Tetrahedron, 1960, Vol. 11, pp. 219 to 225. Pergamon Press Ltd. Printed in Northern Ireland

THE STRUCTURE OF 2,4-DIBROMOMENTHONE

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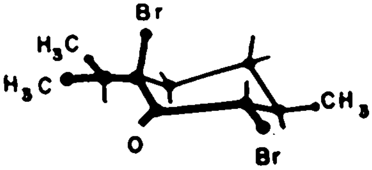
(*Received* 11 *July* 1960)

Abstract—A three-dimensional X-ray diffraction study has shown that the product obtained by bromination of D- or L-menthone is 2,4-dibromomenthone [2(a), 6(e)-dibromo-2(e)-isopropyl-5(e)methyl cyclohexanone]. The two Br atoms are *trans*, and the isopropyl and methyl groups are also *trans*. There are four molecules in the unit cell, which has symmetry $P2_12_12_1$ and dimensions $a = 13\cdot58$, $b = 13\cdot81$ and $c = 6\cdot25$ Å. One intermolecular Br . . . Br contact of 3·52 ± 0·01 Å occurs, a distance which is about 0·4 Å shorter than the van der Waals distance.

INTRODUCTION

Bromination of either D- or L-menthone in chloroform yields a corresponding dibromo derivative first thought to be[1] 1,4 dibromomenthone. Later studies[2–4] of the reactions of this dibromide led to the 2,4 positions as more probable. A recent review[5] of this evidence coupled with infrared spectra and nuclear magnetic resonance results raised a strong possibility that the compound is 2,2-dibromomenthone. The present X-ray diffraction study of a single crystal was undertaken to resolve this problem and to establish the stereochemistry, except for the absolute configuration, of dibromomenthone.



EXPERIMENTAL

Colorless needles, obtained from ethanol solution, were covered with a thin coating of cellulosic cement in order to prevent sublimation and decomposition during X-ray exposure. Weissenberg photographs of an approximately cylindrical single crystal about 0·2 mm in diameter were taken with the use of CuKα radiation. Visual estimates of the intensities were made with the aid of a calibrated intensity scale made from single reflections from a crystal of the same compound. A superimposed powder pattern from aluminum was used as a standard for the unit cell parameters. The density of the crystals was determined by suspending them in isopropyl iodide and adjusting the temperature to −22° until the last crystals just floated.[6]

There are 4 molecules of $C_{10}OH_{16}Br_2$ in an *ortho*-rhombic unit cell having dimensions $a = 13\cdot58 \pm 0\cdot03$, $b = 13\cdot81 \pm 0\cdot05$ and $c = 6\cdot25 \pm 0\cdot03$ Å. The density calculated from the X-ray measurements is 1·78 g cm^{-3}, only 0·01 g cm^3 less than the observed value. Systematic extinctions of h00 for h odd, 0k0 for k odd and 00l for l odd lead uniquely to the space group $P2_12_12_1$. Absorption corrections were made at a later stage of the investigation with $\mu = 90\cdot1$ cm^{-1} as the linear absorption coefficient. A total of 1204 different observed hkl reflections were measured representing 82 per cent

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[1] E. Beckman and H. Eickelberg, *Ber. Dtsch. Chem. Ges.* **29**, 418 (1896).
[2] G. Cusmano, *Chem. Zentr.* **1**, 976 (1914).
[3] O. Wallach, *Liebigs Ann.* **414**, 300 (1918).
[4] P. C. Guha and B. Nath, *Chem. Ber.* **70**, 931 (1937).
[5] M. A. Morgan, M.S. Thesis, University of Minnesota (1957).
[6] J. A. Wunderlich, *Bull. Soc. Fr. Min. Crist.* **81**, 220 (1958).

of the possible total on the levels of the reciprocal lattice which were photographed. All reflections were correlated to a single scale with the aid of Weissenberg photographs of the levels hKl for $0 \le K \le 9$ about the *b* axis, and photographs about the *c* axis of the levels hkl for $0 \le l \le 4$.

Structure determination and refinement

An early attempt to solve the structure from the *c* axis projection was abandoned because of overlap of atomic positions. The three-dimensional Patterson function yielded the Br positions, which were employed to determine the phase angles of the structure factors in a three-dimensional electron density map. A clearly recognizable structure for all atoms except for hydrogens was found for 2,4-dibromomenthone in spite of diffraction ripples especially around the Br atoms.

Three-dimensional least squares refinement of the data uncorrected for absorption, and assuming isotropic thermal parameters and neglecting off-diagonal terms was unsatisfactory, leading to $R = \Sigma||F_0| - |F_c||/\Sigma|F_0| \approx 0{\cdot}30$ or so. A three-dimensional difference map in which isotropic Br atoms were subtracted showed that the Br vibrations were strongly anisotropic, but further least squares refinement with the use of anisotropic temperature factors for Br atoms did not appreciably lower the value of *R*. Analysis of the individual F_0's and F_c's and the behavior of the thermal parameters indicated clearly that absorption corrections were needed. The long square needles were approximated by an equivalent cylinder for these corrections, and only the hk0, hk1, hk2, and hk3 data were felt to be of sufficiently high quality for further refinement. Successive refinement by least squares methods then reached values of $R = 0{\cdot}25$ for all reflections and $R = 0{\cdot}15$ for the hk0 data. Even so, some lack of convergence, due probably to omission of off-diagonal terms, was indicated by abnormally long $C_4—C_5$ and $C_8—C_9$ bond distances, but there also seemed to be special problems associated with the inclusion of unobserved reflections, and with reflections observed at high angles of scattering.

Final refinement was carried out on the I.B.M. 704 with all off-diagonal terms, with the aid of the program of Busing and Levy[7]. Only the 958 observed hkL reflections for which $0 \le L \le 7$ and $\sin\theta \le 0{\cdot}90$ were included. The final agreement factors of $r = \Sigma w(|F_0|^2 - F_c^2)^2/\Sigma w|F_0|^4 = 0{\cdot}168$, $R = 0{\cdot}166$ for all reflections and $R = 0{\cdot}125$ for the hk0 reflections are quite satisfactory. A summary of agreement is shown in Table 1.

The atomic parameters, shown in Table 2, have standard deviations of $\pm 0{\cdot}004$ Å for the *x*, *y*, or *z* parameters of Br, and of $\pm 0{\cdot}03$ for the *x*, *y*, or *z* parameters of C or O, as computed from the full matrix of the least squares analysis. Although the standard deviations of the isotropic temperature factors are $\pm 0{\cdot}5$ A^2, these parameters are very likely subject to large systematic errors owing mostly to the absorption problems in this study.

Discussion of the structure

The structure is shown in Fig. 1. As might be expected if the bromination proceeds through the preferred enol form, the two Br atoms are at the 2 and 4 positions. The well known stereochemical details of methone itself are confirmed: the ring is a chair form, and the methyl and isopropyl groups are in equatorial positions. The Br at C_2 is also equatorial, but it is quite interesting that the Br at C_4 is in the axial position.

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[7] W. R. Busing and H. A. Levy, Report No. 59-4-37, Oak Ridge National Laboratory (1959).

TABLE 1. VALUES OF *R* $\Sigma||F_o| - |F_c||/\Sigma|F_o|$ FOR DIFFERENT CLASSES OF REFLECTIONS

	R	Range of sin θ	*R*	Number of reflections
All planes	0·17	0·00–0·40	0·14	112
h + k + l odd	0·17	0·40–0·50	0·14	94
h + k odd	0·17	0·50–0·60	0·17	146
k + l odd	0·17	0·60–0·65	0·16	89
h + l odd	0·17	0·65–0·70	0·17	96
h odd	0·16	0·70–0·75	0·18	100
k odd	0·17	0·75–0·80	0·19	120
l odd	0·17	0·80–0·85	0·21	111
hk0	0·12	0·85–0·90	0·18	90
0kl*	0·21			
h0l*	0·17			

* Data somewhat incomplete because only observed reflections hkL for 0 ≤ L ≤ 7 and for sin θ ≤ 0·90 are included in this table.

TABLE 2. ATOMIC PARAMETERS*

Atom	*x*	*y*	*z*	Temperature parameters	
Br_1	0·0858	0·2655	0·5004	β_{11}	0·0040
				β_{22}	0·0016
				β_{33}	0·0211
				β_{12}	0·0006
				β_{13}	0·0018
				β_{23}	0·0045
Br_2	−0·0510	0·0636	0·4096	β_{11}	0·0083
				β_{22}	0·0046
				β_{33}	0·0195
				β_{12}	0·0037
				β_{13}	0·0004
				β_{23}	0·0040
C_1	0·038	0·052	0·799	B	1·0 A^2
C_2	0·007	0·051	0·565		1·3 A^2
C_3	0·107	0·062	0·545		2·5 A^2
C_4	0·151	0·156	0·649		0·8 A^2
C_5	0·120	0·150	0·875		1·8 A^2
C_6	0·001	0·139	0·918		2·2 A^2
C_7	0·147	0·038	0·836		2·5 A^2
C_8	0·254	0·155	0·628		1·7 A^2
C_9	0·288	0·164	0·379		2·4 A^2
C_{10}	0·307	0·239	0·754		4·1 A^2
O	0·156	0·001	0·484		4·6 A^2

* *x*, *y* and *z* are expressed as fractions of *a*, *b*, and *c* respectively.

Models suggest that the H . . . H interactions may be serious if the isopropyl groups became axial, although when Br is axial there are some Br . . . H contacts which appear to be somewhat shorter than the sum of van der Waals radii. However, short intramolecular Br . . . H interactions may be less drastic than short H . . . H interactions.

We suspect that the equatorial preference of isopropyl may be lost in the enolic intermediate, and hence the resulting preference of Br for the axial position at C_4 is a question of preferred stability of the final arrangement rather than preservation of the initial stereochemistry about C_4, but we cannot be sure that another mechanism may not also be involved. The complete systematic name of this compound is thus 2(a), 6(e)-dibromo-2(e)-isopropyl-5(e)-methyl cyclohexanone.

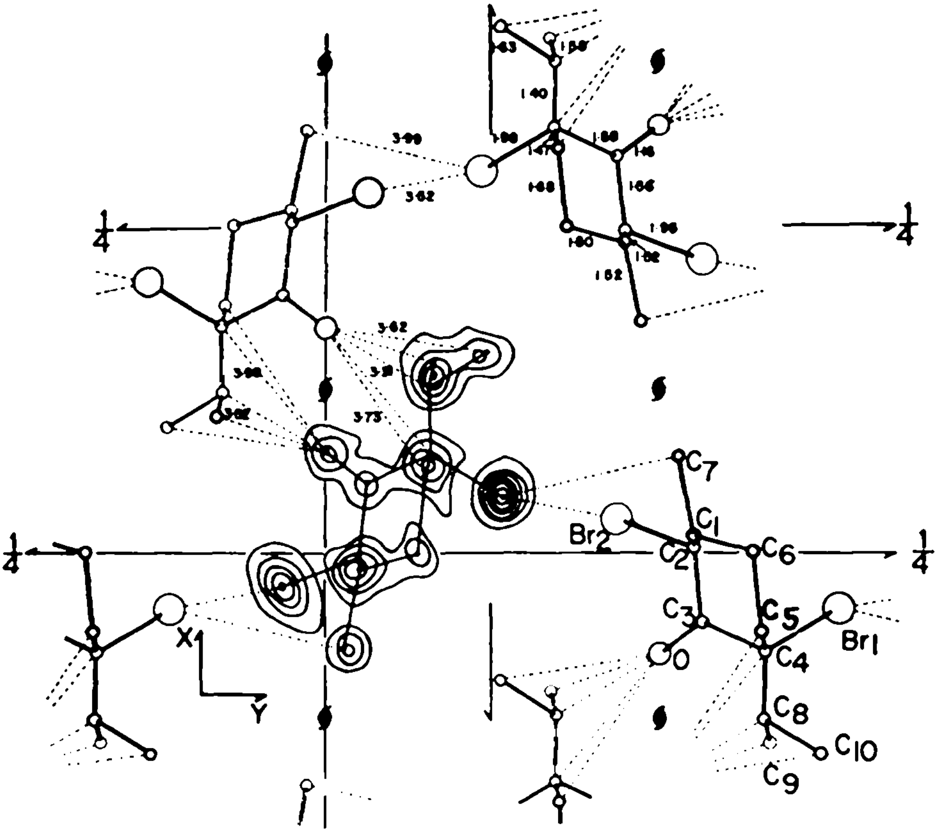

Fig. 1. The molecular arrangement in the crystal structure of 2,4 dibromomenthone. Contours are shown for the projection data (hk0) only at contour levels 0, 5, 10 . . . for C and O atoms and at levels of 0, 20, 40, . . . for Br in units of electrons/Å^2.

Bond distances and angles, shown in Table 3, have fairly high standard deviations of $\pm 0{\cdot}04$ Å for C—C, $\pm 0{\cdot}04$ for C — O, $\pm 0{\cdot}006$ Å for Br . . . Br, $\pm 0{\cdot}03$ Å for C—Br, $\pm 2{\cdot}5°$ for <C—C—C or <C—C—Br and $\pm 3{\cdot}3°$ for <C—C—O. The scatter of bond distances about the values expected upon comparison with other studies[8] is large, but within three times the standard deviations. Thus C—Br distances tend to average[8] around 1·94 Å, but distances as long as 1·99 and 2·10 Å have been found in triphenylmethyl bromide[9] and in 5′-bromo 5′-deoxythimidine,[10] respectively. Also, slightly

[8] *Tables of Interatomic Distances and Configuration in Molecules and Ions.* Special Publication No. 11 of the Chemical Society, London (1948).

[9] C. Stora, *C. R. Acad. Sci., Paris* **236**, 1661 (1953); *Bull. Soc. Chim. Fr.* **20**, 1059 (1953).

[10] M. Huber, *Acta Cryst.* **10**, 129 (1957).

short C—O distances of 1·15 Å in CCl_3CHO[11] and of 1·14 Å in halogenated *p*-quinones[12] are not unreasonable[13] and compare favorably with our value of 1·16 Å, but we cannot claim that a slight shortening is significant.

Van der Waals contacts less than 4 Å are shown in Fig. 1. The shortest C . . . O distance of 3·31 Å between C_8 and O is in reasonable agreement with an expected[13] contact of about 3·4 Å between CH_2 and O. The most interesting feature of the intermolecular interactions is the Br_1 . . . Br_2 distance of 3·52 ± 0·006 Å, which is approximately 0·4 Å shorter than the expected van der Waals contact[13] of 3·9 Å. Such short intermolecular halogen-halogen contacts are not uncommon in crystals, but examples in substituted organic molecules of intermediate complexity are somewhat rare. In the Br_2 crystal[14] the three contacts of 3·30, 3·30 and 3·75 Å are all less than the expected van der Waals contact. Similar shortenings have been found in Cl_2[15] and in I_2[16,17]

TABLE 3a. INTERATOMIC DISTANCES
All distances are in Å units

Br_1—C_4	1·98	C_4—C_5	1·47
Br_2—C_2	1·95	C_4—C_8	1·40
C_1—C_2	1·52	C_5—C_6	1·68
C_1—C_6	1·50	C_8—C_9	1·59
C_1—C_7	1·52	C_8—C_{10}	1·63
C_2—C_3	1·56	O—C_3	1·16
C_3—C_4	1·58		

TABLE 3b. BOND ANGLES

C_2—C_1—C_6	113°	C_3—C_4—C_8	109°
C_2—C_1—C_7	115°	C_3—C_4—Br_1	105°
C_6—C_1—C_7	111°	C_5—C_4—C_8	112°
C_1—C_2—C_3	110°	C_5—C_4—Br_1	111°
C_1—C_2—Br_2	114°	C_8—C_4—Br_1	119°
C_3—C_2—Br_2	110°	C_4—C_5—C_6	116°
C_2—C_3—C_4	115°	C_1—C_6—C_5	109°
C_2—C_3—O	122°	C_4—C_8—C_9	112°
C_4—C_3—O	122°	C_4—C_8—C_{10}	113°
C_3—C_4—C_5	104°	C_9—C_8—C_{10}	107°

The Br . . . Br contacts of 3·77 Å in the *p*-dibromobenzoate diester of iresin[18] are significantly shorter than the van der Waals contact, and are an important feature of the molecular packing in the crystal; indeed, here the thermal vibrations in the crystal are apparently comparatively high. An unusually short Br . . . Br contact of 3·32 Å in triphenylmethyl bromide[9] has been attributed to partial ionization of the C—Br bond. The 3·44 Å Cl . . . Cl contacts in 2-amino-4,6 dichloropyrimidine[19] have been attributed to hydrogen bonding, not present in our crystal. On the other hand,

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[11] C. Degard, *Bull. Soc. Roy. Liège* 7, 36 (1938).

[12] L. L. Boricelli and O. Bastiansen, *Tidsskr. Kjemi Berg.* 9, 3 (1949).

[13] L. Pauling, *Nature of the Chemical Bond* (3rd Ed.). Cornell University Press, New York (1960).

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[17] I. I. Kitaigorodskii, V. Khotsyanova and M. Struchkov, *Zh. fiz. Khim.* 27, 780 (1953).

[18] M. G. Rossmann and W. N. Lipscomb, *Tetrahedron* 4, 275 (1958).

[19] C. J. B. Clews and W. Cochran, *Acta Cryst.* 1, 4 (1948).

the short I--I distance of 3·90 Å in $P_4S_3I_2$[20], the Cl . . . Cl distance of 3·46 Å in *p*-dichlorobenzene[21] and the Br . . . Br distance of 3·76 Å in *p*-dibromobenzene[22] are further examples of distances less than the usual van der Waals contact. These comparisons are interesting and probably significant, but we feel that any detailed comparison of intermolecular contacts in organic crystals should include corrections for the crystal vibrations which are frequently a few to several tenths of an Ångstrom. In particular, we should like to be able to distinguish between the different mechanisms of shortening, such as (a) stronger binding forces in ionic and hydrogen bonded crystals as compared with molecular crystals, (b) effects associated specifically with different thermal amplitudes of crystal vibrations, rarely reliably corrected for, (c) specific charge transfer and valence interactions, probably not completely distinguishable from (a), but perhaps associated with specific electronic transitions in the complex, and, finally, (d) van der Waals contacts which are different depending upon the direction of approach and relative orientations of bonds and lone pair orbitals. The present data, though as yet insufficient, gives us some hope that these various effects can be sorted out, or that the questions can be reformulated so that these abnormal shortenings can be understood.

The C_4—Br_1 . . . Br_2 bond angle of 155·9° and the C_2·-Br_2 . . . Br_1 bond angle of 161·4° are interesting aspects of this abnormally short Br_1 . . . Br_2 distance. These extraordinarily large angles are comparable to the larger of the two X—X . . . X angles of 169° and 105° which occur in solid X_2 crystals, where X is Br[14] or I.[16,17] The meaning of these angles is not clear, even as to whether increased attraction, decreased repulsion or both are occurring, but a study of the nuclear quadrupole coupling constants in the dibromomenthone crystal would be of considerable interest.

The intramolecular Br_2 . . . O distance is only 2·88 Å, considerably shorter than the expected van der Waals contact of 3·35 Å. Such shortenings are quite common, but it is most interesting that the Br_2 atom is only 0·25 Å out of the plane defined by C_2, C_4 and O atoms, in the unexpected direction that C=O just fails to be staggered relative to the two bonds from C_2 to Br_2 and H. A distortion of this order of magnitude is anticipated because of the effect of the expected near planarity of the $C_2C_3C_4O$ group. It is only remarkable that steric interactions between O and Br_2 are not more important, and that the distortion is not greater. It may well be that there are compensating attractive interactions between O and Br_2, somewhat similar to those in 1,4 dioxane-chlorine,[23] an effect which may possibly show up in a charge transfer spectrum.

It seems easiest to understand the bromination reaction as two steps in which the first Br goes into the axial position on C_4 because of the relatively poor steric situation if the isopropyl group were axial. The second Br very probably goes into the equatorial position preferentially to avoid a steric problem with Br_1, already axial.

If α-bromocyclohexanone is taken[5] as a model compound for a comparison of the H^1 resonance spectrum it is to be noted that the H atom on the α-C atom is equatorial[24] in this compound, whereas the corresponding H atom of 2,4-dibromomenthone

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[20] D. A. Wright and B. R. Penfold, *Acta Cryst.* **12**, 455 (1959).

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[24] E. J. Corey, *J. Amer. Chem. Soc.* **75**, 2301 (1953); see also N. L. Allinger, J. Allinger and N. A. LeBell, *Ibid.* **82**, 2926 (1960).

is axial. A shift from about 152·5 c.p.s. (equatorial) to about 185 c.p.s. (axial) at 40 m.c. might be anticipated,[25] but it is not known whether this effect was taken into account.[5] Further substantiation of this difference between 2-bromocyclohexanone and 2,4-dibromomenthone is that the carbonyl infrared absorption is shifted[5] from about 1701 cm^{-1} in L-menthone to about 1721 cm^{-1} in 2,4 dibromomenthone, a shift suggesting approximate coplanarity of CO and CBr (equatorial). This large shift is to be compared with the relatively small shift[24] of only 4 cm^{-1} when cyclohexanone is converted to 2-bromocyclohexanone, which has an axial Br atom. Finally, with respect to the recent chemical evidence,[5] the earlier synthesis[26] of 4-bromomenthone could not be repeated, but monoiodomenthone is known.[27]

Acknowledgements—We wish to thank Professor S. W. Fenton for helpful discussions and for the chemical sample, and we acknowledge support of this research by the Air Force Office of Scientific Research and the National Institutes of Health.

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