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THE EFFECTIVE SIZE OF THE LONE PAIR ON NITROGEN

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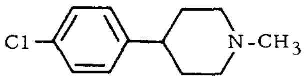
In a paper published in 1958,[1] Aroney and LeFèvre concluded from Kerr constant measurements that the effective size of the lone pair on an amino nitrogen was considerably larger than that of a hydrogen atom, and comparable with that of a methyl group.* Subsequently, evidence has been presented[2] which indicates that the methyl group and hydrogen atom are both effectively larger than the lone pair, but this evidence has been qualitative, and not entirely unequivocal. We wish to report quantitative measurements of equilibrium constants between conformations having axial and equatorial hydrogen atoms or methyl groups on nitrogen in systems of the piperidine and N-methyl-piperidine type, respectively.

Two general kinds of systems were investigated (I and II).



I

IIa, $X=Y=CH_3$
b, $X=CH_3$, $Y=H$
c, $X=Y=H$

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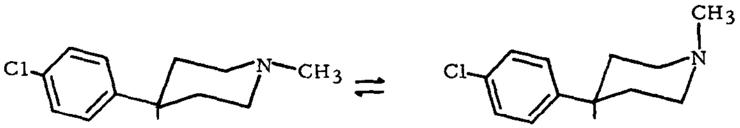
* Theoretical considerations show that the "size" of the lone pair on nitrogen is a function of the way in which it is measured. Here we use "size" to indicate a preference for the equatorial position.

The conformational energy of the phenyl group is sufficient to maintain it almost exclusively in the equatorial position.[3] Compound I, therefore, exists as a mixture of two conformations, as indicated.



From the dipole moments of N-methylpiperidine and *p*-chlorophenylcyclohexane, the resultant moments of these conformations can be calculated to be 2.33 and 0.88 D, respectively (Table I). From the observed moment of 2.25 D, the equilibrium can be calculated to favor the equatorial methyl group to the extent of 95 ± 4%. The conformational energy of the methyl group on nitrogen in N-methylpiperidine is therefore rather similar to that of a methyl on cyclohexane. Because the conformational equilibrium in I is so one-sided, a more accurate measure of the conformational energy of the N-methyl was sought.

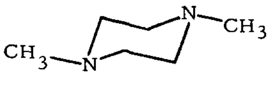
It is well established[4] that the energy of the boat form of cyclohexane can be rather accurately calculated from a consideration of the rotational barrier in ethane. Similar considerations utilizing in addition the observed barrier in methylamine show that the amount of boat form to be expected in piperazine will be negligible, the interpretation of Kerr constant measurements[5] notwithstanding. This conclusion is supported by X-ray diffraction studies on piperazine derivatives[6] and otherwise.[4] For present purposes, we can therefore assume that N,N'-dimethylpiperazine (IIa) exists as a mixture of conformations A, B and C. Conformations A and C have no

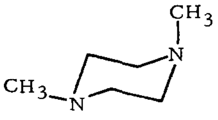
TABLE I

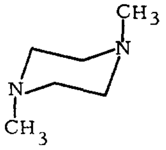
Dipole Moments, 25° C., Benzene Solution

Compound	Moment (D)
N-Methylpiperidine	0.95 ± 0.02
Piperidine	1.16 ± 0.01
N,N'-Dimethylpiperazine	0.50 ± 0.02
Piperazine	1.47 ± 0.02
N-Methylpiperazine	1.14 ± 0.01
p-Chlorophenylcyclohexane	1.83 ± 0.03
N-Methyl-(*p*-chlorophenyl)-piperidine	2.25 ± 0.01

dipole moment, while that of B can be calculated to be 1.55 D. The experimental value is 0.50 D at 25°, which leads to a value for the conformational enthalpy of a methyl group of 1.7 kcal./mole, in good agreement with the number found for the same quantity from compound I, and with that found for a methyl group on cyclohexane.


A


B


C

The same scheme was applied to compound IIc, but here there was a complication because the dipole moment cannot be assumed to point along the axis of the lone pair. The approximation was made that the difference in the dipole moment between N-methylpiperidine and piperidine itself could be attributed to the addition of an N-H bond moment to that of the lone pair; the C-N bond moment here, as in N-methylpiperidine, contributing nothing to the resultant. This approximation is justifiable both theoretically[7] and experimentally.* Calculations exactly analogous to those made for dimethylpiperazine lead here to an energy difference between the lone pair and the hydrogen atom on nitrogen of 0.47 kcal./mole, but it cannot be determined from these data alone which of the two groups is larger. The last point was settled by a study of N-methylpiperazine. Taking the conformational energy of the methyl group as 1.7 kcal./mole, compound IIb exists as a mixture of four conformations, in which the two having an equatorial methyl group predominate. The dipole moment for each conformation was calculated, and the observed moment requires a conformational energy for the hydrogen on nitrogen of either +0.43 kcal./mole (hydrogen larger) or -2.16 kcal./mole. Comparison with the piperazine result shows the former value is the correct one.**

We believe the conformational enthalpies reported herein are accurate and unequivocal. Reasons for the conflicting conclusions by Aroney and LeFèvre are discussed elsewhere.[9] In systems of the type discussed here, it would appear that the most practical point of view is to

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* The angle between the lone pair axis and the resultant moment in methylamine calculated by this approximation, is within 5° of that determined from the microwave spectrum (ref. 8).

** There are a great many sources of error which must be considered in assessing the accuracy of the conformational enthalpies quoted in this paper. These will be discussed in our full publication. The conformational enthalpy of the methyl group (1.7 kcal./mole) is thought to be accurate to about ±0.3 kcal./mole, while that of the corresponding hydrogen atom is taken as 0.4 ± 0.3 kcal./mole. (in benzene solution).

consider the lone pair as simply part of the nitrogen atom, and give it no explicit consideration. This viewpoint can be justified quantum mechanically.[10]

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