8.84 v. for $I_{vert}(C_6H_5O)$. As would be expected, this is considerably higher than the ionization potential of the isoelectronic benzyl radical (7.76 v.).[14] The appearance potential of the $C_6H_5O^+$ fragment ion from anisole was found to be 11.92 ± 0.1 v., in good agreement with the value obtained by Harrison, et al.[15] Assuming this process to be a simple bond rupture in

$$\text{\includegraphics{benzene-O-CH_3}} + \text{e} \rightarrow \text{\includegraphics{benzene-O^+}} + CH_3 + 2e$$
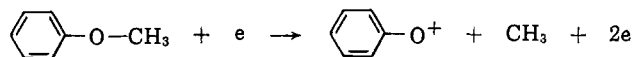
which the structural identity of the C_6H_5O fragment is preserved, the relationship $D(R\text{-}Y) \leq A(R^+) - I(R)$ gives $D(C_6H_5O\text{-}CH_3) \leq 71$ kcal./mole. Evidence for the retention of the phenoxy structure in $C_6H_5O^+$ ions from anisole at the dissociation threshold is provided by the results of Harrison, et al., who found meta-para orientation to be preserved in $RC_6H_4O^+$ ions produced in the dissociative ionization of $RC_6H_4OCH_3$ isomers. One might reasonably expect the O-CH_3 bond in anisole to be appreciably lower than this limit, however. The phenoxy radical is isoelectronic with benzyl radical, and should therefore exhibit considerable resonance stabilization. To a very rough approximation, then, $D(CH_3O\text{-}CH_3) - D(C_6H_5O\text{-}CH_3) \approx D(CH_3\text{-}CH_3) - D(C_6H_5CH_2\text{-}CH_3)$. Taking $\Delta H_f(CH_3) = 32.5$ kcal./mole[16] and $\Delta H_f(C_6H_5CH_2) \sim 43$ kcal./mole,[17] and the standard heats of formation of ethane and ethylbenzene,[18] $D(CH_3\text{-}CH_3) - D(C_6H_5CH_2\text{-}CH_3) \sim 17$ kcal./mole.

If $D(CH_3O\text{-}CH_3) = 77$ kcal./mole,[19] then $D(C_6H_5O\text{-}CH_3) \approx 60$ kcal./mole. On this basis, the appearance potential of $C_6H_5O^+$ from anisole would include 11 kcal./mole of excitational energy. The validity of such a comparison is rather doubtful, however. Other phenoxy derivatives (phenol, phenyl ethyl ether, diphenyl ether) have such small intensities for $C_6H_5O^+$ ion that estimates of $\Delta H_f(C_6H_5O^+)$ cannot be made from them. The value given above for $A(C_6H_5O^+)$, together with ΔH_f(anisole) = −18.5 kcal./mole, leads to $\Delta H_f(C_6H_5O^+) \leq 224$ kcal./mole and $\Delta H_f(C_6H_5O) \leq 20$ kcal./mole. Probable lower limits would appear to be about 10 kcal./mole less.

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(20) Issued as N. R. C. No. 8041.

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Dependency of Vicinal Coupling Constants on the Configuration of Electronegative Substituents

Sir:

Recently, a number of studies have illustrated the decrease in vicinal coupling constants in saturated (I) or unsaturated (II) systems on increasing the electronegativity of a substituent (R) attached to the same carbon atom as one of the vicinally coupled protons.[1] In vinyl compounds (II) it has been demonstrated that the cis-vicinal coupling constant $(J_{HH'})$ is more sensitive than the trans-vicinal coupling constant $(J_{HH''})$ to the electronegativity of R,[1c] in qualitative agreement with the theoretical requirements.[2]

However, the variation of vicinal coupling constants with the orientation of a given electronegative substituent in saturated systems (I) has been virtually neglected. We have at present evidence which suggests that such variations are quite large in the fundamentally important chair form of a cyclohexane ring.

In the downfield region of the 60 Mc. n.m.r. spectrum of 5β-pregnane-3α,12α-diol-20-one diacetate (III), obtained in benzene solution, the resonance of the axial 3β-proton appears as a seven line pattern centered at δ 4.77 p.p.m., while the equatorial 12β-proton signal is evident as a triplet centered at δ 5.12 p.p.m.[3] The seven line pattern is observed because the two diaxial splittings to the 2α- and 4α-protons (10 c.p.s.) are twice the two axial–equatorial splittings to the 2β- and 4β-protons (5 c.p.s.). Evidently, the equatorial 12β-proton approximately bisects the angle between the C-11 methylene protons and the equatorial-axial splitting is equal to the diequatorial splitting (2.5 c.p.s.).

III
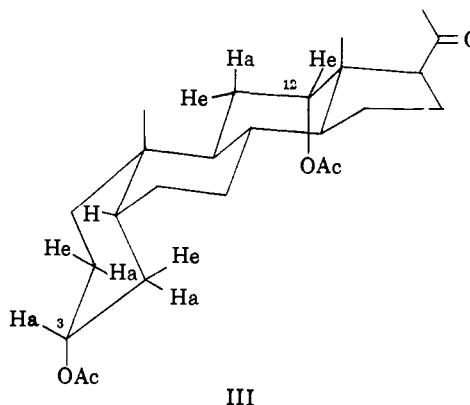
Since there is no obvious reason why both rings A and C in III should not exist in normal chair forms, we felt that the large difference between the axial-equatorial splittings associated with the 3β- and 12β-protons, involving very similar dihedral angles (60°), might arise through the differing configuration of the acetate groups (equatorial and axial, respectively). To test this hypothesis we determined the spectra of a number of other steroids containing acetate functions in rings A and C. Since the hydroxyl group is similar in electronegativity to the acetate function,[1a] its effect was anticipated to be similar and a number of hydroxy steroids were also examined. All spectra were

(1) See, for example: (a) K. L. Williamson, J. Am. Chem. Soc., **85**, 516 (1963); (b) C. N. Banwell and N. Sheppard, Discussions Faraday Soc., **34**, 30 (1962); (c) T. Schaefer, Can. J. Chem., **40**, 1 (1962).

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(3) The resonance position of a proton on the δ scale is related to the frequency (ν) such that δ (p.p.m.) = ν/60 in the 60 Mc. spectrum, when the frequency of the tetramethylsilane reference is arbitrarily taken as zero.

determined in both deuteriochloroform and benzene solutions, since analysis of the spin–spin coupling patterns was usually much easier in the latter solvent.[4]

Before discussing the results, it should be emphasized that the splittings in the X part of an ABX spectrum (or more complicated spectra approximating to AB_2X and A_2B_2X) only furnish J_{AX} and J_{BX} when the chemical shift between A and B is not very small.[5] We have obtained theoretical spectra varying δ_{AB} and employing $J_{AB} = -12$ c.p.s. as a reasonable coupling constant for geminal protons in the systems investigated. The theoretical spectra suggest that the observed splittings will be a good approximation to the coupling constants when $\delta_{AB} \geqslant 20$ c.p.s. This situation probably obtains in most of the compounds examined and, indeed, the first-order approximation has recently been vindicated[6] in systems similar to those under discussion. Moreover, we have determined several spectra at two fields strengths (60 Mc. and 100 Mc.), in effect varying δ_{AB}, and observed no change in the pattern due to the X proton. It is therefore felt that the splittings offer a good approximation to coupling constants and, as will be seen below, imply an important dependency of vicinal coupling constants upon the configuration of electronegative substituents.

In six 5α-steroids containing only equatorial 3β-OH or 3β-OAc substituents in ring A, in one having an equatorial 12β-OAc, and in three 5β-steroids containing only equatorial 3α-OH or 3α-OAc substituents in ring A, J_{ae} was always found to be 5.5 ± 1.0 c.p.s.[7] Similarly, in the spectrum of Δ^4-pregnen-11α-ol-3,20-dione (IV), the coupling constant between the axial 11β-hydrogen and equatorial 12β-proton (J_{ae}) was approximately 5 c.p.s.

IV

V, $R_1 = F$, $R_2 = -COCH_3$
VI, $R_1 = H$, $R_2 = =CHCH_2OH$
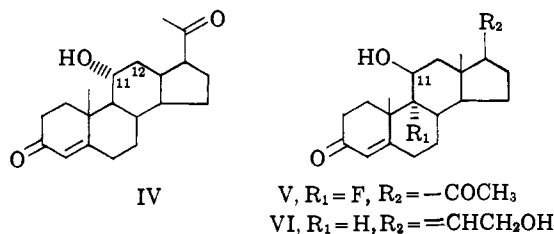
However, in the spectra of cholestan-1α-ol (axial hydroxyl) and two steroids containing only axial 12α-acetoxyl substituents in ring C, $J_{ea} = 2.5$–3.0 c.p.s. Despite the possibility in 11β-hydroxy steroids (axial hydroxyl) of the 1,3-diaxial interaction with the C-18 and C-19 methyl groups resulting in distortion of ring C from the normal chair form, our own studies, and those reported previously,[8] suggest that no significant ring distortion occurs. In two 11β-hydroxy steroids reported earlier,[8] and compounds V and VI studied by ourselves, $J_{ea} = 2.5$–3.2 c.p.s. Finally, in several 5β-steroids and 5β-sapogenins containing an

(4) The spectra were obtained on both Varian A-60 and/or HR-100 spectrometers, with a trace of TMS added to the solutions to act as internal reference. The advantages of employing benzene as solvent for the interpretation of some spin–spin coupling patterns will be the subject of a subsequent publication.

(5) J. D. Roberts, "An Introduction to the Analysis of Spin–Spin Splitting in High Resolution Nuclear Magnetic Resonance Spectra," W. A. Benjamin, Inc., New York, N. Y., 1961, p. 76.

(6) F. J. Schmitz and W. S. Johnson, Tetrahedron Letters, 647 (1962).

(7) The notation J_{ae} is used to denote the coupling of an axial proton on the carbon atom bearing the electronegative substituent to an equatorial proton, whereas J_{ea} is employed for the analogous coupling in which the proton on the electronegatively substituted carbon atom is equatorial.

(8) K. Tori, T. Tomita, H. Itazaki, M. Narisada, and W. Nagata, Chem. Pharm. Bull. (Tokyo), 11, 956 (1963).

axial 3β-hydroxyl or 3β-acetate function, the half-band width of the C-3 proton resonance is only compatible with a value of J_{ea} of 3 c.p.s. or less.

It must therefore be concluded that when a hydroxyl or acetate function is equatorial in a cyclohexane ring chair (VII), the observed J_{ae} value, due to coupling of protons through the bonds indicated by a heavy outline, will be about 5.5 ± 1.0 c.p.s., greater than the J_{ea} coupling (see heavy outline in VIII) of approximately 2.5–3.2 c.p.s. occurring when the substituent is axial.

VII, R = H or Ac   VIII, R = H or Ac
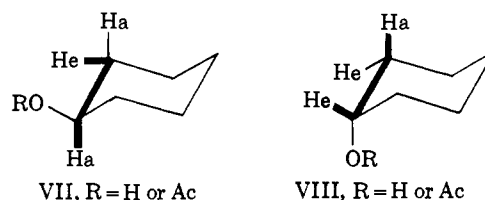
In all compounds of type VIII which were examined, any difference between J_{ee} and J_{ea} was less than 0.5 c.p.s.

Our findings are also compatible with the data available for cyclohexanone ring chair systems. For example, in 2α-acetoxycholestan-3-one (IX) and 3β-acetoxycholestan-2-one (X), containing equatorial acetate functions, the J_{ae} values are 6.6 c.p.s. and 6.2 c.p.s., respectively.[9] When the acetate group is axial, as in the C-3 epimer of X, $J_{ea} = 2.5$ c.p.s. These results have previously been interpreted in terms of conformational distortion in IX and X,[9] but we believe that the change in the configuration of the acetate substituent is primarily responsible for the observed difference in the coupling constants.

IX   X
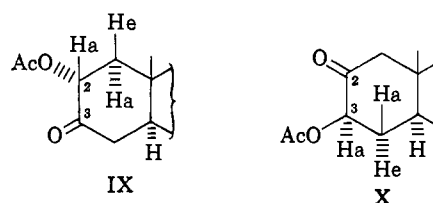
These results will obviously complement existing methods of determining the configuration of acetate and hydroxyl functions. They are also of basic relevance to the whole field of conformational analysis by n.m.r. spectroscopy since an examination of the literature suggests that similar trends are induced by other electronegative substituents, e.g., fluorine[10] and bromine.[11] A great deal of experimental data must be determined on systems of known conformation before the organic chemist can accurately predict dihedral angles in distorted six-membered ring systems.

(9) K. Williamson and W. S. Johnson. J. Am. Chem. Soc., 83, 4623 (1961).

(10) T. A. Wittstruck, S. K. Malhotra, H. J. Ringold, and A. D. Cross, ibid., 85, 3038 (1963).

(11) E. W. Garbisch, ibid., 86, 1780 (1964).

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