Acta Cryst. (1971). B**27**, 1925

The Crystal Structure of 9,10-Bis(chloromethyl)anthracene

By Eric J. Gabe

Department of Energy, Mines and Resources, Ottawa 4, *Ontario, Canada*

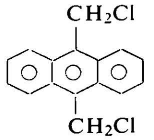
and Jenny Pickworth Glusker

The Institute for Cancer Research, Fox Chase, Philadelphia, Pennsylvania 19111, *U.S.A.*

(*Received* 20 *November* 1970)

9,10-Bis(chloromethyl)anthracene, $C_{16}H_{12}Cl_2$, crystallizes in the monoclinic space group $P2_1/a$ with unit-cell dimensions $a=16{\cdot}658$, $b=4{\cdot}5000$, $c=8{\cdot}5327$ Å, $\beta=103{\cdot}16°$, $Z=2$, observed density 1·45 g.cm^{-3}, calculated density 1·47 g.cm^{-3}. The molecule has a center of symmetry required by the space group. Intensities of 1837 reflections were measured on an automatic diffractometer with Mo $K\alpha$ radiation. Of these reflections, 1315 were above the threshold of observation. The structure was solved by heavy-atom methods. All hydrogen atoms were located from a difference map. Atomic parameters were refined by full-matrix least-squares methods to an R value of 0·043 for the observed data. The molecule is not quite planar, but shows a slight tendency to a boat-chair-boat conformation, the buckling being due to steric hindrance by adjacent groups on the anthracene nucleus. The chlorine atom of a chloromethyl group points towards one carbon atom of an approximately double bond in an outer ring of the anthracene moiety of another molecule.

Antitumor activities of several alkylating agents that are derivatives of polycyclic hydrocarbons have been investigated by Peck, O'Connell & Creech (1970) and Peck & O'Connell (1970). They found that 9,10-bis(chloromethyl)anthracene, for which the formula is



, is an effective agent against Ehrlich ascites tumors in ICR Swiss mice. Therefore, in spite of the simplicity of the compound, a structure analysis was made to determine the interatomic distances with high accuracy, the extent to which the atoms of the anthracene moiety deviate from an idealized planar system, and the manner in which the molecules pack in the crystalline state. These data will then be compared with those from other active antitumor agents that are anthracene derivatives and that are presently being studied.

Table 1. *Parameters of atoms for* 9,10-*bis*(*chloromethyl*)*anthracene*

Positional parameters are expressed as fractions of cell edges. Anisotropic temperature factors are expressed as

$$\exp\left[-(h^2b_{11}+k^2b_{22}+l^2b_{33}+2hkb_{12}+2hlb_{13}+2klb_{23})\right].$$

Isotropic temperature factors for hydrogen atoms are of the form $\exp(-B\sin^2\theta/\lambda^2)$, and values of B are given in Å^2. Standard deviations, determined from the inverted full matrices, are listed below each parameter with respect to the last decimal place given. To avoid confusion in reading the table, the same number of decimal places is listed for a given type of parameter although, because the cell lengths vary considerably, the standard deviations are large for some.

	x	y	z	10^5b_{11}	10^5b_{22}	10^5b_{33}	10^5b_{12}	10^5b_{13}	10^5b_{23}
Cl	0·08882 (2)	0·25465 (12)	0·12679 (4)	456 (2)	6347 (29)	1261 (6)	−143 (8)	378 (3)	−15 (14)
C(1)	0·04024 (13)	0·07803 (43)	0·27193 (21)	436 (9)	4498 (112)	1237 (27)	−71 (28)	308 (13)	−69 (49)
C(2)	0·02004 (9)	0·29810 (34)	0·38674 (16)	380 (6)	2868 (92)	1052 (20)	−189 (21)	281 (9)	43 (39)
C(3)	0·07910 (9)	0·36952 (35)	0·52858 (17)	329 (6)	3462 (88)	1110 (22)	−127 (20)	230 (10)	293 (38)
C(4)	0·16060 (9)	0·24730 (48)	0·56186 (20)	396 (7)	4666 (102)	1544 (27)	0 (31)	294 (12)	116 (61)
C(5)	0·21562 (11)	0·30967 (48)	0·70124 (22)	337 (8)	6232 (153)	1893 (33)	15 (28)	172 (13)	864 (60)
C(6)	0·19453 (12)	0·49644 (47)	0·81629 (23)	407 (9)	6223 (137)	1421 (30)	−351 (29)	46 (13)	436 (58)
C(7)	0·11938 (11)	0·62526 (42)	0·78964 (19)	447 (8)	4649 (109)	1095 (25)	−273 (25)	182 (12)	67 (44)
C(8)	0·05840 (9)	0·56888 (36)	0·64355 (16)	346 (6)	3170 (89)	1001 (21)	−200 (21)	215 (10)	247 (38)

				B	Attached to
H(1)	−0·0074 (9)	−0·0168 (39)	0·2023 (17)	5·2 (4)	C(1)
H(2)	0·0803 (9)	−0·0690 (39)	0·3187 (17)	5·5 (4)	C(1)
H(3)	0·1763 (8)	0·1164 (35)	0·4858 (17)	5·1 (4)	C(4)
H(4)	0·2675 (9)	0·2209 (41)	0·7178 (17)	7·1 (4)	C(5)
H(5)	0·2344 (9)	0·5360 (38)	0·9131 (18)	5·9 (4)	C(6)
H(6)	0·1047 (8)	0·7652 (34)	0·8695 (16)	4·5 (3)	C(7)

Experimental

Large dark-yellow needles of 9,10-bis(chloromethyl) anthracene were provided us by Dr Peck of The Institute for Cancer Research, Philadelphia, Pa. They were prepared by recrystallizing the commercial product (Eastman Organic Chemicals) three times from benzene.

The crystals of the compound, formula $C_{16}H_{12}Cl_2$, F.W. 275·186, are monoclinic. Cell dimensions were derived by the method of least-squares from angular data recorded automatically (Busing, 1970), on 28 reflections in the 2θ range 40–50° with Mo $K\alpha_1$ radiation [$\lambda(K\alpha_1)=0{\cdot}70926$ Å] (Gabe, 1970*a*). The values obtained were $a=16{\cdot}658\pm2$, $b=4{\cdot}5000\pm5$, $c=8{\cdot}5327\pm8$ Å, $\beta=103{\cdot}16\pm4°$, $V=622{\cdot}8\pm2$ Å^3. The density, D_m, was measured by flotation in potassium iodide solution as 1·45 g.cm^{-3} and calculated, for $Z=2$, as $D_x=1{\cdot}47$ g.cm^{-3}. The space group is $P2_1/a$ from the systematic absences $h0l$ with h odd and $0k0$ with k odd. This implies that there is a center of symmetry in the molecule.

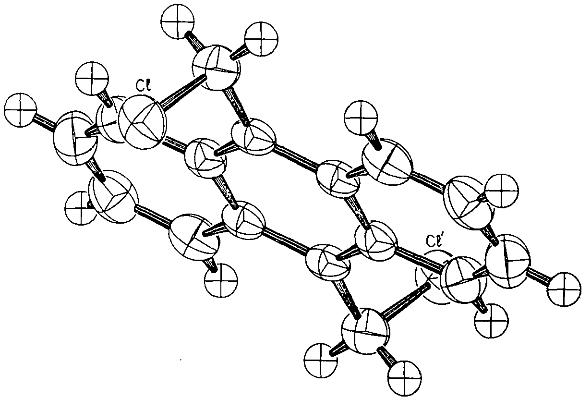


Fig. 1. Thermal ellipsoids in one molecule.

Table 2. *Observed and calculated structure factors*

Each entry lists, in order, h, $|F_{\rm obs}|$, $F_{\rm calc}$ and $\sigma|F_{\rm obs}|$. Unobserved reflections are not included; statistics on them are given in the text.

Three-dimensional data were collected with Mo $K\alpha$ radiation, monochromatized with a graphite crystal on an automatic diffractometer (Gabe, 1970*a*) with the $\theta/2\theta$ scan technique. The crystal used was $0{\cdot}17\times0{\cdot}27\times0{\cdot}47$ mm in size. All reflections in the range $0° < 2\theta \le 60°$ were scanned with a range in 2θ of 1·1° before the $K\alpha_1$ peak, 1·3° after the $K\alpha_1$ peak, and a dispersion factor of $0{\cdot}5\tan\theta$. Background counts of 20 seconds were made on both sides of each peak. The crystal was mounted on an arcless goniometer head with no rational direction parallel to the φ axis to minimize multiple reflection. The internal consistency of the data, as measured from several Friedel related pairs of reflections, is approximately 2% in intensity.

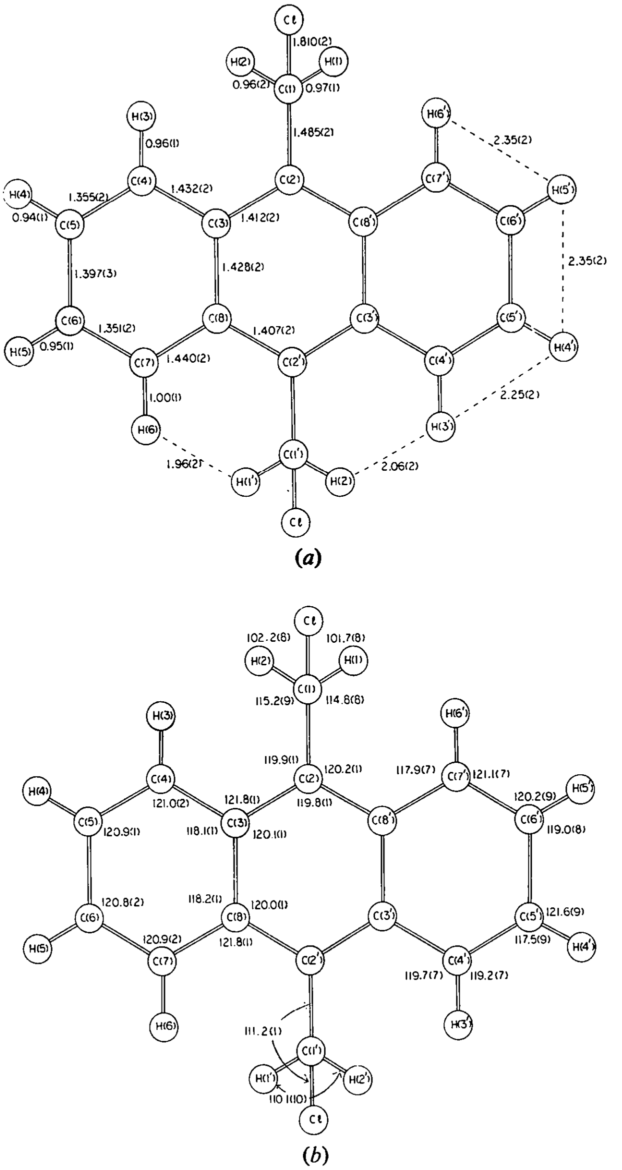


Fig. 2. Bond distances (*a*) and interbond angles (*b*) in 9,10-bis(chloromethyl)anthracene.

Of the 1837 reflections measured, 1315 were considered to be observed on the basis of the test $I \ge 1{\cdot}645\ \sigma(I)$. The values assigned to $|F_{\rm obs}|$ then corresponded to $(I)/3$ for 'unobserved' reflections. Absorption corrections ($\mu = 4{\cdot}94$ cm^{-1}) were applied (Gabe, 1970*b*). The data were corrected for Lorentz and polarization factors and put on an absolute scale by means of a Wilson plot.

Structure determination and refinement

The structure was solved by the location of the chlorine–chlorine vectors in the Patterson map, and by an electron density map phased on this heavy atom. The *R* value for the initial trial structure was 0·32 which was reduced to 0·15 by three cycles of isotropic least-squares. At this stage, all hydrogen atoms were located on a difference map. The structure was then refined by five cycles of anisotropic least-squares with isotropic hydrogen atoms to a final *R* value of 0·043 for the observed data. Of the 522 'unobserved' reflections, 141 have values of $|F_{\rm calc}|$ greater than the value assigned to $|F_{\rm obs}|$ described above and of these, 6 had values of $|F_{\rm calc}|$ between 2 and 3 times the assigned value; none was larger than these. From a comparison of observed and calculated structure factors for intense low-order reflections, no extinction correction was considered necessary. The refined atomic parameters are listed in Table 1. A listing of observed and calculated structure factors is given in Table 2. The thermal motion is illustrated in Fig. 1.

Computations

All calculations were performed on a UNIVAC 1108 with the *X-ray* 67 system of Stewart (1967). The least-squares program (*ORFLS*) uses a full matrix and minimizes the quantity $\sum w(|F_{\rm obs}|-|F_{\rm calc}|)$. The weights, *w*, used were based on counting statistics and instrumental uncertainties. The program used to calculate the molecular geometry was written by A. Caron and H. L. Carrell. The atomic scattering factors were taken from *International Tables for X-ray Crystallography* (1962) except for those for hydrogen atoms which were the values by Stewart, Davidson & Simpson (1965). Fig. 1 was drawn with program *ORTEP* (Johnson, 1965). The program to test for rigid-body motion was provided by Trueblood (1970).

Discussion

The bond lengths and angles in the molecule of 9,10-bis(chloromethyl)anthracene are shown in Fig. 2 with estimated standard deviations. The bonds C(4)–C(5) and C(6)–C(7) most nearly approach a double bond (1·355 and 1·351 Å respectively). Bond lengths in the central ring are longer (1·407–1·428 Å) than expected for a truly aromatic system and there is some double-bond character to the bond C(1)–C(2) (1·485 Å) which is shorter than the value of 1·506 Å in 1,8-dichloro-9-methylanthracene (Dellaca, Penfold & Robinson, 1969). There is a slight shortening of the bond C(5)–C(6) compared with that for anthracene (Cruickshank, 1956) and a lengthening of the bonds C(2)–C(3) and C(2)–C(8′). Bond C(1)–Cl is longer (1·810 Å) than expected for a paraffinic C–Cl bond (1·77 Å). This lengthening of the C–Cl bond may be correlated with the shortening of the C(1)–C(2) bond mentioned above. This may indicate that there is a partial polarization of the C–Cl bond, a possibility consistent with the fact that this compound is known to be a good alkylating agent.

Torsion angles down the C(1)–C(2) bond are shown in Fig. 3. It can be seen that, though the molecular conformation is one that will bring the chlorine atom as far as possible from the anthracene plane, in a similar manner to the $-CH_3$ group in 9-bromo-10-ethylanthracene (Hauw, 1960), this arrangement is not symmetrical. It is found that the chlorine atom lies slightly nearer to the C(3) rather than the C(8′) side of the molecule. The distances from the chlorine atom to aromatic hydrogen atoms are Cl–H(3) = 3·14 Å, Cl–H(6′) = 3·23 Å and from aliphatic to aromatic hydrogen atoms H(2)–H(3) = 2·06 Å, H(1)–H(6′) = 1·96 Å. This lack of symmetry may result from the different packing around H(1) and H(2), the latter being only 2·83 Å from H(4) of another molecule. This H(4) is also 2·81 Å from H(3) in the original molecule. Alternatively, and more probably, it could result from the interaction of the chlorine atom with C(7) of another molecule.

The molecule itself is not planar; that is, this molecule exhibits, to a slight degree, some of the problems of an overcrowded molecule. Deviations of atoms from the best plane through the molecule are shown in Å in Fig. 4. The tendency to a boat-chair-boat arrangement, to keep the atoms of the chloromethyl group and adjacent hydrogen atoms as far apart as possible, is shown in Fig. 5 which overemphasizes distortions from planarity. As shown in Fig. 4 the aromatic hydrogen atoms are displaced from the molecular plane so that each $\mathrm{C}\overset{\mathrm{CH}}{\diagup\;\;\diagdown}\mathrm{C}$ system is planar. Thus, H(3), H(5), C(2) and C(1) are most distorted from the plane, the latter by 0·13 Å, which increases the deviations of H(1) and H(2) of the $-CH_2Cl$ group from the plane of the ring system. Deviations shown in Fig. 4 are in similar directions but approximately twice the magnitude of those found for anthracene itself (Cruikshank, 1956).

Results of a rigid-body analysis are given in Table 3. The maximum librational amplitude is 2·96°, and the effect on bond lengths is small and has not been included in Fig. 2. The values are similar but not equal to those found for anthracene (Cruickshank, 1957), where the root-mean-square amplitudes of translational oscillation in the directions of the molecular axes are 0·20, 0·16 and 0·16 Å and the amplitudes of the angular oscillations are 3·8, 2·2 and 3·1°.

In the packing of molecules in the crystal it is found that the aromatic ring systems do not overlap, but the $-CH_2Cl$ group overlays an adjacent ring so that the chlorine atom is nearest to C(7) of another ring

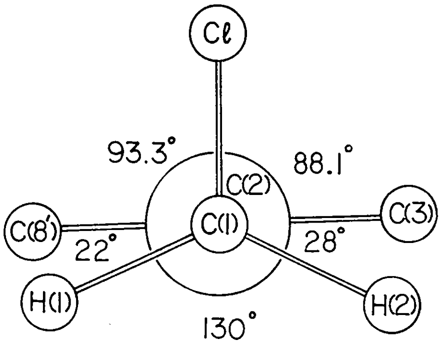


Fig. 3. Torsion angles down the C(1)–C(2) bond.

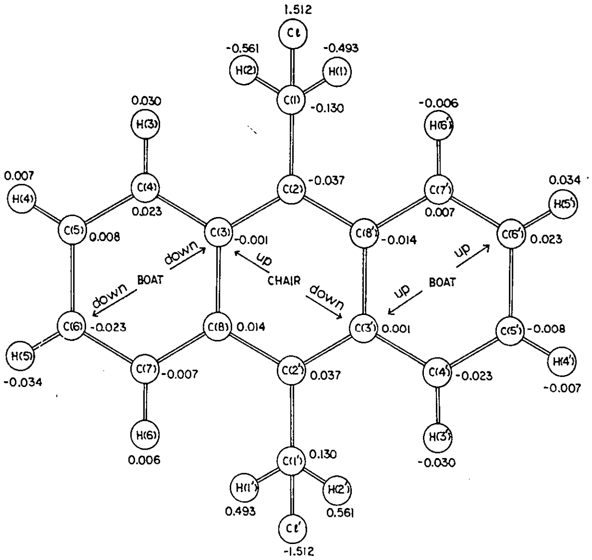


Fig. 4. Deviations of atoms from the best plane through the molecule (Å).

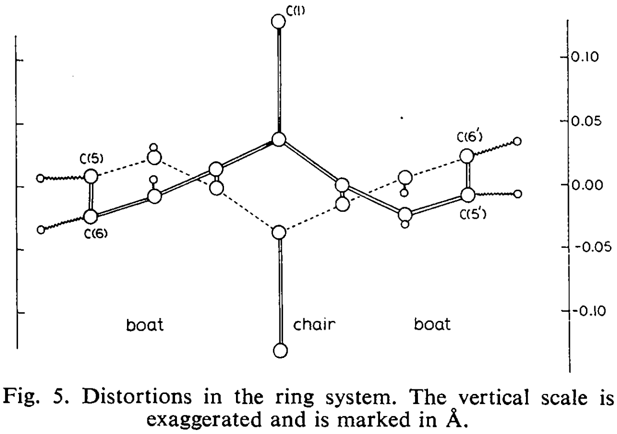


Fig. 5. Distortions in the ring system. The vertical scale is exaggerated and is marked in Å.

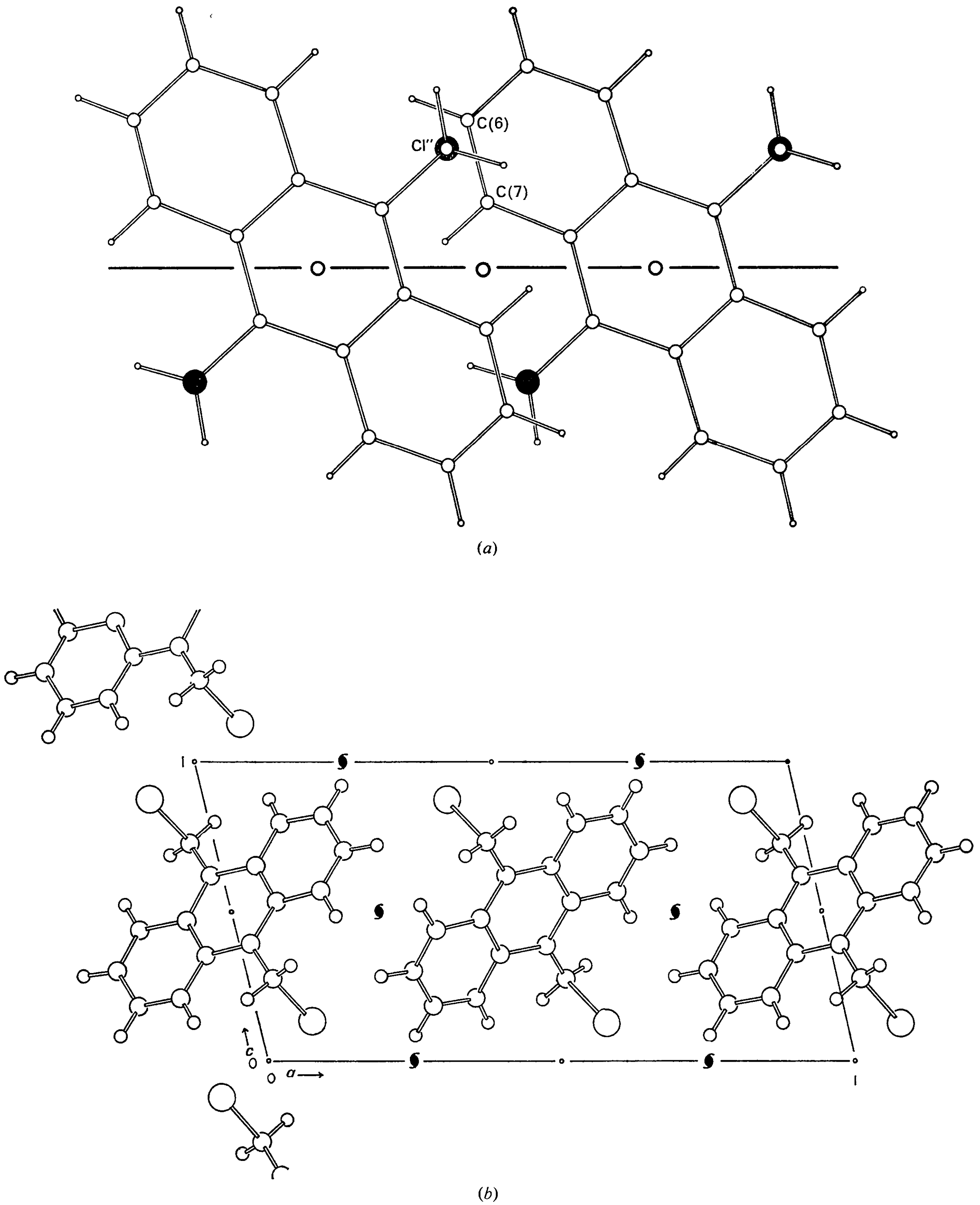


Fig. 6. (*a*) Packing of molecules about centers of symmetry along the *c* axis viewed down the C(1)–Cl bond, (*b*) packing in the unit cell.

Table 3. *Results of rigid-body analysis of thermal parameters**

The translational tensor **T**, represents the translational motion of the center of mass of the molecule and the librational tensor, **L**, describes the libration of the molecule as a whole.

Direction cosines of the eigenvectors are relative to **a**, **b** and **c*** respectively. The molecule is at a centrosymmetric site; thus, **S** is identically zero. The root-mean-square difference between observed and calculated values of $U_{ij}=0{\cdot}0030$ Å^2. Estimated standard deviations of $U_{ij}=0{\cdot}0032$ Å^2. Differences between individual U_{ij} values derived from the temperature factors listed in Table 1 and those calculated for a rigid body are within 3σ of the observed values.

	Eigenvalues	Eigenvectors (direction cosines)		
Translational: tensor, **T**	0·217 Å	0·8676	−0·3131	0·3863
	0·197	0·1043	−0·6407	−0·7607
	0·143	0·4858	0·6994	−0·5243
Librational: tensor, **L**	2·95°	−0·1578	−0·0695	−0·9850
	2·81	−0·7894	−0·5976	0·1402
	2·34	−0·5991	0·7992	0·0488

* Calculated by the method of Schomaker & Trueblood (1968).

system. This is illustrated in Fig. 6 which is a view of a pair of molecules down the C(1)–Cl bond and shows that this points toward the bond C(6)–C(7) which is almost a double bond and is sloped so that the chlorine atom is closest to C(7). This situation may indicate a slight interaction between the chlorine atom and this bond, as if an incipient alkylation is occurring. The distance Cl–C(7) is 3·46 Å compared with a Cl–C(6) distance of 3·66 Å. This packing is reminiscent of the interaction between a silver cation and a double bond in anthracene (Hall & Amma, 1969) although in the case of 9,10-bis(chloromethyl)anthracene the distance of 3·46 Å approximates the sum of the van der Waals radii of carbon and chlorine; in the silver complex the analogous distances are much shorter.

This research was supported in part by grants CA-10925, CA-06927, and RR-05539 from the National Institutes of Health, U.S. Public Health Service, and by an appropriation from the Commonwealth of Pennsylvania.

We wish to thank Mr J. F. Rowland, Dr H. L. Carrell, and Miss Joyce Dargay for assistance with the computations.

References

Busing, W. (1970). *Crystallographic Computing*, pp. 319–330. Edited by F. R. Ahmed. Munksgaard: Copenhagen.

Cruickshank, D. W. J. (1956). *Acta Cryst.* **9**, 915, 1005.

Cruickshank, D. W. J. (1957). *Acta Cryst.* **10**, 470.

Dellaca, R. J., Penfold, B. R. & Robinson, W. T. (1969). *Acta Cryst.* B**25**, 1589.

Gabe, E. J. (1970*a*). Mines Branch Research Report R219, Department of Energy, Mines and Resources, Ottawa, Canada.

Gabe, E. J. (1970*b*). American Crystallographic Association Summer Meeting, Paper A4, Ottawa, Canada.

Hall, E. A. & Amma, E. L. (1969). *J. Amer. Chem Soc.*. **91**, 6538.

Hauw, C. (1960). *Acta Cryst.* **13**, 100.

International Tables for X-ray Crystallography (1962), Vol. III, p. 201. Birmingham: Kynoch Press.

Johnson, C. K. (1965). *ORTEP, A Fortran Thermal-Ellipsoid Plot Program for Crystal Structure Illustrations.* Report ORNL-3794. Oak Ridge National Laboratory, Oak Ridge, Tennessee.

Peck, R. M. & O'Connell, A. P. (1970). *J. Medic. Chem.* **13**, 919.

Peck, R. M., O'Connell, A. P. & Creech, H. J. (1970). *J. Medic. Chem.* **13**, 284.

Schomaker, V. & Trueblood, K. N. (1968). *Acta Cryst.* B**24**, 63.

Stewart, J. M. (1967). *X-ray 67 Program System for X-ray Crystallography.* Technical Report 67–58, Computer Science Center, University of Maryland.

Stewart, R. F., Davidson, E. R. & Simpson, W. T. (1965). *J. Chem. Phys.* **42**, 3175.

Trueblood, K. N. (1970). *TLS* program from UCLA.