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THE VARIATION OF VICINAL PROTON-PROTON COUPLING CONSTANTS WITH ORIENTATION OF ELECTRONEGATIVE SUBSTITUENTS

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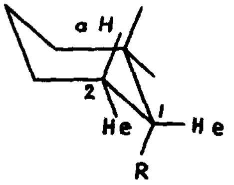
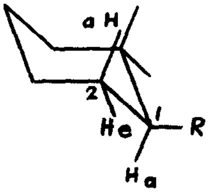
Values of J_{HH} (vicinal) in the fragment (I) depend on bond-angles, bond-lengths, and on the nature of the substituent R.[1]

$-CH-CH(R)-$

(I)



(II)

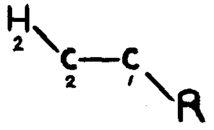


(III)

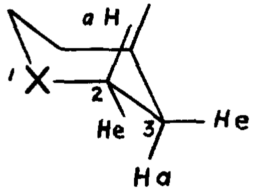
The dependence of J_{HH} (vicinal) on the electronegativity of R has been investigated by a number of workers.[2,3,4] Increase in electronegativity of R causes a decrease in J_{HH}. However, this 'electronegativity' effect itself shows a stereochemical dependence. Bhacca and Williams[5] have recently shown that, for a number of hydroxy- and acetoxy- steroids (partial structures II and III; R = OH or OAc), the *cis*-coupling constant $J_{e_1 a_2}$ (values 2.5-3.2 c./sec.) in the axially substituted (II) is invariably *less* than the *cis*-coupling constant $J_{a_1 e_2}$ (values 4.5-5.5 c./sec.) in the equatorially substituted (III).

The purpose of the present note is to point out that the maximum electronegativity effect on $J_{H_1 H_2}$ appears to coincide with trans-coplanarity of the system $R-C_1-C_2-H_2$ (cf. IV). Three important consequences of this generalisation are now given:

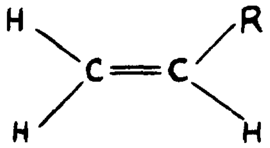
(i) When R is an electronegative substituent directly attached to a cyclohexane ring, the maximum electronegativity effect on J_{HH} (vicinal) occurs in (II), rather than (III). Thus $J_{e_1 a_2}$ in (II) will be smaller than $J_{a_1 e_2}$ in (III), provided that other factors (bond angles, bond lengths, etc.) remain similar.



(IV)



(V)

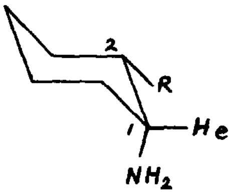


(VI)

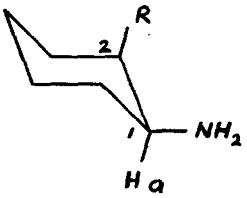
(ii) When an electronegative atom X (e.g. O, N) is part of a reduced six-membered heterocycle having a chair conformation (V), then the maximum electronegativity effect on J_{HH} (vicinal) will be experienced by the equatorial proton at position 3. Thus it is anticipated that $J_{a_2 e_3}$ will be smaller than $J_{e_2 a_3}$.

(iii) In a substituted ethylene (VI), any variation in electronegativity of R will influence J_{HH} (cis) more than J_{HH} (trans).

Experimental support for (i) is now widespread. The isomeric 4-t-butylcyclohexanols and derived acetates of Anet,[6] the hydroxy-, acetoxy- and fluoro- compounds mentioned by Bhacca and Williams,[5,7] and the isomeric 3,5-di-t-butylcyclohexanols of Feltkamp et al.,[8] all yield values of $J_{e_1 a_2}$ in (II) which are smaller than values of $J_{a_1 e_2}$ in (III). In the case of cyclohexylamines (II and III; R = NH_2), only $J_{a_1a_2}$ (~ 10.6 c./sec.) and $J_{a_1e_2}$ (~ 3.2 c./sec.) have been obtained by direct measurement,[9] as the α-proton signals for conformationally homogeneous compounds of type (II; R = NH_2) have not been resolved. Now the band width of the α-proton signal in *cis*-4-t-butylcyclohexylamine leads to a value of 2.75 c./sec. for the mean of $J_{e_1a_2}$ and $J_{e_1e_2}$.[9] The previous assumption[9] that $J_{e_1a_2} = J_{a_1e_2}$ leads to an 'impossible' result[10] for some cis-2-alkylcyclohexylamines (VII ⇌ VIII): thus the observed band width of the α-proton in cis-2-cyclohexylcyclohexylamine is *less* than that calculated for a molecule entirely in conformation (VII).

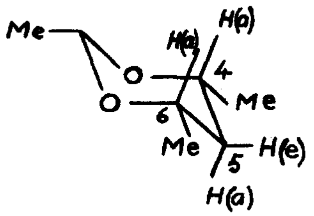


(VII)

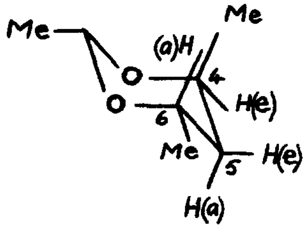


(VIII)

If, however, $J_{e_1a_2}$ is appreciably less than $J_{a_1e_2}$, the results can be rationalised. Rough calculations based on the observed band widths of *cis*-2-alkylcyclohexylamines, and on the ΔG-values of the alkyl groups involved, yield values of ~ 2.5 c./sec. and ~3.0 c./sec. for $J_{e_1a_2}$ and $J_{e_1e_2}$ respectively. There is some experimental support for (ii). Japanese workers[11] have found that $J_{e_5a_6}$ is 2.62 c./sec. in the 1,3-dioxan (IX) and 3.06 c./sec. in the isomer (X), whereas $J_{e_4a_5}$ in (X) was 7.02 c./sec. These differences were attributed entirely to ring distortion, but it seems likely that they are due in part to the different orientation of the e and a bonds at C_5 with respect to the ring oxygen atoms. The exceptionally low value of 0.58 c./sec. for $J_{e_4e_5}$ in (X) is also intelligible.

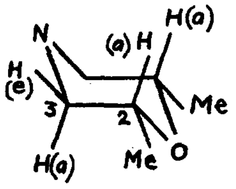


(IX)

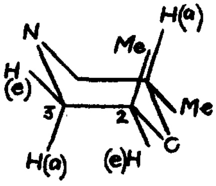


(X)

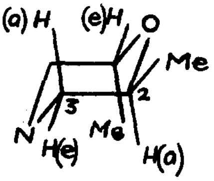
Barbier *et al.*[12] have found that the average of $J_{a_5 e_6}$ and $J_{e_5 a_6}$ for the conformationally mobile molecules of 1,3-dioxan and 4,4-dimethyl-1,3-dioxan was ~3.85 c./sec. Since values of 4.2 - 4.5 c./sec. had been obtained for $J_{a_5 e_6}$ from the spectra of a number of rigid alkyl-substituted 1,3-dioxans, the value of $J_{e_5 a_6}$ lies in the range 3.2 - 3.5, i.e. less than $J_{a_5 e_6}$, again in agreement with expectation. Finally, since oxygen is more electronegative than nitrogen, it is anticipated that, for morpholines, $J_{a_2 e_3}$ will be smaller than $J_{e_2 a_3}$. The p.m.r. spectra of *cis*-2,6-dimethylmorpholine (XI) and *trans*-2,6-dimethylmorpholine (XII ⇌ XIII) yield values of 2.1 and 4.3 c./sec. for $J_{a_2 e_3}$ and $J_{e_2 a_3}$



(XI)



(XII)



(XIII)

respectively.[13] The postulated generalisation predicts that $J_{e_2 e_3}$ in (XII) will be very small; in agreement, the value determined is 0.9 c./sec.

With regard to (iii), the available experimental evidence is in favour of the generalisation, but the effect is slight. Thus the straight line plot of J_{HH} (cis) against electronegativity is slightly steeper than that for J_{HH} (trans).[4]

There remains the possibility that a second, weaker maximum for the electronegativity effect coincides with cis-coplanar arrangement of the system $H-C_2-C_1-R$. Such an effect would be significant for (a) substituted ethylenes, and (b) rigid five-membered rings with adjacent carbon atoms in eclipsed conformations. With regard to (a), the effect would reduce the differential effect of electronegativity on J_{HH} (cis) and J_{HH} (trans) /cf. (iii), above/; in the case of (b), the available evidence[2] is in the anticipated direction, but clearly more results are needed to substantiate the suggestion.

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