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MOLECULAR STRUCTURE OF r-2-(p-BROMOPHENYL)-CIS-4,CIS-6-DIMETHYL-1,3-DIOXANE

F.W. Nader

Organ.-Chemisches Institut der Universität Heidelberg
Heidelberg, Im Neuenheimer Feld W.-Germany

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Differences in conformational energies between substituted cyclohexanes and analogously substituted heterocyclic systems have been interpreted in terms of variations in ring geometry due to the presence of heteroatoms^{+}. In the case of 1,3-dioxane[1] and its disulfur analogue[2] such conclusions have been confirmed by X-ray analysis[3,4]. As postulated from the results of conformational equilibria[1] of the type shown in Fig. 1, and confirmed by structural studies[3], the 1,3-dioxane ring combines a puckered (O-1,C-2,O-3) with a flattened moiety (C-4,C-5,C-6). As a result of the puckering and the shorter (as compared to C-C) C-O distance, _syn_-axial interactions of substituents at C-2 in 1,3-dioxane are substantially higher than in cyclohexane.

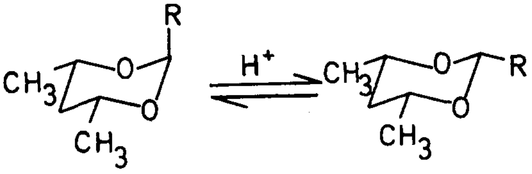
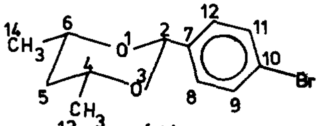


Fig. 1. Conformational equilibrium

Results of equilibria of 2-aryl substituted 1,3-dioxanes (R=aryl in Fig. 1), however, are not in accord with these principles[5]. The ΔG^{o} value for axial phenyl (3.1 kcal/mol) is substantially smaller than for axial methyl (4.0 kcal/mol), which is the reverse of the situation in cyclohexane (3.1 kcal/mol for phenyl versus 1.7 for methyl[6]). The NMR data are even more puzzling: while the more strained 1,3-dioxane (in terms of its ΔG^{o} value) with axial methyl appears to be in a relatively undisturbed chair conformation (according to vicinal coupling constants) the less strained 2-phenyl analogue exhibits substantial distortions. The latter result was confirmed by dipol moment measurements[5].

To try to understand this situation a detailed structural analysis of a pair of _cis_- and _trans_-2-aryl-4-_cis_-6-dimethyl-1,3-dioxanes was undertaken. The structure of the equatorially substituted isomer, of _r_-2-(_p_-bromophenyl)-_cis_-4,_cis_-6-dimethyl-1,3-dioxane (**1**) is reported here; while the structural study of an axially substituted 1,3-dioxane is in progress and will be published in due course.

$^{+}$ This holds true only in the case of non-polar substituents.



(1)

Single crystals of (1) were obtained by slow evaporation of petroleum ether solutions. Crystals were monoclinic, space group $P\ 2_1/n$, and had cell dimensions: a = 9.164 Å, b = 14.416 Å, c = 8.974 Å, β = 94.50°. X-ray diffraction data were collected on an automatic Siemens three-circle diffractometer controlled by a Siemens 305 on-line computer. The structure was solved by a sharpened Patterson function and a subsequent Fourier synthesis. Positions of hydrogen atoms resulted from an F_o-F_c Fourier map. Refinement with anisotropic temperature factors for all heavy atoms and isotropic temperature factors for hydrogen atoms with 2864 independant reflections yielded a final agreement factor R = 0.047.

As expected the 1,3-dioxane ring appears in the chair conformation with all substituents in equatorial positions. The high degree of substitution causes an overall flattening of the ring as demonstrated by a comparison of torsional angles with values reported for 2-(p-chlorophenyl)-1,3-dioxane[3] (Fig. 2, values in parentheses). The orientation of the phenyl group in respect to the plane of the heterocycle is a close-to-bisecting arrangement in contrast to 2-(p-chlorophenyl)-1,3-dioxane which displays a close-to-perpendicular orientation[+].

This indicates that the conformation of the phenyl group is determined predominantely by packing forces in the solid state, there being little intrinsic preference for either the "bisecting" or the "perpendicular" conformation.[8] The deviation from the bisecting conformation amounts to a 29° twist

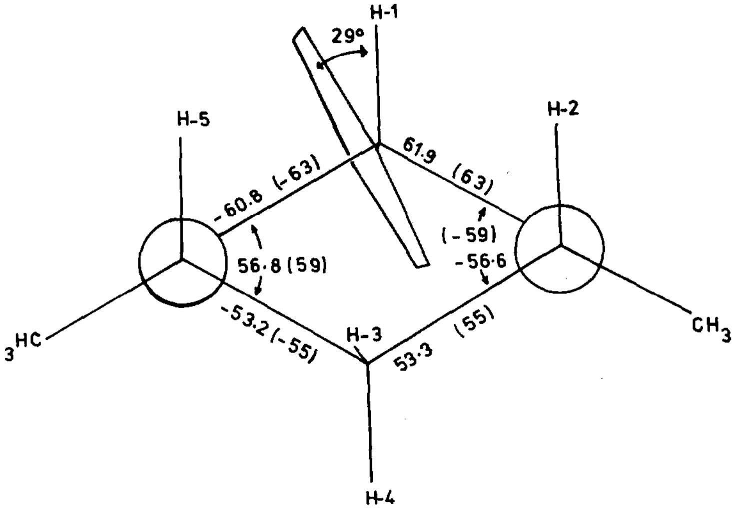


Fig. 2. Torsional angles of the 1,3-dioxane ring of (1) with the data of de Kok and Romers[3] in parentheses.

[+] Following a suggestion by Prof. Eliel, the phenyl rotamers are described by the terms "bisecting" and "perpendicular" (to the mirror plane of the ring) avoiding thereby a relation to the geminal substituent[7].

around the C-2 - C-7 bond (s. Fig. 2) and corresponds to an intramolecular separation of H-1....H-9 (o-phenyl hydrogen) - the closest contact - of 2.4 Å. This value seems to be about the limit of a none-repulsive approach of two hydrogen atoms.

The experimental bond lengths found in Fig. 3 compare reasonably well with those reported for 2-(p-chlorophenyl)-1,3-dioxane[3] (values in parentheses) In both structures the intracyclic bond lengths are significantly shorter (1.507 Å) than normal C_{sp^3} - C_{sp^3} bonds (1.535 Å).

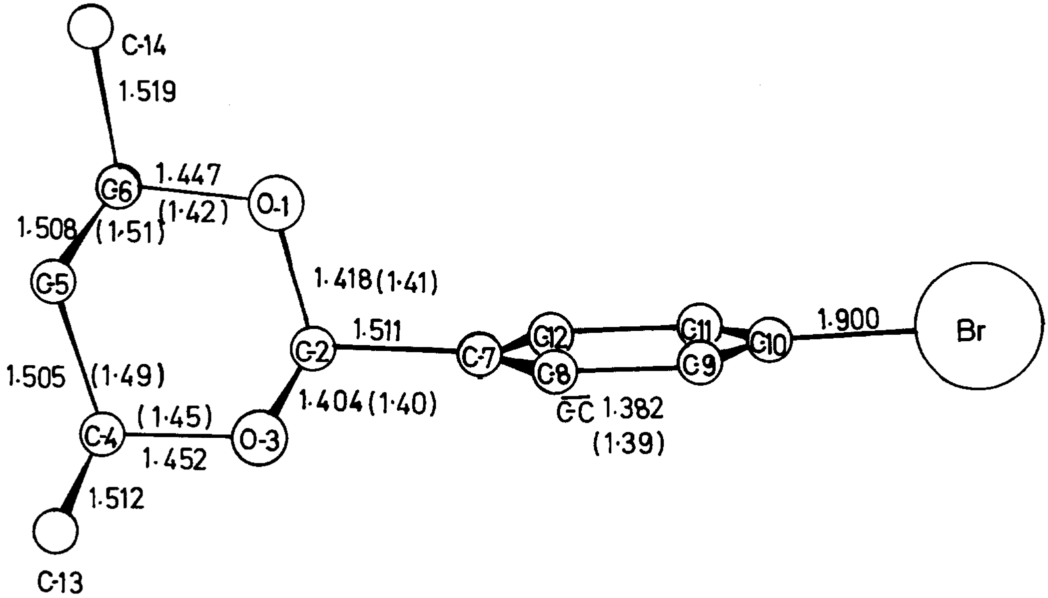


Fig. 3. Experimental bond lengths of (1) with de Kok and Romers data[3] in parentheses.

Bond angles found in Fig. 4 also agree well with the exception of the C-4,C-5,C-6 angle (111.3° versus 108°) which seems to have significance in connection with the presence of the two equatorial methyl groups in (1). The most significant geometrical alteration due to the diequatorial methyl substitution of the 1,3-dioxane ring was found for bond angles involving the methyl carbon atoms, i.e. angles: C-5,C-4,CH_3 / C-5,C-6,CH_3 and O-3,C-4,CH_3 / O-1,C-6-CH_3. The steric interactions of the equatorial methyl groups cause the C-C-Me angles to open up by about 4° (mean value 113.3°) mainly at the cost of the O-C-Me angles which are compressed by about 3° (mean value 106.6°). This finding is not quite compatible with the expected[9] so-called "Allinger-buttressing-effect"[10] by which equatorial alkyl groups should buttress the geminal axial hydrogen atoms by decreasing the C-C-H valency angle and therefore increasing its syn-axial interaction. In the present case, due to the lack of symmetry at C-4 and C-6 respectively (C-5 versus O-1/O-3) the minimization of steric interaction is achieved mainly by exocyclic bending (Me-C-O) rather than by an endocyclic process (Allinger buttressing). A buttressing effect may however be involved to some extent as both Me-C-H valency angles amount to 106° compared to all other bond angles involving hydrogen of 109-111°.

The present structural data rule out one possible explanation for the difference of conformational equilibria with 2-aryl and 2-alkyl substituted 1,3-dioxanes: Since the experimental ΔG^o value represents the energy difference between equatorial and axial substitution one might have argued that *r*-2-phenyl-*cis*-4,*cis*-6-dimethyl-1,3-dioxane is more strained than its 2-methyl analogue and that this difference accounts for the relatively small ΔG^o value of the axial phenyl. The present data however lend no support whatsoever to the hypothesis that additional strain is introduced by equatorial phenyl substitution.

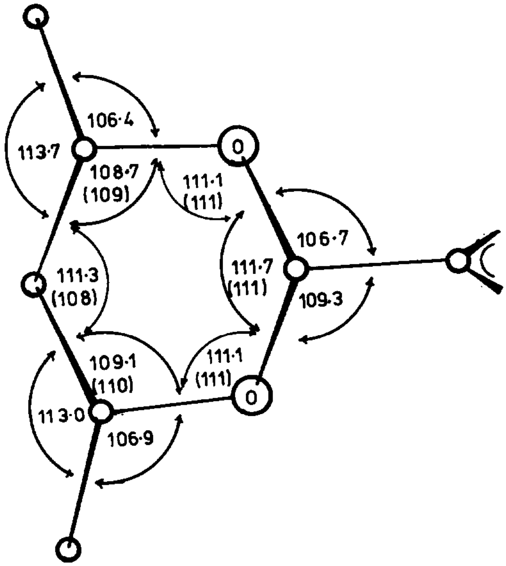


Fig. 4. Experimental bond angles of (**1**) with de Kok and Romers data[3] in parentheses.

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