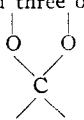


[CONTRIBUTION FROM THE SCHOOL OF PHARMACY OF THE UNIVERSITY OF CALIFORNIA, SAN FRANCISCO, AND THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA, LOS ANGELES]

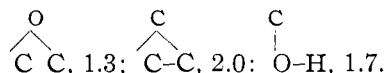
Dipole Moments of Some Five-membered Ring Compounds

BY W. D. KUMLER, ALAIN C. HUITRIC AND H. K. HALL, JR.

RECEIVED APRIL 2, 1956

The dipole moments of ten five-membered carbon ring compounds have been measured in dioxane and three of these have been measured in benzene. The compounds have the substituents bromine, hydroxyl, epoxy and an  bridge. The moments were measured and compared with the calculated moments for various configurations to obtain evidence with regard to the relative orientation of the substituents.

The moments for the various possible configurations were found by obtaining the moments of the polar groups from the measured moments of model compounds. The following moment values were used C-Br, 2.2;



Since these calculations were made, evidence has been presented that the C-Br and C-Cl dipoles have a value around 1.9 when two such dipoles are on adjacent carbon atoms^{1,2} instead of the value 2.2 which we used. If this smaller value had been taken the calculated values would have been closer to the experimental values and the conclusions about the structure would be the same in every case. Thus for 1,2-dibromocyclopentane, b.p. 94° (32.5 mm.), the calculated values would be 1.79 *trans* and 3.58 *cis* with 1.51 observed. Another factor that will tend to make the observed moment smaller than the calculated is dipole interaction, which will tend to spread the angle between the individual dipoles. This effect will be larger in those compounds where spreading can result from rotation about single bonds, without greatly altering the normal valence angles of the atoms.


A set of reference axes were set up in each molecule and the component of each group moment calculated thereon. The resultant was obtained as the square root of the sum of the squares of these components. The ring was assumed to be a flat pentagon.

Dibromides.—In Table I are given the results. In the case of 3,5-dibromocyclopentene, m.p. 45°, the observed moment 3.40 *D* is near that calculated for the *cis* configuration XVII, 3.68 *D* and far from the calculated moment for the *trans* XVIII, 0.79 *D*, indicating that the structure is *cis*. This result came as something of a surprise and is completely at variance with the assumptions of previous workers. Nevertheless, the evidence is conclusive and is further supported by various bits of less direct chemical evidence.³

For 3,4-dibromocyclopentene, m.p. 15°, the observed dipole moment of 1.37 *D* clearly indicates the compound has the *trans* configuration XX and not the *cis* XIX. Likewise, 1,2-dibromocyclo-


pentane, b.p. 94° (32.5 mm.), has the *trans* configuration XXII and not the *cis* XXI. These results are in keeping with the previous chemical evidence.

Acetonides.—The results on *cis*-1,2-cyclopentanediol acetonide, b.p. 147–148°, are somewhat unexpected because of the large difference in dipole moment in dioxane as compared with benzene. There is no possibility of this molecule hydrogen bonding with either of these solvents. The difference 0.56 *D* is large compared with the values of the moments 0.81 and 1.37 *D* and is a much larger difference than would be expected just due to a solvent effect arising from the difference in dielectric constants of the two solvents. The explanation may be that the five-membered ring containing the two oxygen atoms has two or more configurations in

which the resultant dipoles of each  C-C group make different angles with one another. The configuration with the smallest angle between these and having the largest moment would be favored in the solvent dioxane, in which there are local dipoles.

With the compound 3,5-dibromocyclopentanediol acetonide, m.p. 27.2°, structure XXIV is clearly ruled out and structure XXV is definitely favored over structure XXVI, since for reasons pointed out previously the observed moments are expected to be a few tenths smaller than those calculated for the correct structure.

The other 3,5-dibromocyclopentanediol acetonide, m.p. 72.5–73.5°, has the structure XXVI. That this observed moment is greater in dioxane by 0.35 than the calculated moment probably results from steric and dipole interaction between one of the oxygens in the bridge and the bromine that is *cis* to the bridge. Here the spreading between the

 C-C dipole and the C-Br dipole could increase the over-all resultant moment because it decreases the angle between the two C-Br dipoles.

For 3,4-dibromocyclopentanediol acetonide, m.p. 78°, structure XXVII is definitely ruled out and the calculated dipole moment of XXVIII with bromine *cis* but *trans* to the bridge agrees well with the observed dipole moment. The chemical evidence, while not conclusive, definitely favors a *trans* configuration for the bromine atoms, which suggests the compound has either structure XXIX or XXX. Of these, structure XXX would be favored because it has a bromine *cis* and adjacent to the bridge, a configuration which could cause the observed

(1) A. Tulinski, A. DiGiacomo and C. P. Smyth, *THIS JOURNAL*, **75**, 3552 (1953).

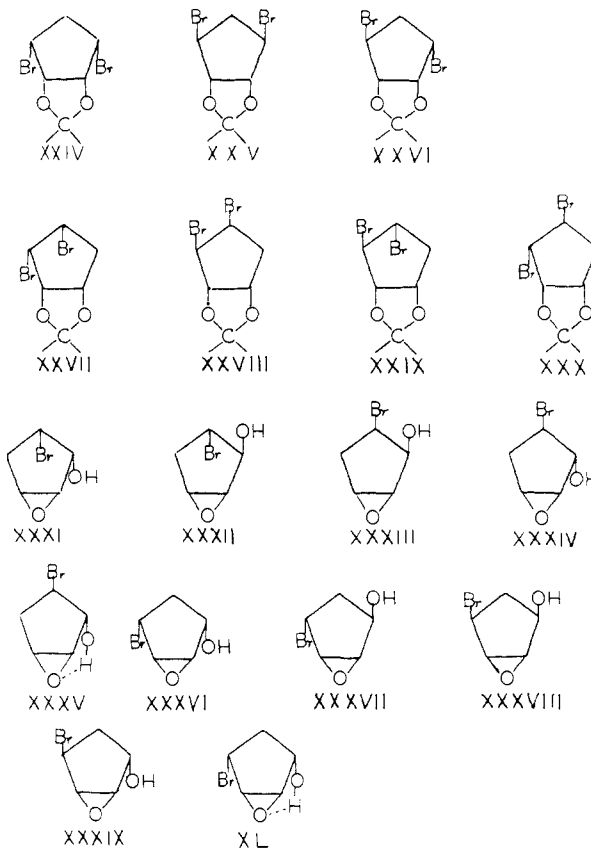
(2) P. Bender, D. L. Flowers and H. L. Goering, *ibid.*, **77**, 3463 (1955).

(3) W. G. Young, S. Winstein and H. K. Hall, Jr., *ibid.*, **78**, 4338 (1956).

TABLE I: DIPOLE MOMENTS, OBSERVED AND CALCULATED FOR POSSIBLE STRUCTURES

Compound	S _u	ε _i	n _D	α	β	P ₂₉	P _{E₃}	μ in Debyes		μ in Debyes calcd. for
								Obsd.	XVII	
3,5-Dibromocyclopentane, m.p. 45°	D	2.2024	0.97390	6.36	-0.47	270.30	38.16	3.40	cis 3.68	trans 0.79 XVIII
3,4-Dibromocyclopentane, m.p. 15°	D	2.2048	.97384	1.16	-.472	75.05	38.16	1.37	cis 4.14	trans 2.04 XX
1,2-Dibromocyclopentane, b.p. 94° (32.5 mm.)	D	2.2029	.97380	1.27	-.417	84.20	38.63	1.51	cis 4.14	trans 2.04 XXII
cis-1,2-Cyclopentane diol acetone, b.p. 147-148°	D	2.2030	.97384	1.48	+.036	75.90	38.04	1.37	1.05	
3,5-Dibromocyclopentane diol acetone, m.p. 27.2°	B	2.2689	1.4748	0.971	-1.057	51.18	38.04	0.81	XXIII	
3,5-Dibromocyclopentane diol acetone, m.p. 27.2°	D	2.2028	0.97380	2.28	-0.364	165.48	111.92	2.36	4.99	1.81 XXIV
3,5-Dibromocyclopentane diol acetone, m.p. 72.5-73.5°	D	2.2020	.97380	1.92	-.364	147.64	53.56	2.16	4.99	1.81 XXV
3,4-Dibromocyclopentane diol acetone, m.p. 78°	B	2.2684	1.1475	1.117	-.540	117.45	53.56	1.78	XXIV	2.75 XXVI
3,4-Dibromocyclopentane diol acetone, m.p. 78°	D	2.2046	.97386	4.26	-.392	261.22	53.56	3.21	5.44	2.79 XXVII
3,4-Dibromocyclopentane diol acetone, m.p. 48.0-49.7°	B	2.2688	1.14764	3.36	-.596	239.64	53.56	3.02	XXVIII	2.79 XXX
3,4-Dibromocyclopentane diol acetone, m.p. 48.0-49.7°	D	2.2047	0.97379	1.98	-.386	148.68	53.56	2.17	5.44	2.79 XXXI
1,2-Bromohydrin epoxide, m.p. 53.2-53.7°	D	2.2036	.97386	4.13	-.47	148.16	32.08	2.40	4.12	0.96 XXXII
1,3-Bromohydrin epoxide, m.p. 64.8°	D	2.20365	.97387	5.90	-.50	198.99	32.08	2.88	4.20	0.96 XXXIII

α S, solvent; D, dioxane; B, benzene.



Epoxides.—With the bromohydrin epoxides the dipole moment values for the different structures in Table I were calculated assuming the hydroxyl group has freedom of rotation. With 1,2-bromohydrin epoxide, m.p. 53.2-53.7°, structure XXXII with bromine *cis* and hydroxy *trans* to the epoxy has a calculated moment nearest the observed moment. The chemical evidence, however, indicates the bromine is *trans* and the hydroxyl *cis* to the epoxy which is structure XXXIV, which has a calculated dipole moment of only 0.22 *D* in contrast to the observed moment of 2.40 *D*. The chemical evidence in this case is fairly good so it is fairly obvious that our assumption of freedom of rotation for the hydroxyl group does not hold. This group might be expected to be fixed with the hydrogen forming a hydrogen bond with the epoxy oxygen. The calculated moment for structure XXXV with the hydroxyl fixed in this manner is 1.94 which is still a bit small but within reason considering the uncertainties involved in calculat-

moment to be larger than the calculated value, a situation similar to that mentioned above with 3,5-dibromocyclopentane diol acetone.

The 3,4-dibromocyclopentane diol acetone, m.p. 48.0-49.7°, with an observed dipole moment of 2.17 *D* then would logically be assigned structure XXIX. This assignment is in agreement with both the chemical evidence, which indicates that one bromine in I is *trans* to the hydroxyl, and with the dipole moment evidence which proved the bromines were *trans* in the parent dibromocyclopentane.

ing the dipole moment of a compound containing a hydrogen bond.

With 1,3-bromohydrin epoxide, m.p. 64.8°, the structure whose dipole assuming freedom of rotation of the hydroxyl is nearest the observed value is XXXVII with the bromine *cis* and the hydroxyl *trans* to the epoxy. The chemical evidence rather strongly indicates that both the bromine and hydroxyl are *cis* to the epoxy. Assuming such a structure and having the hydroxyl hydrogen bonded to the epoxy oxygen XL, the calculated moment is 3.22 *D* which again is a reasonable value when compared with the observed moment.

Experimental

The measurements were carried out at 30° using the apparatus described previously⁴ and the dipole moments were calculated using the equation and method of Halverstadt and Kumler⁵

$$p_{20} = \frac{3\alpha\nu_1}{\epsilon_1 + 2} + (\nu_1 + \beta) \frac{\epsilon_1 - 1}{\epsilon_1 + 2}$$

$$P_{20} = p_{20}M_2$$

$$\mu = 0.0128 \sqrt{(P_{20} - P_{E_2})T}$$

The plots of ϵ_{12} versus ω_2 and ν_{12} versus ω_2 were straight lines within the limits of the experimental error and the values

(4) W. D. Kumler and I. F. Halverstadt, *THIS JOURNAL*, **62**, 2182 (1941).

(5) I. F. Halverstadt and W. D. Kumler, *ibid.*, **64**, 2988 (1942).

of ϵ_1 and ν_1 were obtained by extrapolating the ϵ_{12} and ν_{12} values to zero weight fraction.

Preparation of Compounds.—A number of the compounds were prepared in the course of the previous investigation.³

trans-1,2-Dibromocyclopentane was prepared by the addition of bromine to cyclopentene. The product was distilled once, b.p. 93–95° (32.5 mm.), and was crystallized twice from petroleum ether (b.p. 30–60°) cooled in Dry Ice-acetone. Distillation gave material of b.p. 94° (32.5 mm.).

cis-1,2-Cyclopentanediol, b.p. 87° (1.5 mm.), was prepared by the oxidation of cyclopentene with potassium permanganate.⁶ This was converted in good yield to the cyclic acetamide, b.p. 148°, by treatment with anhydrous copper sulfate and acetone as described for the dibromocyclopentanediols.³

1-*trans*-2-Dibromo-*trans*-3,4-acetylidenecyclopentane (XVII) was prepared as follows. A solution of 0.95 g. (0.00595 mole) of bromine in 4 ml. of C.P. chloroform was added over 5 minutes to a solution of 0.90 g. (0.00643 mole) of unsaturated acetamide³ (XIII) in 4 ml. of chloroform at –80°. The solution was warmed to room temperature, washed with 5% sodium thiosulfate solution, and evaporated. Crystallization of the residue at –80° and filtration gave 0.95 g. of crystalline XVII. One recrystallization from petroleum ether (b.p. 29–53°) gave 0.80 g. (45.0%) of XVII, m.p. 78°. A mixed m.p. with compound m.p. 48° was depressed.

Anal. Calcd. for C₈H₁₂O₂Br₂: C, 32.02; H, 4.03. Found: C, 31.75; H, 4.17.

(6) C. van Loon, *C. A.*, **17**, 1956 (1923).

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

Neighboring Carbon and Hydrogen. XXII. Homoallylic Systems. The Preparation and Behavior of Certain 3,5-Cyclosteroids

BY EDWARD M. KOSOWER¹ AND S. WINSTEIN

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Homoallylic systems offer an interesting departure from the more familiar allylic ones. In this connection, 5-cholesten-3 β -yl and the related 3,5-cyclocholestan-6 β - and 6 α -yl derivatives are interesting. In the present work, the preparation of "i-cholesterol" has been improved, and the configurations of the 3,5-cyclocholestan-6-ols have been discussed. Both 3,5-cyclocholestan-6-yl trichloroacetates have been prepared, and their rearrangement and solvolysis have been studied. While cholesteryl trichloroacetate methanolyses with acyl-oxygen cleavage, both 3,5-cyclocholestan-6-yl trichloroacetates do so with alkyl-oxygen cleavage. In methanol-chloroform, cholesteryl toluenesulfonate and the 3,5-cyclocholestan-6-yl trichloroacetates yield a mixture of methyl ethers, 90 \pm 2% 3,5-cyclocholestan-6 β -yl and 10 \pm 2% cholesteryl. These results are ascribed to the occurrence of a common homoallylic hybrid carbonium ion intermediate in the solvolysis of all three compounds. The results cannot be discussed on the basis of only dissociated forms of the carbonium ions. In 90% dioxane, substantial ion pair return accompanies hydrolysis of both 3,5-cyclocholestan-6-yl trichloroacetates. Thus, cholesteryl trichloroacetate is produced during hydrolysis. Even in methanol-chloroform, a few per cent. of cholesterol, by way of cholesteryl trichloroacetate, is obtained from either 3,5-cyclocholestan-6-yl ester.

Homoallylic² systems offer an interesting departure from the more familiar allylic ones because of the striking difference in geometric requirements involved in the formation of intermediates and products. In this connection, 5-cholesten-3 β -yl and the related 3,5-cyclocholestan-6 β -yl and 3,5-cyclocholestan-6 α -yl derivatives are interesting.

Since the discovery of 3,5-cyclocholestan-6 β -yl methyl ether (formerly "i-cholesteryl" methyl ether) by Stoll³ in 1932, various reactions^{4–8} have

(1) Research Fellow of the National Institutes of Health, 1949–1952.

(2) M. Simonetta and S. Winstein, *THIS JOURNAL*, **76**, 18 (1954).

(3) W. Stoll, *Z. physiol. Chem.*, **207**, 47 (1932).

(4) T. Wagner-Jauregg and L. Werner, *ibid.*, **213**, 119 (1932).

(5) (a) J. H. Beynon, I. M. Heilbron and F. S. Spring, *J. Chem. Soc.*, 907 (1936); (b) 406 (1937); (c) 1459 (1937)

(6) I. M. Heilbron, J. Hodges and F. S. Spring, *ibid.*, 759 (1938).

been carried out, with 3,5-cyclosteroids. Winstein and Adams⁹ have shown that the 5,6-double bond of cholesteryl *p*-toluenesulfonate participates in the rate-controlling ionization during solvolysis, and they proposed a hybrid ion intermediate. This suggestion was supported by the discovery¹⁰ that 3,5-cyclocholestan-6 β -yl methyl ether could be converted partially to the corresponding ethyl ether by treatment with dilute acid in ethanol. With a view to establishing the hybrid ion intermediate I in a more definitive manner, the preparation of suitable 3,5-cyclocholestan-yl derivatives and a

(7) E. S. Wallis, E. Fernholz and F. T. Gephart, *THIS JOURNAL*, **59**, 137 (1937).

(8) E. G. Ford and E. S. Wallis, *ibid.*, **59**, 1415 (1937).

(9) S. Winstein and R. Adams, *ibid.*, **70**, 838 (1948).

(10) S. Winstein and A. H. Schlesinger, *ibid.*, **70**, 3528 (1948).