatter, *J. Amer. Chem. Soc.*, 1961, **83**, 994.
[23] Waegell and Ourisson, *Bull. Soc. chim. France*, 1963, 495, 496, 503.
[24] Kasai and Myers, *J. Chem. Phys.*, 1959, **30**, 1096.
[25] Stolow and Boyce, *J. Amer. Chem. Soc.*, 1961, **83**, 3722.
[26] Groth and Hassel, *Proc. Chem. Soc.*, 1963, 218.
[27] Mossel, Romers, and Havinga, *Tetrahedron Letters*, 1963, 1247.
[28] Hassel and Naeshagen, *Tidsskr. Kjemi*, 1930, **10**, 81; Le Fèvre and Le Fèvre, *J.*, 1935, 1696.
[29] Groth and Hassel, *Tetrahedron Letters*, 1964, 65.

filtration in pentane solution through alumina (activity 2) and recrystallization, melted at 82° (Found: C, 68·7; H, 8·8. $C_{12}H_{18}O_3$ requires C, 68·5; H, 8·6%). The compound is surprisingly volatile and starts to sublime at ~60°. Its infrared spectrum, recorded in a Perkin-Elmer double-beam instrument, model 21, is given in Fig. 1. The ultraviolet spectrum (in cyclohexane) had a broad maximum at 300 mμ (ε 80).

At 140° the yield was also 62%; at 100° it was 25%. Refluxing at atmospheric pressure for 24 hr. resulted in a yield of only 17%.

Replacement of the system NaOH–H_2O by MeONa–MeOH or t-BuOK–t-BuOH gave lower yields, neutral *O*-alkylated oily isomers being formed.

The deuterated trione, m. p. 80—81°, was prepared exactly as above, once by using trideuteromethyl iodide (97% D) and once by using the bromide (99% D). The degree of deuteration of the triones was determined by field ionization mass-spectrometry and corresponded well: 53% d_{18}, 34% d_{17}, 13% d_{16} in the former case and 80% d_{18}, 17% d_{17}, 3% d_{16} in the latter case. The infrared spectra were, however, hardly different; for the latter it is given in Fig. 1.

1-*Hydroxy*-2,4,4,6,6-*pentamethylcyclohexene*-3,5-*dione* (II).—The aqueous layer from the methylation of phloroglucinol (above) was acidified and extracted with ether. After removal of the solvent, the solid (37·5 g., 31%) was recrystallized from benzene, giving the *dione*, m. p. 115° (Found: C, 67·2; H, 8·1. $C_{11}H_{16}O_3$ requires C, 67·3; H, 8·2%). Infrared bands (KBr disc) were at ~3100 (broad; assoc. enolic OH), 1712 (nonconjugated C=O), 1637 (C=C), 1588 (broad; conjugated, assoc. C=O), 1178, and 1057 cm.$^{-1}$; in carbon tetrachloride solution, at 3535 (free OH), ~3120 (broad, weak), 1708, 1637, ~1610 (broad; conjugated free C=O), 1160, and 1060 cm.$^{-1}$; many bands between 6 and 10 μ which were strong in the solid became weak in solution. The ultraviolet spectrum (in propyl alcohol) showed a maximum at 260 mμ (ε 12,700).

From the reaction performed at 100° the yield of (II) was 46%; refluxing at atmospheric pressure for 24 hr. gave 56%. Replacement of the water by alcohols as above gave lower yields.

The isolated pentamethylated compound, when treated again with methyl iodide and aqueous alkali, could be more or less completely transformed into the hexamethylated trione (III), depending on the conditions as above.

1-*Ethoxy*-2,4,4,6,6-*pentaethylcyclohexene*-3,5-*dione*.—Phloroglucinol dihydrate (26 g.) and sodium hydroxide (80 g.) were dissolved in water (400 ml.) and refluxed with ethyl iodide (220 g.) with stirring until neutral, *i.e.*, for about 40 hr. The solution was made alkaline and extracted with ether, ether and excess of ethyl iodide were evaporated, and the residual *ethoxydione* (39%) was distilled at 126—128°/0·8 mm. (Found: C, 73·0; H, 10·1. $C_{18}H_{30}O_3$ requires C, 73·4; H, 10·3%). The infrared spectrum showed bands at 1710 (non-conjugated C=O), 1650 (conjugated C=O), 1610 (conjugated C=C), 1155, and 1020 cm.$^{-1}$ (enol ether); this excludes the hexaethylcyclohexane-1,3,5-trione structure, as well as higher *O*-ethylated compounds (one or no carbonyl groups). The ultraviolet spectrum corresponds to that of an αβ-unsaturated ketone; $\lambda_{max.}$ (in cyclohexane) 245 and ~320 mμ (ε 9000, 150).

Dipole-moment Determination.—Measurements were made at 25° of four solutions in benzene at different concentrations following the procedure described by Weiss.[30] Dielectric constants were measured in a Slevogt Dipolmeter DM 01,[30] the densities pyknometrically, and the refractive indices at the sodium *D*-line in an Eintauchrefraktometer (Carl Zeiss, Jena). Extrapolation to infinite dilution was made according to Hedestrand;[31] the values lay on a straight line. The measured total molar polarization of the solute ($P\infty$) was 82·37 cm.^{3} and the electronic polarization (P_E), or molar refraction, 55·18 cm.^{3}; from these values a dipole moment of 1·15 ± 0·03 D was calculated. Assuming the atomic polarization to be 10% of P_E, a dipole moment $\mu_{10\%}$ = 1·03D was calculated.

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[30] Weiss, *Z. anorg. allg. Chem.*, 1956, **287**, 223.

[31] Hedestrand, *Z. phys. Chem.*, 1929, *B***2**, 428.