B. From Duryl *o*-Isopropylphenyl Ketone.—By a procedure very similar to that just given, 1.5 g. of this ketone was treated with *t*-butylmagnesium chloride (0.0321 mole). The product (m.p. 141.5–143°, yield 77.8%) was shown by the method of mixed melting points to be identical to the 4-*t*-butyl-2-isopropylphenyl duryl ketone made by method A.

C. From 4-*t*-Butyl-2-isopropenylphenyl Ketone.—The procedure described for duryl *o*-isopropylphenyl ketone was followed except that the treatment was continued for 24 hours. The product (m.p. 142–143°) did not depress the melting point of an authentic specimen of 4-*t*-butyl-2-isopropylphenyl duryl ketone.

***p*-Mesitoylstilbene A. From *p*-Carboxystilbene.**—A mixture of 23.5 g. of *p*-carboxystilbene and 86.9 g. of thionyl chloride was heated under reflux for 3 hours, and the unchanged thionyl chloride removed under reduced pressure. The acid chloride[12] separated from high-boiling petroleum ether in light, buff needles, m.p. 131–133° (uncor.), yield 18.4 g. (72%). To a mixture of 10.4 g. of the chloride in 50 ml. of dry ether was added a Grignard reagent prepared from 9.0 g. of bromomesitylene, 1.1 g. of magnesium and 15 ml. of ether. The mixture was heated under reflux for 5 minutes and decomposed in the usual way. The ketone separated from methanol as colorless crystals, yield 2.1 g. (16%). After repeated recrystallization from ether and methanol it melted at 132–133°.

Anal. Calcd. for $C_{24}H_{22}O$: C, 88.30; H, 6.79. Found: C, 88.35; H, 6.81.

B. From *p*-Nitrobenzoyl Chloride.—To a chilled solution of 25 g. of *p*-nitrobenzoyl chloride, 16.2 g. of mesitylene and 15 ml. of dry benzene was added, in small portions and with stirring, 19.8 g. of aluminum chloride over a period of 20 minutes. Stirring was continued at 0° for 2 hours and the resulting pasty mass was decomposed with cold, dilute sulfuric acid. Ether was added and the organic layer was washed with water, and a 5% sodium bicarbonate solution and again with water. The solution was concentrated by evaporation of solvent; yellow prisms separated, m.p. 125.5–127°, yield 33 g. (91%). Recrystallization from methanol gave the pure mesityl *p*-nitrophenyl ketone, m.p. 126.5–127.5°.

Anal. Calcd. for $C_{16}H_{15}NO_3$: C, 71.40; H, 5.62; N, 5.20. Found: C, 71.67; H, 5.77; N, 5.12.

Catalytic reduction was accomplished by treating a slurry of 110 g. of the nitro ketone in ethanol with hydrogen at an initial pressure of 2000 lb. per sq. in. over 10 g. of Raney nickel. The hydrogenation required 4 hours at a temperature below 60°. The crude orange-buff amine melted at 152–154°, yield 80–85%. The pure *p*-aminophenyl mesityl ketone crystallized from high-boiling petroleum ether in long, white needles, m.p. 154–155°.

Anal. Calcd. for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.47; H, 7.24; N, 5.86.

The catalytic reduction was carried out also with Adams catalyst, and chemical reduction was accomplished with hydrochloric acid and mossy tin.

Diazotization was effected by dropwise addition, at 0° with stirring, of a saturated, aqueous solution of 8.79 g. of sodium nitrite to a slurry of 30 g. of the amino ketone, 35.1 g. of concentrated hydrochloric acid and 35.1 g. of ice. Saturated solutions of 40.5 g. of sodium acetate in water and 48.4 g. of *trans*-cinnamic acid in acetone were added to the solution of diazotized amine, and then a saturated, aqueous solution of 6.81 g. of cupric chloride was added dropwise. The mixture was stirred several hours at 0° and allowed to stand overnight. The product crystallized from ether in colorless needles, m.p. 132–133°, yield 21.7 g. (53%). A mixture with *p*-mesitoylstilbene made by method A showed no lowering of the melting point.

Treatment of *p*-mesitoylstilbene with benzylmagnesium chloride gave a product (m.p. 120–121°) that had the composition of a dibenzyl derivative.

Anal. Calcd. for $C_{33}H_{36}O$: C, 89.72; H, 7.13. Found: C, 89.88; H, 7.25.

The infrared spectrum indicates the presence of a normal hindered ketone group and the absence of an olefinic double bond.

URBANA, ILLINOIS

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(12) G. A. R. Kon, *J. Chem. Soc.*, 224 (1948).

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Calculation of Molecular Geometry by Vector Analysis. Application to Six-membered Alicyclic Rings[1]

BY ELIAS J. COREY AND RICHARD A. SNEEN

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A method for the accurate calculation of molecular geometry by vector analysis is outlined and applied to cyclohexane, cyclohexylidene, cyclohexene, *trans*-Δ^1-octalin and *trans*-Δ^2-octalin. The effect of the double bond on the stability and reactivity of these systems is discussed. For example, the calculated data are used to explain the extra strain in cyclohexene over 2-butene (1 kcal./mole), the greater stability of 1-methylcyclohexene over methylenecyclohexane and the tendency of 3-ketoallosteroids to enolize to the Δ^2-enols rather than the Δ^3-enols.

Continued progress in the study of the chemistry of compounds containing isolated, fused or bridged rings requires in many cases an accurate knowledge of the molecular geometry of these systems. The problem of determining the effect of introducing exo- and endocyclic double bonds on the geometry of the cyclohexane ring, for example, is one of salient importance. Because of our interest in the general subject and in this particular example we have devised a method by which molecular geometry can be calculated accurately, and which, in principle, is applicable to all molecules. This paper presents the essentials of this method, which involves vector analysis, and the results of the calculations for some six-membered alicyclic systems. The examples used herein illustrate the utility of the vector analytical approach in the solution of problems for which even the finest mechanical models available are inadequate.

Calculations

The general method of vector analysis was used for all calculations in the following way. The molecule in question was located in a three-dimensional coördinate system having X, *Y* and *Z* axes in a manner convenient for the calculations and for the subsequent interpretation of results. The bonds between atoms were designated as vectors in terms of (1) *i*, *j* and *k* which represent the unit vectors in the positive X, *Y* and *Z* directions, respectively, and (2) the various atomic coördinates (both known and unknown). Standard values for bond lengths and bond angles were employed except, as is indicated below, where these values were not physically possible. The unknown coördinates and bond angles then were calculated by means of standard trigonometric and vector relationships, especially important among these

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(1) Presented in part at the Fifth Conference on Organic Reaction Mechanisms, Durham, N. H., September, 1954.

being the formula for the dot product of two vectors having a common origin, *a*, and separated by an angle θ, *i.e.*

$$\overrightarrow{ab}\cdot\overrightarrow{ac} = BC\cos\theta$$

where $\overrightarrow{ab}\cdot\overrightarrow{ac}$ is the dot product of the two vectors and B and C are their absolute magnitudes.

To obtain unknown quantities it was necessary in general to solve n simultaneous quadratic equations in n unknowns. The solutions of these were obtained most readily by use of the variation method for linearizing quadratic equations.

The calculations for several structures of interest, including cyclohexane, cyclohexene, cyclohexylidene, Δ^1-octalin and Δ^2-octalin are described in the following sections. The case of cyclohexane is included because it is a simple illustration of the method and also provides values for comparison with the other cases.

Cyclohexane.—The following conditions were imposed on the molecule: chair form, C–C distance 1.55 Å.; C–H distance, 1.09 Å.; ring angles 109°28′. This model was placed in the coördinate system as shown in Fig. 1. The coördinates of b and f (x,y,z) are $(0, -1.266, 0)$ and $(0, +1.266, 0)$, respectively, since

$$|\overrightarrow{of}| = |\overrightarrow{ob}| = 1.55 \sin\frac{109°28'}{2} = 1.266$$

The remaining coördinates are a$(x_1,0,z_1)$, c$(x_2, -1.266, z_1)$, e$(x_2, +1.266, z_1)$ and d$(x_1+x_2, 0,0)$.

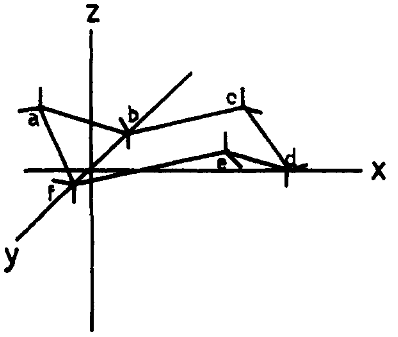

Fig. 1.—Cyclohexane. All angles 109°28′; carbon coördinates (x,y,z): a $(-0.729, 0, 0.521)$, b, f $(0, \mp 1.27, 0)$, c, e $(1.46, \mp 1.27, 0.521)$, d $(2.19, 0, 0)$; axial substituents $(x,y,z)^a$: a, b, c, d, e, f, $(0, 0, \pm 1.09)$; equatorial substituents $(x,y,z)^a$: a, d $(\pm 1.03, 0, \mp 0.362)$; b, c, e, f $(\pm 0.513, \pm 0.889, \pm 0.364)$.

First the three unknown coördinates of the carbon atoms were determined using the vectors

$$\overrightarrow{ba} = -x_1 i - 1.266j + z_1 k$$

$$\overrightarrow{bc} = x_2 i + z_1 k$$

$$\overrightarrow{af} = x_1 i + 1.266j - z_1 k$$

and the equations

$$\overrightarrow{ba}\cdot\overrightarrow{bc} = -x_1x_2 + z_1^2 = 1.55^2 \cos 109°28' \quad (1)$$

$$\overrightarrow{ab}\cdot\overrightarrow{af} = x_1^2 - 1.266^2 + z_1^2 = 1.55^2\cos 109°28' \quad (2)$$

$$x_2^2 + z_1^2 = 1.55^2 \quad (3)$$

which yield the solution $x_1 = 0.729$, $z_1 = 0.521$ and $x_2 = 1.46$.

The coördinates of the two hydrogen atoms on a given carbon atom, *e.g.*, *f*, were next determined by placing the carbon atom at the origin, placing the hydrogen substituents tetrahedrally at h and h′ and using the vectors

$$\overrightarrow{fh} = x_h i + y_h j + z_h k$$

$$\overrightarrow{fa} = -0.729i - 1.266j + 0.521k$$

$$\overrightarrow{fe} = 1.46i + 0.521k$$

and the equations

$$\overrightarrow{fa}\cdot\overrightarrow{fh} = -0.729x_h - 1.266y_h + 0.521z_h = (1.09)(1.55)\cos 109°28' \quad (1)$$

$$\overrightarrow{fe}\cdot\overrightarrow{fh} = 1.46x_h + 0.521z_h = (1.09)(1.55)\cos 109°28' \quad (2)$$

$$x_h^2 + y_h^2 + z_h^2 = 1.55^2 \quad (3)$$

which yield the coördinates of both axial and equatorial hydrogen atoms attached to carbon f (f = origin): axial hydrogen (0.00, 0.00, 1.09); equatorial hydrogen (0.513, 0.889, −0.363). In this way the coördinates of all the atoms in cyclohexane can be calculated (Fig. 1).

Distances between substituents can be calculated readily by choosing a polygon containing the unknown distance as one side and known vectors as the remaining sides and solving for the unknown vector. Thus, for example, the internuclear distance between adjacent equatorial hydrogen atoms and the internuclear distance between two *cis*, axial hydrogens can be determined simply as 2.50 and 2.53 Å., respectively.

Cyclohexylidene.—The geometry of the six-membered carbocyclic, chair-formed ring having an exocyclic double bond was calculated by orienting the molecule as shown in Fig. 2 and setting up simultaneous quadratic equations in the manner described for cyclohexane. The trigonal bond angle was taken to be 120°. The results, which apply to ketones, olefins, etc., are summarized in Fig. 2.

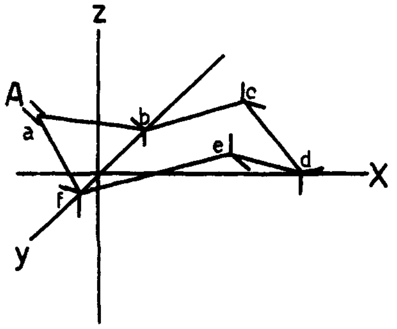

Fig. 2.—Cyclohexylidene. Angles: a, 120°; b, c, d, e, f, 109°28′; carbon coördinates (x,y,z): a $(-0.732, 0, 0.258)$, b, f $(0, \mp 1.34, 0)$, c, e $(1.43, \mp 1.27, 0.554)$, d $(2.13, 0, 0)$; axial substituents $(x,y,z)^a$: b, f $(+0.028, \mp 0.197, -1.06)$, c, e $(-0.031, \mp 0.049, 1.09)$, d $(-0.058, 0, -1.09)$; equatorial substituents $(x,y,z)^a$: b, f $(-0.538, \mp 0.806, 0.481)$, c, e $(0.557, \mp 0.886, -0.300)$, d $(1.04, 0, 0.313)$.

Cyclohexene.—It was found that in the case of cyclohexene it is impossible to impose on the molecule all the desired conditions, *i.e.*, normal tetrahedral and trigonal bond angles and normal bond distances.[2] This holds true for both the modified chair form and the less stable modified boat form. In order to construct the most reasonable model for the modified chair form two conditions were invoked: (1) the total distortion in all angles should be as small as possible and (2) the various angles should be distorted to approximately the same extent. In addition the ethylenic system was assumed to be planar.

The approximation required was obtained for the modified chair form by trial and error in the following way. Preliminary calculations were made, using the orientation shown in Fig. 3, in which it was assumed that all the distortion was absorbed in one pair of equivalent angles, the allylic, homoallylic or trigonal angles. First it was assumed that the allylic angles, a and d, had a value θ and that the remaining angles and bonds had the normal values. The quantity θ which represents the most distorted angle possible for a and d then was calculated by the usual vector method and was found to be 119°14′ (distortion = +9°46′). Similarly the angle of maximum distortion was calculated for the homoallylic angles, b and c, and was found to be 98°17′ (distortion = −11°11′). It was determined further that an increase in the trigonal angles, e and f, decreases the

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(2) It generally has been assumed that there is no distortion of ring angles in cyclohexene. *Cf.* M. A. Dolliver, T. L. Gresham, G. B. Kistiakowsky and W. E. Vaughan, THIS JOURNAL, **59**, 831 (1937).

distortion necessary for both the allylic and homoallylic angles. After several trial calculations the final assignment chosen was a value of 107°43′ for the homoallylic angles (distortion = −1°45′) and 122°30′ for the trigonal angles (distortion = +2°30′) which results in a value of 111°17′ for the allylic angles (distortion = +1°45′). The space coördinates for the carbon atoms in this model are given with Fig. 3.

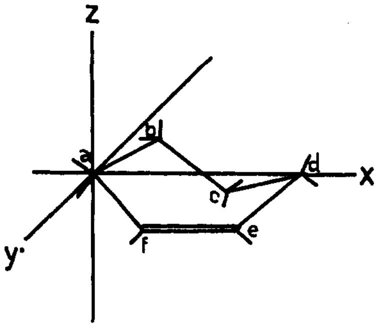

Fig. 3.—Cyclohexene. Angles: e, f, 122°30′; a, d, 111°17′; b, c, 107°43′; carbon coördinates (*x*,*y*,*z*): a (0, 0, 0), b (0.860, −1.22, 0.431), c (2.15, −1.22, −0.431), d (3.01, 0, 0), e (2.17, 1.31, 0), f (0.833, 1.31, 0); axial substituents (*x*,*y*,*z*)[a]: a, d (∓0.386, ∓0.175, ∓1.01), b, c (±0.262, 0.089, ±1.05); equatorial substituents (*x*,*y*,*z*)[a]: a, d (∓0.834, ±0.109, ±0.682), b, c (∓0.556, −0.923, ∓0.166).

[a] Origin at substituent bearing carbon atom.

In calculating the coördinates of the hydrogen substituents the assumption was made that for a given carbon atom, the C–C–H and H–C–H angles are equal. This assumption should be quite good in the case of cyclohexene since the ring-angle distortions involved are relatively small. The two hydrogen atoms on a given carbon were located in the usual way in terms of the cosine of the C–C–H angle which in turn was determined by the solution of a dot-product expression requiring the H–C–H and C–C–H angles to be equal.

***trans*-Δ²-Octalin.**—The extension of these calculations to the bicyclic case of *trans*-Δ²-octalin was carried out as follows. The model used for the calculation was constructed by attaching four carbon atoms to the model of cyclohexene which has just been described above.

It was found in preliminary calculations that the internal angles of the saturated ring could not have the tetrahedral values and, hence, that some angular distortion is necessary. Since the chief purpose of the present calculations was to compare Δ²- and Δ¹-octalins, the calculations were simplified in both cases to a determination of the distortions involved in the models in which all of the strain was assumed to be absorbed in the two angles farthest from the ring juncture. These models also were used to compare the displacement of substituents in Δ¹- and Δ²-octalins caused by the presence of the double bond, and although the displacements so determined are not exact, they are sufficiently accurate to allow interpretation.

The bicyclic nucleus was placed in the coördinate system as shown in Fig. 4A and the vector $\overrightarrow{gh}$, the angle hgb and the angle ghc were calculated. The atomic coördinates then were transformed to those shown in Fig. 4B with g and h being transformed into g′ and h′, etc. The coördinates of b′ and c′ were calculated in the usual way employing the known vector $\overrightarrow{g'h'}$ and these values were used to calculate the coördinates of p′ and q′ and subsequently the angles g′p′q′ and h′q′p′. These angles were found to be 103°7′ (distortion = −6°21′). It was of interest in connection with a comparison of *trans*-Δ¹- and Δ²-octalin types to calculate the distance between an axial substituent on b′ and an axial substituent on h′ since this distance, and hence interaction, is subject to the greatest change in going from the Δ²- to the Δ¹-structure. In the above model the internuclear distance for axial hydrogen atoms on b′ and h′ is 2.63 Å. and that for an axial methyl group on b′ and a hydrogen on h′ is 2.71 Å.

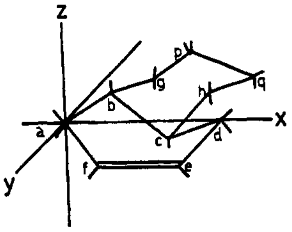

Fig.4A

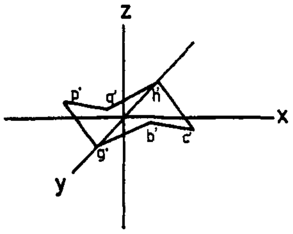

Fig.4B

When calculations were made in a similar way for the model of *trans*-Δ²-octalin in which the angular distortion was distributed equally between the pair of angles adjacent to the ring juncture (∠b′g′p′ and ∠c′h′q′) and the pair of angles farthest removed from the ring juncture (∠h′q′p′ and ∠g′p′q′), the interatomic distance for axial hydrogen atoms on b′ and h′ is only slightly greater, 2.64 Å., than that calculated for the model discussed above. The corresponding distance between an axial methyl group at b′ and a hydrogen at h′ is 2.72 Å.

***trans*-Δ¹-Octalin.**—The calculations in this case were carried out using the same operations as for Δ²-octalin. The angles farthest removed from the ring juncture were found to be 116°31′ (distortion = +7°3′) in the model where the angles adjacent to the ring juncture are tetrahedral. The internuclear distance between the axial substituents on the carbons corresponding to b′ and h′ in Fig. 4B was calculated to be 2.46 Å. where both substituents are hydrogen and 2.48 Å. where one substituent is a methyl group and the other is a hydrogen atom.

For the model in which the angular distortion in the saturated ring is distributed between angles b′g′p′, c′h′g′, h′q′p′ and g′p′q′ the interatomic distance for axial hydrogen atoms on b′ and h′ is 2.40 Å. and the corresponding distance for an axial methyl group on b′ and an axial hydrogen on h′ is 2.42 Å. It is important to note that these distances calculated for Δ¹-octalin are less than the corresponding distances for Δ²-octalin by 0.2–0.3 Å.

Discussion

The geometry of the cyclohexylidene ring (Fig. 2) requires no distortion of internal angles from the preferred values. Comparison with cyclohexane (Fig. 1) indicates that the axial substituents at C_b and C_f are displaced to an appreciable extent in the negative and positive *Y* directions, respectively, and also in the positive *X* direction. The internuclear distance between the two *cis* axial α-hydrogen substituents in this chair-formed cyclohexylidene is calculated to be 3.04 Å., whereas the internuclear distance between two *cis* axial α- and γ-hydrogens is only 2.37 Å. and that between the two *cis* axial hydrogens in cyclohexane is 2.53 Å. On the basis of these figures it seems quite reasonable that the constant for the Br(axial) ⇄ Br(equatorial) equilibrium is greater for 2-bromo-4,4-dimethylcyclohexanone (>100) than for 2-bromo-6,6-dimethylcyclohexanone (~2.5).[3a,b] The data on the modified chair form[4] of cyclohexene with least angular distortion indicate that the introduction of a double

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[3] (a) E. J. Corey, THIS JOURNAL, **76**, 175 (1954); (b) the buttressing effect of the two α-methyl groups in 2-bromo-6,6-dimethylcyclohexanone may also be a significant factor in explaining this difference since Br–O–CH_3(eq.) repulsions would be more serious in this case than Br–O–H(eq.) repulsions in the 2-bromo-4,4-dimethyl isomer. However, it is probably not as important as that mentioned above.

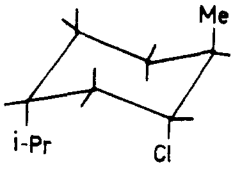
[4] The modified chair form of cyclohexene has been found to be considerably more stable than the modified boat form (Δ*E* = 2.7 kcal./mole); C. W. Beckett, N. K. Freeman and K. S. Pitzer, *ibid.*, **70**, 4227 (1948). This difference in stability is not enough to ensure that the chair-formed ring will be the more stable in the case of various substituted cyclohexenes.

bond into the cyclohexane ring causes a displacement of substituents on *both the allylic and homoallylic carbon atoms.* The axial bonds which become *allylic* upon introduction of the double bond are displaced through an arc of 23° from the vertical mainly in the X direction, whereas the axial bonds which become *homoallylic* are displaced through an arc of 11° from the vertical mainly in the X direction and slightly toward the ring center; equatorial bond directions change correspondingly.[5] An important result of these displacements is the increased eclipsing of *cis* allylic and homoallylic substituents on adjacent carbons.

It is of interest in connection with these calculations to compare the data on the heats of hydrogenation of *trans*-2-butene and cyclohexene, −27.6 and −28.6 kcal./mole, respectively.[6a] The difference between the two (1 kcal./mole) is not unexpected and appears to be a result of angular distortion and eclipsing of adjacent substituents in cyclohexene.[6b]

The greater stability of 1-methylcyclohexene over methylenecyclohexane ($\Delta H = -3.1$ kcal./mole) is another point of interest. Since the ring angles of methylenecyclohexane can assume the undistorted values and since the cyclohexene ring is subject to ring and eclipsing strains, the instability of methylenecyclohexane relative to 1-methylcyclohexene is probably due to steric interactions between the exocyclic methylene hydrogens and the nearby equatorial hydrogens in the former molecule as has been suggested recently by Brown, *et al.*[7]

An important conclusion which follows from the data on cyclohexene is that large axial substituents on a cyclohexane ring which are not being eliminated will speed the rate of reactions in which endocyclic double bonds are formed, whereas large equatorial substituents will have the reverse effect. Thus, for example, menthyl chloride (I) forms Δ^2-menthene much faster relative to neomenthyl chloride (II) than would be predicted from the equilibrium constant for the change *trans*-menthane (Me, *i*-Pr axial) ⇄ *trans*-menthane (Me, *i*-Pr equatorial).[8]



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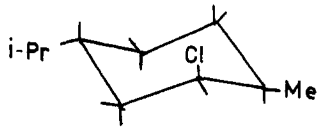
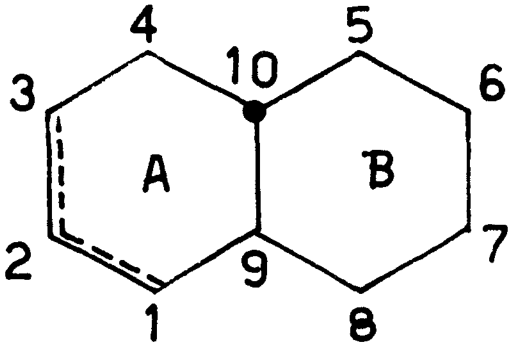


II

The data for *trans*-Δ^1- and Δ^2-octalins (III) reveal that the presence of a double bond in the A ring of these structures causes angular distortion not only in that ring but also in the B ring. The calculated distortion of angles in the B ring is only slightly greater for Δ^1-octalin than for Δ^2-octalin and, interestingly, is in opposite directions in the two cases. A more important difference between the two structures is the difference in internuclear distance between the axial substituents at C_8 and C_{10}. This difference which is *ca.* 0.25 Å. for the octalins themselves and *ca.* 0.30 Å for the 10-methyloctalins favors the Δ^2-structure and in addition becomes more important as the size of the axial groups at C_8 and C_{10} are increased. It therefore is to be anticipated that *trans*-Δ^2-octalins will be more stable than *trans*-Δ^1-octalins and that an even larger difference will exist between the *trans*-Δ^2- and Δ^1-10-methyloctalins or the Δ^2- and Δ^3-allosteroids (steroid numbering). Such a difference in favor of Δ^2-allosteroids over Δ^3-allosteroids is, of course, well known.[9]



III

We have applied these considerations to the problem of the α-bromination of $5\alpha,6\beta$-dibromocholestan-3-one. The bromination leads to a pair of epimeric tribromides in which the newly attached α-bromine usually has been assumed to be at C_4 instead of at C_2.[10,2] According to the argument presented above, $5\alpha,6\beta$-dibromocholestan-3-one should form the Δ^2-enol and not the Δ^3-enol with the Δ^2-enol being favored even more than with cholestanone itself. Hence the α-bromine atom in the tribromides must be at C_2. This surmise is confirmed by the work of Djerassi, *et al.*, on the bromination of cholestenone.[11,12]

If the above arguments are true, the very useful generalization can be made that in substituted *trans*-octalins possessing an angular substituent at the ring juncture and a six-membered ring fused onto the saturated ring, the Δ^2-type structure should be more stable than the Δ^1-type.

In closing it should be pointed out that although the vector analysis method is in principle applicable even to very complex molecules, it is practical in these cases only when techniques are available for simplifying the mathematics involved. Even a problem such as the comparison of Δ^5- and Δ^7-steroids is beset by formidable mathematical difficulties because the distortion caused by the presence of the double bond is distributed, at least, over rings A, B and C. It is hoped, nevertheless, that these

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(5) It therefore is suggested that *both* allylic and homoallylic substituents be designated as a′ and e′ after the terminology of D. H. R. Barton, R. C. Cookson, W. Klyne and C. W. Shoppee, *Chem. and Ind.*, 21 (1954).

(6) (a) G. B. Kistiakowsky, J. R. Ruoff, H. A. Smith and W. E. Vaughan, THIS JOURNAL, **57**, 876 (1935); **58**, 137 (1936); (b) K. S. Pitzer, *Science*, **101**, 672 (1945).

(7) H. C. Brown, J. H. Brewster and H. Shechter, THIS JOURNAL, **76**, 467 (1954).

(8) D. Y. Curtin, *Rec. Chem. Prog.*, **15**, 111 (1954).

(9) For another explanation of this difference see D. A. H. Taylor, *Chem. and Ind.*, 250 (1954).

(10) (a) L. F. Fieser and M. Fieser, "Chemistry of Natural Products Related to Phenanthrene," Reinhold Publ. Corp., New York, N. Y., p. 273; (b) D. H. R. Barton and E. Miller, THIS JOURNAL, **72**, 1066 (1950).

(11) C. Djerassi, G. Rosenkranz, J. Romo, St. Kaufmann and J. Pataki, *ibid.*, **72**, 4534 (1950).

(12) A similar conclusion on the structure of the tribromides has been reached by Dr. H. H. Inhoffen (private communication).

difficulties will not be insuperable and that the vector method will provide a means of determining molecular geometry in such complex systems.

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Specific Solvent Effects in the Hydrolysis of *p*-Nitrobenzhydryl Bromide

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The hydrolysis of *p*-nitrobenzhydryl bromide in aqueous acetone is accelerated and the activation enthalpy changed when part of the acetone is replaced by hexane or by aromatic compounds. An explanation in terms of preferential solvation and complex formation is proposed.

Although certain macroscopic properties of the solvent, as for example the dielectric constant, are of importance in determining the effect of solvent changes on reaction rates, such macroscopic properties are quite inadequate for any complete explanation of solvent effects. This is especially noticeable in the case of mixed solvents[1] or when an attempt is made to explain the effect of solvent changes on activation parameters as well as on rates.[2] One of the special solvent effects that must be considered is the formation of molecular complexes. Another is the tendency of solvent in the vicinity of a solute molecule to have a different composition from that in the bulk of the solvent in the case of mixed solvents.

The partial positive charge on the central carbon atom of the transition state for *p*-nitrobenzhydryl bromide hydrolysis should confer an enhanced stability on π-complexes formed by the transition state as compared to those formed by the ground state. As a result the free energy of activation of the hydrolysis should be lower in the presence of appropriate complexing agents even though the addition of the complexing agent may lower the dielectric constant of the solvent. We have carried out the indicated experiments and find a rate effect in the predicted direction. The effect is a small one, however, and seems to be superimposed on a larger effect having nothing to do with the formation of π-complexes.

Table I shows the effect of replacing part of the acetone in a standard aqueous acetone solvent with various aromatic compounds and with hexane in concentrations about 1 molar. The most conspicuous result is the acceleration (14 to 39%) of the reaction in any of the other mixtures as compared with aqueous acetone. The null hypothesis for these rate differences has a negligible probability.[3] The difference in activation enthalpy for the reaction in aqueous acetone and in aqueous acetone–*p*-dimethoxybenzene has only a 15% probability of being null while the differences in entropy of activation have a rather high probability of being null except in the case of hexane. It is therefore reasonable to seek explanations of the rate effect that predict it on the basis of a decrease in activation enthalpy. The next most conspicuous feature of Table I is the fact that hexane not only accelerates the reaction but has a larger effect on the activation parameters than any of the other addends. Since π-complexing can be neglected in the case of hexane, and since hexane certainly does not make the reaction mixture more polar, at least one additional factor must be at work.

In a three-component solvent system there is no difficulty in finding explanations of the experimental facts but only in defending a preferred explanation selected from many. The explanation presented here is by no means the only possible one but does make use of the predicted effect of complexing by aromatic compounds. Large, relatively non-polar organic molecules like *p*-nitrobenzhydryl bromide and its transition state for hydrolysis will tend to surround themselves preferentially with the organic components of a mixed solvent. Some, but not all, of the organic solvent molecules must be displaced to make room for water molecules in the transition state. The most easily displaced solvent component will be hexane. The solvent that contains hexane in place of some of the acetone therefore has a lower activation enthalpy. Acetone and the aromatic compounds interact more than hexane with the alkyl bromide and are less easily ejected to make room for water molecules. Since they are more firmly held, their release is attended by an increase in entropy, hence the generally higher activation enthalpies and less negative entropies for acetone and the aromatic compounds. In the case of the aromatic compounds those molecules that remain in the aggregation about the transition state partly counteract the general increase in activation energy by complexing with the transition state. Thus the aromatic molecules give a lower activation energy than acetone, an effect which is greater with the substituted benzenes than with benzene itself.

Table II shows the effect of increasing the water content on the rates in aqueous acetone. Since added water seems to accelerate the reaction almost entirely by an entropy effect, the activation enthalpies being unchanged within their probable errors, it is unlikely that the non-polar solvents produce their acceleration by releasing water, for example from an acetone–water complex. Any purely entropy effect on changing the concentration of a reagent can be described either as a medium effect or as a concentration effect. If the effect of adding water to these solutions is merely that of changing

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[1] N. Farinacci and L. P. Hammett, THIS JOURNAL, **59**, 2542 (1937); **60**, 3097 (1938).

[2] H. E. Cox, *J. Chem. Soc.*, **119**, 142 (1921).

[3] W. J. Youden, "Statistical Methods for Chemists," John Wiley and Sons, Inc., New York, N. Y., 1951.