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CONFORMATIONAL ANALYSIS. LXXVIII. THE CONFORMATION OF PHENYLCYCLOHEXANE, AND RELATED MOLECULES.[1, 2]

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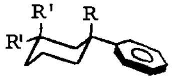
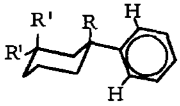
The recent appearance of a paper describing an experimental nmr study by B. L. Shapiro and coworkers[3] prompts us to report some of our calculations on molecules which contain a phenyl group attached to a cyclohexane ring. These calculations were carried out with the aid of a force field method previously described,[4] to which must be added only a few numerical constants characteristic of the phenyl group which were also worked out earlier.[5] Shapiro suggested that 3-phenyl-3, 5, 5-trimethylcyclohexanone had a conformation in which the phenyl group was in an axial position. Since the conformational energy of the phenyl (3.0 kcal/mole[6]) is larger than that of the methyl (1.7 kcal/mole[6]), this is quite unexpected. No explanation for this anomaly was offered.

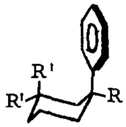
For phenylcyclohexane itself, one needs to consider four conformations with the ring in the chair form.



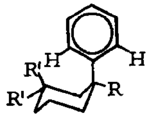
Equatorial
Perpendicular
e ∅ ⊥ R



Equatorial
Parallel
e ∅ ‖ R



Axial
Perpendicular
a ∅ ⊥ R



Axial
Parallel
a ∅ ‖ R

The phenyl group can be equatorial or axial, and it can be oriented so that the plane of the phenyl is either perpendicular to the bond connecting the cyclohexane substituent attached at the same carbon, or the latter may be in and parallel to the phenyl plane. The calculations show (Table 1) that the most favorable conformation of phenylcyclohexane has the parallel geometry (the C-R bond to the substituent geminal to the phenyl is parallel to the aromatic plane), with the phenyl equatorial.

TABLE 1. Calculated Conformational Energies

	$e\phi \parallel R$	$e\phi \perp R$	$a\phi \parallel R$	$a\phi \perp R$
R=R'=H	0.00	3.92	5.22	3.66
R=CH_3, R'=H	2.06	0.90	6.43	0.00
R=R'=CH_3	4.95	3.26	----[a]	0.00
3-Phenyl-3,5,5-trimethylcyclohexanone	4.10	2.99	----[a]	0.00

(a) These conformations do not correspond to energy minima.

The perpendicular equatorial phenyl exhibits serious van der Waals repulsions between the ortho hydrogens on the phenyl ring, and the equatorial hydrogens attached at C-2 and C-6 on the cyclohexane ring. On the other hand, if the phenyl is axial, the perpendicular conformation is the more comfortable, mainly because in the parallel conformation the ortho hydrogen on the phenyl which is over the cyclohexane ring interacts seriously with the syn-axial hydrogens of the cyclohexane. The calculated energy difference between the preferred conformations of the axial and equatorial phenyl, is 3.66 kcal/mole, and this may be compared with values of 2.0 - 3.1 kcal/mole reported in the literature.[6]

Geminal substitution of a methyl group and a phenyl at the same carbon of a cyclohexane ring leads to a different situation. In this case the equatorial phenyl, if in the parallel conformation, would have a serious repulsion between the nearest ortho hydrogen and the geminal methyl. With 1-methyl-1-phenylcyclohexane, the perpendicular conformation is therefore preferred for the equatorial phenyl. With the axial phenyl, again the perpendicular conformation is preferred. In this case the energy difference between the equatorial and axial phenyls amounts to 0.90 kcal/mole, with the axial conformation being preferred. This is not even qualitatively what one would have estimated, assuming additivity of the conformational energies of the phenyl and the methyl

(3.0 - 1.7 = 1.3 kcal/mole favoring equatorial phenyl). The main reason for the lack of additivity is, of course, that the phenyl is forced to assume a different conformation in the equatorial position, depending on whether or not the methyl is located on the same carbon.

Next, we may consider the 1-phenyl-1,3,3-trimethylcyclohexane case. If the phenyl is equatorial, there is a syn-diaxial methyl-methyl interaction, which is known to be very serious (3.7 kcal/mole).[7] The main cause of this interaction is the severe van der Waals repulsion between the nearest hydrogens on the two axial methyls. On the other hand, if the methyl goes equatorial and allows the phenyl to be axial, and the phenyl is in the perpendicular conformation (actually it rotates slightly to avoid the syn-axial methyl), there is no syn-axial hydrogen-hydrogen interaction, although there is a syn-axial hydrogen-carbon interaction between methyl and phenyl, respectively. Nonetheless, the latter is much to be preferred, and the conformation with the axial phenyl is better than the one with the equatorial phenyl by a calculated 3.3 kcal/mole. The corresponding ketone 3-phenyl-3,5,5-trimethylcyclohexanone similarly has the axial phenyl in the preferred conformation, by 3.0 kcal/mole, and these numbers are quite consistent with what Shapiro has found. Further calculations show that the twist form into which the molecule might retreat in order to avoid any syn-diaxial interaction is higher in energy than the axial phenyl chair, and, as Shapiro has indicated, the ketone plays no special role here; the same qualitative statements can be made about the hydrocarbon as well.

Previous evidence for the exact lack of additivity of the conformational energies of substituents when they are geminal has been obtained, although the differences have usually been rather small.[8,9] Here, because of the severe geometric anisotropy of the phenyl group, the differences are dramatic, and even qualitatively reversed from what additivity would predict. The parallelism between calculation and experiment seems quite satisfactory, and an understanding of Shapiro's results follows in a straightforward manner from the present calculations.

Other examples are already known in which the phenyl group appears to be quite small,[10] and in which the size of the phenyl is a function of the geminal substituent.[11] In the latter case, the earlier interpretation of the data is similar to that given here.

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