Steric Interference in Allylic and Pseudo-allylic Systems:[1] $A^{(1,2)}$ Strain between Methyl Group and Hydrogen

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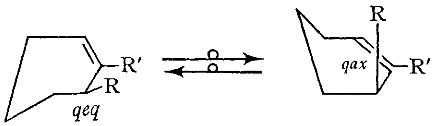
WE have recently described two stereochemical theorems dealing with steric interference associated with substituted allylic systems that constitute part of six-membered rings.[2] In one of the theorems it was pointed out that molecules containing endocyclic double bonds as shown in (I) possess nonbonded steric interaction between substituents R and R′. This interaction was classified as $A^{(1,2)}$ strain. When the substituents are moderate-to-large in size, relief from strain is easily attained by conformational inversion of (I) to (II) thus changing the dihedral angle between the substituents from ~35° to ~85°. Now we report the approximate magnitude of the $A^{(1,2)}$ strain in (I) when R = Me and R′ = H.

The pyrrolidine enamine of 3-methylcyclohexanone was found from its n.m.r. spectrum† to be a 3 : 7 mixture of the Δ^1- and Δ^6-isomers, (III) and (IV). Vinylic protons corresponding to these isomers appear, respectively, as a doublet at 244 c./sec. [due to C-2 proton split by proton at C-3 as in (III)] and a triplet at 253 c./sec. [(due to C-6 proton split by protons at C-5 as in (IV)]. This isomeric composition would indicate that $A^{(1,2)}$ strain between the C-3 methyl group and the C-2 proton destabilizes the Δ^1-isomer by 0·6 kcal./mole.[3]

(I)



(II)

Further proof regarding the magnitude of this interaction came from the isomeric composition of the pyrrolidine enamine of 2,5-dimethylcyclohexanone. Since the pyrrolidine enamine of 2-methylcyclohexanone consists almost exclusively of the trisubstituted ethylenic isomer with the C-2 methyl group in the quasi-axial orientation,[4] the value of 0·6 kcal./mole for $A^{(1,2)}$ Me–H interaction would imply that the pyrrolidine enamine of 2,5-dimethylcyclohexanone (prepared under equilibrating conditions) should be approximately a 3 : 2 mixture of isomers (V) and (VI). This composition

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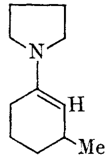
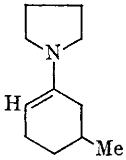
† Determined at 60 Mc./sec. with a Varian A-60, N.M.R. Spectrophotometer-downfield from Me_4Si (internal reference).

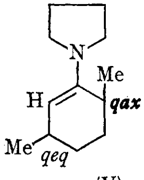
is based on the strain-energy difference between (VI) and (V) [(2 × 1,3-diaxial Me–H interaction)—(1 × 1,3-diaxial Me–H interaction + 1 × $A^{(1,2)}$ Me–H interaction) = 2 × 0·9 − (1 × 0·9 + 0·6) = 0·3 kcal./mole]. In the n.m.r. spectrum of this enamine‡ the C-6 vinylic proton appeared as two doublets at 244 (J = 2) and 253 c./sec. (J = 4 c./sec.) due to the coupling with the C-5 quasi-axial and quasi-equatorial protons, respectively. From the areas under these doublets the enamine was estimated to be a 62 : 38 (±2%) mixture of (V) and (VI). Its hydrolysis with dilute acetic acid[4] led to a 3 : 2 mixture of *cis*- and *trans*-isomers of 2,5-dimethylcyclohexanone,§ thus confirming the assignments made to the enamine components.



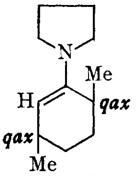
(III)



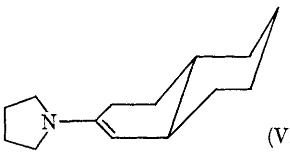
(IV)



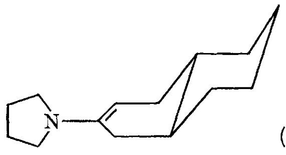
(V)



(VI)



(VII)



(VIII)

The significance of this interaction becomes quite apparent in the direction of enolization of *trans*-2-decalone. The pyrrolidine enamine of this ketone was estimated to be a 28 : 72 mixture of Δ^1- and Δ^2-isomers, (VII) and (VIII), from its n.m.r. spectrum showing that here again the $A^{(1,2)}$ strain between the C-8 methylene group and the C-1 proton destabilizes the Δ^1-isomer (VII) by *ca.* 0·6 kcal./mole and is thus primarily responsible for the preferred enolization towards C-3.[5] In a similar study House and Trost have reported that the enol acetate derived from *trans*-2-decalone on equilibration with toluene-*p*-sulphonic acid at 100° led to a 28 : 72 mixture of Δ^1- and Δ^2-isomers.[6]

In the light of these results, we conclude that in respect of the 3- and 4-methylcyclohexenes, the methyl group in the latter should have a stronger preference for equatorial orientation than in the former and not *vice versa* as has recently been suggested.[7]

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‡ The enamine was prepared by treating the ketone with pyrrolidine in the presence of Dowex-50 (acid form) as the catalyst in refluxing benzene for 4 days. The equilibration probably proceeds through the tetrasubstituted ethylenic isomer.

§ Composition determined by g.l.c. with a column packed with 30% McNairs on Chromosorb P.

[1] Previous paper in this series: S. K. Malhotra, D. F. Moakley, and F. Johnson, *Tetrahedron Letters*, 1967, 1089.

[2] F. Johnson and S. K. Malhotra, *J. Amer. Chem. Soc.*, 1965, **87**, 5492; S. K. Malhotra and F. Johnson, *ibid.*, 1965, **87**, 5493.

[3] Free energy difference at 80°, the temperature at which the enamine was prepared. In the absence of this strain, the ratio of (III) and (IV) should have been 1 : 1. The strain energy value of *ca.* 0·6 kcal./mole implies that the isomer (III) is approximately a 2 : 3 mixture of two conformers with quasi-axial and quasi-equatorial methyl groups respectively. Also *cf.* J. Champagne, H. Favre, D. Vocelle, and J. Zwibowski, *Canad. J. Chem.*, 1964, **42**, 212.

[4] S. K. Malhotra and F. Johnson, *Tetrahedron Letters*, 1965, 4027.

[5] For alternative views in this regard see (a) E. J. Corey and R. A. Sneen, *J. Amer. Chem. Soc.*, 1955, **77**, 2505; (b) R. B. Turner, W. R. Meador, and R. E. Winkler, *ibid.*, 1957, **79**, 4122.

[6] H. O. House and B. M. Trost, *J. Org. Chem.*, 1965, **30**, 1341.

[7] B. Rickborn and S. Lwo, *J. Org. Chem.*, 1965, **30**, 2212.