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THE CHAIR-BOAT ENERGY DIFFERENCE IN 1,3-DIOXANE

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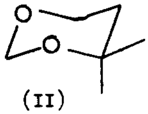
There is continuing interest in the possibility of six membered rings existing in boat conformations, and the energy differences between boat and chair forms are of fundamental importance in conformational analysis. Recently the enthalpy difference between the boat and chair forms of 1,3-dioxane has been calculated to be 2.2 kcal/mole,[2] and, seemingly in agreement with this value, a boat conformation has been proposed for 4-methyl-4-t-butyl- 1,3-dioxane (I).[3]

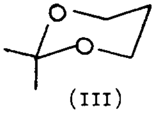
Our reasons for doubting the validity of the calculations giving the value of 2.2 kcal/mole have been expressed in full elsewhere.[4,5] Briefly they are based on the inadequacy of methanol (barrier to internal rotation 1.1 kcal/mole)[6] as a model for predicting torsional strain in the boat conformation of an oxygen-containing heterocycle, for which dimethyl ether (barrier 2.7 kcal/mole)[7] should be a better model. All the reliable experimental evidence available points to the free energy of the boat form being more than 3 kcal/mole greater than that of the chair form.

For a variety of reasons we consider it unlikely that an axial 4-methyl group introduces sufficient strain into a 1,3-dioxane ring to force it into a boat conformation. Firstly, 4,4-dimethyl-1,3-dioxane (II) shows the expected coalescences in its low temperature nmr spectrum for interconversion between chair conformations.[8] It is unlikely that the observed free energy of activation (9.1 kcal/mole at -110°) corresponds to a psuedorotation barrier between two flexible forms. More significantly, 2,2-dimethyl-(III) and 2,2,5,5-tetramethyl-(IV) 1,3-dioxanes, in which the non-bonded interactions caused by the axial 2-substituent may be expected to be greater than those caused by an axial 4-methyl group,[4,9] also show the expected chair-chair interconversion barrier in their low temperature nmr spectra [10]

(I)



(II)



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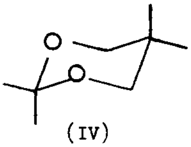
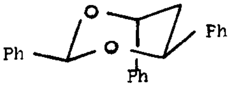


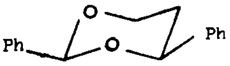
(IV)

Comparison of the coupling constants of the ring protons in the 60 Mcs nmr spectrum of cis-trans-2,4,6-triphenyl-1,3-dioxane (V) with those in analogous compounds of undisputed chair conformation, such as 4-phenyl-1,3-dioxane[11] (VI) and cis-2,4-diphenyl-1,3-dioxane (VII), leads to the conclusion that this compound has a chair conformation with an axial phenyl group.[12] This result has been confirmed by spectra obtained at 100 Mcs, with benzene as solvent. (Table) An axial phenyl group is expected to introduce more strain into a six membered ring than an axial methyl group. If (V) were in a twisted boat conformation similar to that proposed for (I) by Delmau and Duplan then J4a,5a (11.7 cps) and J5e,6e (1.5 cps) should be roughly equal. The contrast with the coupling constants expected for the boat, and the agreement with the values for other chair conformations make the results on (V) highly significant. Furthermore, the coupling constants obtained by analysis of the spectra of 4,4,6-trimethyl-(VIII) and 2-t-butyl-4,4-dimethyl-(IX) 1,3-dioxanes are in accord with chair conformations. Finally, in a series of 5,5-dimethyl-1,3-dioxanes, as the 2-substituents are changed from 2-methyl (X) to 2-t-butyl (XI) to 2-t-butyl-2-methyl (XII) the relative chemical shift difference of the 5,5-dimethyl groups does not alter significantly, as would be expected if the third compound in this series were forced into a boat conformation by the axial 2-methyl group.

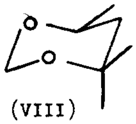


(V)

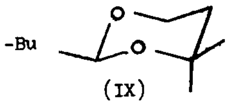
(VI)



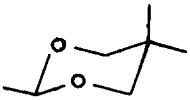
(VII)



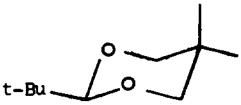
(VIII)



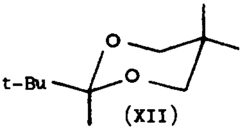
(IX)



(X)



(XI)



(XII)

The two principal arguments employed by Delmau and Duplan in assigning a boat conformation to (I) are the differences between observed and "predicted" geminal chemical shift differences, and slight deviations of coupling constants from the expected values.

The most reliable evidence in the literature for shielding of alkyl substituents on six membered rings[13] permits qualitative predictions of the changes caused by the 4-alkyl substituents on the C-2 and C-5 geminal chemical shift differences. The predicted changes are in the directions observed. In any event C-2 geminal chemical shift differences are at present an uncertain criterion for conformational assignments. The relative spectral positions of the C-2 protons are solvent and concentration dependent,[14] and we have found that the relative chemical shifts of the C-2 protons in (I) and (VIII) change sign on changing the solvent from benzene to chloroform.

A re-examination of the spectrum of (I) shows that while some of the differences between the reported[3] and expected coupling constants for a chair conformation for (I) may have resulted from an inappropriate first order analysis,the apparently most significant coupling constants were wrongly assigned. In particular the methyl group was reported to show a long distance coupling (1 cps) with one of the C-5 protons (H5),[3] implying an approximately antiperiplanar relationship,[15,16] while the other C-5 proton (H5*)[3] was reported to have a 13 cps vicinal coupling (which was regarded as anomalously large)[3] with the boat-axial C-6 proton (H6a),[3] again implying an antiperiplanar relationship. The C-5 protons can only take part in antiperiplanar relationships in this way if the ring is in a twisted boat conformation. The spectrum of a benzene solution of (I), however, shows unambiguously that the 13 cps coupling is between geminal and not vicinal protons, and that the long range coupling of 1 cps is to the C-5 proton at lower field which also shows a large axial axial vicinal coupling, 12.0 cps, with the axial C-6 proton. Thus one of C-5 protons is involved in two antiperiplanar relationships. This is conclusive evidence for a chair conformation, without excluding slight distortions which do not appear to affect the vicinal coupling constants greatly (Table).

The above arguments, based on both chemical shift and coupling constant measurements, have led both ourselves, and recently Delmau and Duplan[17] to the conclusion that 4-methyl-4-*t*-butyl-1,3-dioxane has a chair conformation.

It has recently been shown that the free energy difference between an axial and equatorial 4-methyl group in a 1,3-dioxane is about 3.0 kcal/mole.[9] Since the strain in some of the compounds discussed above and shown to have chair conformations is greater than the strain due to an axial 4-methyl group alone, one is led to the conclusion that the free energy difference between the chair and boat forms of 1,3-dioxane is greater than 3 kcal/mole, and quite probably close to that of cyclohexane.

Table of Vicinal Coupling Constants

Compound	4a5e	4a5a	5e6e	5e6a	5a6e	5a6a	Reference
I	--	--	1.2	4	5	13	3
I*	--	--	1.6	2.6	6.3	12.0	This work
V*	2.5±0.2	11.7±0.2	1.5±0.2	--	6.0±0.2	--	This work
VI	2.8	11.0	1.7	2.8	5.0	11.0	11
VII**	3.0±0.2	10.0±0.4	1.7±0.2	2.7±0.2	5.0±0.2	11.1±0.4	12
VIII**	--	--	--	3.1	--	10.6	This work
IX**	--	--	1.9	2.6	6.6	11.5	This work

Table of Geminal Coupling Constants

Compound	5e5a	6e6a	Reference
I	13.2	11.2	This work
VI	13.2	11.2	11
VII**	13.1	11.1	12
VIII**	13.1	--	This work

* Based on ABRX approximation.

** Based on an approximate first order analysis.

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