

CONFORMATIONAL EFFECTS IN COMPOUNDS WITH SIX-MEMBERED RINGS—VIII

THE PREFERRED ORIENTATIONS OF ALKYL GROUPS IN ALLENES AND IN 2-ALKYL-1,3-DIOXANES AND -DIOXOLANES

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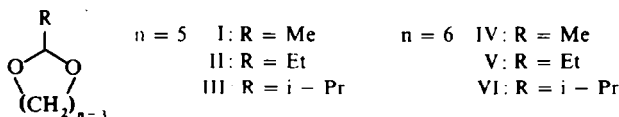
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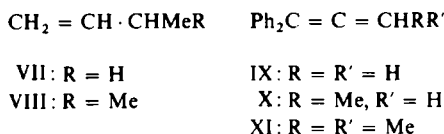
Abstract—The preferred orientations of ethyl and isopropyl groups in 1-alkyl-3,3-diphenylallenes and in 2-alkyl-1,3-dioxanes and -dioxolanes have been determined from the temperature dependence of the spin-spin coupling constants for appropriate vicinal protons. In the allenes a methyl group rather than a hydrogen atom eclipses a double bond but in the cyclic acetals skew interactions between methyl groups and oxygen atoms are minimised in the preferred conformations. It is concluded that the conformational preferences in simple ketones and aldehydes depend primarily on the double bonds rather than on the electronegativity of the oxygen atom of the carbonyl group.

CONFORMATIONAL equilibria in simple aldehydes and ketones show a preponderance of those conformations in which an alkyl group rather than a hydrogen atom eclipses the double bond.¹ Hitherto this conformational preference in carbonyl compounds has often been supposed to be due to one or more factors such as dipole-dipole interactions or London dispersion forces with the electronegative oxygen atom as the significant structural factor, but for reasons we will fully explain elsewhere¹ we suspected that the essential structural feature determining the conformational preferences in simple aldehydes and ketones was the double bond and not the electronegative oxygen atom. A comparison between conformational equilibria in carbonyl compounds and in compounds with singly bonded oxygen atoms would be a crucial test of the role we ascribe to the double bond in the former. In order to study the skew



interactions between alkyl, more particularly Me, groups and oxygen atoms in the absence of double bonds we have determined the conformational equilibria in the cyclic acetals II, III, V and VI as well as in 5-alkyl-1,3-dioxanes.² In these compounds with singly bonded oxygen atoms the distances (calculated from standard bond lengths and bond angles)² between Me groups and oxygen atoms in gauche relationships (2.79 Å between the oxygen atoms and the nearest hydrogen atoms of the Me groups in V and VI) are very similar to the analogous distances (2.81 Å) in the preferred

conformations of simple aldehydes and ketones. If London dispersion forces between Me groups and oxygen atoms are important in the latter they should also be important when oxygen atoms are singly bonded since the Van der Waals radii of singly and doubly bonded oxygen atoms are very similar.³ If dipole-dipole interactions are important in the carbonyl compounds they should be significant in the acetals (see later).



In contrast to aldehydes and ketones, 1-butene (VII) and 3-methyl-1-butene (VIII) have conformations of nearly equal stability.⁴ The absence of any marked conformational preference in these olefines has been accepted as indicating that there are no structural features present that might lead to differences in the stabilities of the conformations,⁴ but we considered it more likely that this resulted from the mutual cancellation of two effects, namely a preference for a Me group rather than a hydrogen atom to eclipse the double bond being opposed by steric hindrance between the terminal Me and methylene groups. The shortest distance between the hydrogen atoms at opposite ends of the molecule is only 2.25 Å,* which is similar to the shortest distance between hydrogen atoms in (ax)-methyl-cyclohexane.²

The first effect would be qualitatively, but not necessarily quantitatively, similar to that which we suppose to operate in aldehydes and ketones. The second effect would be substantially reduced, if not entirely eliminated, in allenes and we selected the allenes IX-XI as most suitable for study.

The allenes were prepared from the corresponding olefines by Skattelbøls general method,⁶ and were oils which could not be distilled or crystallized. They decomposed within a few days at 0° and satisfactory elemental analyses could not be obtained but their NMR and mass spectra were consistent with the proposed structures. The cyclic acetals were prepared from the appropriate combinations of diol and aldehyde in the presence of an acid and a dehydrating agent.

RESULTS AND DISCUSSION

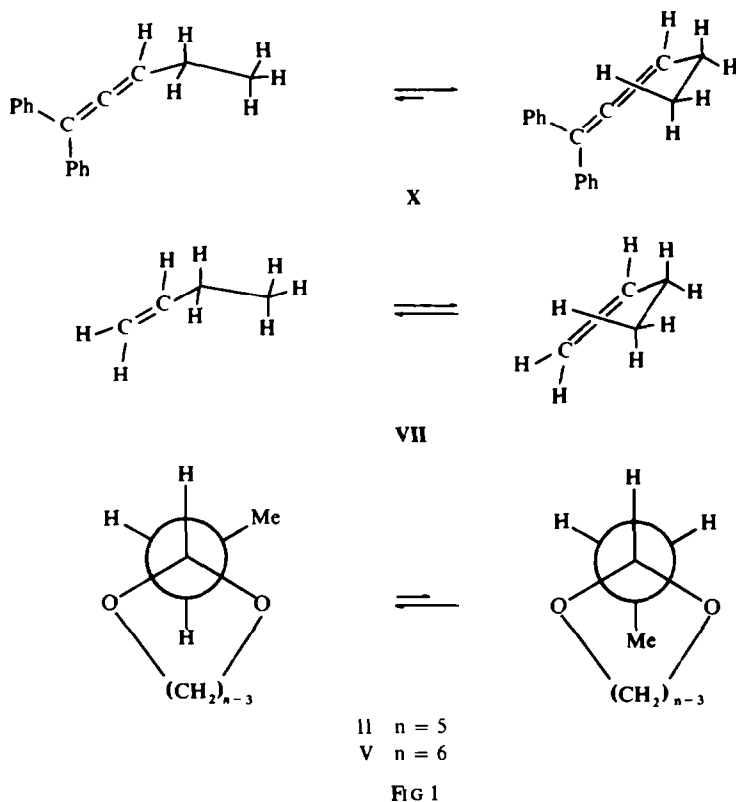
We assume that the alkyl groups (Et or iso-Pr) in each of the allenes and the acetals can adopt three orientations, which, by analogy with other olefinic and saturated compounds,⁶ will be taken to be those shown in Fig. 1. The observed time-average coupling constants, J , for the 3- and 4-hydrogen atoms in the 1,1-diphenylallenes (IX-XI) and for the 2- and 1'-hydrogen atoms in the cyclic acetals, may be expressed as a function of the coupling constants J_g and J_t (for gauche and *trans* vicinal hydrogen atoms) and of the enthalpy, ΔH , and entropy, ΔS , differences for the conformational equilibrium. The relationships are

$$J = J_g + (J_t - J_g)/[2 + \exp(\Delta H/RT - \Delta S/R)] \quad (\text{ethyl group}) \quad (1)$$

$$J = J_t - 2(J_t - J_g)/[2 + \exp(\Delta S/R - \Delta H/RT)] \quad (\text{isopropyl group}) \quad (2)$$

* This is based on accepted bond lengths and bond angles;³ no attempt to minimize strain has been made.

In order to obtain reasonably secure values of ΔH , let alone ΔS , from the observed variation of J with temperature it is necessary to eliminate potential systematic errors so far as possible. The most obvious is the possible variation of J_g and J_t with temperature. Proton-proton coupling constants are generally insensitive to changes of temperature and the coupling constants, equal to $(2J_g + J_t)/3$, for Me groups provide a check on this assumption.*



A less obvious but easily tested source of error is the temperature dependence of the dielectric constant of the solutions. If the conformations differed in polarity ΔH would vary with the dielectric constant and hence with the temperature. No significant effect on the coupling constants resulting from a difference in polarity was observed for 2-ethyl-1,3-dioxane when the solvent was changed from the non-polar heptane ($J = 4.90 + 0.02$ c/s), to the very polar acetone ($J = 4.91 \pm 0.02$ c/s) at 35° . In CHCl_3 , the best solvent experimentally, the coupling constant was slightly higher ($J = 4.96 \pm 0.02$ c/s), an effect which might be due to a very small difference in hydrogen bonding between the different conformations but which we did not consider to be important. Since the possible effect of the temperature dependence of the dielectric constant of the solutions appeared to be negligible for the polar acetals no error from

* If J_g and J_t vary with temperature in such a way as to leave the Me coupling constants unchanged then the derived values ΔH for Et and isopropyl groups will be somewhat changed in magnitude but *not* in sign and our main conclusions will be unchanged.

this source was to be expected for the almost non-polar allenes. The solvent dependence observed for the conformational equilibria in aldehydes⁸ has been explained as the effect of changing dielectric constant on dipole-dipole interactions. Since the importance of the difference between the group dipole moments of hydrogen and Me attached to a *saturated* carbon atom is uncertain,* specific solvent-solute interactions rather than the change in dielectric constant should be considered for carbonyl compounds since the acetals show so little sensitivity to solvent effects.

As an approximation we have assumed that the observed splittings for the low field protons equal the coupling constants. This could lead to a significant error if the chemical shifts, particularly the difference in the chemical shifts of the protons on the α and β carbon atoms of the alkyl groups, were temperature dependent but such changes are very small.

The observed coupling constants for the cyclic acetals do not show much dependence on the structure of the alkyl group *at room temperature* and using the arguments Bothner-By and his collaborators⁴ applied to simple olefines it might be supposed that the three orientations of the Et and of the iso-Pr groups are equally probable at all temperatures. In contrast the coupling constants for the allenes at room temperature are consistent with a preference for conformations with a Me group rather than a hydrogen atom eclipsing the double bonds. Both interpretations must be considered naive for several reasons. Vicinal coupling constants vary with the electronegativity of the other substituents and replacement of a hydrogen atom by a Me group leads to a reduction in vicinal coupling constants in the series ethane, propane, isobutane.¹¹ Furthermore, measurements at a single temperature can at best give only a free energy difference and there is no good reason to believe that entropy differences may be neglected, although this is often done. Since enthalpy differences in conformational equilibria are generally more easily related to structural factors than are entropy differences we considered it necessary to consider non-zero values of ΔS .

By means of a suitable computer programme the parameters in equations (1) and (2) were varied systematically over wide ranges and sets of values were selected as consistent with the experimental data if the sum of the squares of the differences between the observed and calculated coupling constants was less than the sum of the squares of the experimental errors for each observation. It was not unexpected that when all four parameters were varied completely independently wide ranges of J_g , J_t and ΔS were consistent with the observed coupling constants but all acceptable values of ΔH were positive for the allenes and negative for the acetals.† Qualitatively, therefore, there seems to be no doubt that these allenes resemble aldehydes in that the low enthalpy conformations have a Me group rather than a hydrogen atom eclipsing the double bond, although the magnitude of the effect is smaller. In contrast to the aldehydes the preferred orientations of the alkyl groups in the cyclic acetals are such as to minimize close approach of Me groups and oxygen atoms, so that there is no reason to explain the conformation equilibria in aldehydes by reference to attraction

* Dipole-dipole interactions could be important in *e.g.*, propionaldehyde, if there was a substantial difference in polarity between carbon-hydrogen bonds and carbon Me bonds when the carbon atom is *saturated*, but the dipole moments of propane (0.083 D)⁹ and isobutane (0.132 D)¹⁰ suggest that the difference is too small to be important.

† The observed coupling constants for 2-ethyl-1,3-dioxolane did not appear to be sufficiently precise for computer analysis of the small temperature variation to be worth attempting although the change is qualitatively the same as for the other cyclic acetals.

between Me groups and the electronegative oxygen atoms. The difference between the Van der Waals radii of singly and doubly bonded oxygen atoms is negligible.³

A reasonable way to reduce the number of independent parameters in the equations (1) and (2) to three is to relate $(J_t + 2J_g)/3$ for the Et and iso-Pr groups to the observed coupling constants for Me substituents. The effects of electronegativity changes were allowed for by reducing the observed J for the Me compounds by the factor 7.26/8.0 (= ratio of coupling constants in propane and ethane)¹¹ for an Et group, and by 6.8/8.0 (= ratio of coupling constants in isobutane and ethane)¹¹ for an isopropyl group to give values of $(J_t + 2J_g)/3$. With this restriction much narrower ranges of J_g and J_t were obtained with a modest narrowing of the range for ΔS and very little effect on ΔH (Table 3).

The results in Table 3 allow several comparisons which increase the degree of certainty of our conclusions. Firstly, the values of J_g and J_t in the allenes compare reasonably well with values found for analogous olefines,^{4, 12} and similarly the values found for the acetals may be compared with those for derivatives of 2-hydroxypyran.¹³ Since our results have been obtained by a rather long extrapolation and are therefore very sensitive to random and systematic errors this agreement with coupling constants determined in compounds with fixed conformation suggests strongly that our parameters, particularly the vital and relatively insensitive enthalpy differences, are not distorted by faults in our assumptions. If we reverse this comparison with published data by using Bothner-By, Naar-Colin and Gunther's values for J_g and J_t in olefines⁴ as assumed values for our allenes then for the allene (X) we obtain $\Delta H = +0.5$ kcal./mole and $\Delta S = +1.0$ e.u., almost in the middle of the ranges given in Table 3. The similarity in results for Et and iso-Pr groups in each series is noteworthy, as is the possibly significant difference between the five- and six-membered ring acetals.

The entropy differences* are individually barely significant but the close correspondence for related pairs of compounds increases the probability that they are real

TABLE 1. ANALYTICAL DATA FOR 3-ALKYL-2,2-DIBROMO-1,1-DIPHENYL CYCLOPROPANES

Alkyl group	m.p.	Formula	C		H	
			Found	Req.	Found	Req.
Methyl	88–89°	C ₁₆ H ₁₄ Br ₂	52.69	52.48	3.85	3.85
Ethyl	94–97°	C ₁₇ H ₁₆ Br ₂	53.81	53.71	4.19	4.22
Isopropyl	137–138°	C ₁₈ H ₁₈ Br ₂	54.99	54.83	4.60	4.60

and are too large to be neglected in conformational equilibria in acyclic compounds. Entropy differences between isomeric cyclic compounds or conformations such as derivatives of cyclohexane should, therefore, only be interpreted as evidence for changes in ring conformation if they are much larger than 1 e.u.

The qualitative similarity between the conformational equilibria in aldehydes and allenes, and the contrast with the cyclic acetals, is consistent with a stereoelectronic effect, probably involving overlap between hydrogen 1s and carbon 2p orbitals, being the basic common factor influencing conformational equilibria in unsaturated

* The entropies of mixing for mirror image pairs of conformations are automatically allowed for in equations (1) and (2).

systems,¹ although steric hindrance or dipole-dipole interactions may obscure this in many cases. The significance of the quantitative differences between aldehydes and allenes remains to be determined.

TABLE 2. TEMPERATURE DEPENDENCE OF COUPLING CONSTANTS (J , c/s) IN 2-ALKYL-1,3-DIOXOLANES AND -1,3-DIOXANES ($J_{2,1'}$) AND IN 3-ALKYL-1,1-DIPHENYLALLENES ($J_{3,4}$) IN CHLOROFORM

System	Alkyl group					
	Methyl		Ethyl		Isopropyl	
	Temp. °C	J	Temp. °C	J	Temp. °C	J
1,3-Dioxolane	+ 31	4.84	+ 79	4.53	+ 82	4.52
	- 44	4.84	51	4.52	48.5	4.59
			31	4.55	31.5	4.62
			- 11.5	4.59	30	4.61
			29.5	4.60	- 8	4.68
			47.5	4.65	26	4.79
					50	4.89
					51.5	4.86
1,3-Dioxane	+ 31	5.02	+ 80	4.88	+ 80	4.76
	- 38	5.06	52.5	4.90	51	4.81
			34	4.96	33	4.85
			30	4.97	30	4.82
			- 3	5.03	- 1	4.92
			38	5.14	9.5	5.05
			49	5.20	22.5	5.10
					38	5.23
				48	5.29	
1,1-Diphenylallene	+ 31	7.09	+ 81	6.21	+ 80	5.84
	- 42	7.03	56	6.14	57	5.76
			31	6.10	31	5.73
			- 17	6.02	- 1	5.66
			35	5.95	17	5.64
			50	5.85	35	5.57
			54	5.84	48	5.52

TABLE 3. COUPLING CONSTANTS (J_2 AND J_1) AND THERMODYNAMIC FUNCTIONS FOR THE CONFORMATIONAL EQUILIBRIA IN ALKYL DERIVATIVES OF 1,1-DIPHENYLALLENES, 1,3-DIOXANE AND 1,3-DIOXOLANE

Compound	J_2 (c/s)	J_1 (c/s)	ΔH (kcal/mole)	ΔS (e.u.)
3-Ethyl-1,1-diphenylallene (X)	4.2 ± 1.2	10.3 ± 2.2	$+0.5_6 \pm 0.2$	$+1.2 \pm 1.0$
3-Isopropyl-1,1-diphenylallene (XI)	4.8 ± 1.6	8.4 ± 3.2	$+0.6_5 \pm 0.4$	$+1.3 \pm 1.3$
2-Ethyl-1,3-dioxane (V)	2.1 ± 1.0	9.4 ± 2.5	$-0.7_4 \pm 0.4$	-1.2 ± 1.0
2-Isopropyl-1,3-dioxane (VI)	3.1 ± 0.7	6.8 ± 1.6	$-0.8_6 \pm 0.4$	-1.5 ± 0.7
2-Isopropyl-1,3-dioxolane (III)	2.7 ± 1.0	7.0 ± 2.0	$-0.4_0 \pm 0.2$	-0.3 ± 0.7

EXPERIMENTAL

NMR spectra, calibrated with sidebands generated by a Muirhead-Wigan D-8090-A oscillator, were measured with a Varian A60 spectrometer with a V 6057 variable temperature system. Probe temperatures ($\pm 1^\circ$) were measured with MeOH and ethylene glycol samples supplied by Varian Associates and were checked before and after each group of spectra for a given compound. Coupling constants were measured for 20% (w/v) solutions (dried with silica gel) in CHCl_3 , except for a few measurements in other solvents, with a sweep rate of 0.4 c/s² on the 100 c/s sweep width. At least 10 sweeps for each acetal and 16 for each allene were run for each temperature studied. Owing to the ease of oxidation of both acetals and allenes freshly distilled samples of the acetals and freshly prepared samples of the allenes were used each day spectra were measured.

3-Alkyl-1,1-diphenylallenes. A 1,1-diphenylcarbinol (prepared by the action of PhMgBr on ethyl propionate, butyrate or isovalerate) was dehydrated with iodine at $140^\circ/30$ min. The resulting olefine dissolved in pentane was freed from polar impurities with alumina and used immediately. 1,1-Diphenylpropene, m.p. 52° , crystallized from pentane but the other olefines were oils. An olefine dissolved in pentane (500 ml/mole) was stirred with a 50% excess of *t*-BuOK while CHBr_3 was slowly added at $-10^\circ/2$ hour: stirring was then continued for a further 2 hr at room temperature. One such treatment was sufficient for 1,1-diphenyl-1-butene and its 3-methyl derivative but 1,1-diphenylpropene had to be re-cycled and the product required extensive purification by chromatography on alumina. The dibromocyclopropanes (Table 1) were re-crystallized from pentane.

M₂LiBu in pentane was added dropwise to a stirred solution or suspension of a dibromodiphenylalkylcyclopropane (100 mg) in ether (1.5 ml) at -30° until a permanent yellow colour appeared. The solution was rapidly warmed to room temperature, washed three times with water, dried with MgSO_4 , and volatile material removed at room temperature/0.1 mm. The residues gave mass, IR and NMR spectra consistent with the allenes IX–XI but did not give satisfactory microanalyses. When attempts were made to purify the allenes additional bands appeared in the IR and NMR spectra.

2-Alkyl-1,3-dioxolanes. Anhyd. CaCl_2 was added to a cooled mixture of ethylene glycol (50 ml), an aldehyde (25 ml) and conc. HCl (1 ml) until one liquid layer remained. The latter was distilled, dried with K_2CO_3 and KOH, distilled from Na and stored in sealed ampoules.

2-Alkyl-1,3-dioxanes. These were prepared by the general method described previously.²

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