The mole percentages of I and II cannot be determined accurately by the present experimental method, for the magnitude of the "anomeric effect" in 2-chloro- and 2-bromotetrahydropyran is still so large that the percentage of the equatorial conformer is too small to be detected by nmr analysis. The fact that the X resonance remains as a broad partially resolved multiplet similar to that observed for *trans*-2-bromo-4-*t*-butylcyclohexanone[14] and does not broaden to any significant extent in solvents of increasing dielectric constant is strong evidence for the exclusive existance of the axial conformer. This conclusion is independent of any assumptions regarding the magnitude of J°.

The effect of solvent polarity on the conformational equilibrium in 2-bromocyclohexanone is well known.[10] The solvent stabilization of the equatorial conformer of 2-bromocyclohexanone in going from heptane to dioxane is approximately 0.5 kcal/mole. In order for such a factor to be undetected in the 2-bromotetrahydropyrans, in which an even greater dipole–dipole term is operative, the equilibrium constant for the equatorial–axial conversion would have to be of the order of 20 or greater. The free-energy change for such an equilibrium constant is of the order of 1.8 kcal/mole. Since the conformational preferences of bromine and chlorine in cyclohexane are approximately 0.5 kcal/mole,[16] the magnitude of the "anomeric effect" is approximately 2.3 kcal/mole. That the observed J° for 2-bromotetrahydropyran is similar to that of the *trans*-2-bromo-4-*t*-butylcyclohexanone is reasonable, but the conclusions are independent of this fact.

The J° of 2-chlorotetrahydropyran is identical with that of 2-bromotetrahydropyran. This was anticipated, as substituted α-D-glucopyranosyl chlorides and bromides exhibit the same coupling constants.[17] Apparently the "anomeric effect" is still so significant in 2-chlorotetrahydropyran to preclude any significant amount of the equatorial conformer even in dioxane. In dioxane, 2-chlorocyclohexanone exists to the extent of 63% of the equatorial conformer.[10] The solvent stabilization in 2-chlorotetrahydropyran would be expected to be similar to that of 2-chlorocyclohexanone. However, the conformational equilibrium constant of the former compound favors the axial isomer to such an extent as to make such solvent free-energy changes of diminished importance in detecting a change in equilibrium constant by the nmr method.

The chemical shifts of the X hydrogen vary as a function of solvent. The largest change is for that of dioxane. While the shifts are in the order of magnitude that would be expected if a major change in conformer population occurred, such a change is not possible without simultaneously noting an increase in J°. The shift as a function of solvent must be due to either bulk diamagnetic susceptibility of the solvent or a specific intermolecular interaction with solvent. An intermolecular interaction would not be unreasonable in the case of dioxane as the oxygen atom and the X hydrogen might be expected to associate. Even the less acidic iodomethane is affected by dioxane in a similar manner.[18]

The qualitative observation that the conformer with an axial halogen is the more stable in both 2-chloro- and 2-bromotetrahydropyran was anticipated. Unfortunately, even in the simplest system in which the "anomeric effect" can be examined, only a limit of the dipole–dipole interaction can be set. By analogy with the 2-halocyclohexanones, 2-fluorotetrahydropyran might be expected to exist to a larger extent as the equatorial conformer. However, the level of the "anomeric effect" is so high that probably even 2-fluorotetrahydropyran, which has not been synthesized to date, would exist predominately in the axial conformation and the nmr method could not provide a quantitative value for the conformational equilibrium constant.

Experimental Section

The 2-chloro- and 2-bromotetrahydropyran were prepared fresh by bubbling the appropriate gaseous hydrogen halide into dihydropyran in anhydrous ethyl ether at 0°. Distillation under reduced pressure yielded 2-chlorotetrahydropyran, bp 35–36° (12 mm), and 2-bromotetrahydropyran, bp 61–63° (16 mm), as colorless liquids. The samples were immediately dissolved in solvents, and their nmr spectra were determined, utilizing a Varian A-60 instrument operated at 38°. Chemical shift coupling constants are reproducible to ±0.02 ppm and ±0.2 cps, respectively.

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Conformational Analysis. VI.[1,2] 1-Vinylcyclohexanol

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Dilution studies have been carried out to determine the chemical shift of the hydroxyl proton at infinite dilution of 1-vinylcyclohexanol, 1-vinyl-*cis*-4-*t*-butylcyclohexanol, and 1-vinyl-*trans*-4-*t*-butylcyclohexanol. Utilizing 0.75 kcal/mole for the conformational preference of the hydroxyl group and assuming that the free-energy terms are additive, the conformational preference of the vinyl group is calculated to be 1.35 kcal/mole.

In two early papers in this series[4] a method was developed for determination of the conformational preference of substituents in the cyclohexane series. The method depends on the difference in magnetic environment of the axial and equatorial hydroxyl protons in cyclohexanols. The principal advantage

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(1) Paper V: G. E. Booth and R. J. Ouellette, *J. Org. Chem.*, **31**, 544 (1966).

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(3) National Science Foundation Undergraduate Summer Research Participant.

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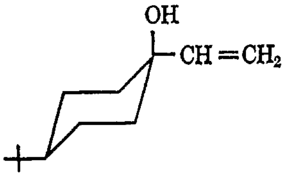
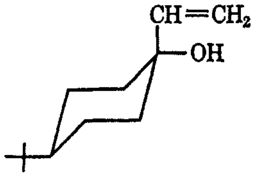
of the procedure is that the chemical shift of the hydroxyl proton is rather insensitive to substitution and lies in the high-field region near tetramethylsilane at infinite dilution. Previous procedures depend on the 1-proton of a monosubstituted cyclohexane being sufficiently different magnetically so as to place it in an uncomplicated region of the spectrum.[5] In addition, the proton is usually broad owing to spin coupling, and some uncertainty exists in the choice of the chemical shift. The problem of spin coupling is eliminated in the 1-substituted cyclohexanols, and the choice of the chemical shift is more direct. The chief disadvantage of the method is the necessity of employing dilution studies to eliminate the concentration dependence of the hydroxyl resonance.

In this paper the hydroxyl dilution method will be employed to determine the conformational preference of the vinyl group in 1-vinylcyclohexanol. The vinyl group is of considerable interest as it would serve to complete the series of sp^1 through sp^3 hybridized carbon atoms attached to a cyclohexane ring. The ethyl group has been examined by a variety of methods and its conformational preference is in the order of 2.0 kcal/mole.[6] The conformational preference of the ethynyl group has been determined and found to be 0.18 kcal/mole.[4]

Results and Discussion



II



III

The linear dependence of the chemical shift of the hydroxyl proton in carbon tetrachloride as solvent was obtained by extrapolation to infinite dilution. The concentration dependence for 1-vinylcyclohexanol (I), 1-vinyl-*cis*-4-*t*-butylcyclohexanol (II), and 1-vinyl-*trans*-4-*t*-butylcyclohexanol (III) are represented in Figure 1. All chemical shifts were determined relative to tetramethylsilane which was present in approximately 0.002 mole fraction. The extrapolated chemical shifts of the axial and equatorial hydroxyl protons in the two locked compounds are 40.5 and 60.0 cps, respectively, downfield relative to tetramethylsilane. The chemical shift of the hydroxyl proton in 1-vinylcyclohexanol extrapolates to 45.6 cps. The equilibrium constant for the transformation of Ia to Ib, as calculated from the equation $K = (\delta_{II} - \delta_I)/(\delta_I - \delta_{III})$, is 2.82.

The conformational preference of the hydroxyl group in carbon tetrachloride at infinite dilution is 0.75 kcal/mole.[4] The ΔG for the conversion of Ia to Ib at 38° is -0.64 kcal/mole. If it is assumed that the conformational preferences of two groups attached to the same carbon atom on a cyclohexane ring are additive, then the conformational preference of the vinyl group is 1.39 kcal/mole.

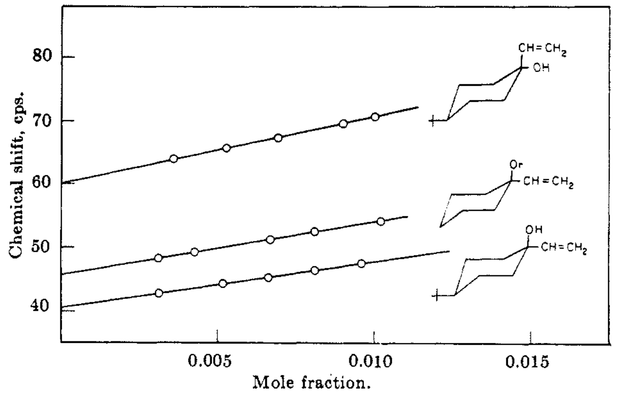
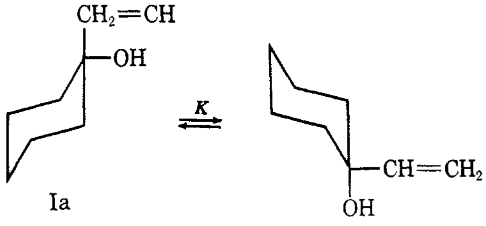


Figure 1.—Chemical shift dependence of the hydroxyl proton with concentration at 38°.



Ia Ib

The determination of the conformational preference of the vinyl group by examining 1-vinylcyclohexanol by the hydroxyl dilution method is advantageous over the alternative possibility of utilizing 1-vinylcyclohexane and examining the chemical shift of the 1-proton. The proton in 1-vinylcyclohexane would be strongly coupled with three hydrogens and weakly coupled with four protons to yield a resonance signal in which the determination of the chemical shift would be quite uncertain.

The conformational preference of the vinyl group is in the general range expected for trivalent substituents. In general, the magnitude of $-\Delta G°$ for a substituent is controlled by the number rather than the type of substituents on the atom next to the ring. Therefore, the vinyl group might be expected to be of similar effective steric size as the carbomethoxy group whose $-\Delta G°$ is 1.1 kcal/mole. However, other secondary factors control the conformational preference of substituents, and it is to assess these terms that the determination of $-\Delta G°$ for substituents in the cyclohexane system is important.

As a first approximation, the vinyl group might be considered to be of the same steric size as an aldehyde group, because, in general, substituents attached to the second atom from the ring are unimportant. Unfortunately, the aldehyde group has not been examined. The carbomethoxy group which has been examined would be expected to be of somewhat larger effective steric size relative to the aldehyde although the difference may not be large, as the groups may exist in certain preferred rotational conformations in which the structural differences are minimized. Therefore, *a priori* the vinyl group might actually be considered to be smaller than the carbomethoxy group.

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Since the experimental value for the conformational preference of the vinyl group indicates that it is larger than the carbomethoxy group, it is necessary to examine in closer detail the actual geometry anticipated for these two groups with respect to the cyclohexane ring. The vinyl group would be expected to prefer an orientation in the axial position such that the plane of the group is parallel to the plane defined by the 3,5-*syn*-axial carbon–hydrogen bonds. If the plane of the vinyl group were perpendicular to the plane of the 3,5-*syn*-axial carbon–hydrogen bonds, two orientations could be considered. If the methylene carbon were directed toward the *syn*-axial hydrogens plane, a strong repulsion would be expected, and this orientation is very unlikely. If the methine hydrogen were directed toward the plane, the interaction would be similar to that of a methyl group, whose conformational preference is approximately 1.8 kcal/mole.[6] By comparison, the carbomethoxy group has less option in its conformations and should tend to be oriented parallel to the 3,5-*syn*-axial plane. The orientations in which either the carbonyl or ester oxygens are directed toward the 3,5-*syn*-axial plane should be of prohibitively high energy. The value of 1.35 kcal/mole for the $-\Delta G°$ of the vinyl group might be the result of some interaction of the group in the arrangement parallel to the *syn*-axial plane, which is absent in the case of the carbomethoxy group. The terminal methylene hydrogens are directed toward the equatorial 2-hydrogen, and the resultant repulsion can be eliminated by a slight rotation of the entire vinyl group. The difference between the vinyl group and the carbomethoxy group could be due to this interaction. The methoxy group can easily orient itself so as to eliminate this interaction without rotating the plane of the carbomethoxyl system.

Alternative conformations that must be considered involve eclipsing of the unsaturated portion of the vinyl group with either a carbon–hydrogen or carbon–carbon bond. Both propene[7] and acetaldehyde[8] exist in eclipsed conformations. In the case of a vinyl group attached to cyclohexane, the conformation corresponding to the eclipsed form of propene contains the vinyl group perpendicular to the 3,5-*syn*-axial plane with the methine hydrogen directed toward the plane. This conformation was discussed above and would be expected to be of higher energy than the experimentally observed value. A conformation in which the vinyl group eclipses the 1,2 carbon–carbon ring bond might also be considered. This conformation corresponds to the methyl–methylene-eclipsed conformation of 1-butene, which is as populated as that of the hydrogen-eclipsed conformation.[9] However, 1-butene is not a completely satisfactory model. In the 1-vinylcyclohexane system, the 3-*syn*-axial proton should cause strong steric repulsion which is absent in 1-butene. Neopentylethylene, which exists in a hydrogen-eclipsed rather than the *t*-butyl-eclipsed conformation, is a more suitable model. The *t*-butyl-eclipsed conformation of neopentylethylene always contains two methyl hydrogens which are situated in a geometrical relationship to the methylene identical with that of the 3-*syn*-axial hydrogen in the 1-vinylcyclohexanol conformation under discussion. Therefore, the most favorable conformation for the vinyl group appears to be the coplanar vinyl, 3,5-*syn*-axial arrangement or perhaps a slightly twisted form with the methylene group directed away from the ring.

The discussion above is not meant to imply severely restricted rotation of the substituent but rather is only a dissection of the factors which may be operative in certain readily recognized conformations. Since the vinyl group is unsymmetrical and cannot be treated as a pseudo-atom, it is possible that an entropy term may be operative in the determination of the conformational preference of the group. To date only a few entropy terms have been determined and these are small[10] except for the unusually large entropy of isomerization of *cis*- and *trans*-β-decalones.[11] However, groups containing trigonally substituted carbon attached to the ring would be expected to exhibit the largest entropy terms, but this possibility has not been examined extensively.

The value of $-\Delta G°$ for the vinyl group calculated in this work must be viewed with some reserve. The assumption of additivities of free-energy terms may not be correct. In two previous applications of this method the conformational preference of the hydroxyl group with respect to hydrogen and the conformational preference of the ethynyl group with respect to hydroxyl were determined. In neither case was there any serious additional energy term that would be expected to contribute to the equilibrium. However, with acetyl and hydroxyl, small deformations of the ring, hindrance to rotation of the groups, and perhaps even solvation effects may contribute to make the resultant value only approximately indicative of the conformational preference of the vinyl group.

Experimental Section

The nmr method has been previously described. Deuterium oxide was added to each sample after the determination of its spectrum to confirm the assigned hydroxyl resonance.

1-Vinyl-4-*t*-butylcyclohexanols.—Vinyl Grignard was added to 4-*t*-butylcyclohexanone in ether as solvent. Conventional workup yielded an oil which consisted of two components in approximately a 3:2 ratio. The smaller component had the shorter retention time on a 6 ft × 0.25 in. column which contained 45% QF-1 on Chromosorb W. The smaller component was assigned as the *cis* isomer, as in both the 4-*t*-butylcyclohexanols and the 1-ethynyl-4-*t*-butylcyclohexanols the *cis* isomer has the shorter retention time. Assignment was consistent with the observed extrapolated chemical shift of the hydroxyl protons in the two compounds which were collected by vpc. Finally, reduction of 1-ethynyl-*trans*-4-*t*-butylcyclohexanol[12] by the method of Tedeschi and Clark[13] yielded a compound whose retention time was identical with that of the larger component which confirmed its *trans* assignment.

1-Vinyl-*cis*-4-*t*-butylcyclohexanol had mp 42–43°.

Anal. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16. Found: C, 79.18; H, 12.29.

1-Vinyl-*trans*-4-*t*-butylcyclohexanol had mp 56–57°.

Anal. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16. Found: C, 78.89; H, 12.01.

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