Tetrahedron, 1966, Vol. 22, pp. 183 to 187. Pergamon Press Ltd. Printed in Northern Ireland

THE CONFORMATION OF NON-AROMATIC RING COMPOUNDS—XIX*

THE DIPOLE MOMENTS OF *TRANS*-2,3- AND *TRANS*-5,6-DIHALOGENO-5α-CHOLESTANES

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(*Received* 28 *June* 1965; *in revised form* 24 *July* 1965)

Abstract—Dipole moments of some *trans*-2,3- and *trans*-5,6-dihalogeno-5α-cholestanes are determined in benzene and in carbon tetrachloride. A discussion is given on the basis of the geometry of the molecules as revealed by X-ray analysis. It is concluded that besides the deviations of the 6-membered ring system from the ideal chair form (i.e. the flattening of the rings) also induction effects and interaction of dipoles have to be taken into account to arrive at a satisfactory interpretation of the dipole moment values of the diaxial as well as of the diequatorial dihalogenides.

INTRODUCTION

THE investigation presented in this paper forms a continuation of the conformational studies made in this laboratory on dihalogeno-substituted cyclohexane,[1–3] dioxane,[4] and dithiane[5] derivatives. The dipole moments of 1,2-dihalogeno-cyclohexane derivatives with fixed conformation have been found to deviate significantly from the values obtained by vector addition of partial carbon–halogen moments, using the regular chair-form as the molecular model.[2,3,6,7] This holds for the diequatorial as well as for the diaxial compounds.

Similar conclusions have been reached for the halogeno–dioxanes and the halogeno–dithianes, where the molecular geometry could be determined by X-ray analysis.[8,9,10] With the axially halogen-substituted heterocyclic compounds, however, incompletely understood "electronic" interactions occur, affecting bond lengths and bond angles and making theoretical treatment still more complicated.

In order to arrive at a fruitful discussion of the dipole moments of the halogeno-cyclohexanes it was deemed essential to combine the knowledge of the exact geometry obtained by X-ray analysis with the value of the moment of one and the same molecule. Dihalogenides of cholestane were chosen for this purpose because these compounds

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[*] Part XVIII C. Romers, B. Hesper, E. v. Heykoop and H. J. Geise, *Acta Cryst.* in the press.

[1] W. Kwestroo, F. A. Meyer and E. Havinga, *Rec. Trav. Chim.* **73**, 717 (1954); W. Kwestroo, Thesis Leiden (1954).

[2] E. C. Wessels, Thesis Leiden (1961).

[3] J. A. v. d. Linden, Thesis Leiden (1958).

[4] C. Altona, Thesis Leiden (1964); C. Altona, C. Romers and E. Havinga, *Tetrahedron Letters* No. 10, 16 (1959).

[5] H. T. Kalff and E. Havinga, *Rec. Trav. Chim.* **81**, 282 (1962); H. T. Kalff, Thesis Leiden (1964).

[6] E. L. Eliel and R. G. Haber, *Chem. & Ind.* 264 (1958); *J. Org. Chem.* **24**, 143 (1959); E. L. Eliel and R. V. Acharya, *J. Org. Chem.* **24**, 151 (1959).

[7] W. Hückel, H. Waiblinger and H. Feltman, *Liebigs. Ann.* **678**, 24 (1964).

[8] C. Altona, C. Knobler and C. Romers, *Rec. Trav. Chim.* **82**, 1089 (1963); *Acta Cryst.* **16**, 1217 (1963).

[9] C. Altona and C. Romers, *Rec. Trav. Chim.* **82**, 1080 (1963); *Acta Cryst.* **16**, 1225 (1963).

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can be prepared in a pure crystalline state and because the molecules can be expected to have a fixed, rather rigid conformation, the details of which are interesting from several points of view (e.g. Halkes and Havinga l.c. 11). The results of the X-ray analyses are reported in other papers of this series.[12,13,14] The data on the dipole moments and the discussion are presented in this publication.

EXPERIMENTAL

Characterization and purity of the compounds. A number of diaxially and diequatorially substituted dihalogeno-5α-cholestanes were synthesized by methods indicated in the literature.* 2β-chloro 3α-bromo-5α-cholestane was obtained by direct addition of BrCl to cholest-2-ene. Some physical constants are summarized in Table 1.

The purity of the 2,3-derivatives was tested by means of thin layer chromatography using heptane as an eluent. A single spot was observed in all cases. The 5α,6β-derivatives could not be tested in this way because of their tendency to decompose. IR absorption spectra of the diaxial compounds showed no indications of contamination with the diequatorial isomers. Neither were indications found of contamination of the diequatorial compounds with the diaxial derivatives. It is of great importance to the discussion of the molecular conformation and the dipole moments in solution that the IR spectra taken from solutions in CS_2 are practically identical with those obtained from crystalline material (KBr discs).

TABLE 1. CHARACTERISTIC DATA OF THE DIHALOGENO-CHOLESTANES

Compound	Conformation	m.p.* (°C)	$[\alpha]_D^{20}$ in $CHCl_3$	% hal. Found	% hal. Calc.
2β,3α-Cl,Cl[16]	a,a	110–112 (108–112)	+62 (+63)	16·0	16·1
2β,-Cl,3α-Br	a,a	97–99 (90–92)†	+70 (+62)	23·7	23·7
2β-Br,3α-Cl[16]	a,a	130–133 (130–132)	+64 (+66)	23·5	23·7
2β,3α-Br,Br[16]	a,a	122–124 (124)	+74 (+76)	29·8	30·1
5α,6β-Cl,Cl[17]	a,a	121–123 (121–122)	−29 (−28)	16·0	16·1
5α-Br,6β-Cl[17]	a,a	111–113 (109–110)	−32 (−46?)	23·3	23·7
5α,6β-Br,Br[17]	a,a	105–106 (109–110)	−40 (−40·5)	29·9	30·1
2α,3β-Cl,Cl[16]	e,e	150–152 (150–152)	− 9 (− 7)	16·1	16·1
2α-Cl,3β-Br[16]	e,e	156–157 (150–152)	−17 (−16)	23·9	23·7
2α-Br,3β-Cl[16]	e,e	135–137 (134–136)	−18 (−17)	23·4	23·7
2α,3β-Br,Br[16]	e,e	146–148 (143–144)	−32 (−29)	29·8	30·1
5β,6α-Br,Br[17]	ae,e	146–148 (143–144)	+50 (+50)	30·2	30·1
3α-Cl[18]	a	103–104 (103–105)	+29 (+31)	9·1	8·7
3β-Cl[19]	e	113–114 (114–115)	+29 (+27)	9·0	8·7
cholestane[20]	—	79–80 (79–80)	−25 (−25)	87·0 (%C) 12·9 (%H)	87·0 (%C) 13·0 (%H)

* Given in parentheses are the values from the literature.

† Synthesized in a different way.[21]

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* Details of the syntheses can be found loc. cit. 12.

[11] S. J. Halkes and E. Havinga, *Rec. Trav. Chim.* **84**, 889 (1965).

[12] H. J. Geise, Thesis Leiden (1964).

[13] H. J. Geise, C. Romers and E. W. M. Rutten, *Acta. Cryst.* in the press.

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[19] R. E. Marker, F. C. Whitmore and O. Kamm, *J. Amer. Chem. Soc.* **57**, 2359 (1935).

[20] L. Ruzicka, M. Furter and G. Thomann, *Helv. Chim. Acta* **16**, 327 (1933).

[21] L. F. Fieser and W. Y. Huang, *J. Amer. Chem. Soc.* **75**, 4837 (1953).

Dipole moments. The dipole moments were calculated from measurements of the dielectric constants of dilute solutions in benzene and CCl_4 using the extrapolation formula of Halverstadt and Kumler.[15] The concentration of the solute was less than ·01M throughout. Therefore, the refractive indices could not be measured accurately and the molar refractions were calculated from the refractive indices of *trans*-decalin, cyclohexane, cyclopentane and 2-methylheptane and the atomic refractions of H, Cl and Br. Densities were measured with 6 ml pycnometers; wts were corrected to 25° and 76 cm Hg press. The dielectric constants were determined with a Schering bridge. The apparatus is described by de Vos[22] and Altona.[4] The accuracy calculated according to a method described by Wessels,[3] is about ·04 D in the case of a dipole moment of 1·5 D, ·03 D with a moment of 2·5 D and ·02 D with a moment of 3·5 D. The results are summarized in Table 2.

TABLE 2. DIPOLE MOMENTS (AT 25°) OF THE DIHALOGENO-CHOLESTANES IN DEBYE UNITS

Compound	Confor-mation	Moment in CCl_4	C_6H_6
2β,3α-Cl,Cl	a,a	1·27	1·25
2β-Cl,3α-Br	a,a	1·30	1·29
2β-Br,3α-Cl	a,a	1·35	1·35
2β,3α-Br,Br	a,a	1·39	1·40
5α,6β-Cl,Cl	a,a	1·11	1·16
5α-Br,6β-Cl	a,a	1·28	1·33
5α,6β-Br,Br	a,a	1·38	—
2α,3β-Cl,Cl	e,e	3·44	3·42
2α-Br,3β-Cl	e,e	3·41	3·44
2α-Cl,3β-Br	e,e	3·52	3·48
2α,3β-Br,Br	e,e	3·42	3·44
5β,6α-Br,Br	ae,e	3·56	3·60
3α-Cl	a	2·05	2·06
3β-Cl	e	2·30	2·31
5α-Cholestane	—	0·18	—

Discussion of the dipole moments

One of the features emerging from the data of Table 2 is that the dipole moments are independent of the nature of the solvent. On the basis of the experience gained in former investigations[1–5] we would interpret this as an indication that in solution the molecules concerned exist predominantly in one conformation. The fact that IR absorption spectra in solution and in the crystalline state are almost identical, induces us to postulate that this conformation has the same geometry as found by X-ray analysis for the molecules in the crystal (Figs 1 and 2).

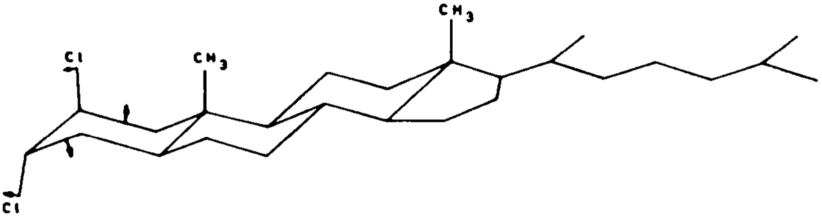

FIG. 1. Perspective view of the molecule of 2β,3α-dichloro-5α-cholestane. The arrows suggest the torsion around C(2)–C(3) (flattening of ring A) which causes the chlorine atoms to deviate from their "ideal" positions.

It is well known that the dipole moments in the series primary, secondary, tertiary halogenides increase as a consequence of increasing inductive effects.[23] These effects play an important role in cyclohexane derivatives and are thought to be responsible for the difference between an equatorial and an axial carbon–halogen moment. According to Ingold,[23] a longitudinal moment—a moment in the direction of the carbon chain—is enhanced by induction whereas a transversal moment—perpendicular to the carbon chain—will be lowered. Wessels[2] following this line of thought, discussed that an equatorially placed halogen gives rise to a larger moment than a halogen in axial position. In the axial case the induced moment is nearly perpendicular to the carbon–halogen bond moment, so that the total moment will not be enhanced by induction whereas in the equatorial case the induction moment is nearly parallel to the carbon–halogen bond, resulting in an enhanced total moment.

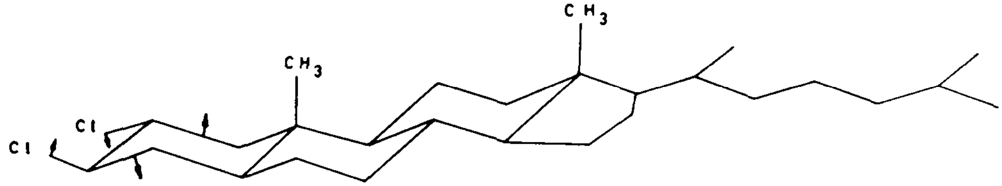

FIG. 2. Perspective view of the molecule of 2α,3β-dichloro-5α-cholestane. The torsion around C(2)–C(3) is suggested by arrows.

The moments observed for 3β[e]-chloro-5α-cholestane (Table 2) (2·30 D) and *trans*-1[e]-bromo-4-t-butylcyclohexane[2] (2·25 D) are significantly larger indeed than the normal values (2·04–2·12 D) found for secondary halogenides. Such an increase is not observed for the axial isomers (3α[a]-chloro-5α-cholestane: 2·05 D and *cis*-1[a]-bromo-4-t-butyl cyclohexane: 2·15 D).

The dipole moments of the diaxially substituted 5α,6β- and 2β,3α-dihalogeno-5α-cholestanes have values between 1·11 D and 1·40 D. We will discuss this phenomenon in a semiquantitative way taking the 2β,3α-dichloro-derivative as an example.

If the C—Cl bonds were strictly antiparallel the partial moments would cancel.*

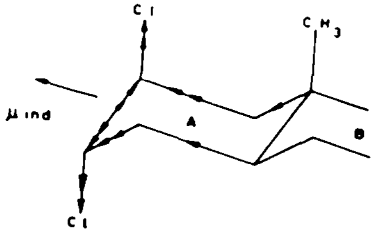

FIG. 3. Induction in ring A of 2β,3α-dichloro-5α-cholestane.

The angle between the two C—Cl bonds is found to be 157° (loc. cit. 12, 13). Taking 2·05 D as the partial moment for an axial C—Cl bond, a value of 0·82 D is calculated by vector addition. This moment thus considered to be due to the deviations of ring A from the ideal chair form, leaves a difference of ~ 0·5 D with the experimentally observed moment. The simplest description that accounts for this difference is by way

* It was checked that 5α-cholestane itself has zero dipole moment (calculated from the experimental data: ·18 D).

[22] F. C. de Vos, Thesis Leiden (1958).

[23] C. K. Ingold, *Structure and Mechanism in Organic Chemistry* p. 98; Cornell U.P., New York (1953).

of inductive effects: the two chlorine substituents induce extra moments in the ring system that do not cancel (Fig. 3) and that contribute significantly to the total molecular dipole moment.*

Comparable moments (1·0–1·2 D) have been observed for several fixed 1,2[a,a]-dihalogeno-cylcohexane derivatives by Hageman[24] and for 2,3[a,a]-dibromo-*trans*-decalin by v.d. Linden[8] and by Hückel[25] a.o. The deviation from the ideal chair form consisting in a flattening of the six-membered ring, occurs in all cyclohexane derivatives investigated[14,26,27] and the splaying outwards of the axial valencies is a general phenomenon in this type of molecules. On the ground of this geometry and on account of inductive effects the moments of fixed 1,2[a,a]-dihalogeno-cyclohexane derivatives and *vic.*[a,a]-dihalogeno-cholestanes may generally be expected to have values of 1·1 ± 0·5 D (cf. also loc. cit. 24).

In diequatorially substituted cyclohexanes the ideal value of the angle between carbon–halogen bonds is 70·5°. X-ray investigations on 2α,3β[e,e]-dichloro- and 2α,3β[e,e]-dibromo-5α-cholestane[12,14] reveal angles of 72° and 75°, respectively, corresponding to a flattening of the ring system. Assuming an angle of 73° and a moment of 2·30 D for an equatorial C—Cl bond, a moment of 3·70 D is calculated for 2α,3β-dichloro-5α-cholestane (observed: 3·43 D). In this type of compounds inductive effects again play an important role. The partial carbon–halogen moments will be decreased by mutual induction. Also, the moments induced in the ring by the chlorine atoms will influence, although not fully cancel each other. The resultant of these interactions reduces the total dipole moment to an extent of 0·3–0·6 D, as compared to the value calculated, using the "induction-increased" equatorial C—Cl bond moment of 2·30 D.

Moments in the range 3·3–3·6 D have been observed[2,3,7] for similar diequatorially substituted cyclohexane derivatives with vicinal halogen atoms. In none of these compounds an abnormally strong distortion of the cyclohexane ring is to be expected. Flattening of the ring system will cause an enlargement of the angle between 1,2-equatorial carbon-halogen bonds and therefore a reduction of the total moment. Possibly, compounds such as 4,4′-dimethyl-2α,3β-dihalogeno- and 2β-methyl-2α,3β-dihalogeno-5α-cholestane may, on account of strong distortion (flattening) of the ring system, have moments smaller than 3 D.

The main conclusion from this investigation is that the deviation of the 1,2 diaxial and diequatorial dihalogeno cyclohexane derivatives from the "theoretical" values is only partly accounted for by the geometry of the molecules (flattening of the 6-membered ring). In order to bring the values obtained by vector addition of partial moments in agreement with experimental data mutual interactions and inductive effects have also to be taken into consideration.

Acknowledgement—The authors wish to thank Mrs. Drs. M. J. M. de Kort-Schulpen and Drs. M. v. Vreedendaal for their help with the syntheses. The IR spectra were obtained through the co-operation of Dr. A. L. Koevoet. We are indebted to Dr. C. Altona for many helpful discussions.

* In contrast to compounds with a single axial halogen atom, induction can increase the total moment of derivatives with two vicinal, axial halogen atoms, because the resultant of the partial C—Cl bond moments (not strictly anti-parallel) is now in the same direction as the induction moment.

[24] H. Hageman, Thesis Leiden (1965).

[25] W. Hückel and H. Waiblinger, *Liebigs Ann.* **666**, 17 (1963).

[26] A. Davis and O. Hassel, *Acta Chem. Scand.* **17**, 1181 (1963).

[27] Ref. 12 and papers cited there.