A Method for Determination of 1,3-Diaxial Interactions

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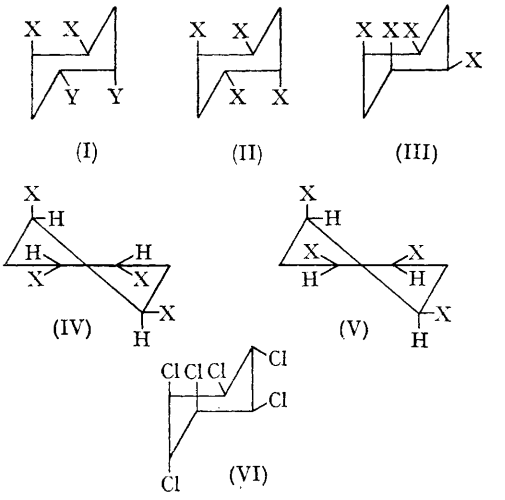
EVIDENCE has been presented[1] which indicates that the ring inversion of a heavily substituted cyclohexane proceeds *via* the half-chair transition state of lowest energy. In a compound of type (I) two transition states are possible, *viz.*, X's coplanar or Y's coplanar; but in compounds of type (II) and (III) only one transition state need be considered. If it is assumed that the enthalpies of the half-chairs (IV) and (V) derived, respectively, from (II) and (III) are the same, then differences in $\Delta H^{\ddagger}$ for ring inversion reflect ground-state enthalpy differences. Since (II) and (III) differ by the existence of a 1,3-diaxial interaction in the latter compound, the magnitude of this interaction ought to be accessible from the temperature dependence of the n.m.r. spectra of the two isomers.[2]



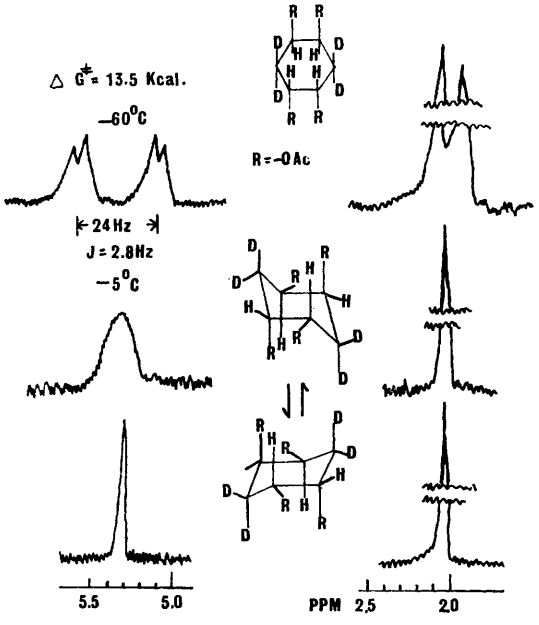


FIGURE 1. *The n.m.r. spectrum at various temperatures of* cis,anti,cis-1,2,4,5-*tetra-acetoxy*[3,3,6,6-$^2H_4$]-*cyclohexane.*

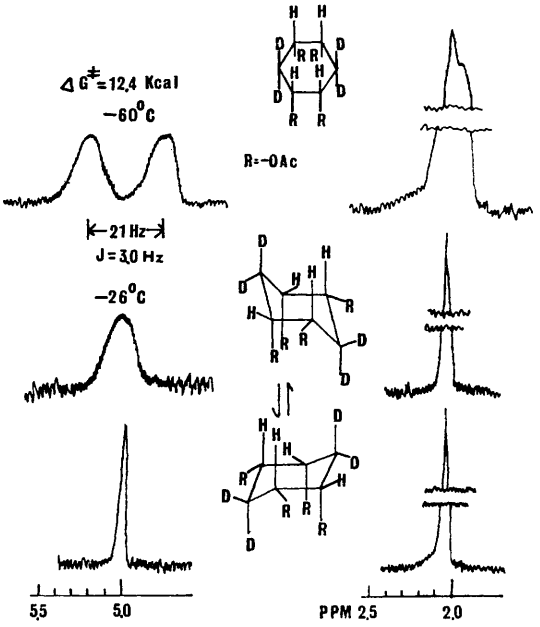


FIGURE 2. *The n.m.r. spectrum at various temperatures of* cis,syn,cis-1,2,4,5-*tetra-acetoxy*[3,3,6,6-$^2H_4$]*cyclohexane.*

Figures 1 and 2 show such data for the *cis,anti,cis-* and *cis,syn,cis*-1,2,4,5-tetra-acetoxy[3,3,6,6-$^2H_4$]cyclohexanes (II and III, X = OAc). The compounds were synthesized by acetylation of the two tetraols prepared from [3,3,6,6-$^2H_4$]cyclohexa-1,4-diene[3] with osmium tetroxide.[4] Analysis of the data is straightforward, coalescence of the low-field signals being observed at −6° for the

cis,anti,cis- and at −26° for the *cis,syn,cis*-isomers. Preliminary estimates of $\Delta G^{\ddagger}$ are 13·5 and 12·4 kcal./mole, the smaller value being obtained, as expected, from the *cis,syn,cis*-compound. We are extending our observations to temperatures above and below T_c in order to obtain $\Delta H^{\ddagger}$ values for these two compounds. Other X-containing systems are also being synthesized for study in this way.

From the low-temperature spectrum of γ-hexachlorocyclohexane (VI; a *cis,syn,cis*-isomer) $\Delta G^{\ddagger}$ was calculated to be at least 13·8 kcal./mole. The $\Delta G^{\ddagger}$ value for a *cis,anti,cis*-chlorinated cyclohexane would then be greater than 13·8 kcal./mole by 1–2 kcal./mole.

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[1] S. Wolfe and J. R. Campbell, preceding Communication.
[2] For references to other methods of obtaining 1,3-diaxial interactions see E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis", Interscience, New York, 1965, p. 52.
[3] S. Wolfe and J. R. Campbell, unpublished results.
[4] G. E. McCasland, S. Furuta, L. F. Johnson, and J. N. Shoolery, *J. Org. Chem.*, 1963, **28**, 894.