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# The Crystal Structure of 9-Chloromethylacridine Hydrochloride

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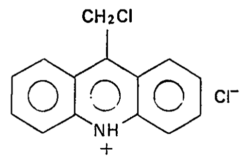
Crystals of $C_{14}H_{11}Cl_2N$ are triclinic, space group $P\bar{1}$, with $Z=2$, $a=9{\cdot}979$ (3), $b=9{\cdot}901$ (2), $c=8{\cdot}680$ (1) Å, $\alpha=107{\cdot}97$ (2), $\beta=118{\cdot}12$ (2), $\gamma=106{\cdot}94$ (2)°, $V=614{\cdot}3$ (2) Å$^3$, $D_x=1{\cdot}428$, $D_m=1{\cdot}415$ g cm$^{-3}$. The structure has been determined from three-dimensional X-ray diffraction data by the Patterson method and refined by full-matrix least-squares calculations to a final $R$ of 0·049 for 1963 observed reflections. There is a hydrogen bond [2·991 (1) Å] from the protonated ring nitrogen atom to the chloride ion. The molecules stack in planes 3·4 Å apart throughout the crystal.

## Introduction

A crystallographic study of several acridine derivatives, including some that are mutagens, has been in progress in this laboratory (Glusker, Berman & Carrell, 1972). Some of these compounds are believed to intercalate in DNA (Lerman, 1964). They may also interact with polymerases, and certain bromomethylbenzo[*c*]-acridines have been reported to inhibit DNA and RNA synthesis (Daudel, Gachelin, Delcey, Jacquignon, Buu Hoi & Queval, 1971/1972). This study was undertaken in order to determine the dimensions of a chloromethylacridine and to compare the results with those for other simple acridine derivatives and for the larger alkylating derivatives, some of which are mutagens.

## Experimental

The salt (I) was prepared and crystals were grown and provided by Dr R. M. Peck (1974, unpublished).




(I)

Table 1. *Crystal data for 9-chloromethylacridine hydrochloride*

| | |
|---|---|
| Formula: $C_{14}H_{11}Cl_2N$ | F.W. 264·12 |
| Crystal system: triclinic | Space group: $P\bar{1}$, no systematic absences |
| $a=9{\cdot}979$ (3) Å | $\alpha=107{\cdot}97$ (2)° |
| $b=9{\cdot}901$ (2) | $\beta=118{\cdot}12$ (2) |
| $c=8{\cdot}680$ (1) | $\gamma=106{\cdot}94$ (2) |
| $V=614{\cdot}3$ (2) Å$^3$ | $F(000)=272$ |
| $D_x=1{\cdot}428$ g cm$^{-3}$ | $Z=2$ |
| $D_m=1{\cdot}415$ g cm$^{-3}$ (in bromobenzene and dichloromethane) | |
| $\mu$(Cu $K\alpha$)$=45{\cdot}41$ cm$^{-1}$ | |
| Crystal size: $0{\cdot}15\times0{\cdot}29\times0{\cdot}30$ mm | |

Table 2. *Final atomic parameters*

Positional parameters are given as fractions of cell edges $\times 10^4$ ($\times 10^3$ for hydrogen). Anisotropic temperature factors are expressed as $\exp[-\frac{1}{4}(h^2a^{*2}B_{11}+k^2b^{*2}B_{22}+l^2c^{*2}B_{33}+2hka^*b^*B_{12}+2hla^*c^*B_{13}+2klb^*c^*B_{23})]$ and isotropic temperature factors as $\exp(-B\sin^2\theta/\lambda^2)$ with $B$ values given in Å$^2$. The estimated standard deviations for each parameter, determined from the inverted full matrix, are given in parentheses and apply to the last specified digits. The numbering system of *Chemical Abstracts* is used with 4a, 8a, 9a and 10a replaced by 11–14 respectively.

| | $x$ | $y$ | $z$ | $B_{11}$ | $B_{22}$ | $B_{33}$ | $B_{12}$ | $B_{13}$ | $B_{23}$ |
|---|---|---|---|---|---|---|---|---|---|
| Cl(1) | −477 (1) | 2525 (1) | −806 (1) | 3·24 (1) | 7·00 (3) | 5·20 (2) | 1·61 (2) | 2·48 (2) | 2·26 (3) |
| Cl(2) | 10373 (1) | 8271 (1) | 6376 (1) | 3·19 (1) | 4·02 (2) | 3·85 (2) | 1·05 (1) | 1·19 (1) | 1·85 (2) |
| C(1) | 2637 (3) | 5801 (3) | −611 (4) | 3·48 (5) | 4·83 (8) | 3·91 (7) | 2·34 (7) | 2·21 (7) | 2·19 (10) |
| C(2) | 3427 (3) | 7337 (3) | −268 (4) | 4·99 (6) | 5·50 (8) | 5·09 (7) | 3·55 (8) | 3·40 (8) | 3·40 (12) |
| C(3) | 5241 (3) | 8512 (3) | 1404 (4) | 5·00 (6) | 4·24 (8) | 5·47 (8) | 2·75 (7) | 3·78 (9) | 2·83 (11) |
| C(4) | 6230 (3) | 8136 (3) | 2716 (4) | 3·92 (5) | 3·56 (8) | 4·41 (7) | 1·74 (6) | 2·76 (8) | 1·71 (9) |
| C(5) | 6873 (3) | 4374 (3) | 4941 (4) | 3·56 (6) | 4·44 (9) | 3·47 (7) | 1·96 (7) | 1·74 (7) | 1·68 (9) |
| C(6) | 6211 (3) | 2886 (3) | 4776 (4) | 5·08 (7) | 5·20 (9) | 4·39 (7) | 3·17 (8) | 2·79 (8) | 2·76 (11) |
| C(7) | 4388 (3) | 1627 (3) | 3182 (4) | 5·22 (7) | 3·97 (8) | 4·74 (8) | 2·35 (7) | 3·10 (9) | 2·33 (10) |
| C(8) | 3284 (3) | 1871 (3) | 1782 (4) | 3·99 (6) | 3·38 (8) | 3·85 (7) | 1·57 (7) | 2·27 (8) | 1·41 (9) |
| C(9) | 2873 (2) | 3733 (3) | 433 (3) | 3·04 (4) | 3·56 (7) | 2·67 (5) | 1·57 (6) | 1·79 (6) | 1·04 (8) |
| N(10) | 6408 (2) | 6144 (2) | 3693 (3) | 2·91 (4) | 3·29 (6) | 3·06 (5) | 1·30 (5) | 1·64 (5) | 1·12 (6) |
| C(11) | 5421 (2) | 6537 (3) | 2400 (4) | 3·20 (4) | 3·36 (7) | 3·37 (6) | 1·73 (6) | 2·21 (7) | 1·43 (8) |
| C(12) | 3912 (2) | 3397 (3) | 1862 (3) | 3·23 (5) | 3·20 (7) | 3·00 (6) | 1·55 (6) | 1·91 (7) | 1·13 (8) |
| C(13) | 3592 (2) | 5314 (3) | 697 (3) | 3·14 (4) | 3·51 (7) | 3·10 (6) | 1·71 (6) | 2·02 (6) | 1·42 (8) |
| C(14) | 5745 (2) | 4663 (3) | 3509 (3) | 3·12 (5) | 3·41 (7) | 2·94 (6) | 1·65 (6) | 1·84 (6) | 1·28 (8) |
| C(15) | 989 (3) | 2389 (3) | −1405 (4) | 3·06 (6) | 4·03 (8) | 3·15 (7) | 1·24 (7) | 1·45 (7) | 1·35 (9) |

Table 2 (*cont.*)

| | $x$ | $y$ | $z$ | $B$ |
|---|---|---|---|---|
| H(N10) | 785 (3) | 700 (3) | 479 (5) | 7·1 (8) |
| H(1) | 148 (3) | 501 (3) | −167 (4) | 4·5 (6) |
| H(2) | 270 (3) | 757 (3) | −122 (4) | 5·2 (7) |
| H(3) | 579 (3) | 952 (3) | 157 (4) | 4·7 (7) |
| H(4) | 749 (3) | 897 (3) | 388 (4) | 5·4 (7) |
| H(5) | 814 (3) | 529 (3) | 597 (4) | 5·0 (6) |
| H(6) | 708 (3) | 274 (3) | 587 (5) | 7·3 (9) |
| H(7) | 399 (3) | 65 (3) | 319 (4) | 5·8 (8) |
| H(8) | 200 (2) | 98 (3) | 67 (4) | 4·6 (6) |
| H(151) | 94 (3) | 133 (4) | −161 (5) | 7·2 (9) |
| H(152) | 66 (3) | 257 (3) | −257 (4) | 5·3 (7) |

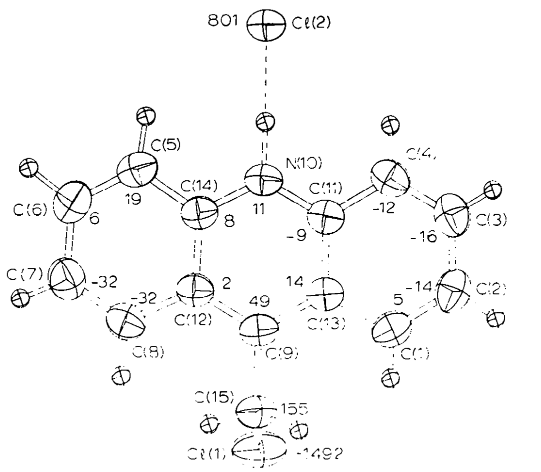



Fig. 1. A view of the molecule perpendicular to the molecular plane (plane 1, Table 3). Deviations from this plane (in Å × 10³) are listed beside each atom.

The crystal data are given in Table 1. Three-dimensional data were collected on a Syntex automated diffractometer with a graphite monochromator and Cu $K\alpha$ radiation using the $\theta$–$2\theta$ scan technique. Intensities were measured for 2335 reflections in the range $\sin\theta/\lambda = 0$ to 0·61 Å$^{-1}$. Values for $\sigma(I)$ were derived from counting statistics. Reflections for which the measured intensity, $I_{obs}$, was less than 3·0 $\sigma(I)$ were considered to be below the threshold of measurement. Values of $\sigma(F)$ were computed from the expression $(F/2)\{[\sigma^2(I)/I^2]+\delta^2\}^{1/2}$ where $\delta$, the measured instrumental uncertainty, was found to be 0·0136. The intensity data were converted to structure amplitudes by application of Lorentz and polarization factors and an ellipsoidal absorption correction (Johnson, 1963), and placed on an absolute scale with a Wilson plot. An isotropic extinction correction (Zachariasen, 1963) with $\alpha = 5{\cdot}71 \times 10^{-6}$ was also applied to the data in the final stages of the refinement.

## Structure determination and refinement

The structure was solved by direct inspection of the Patterson map. The initial trial structure gave an $R$ of 0·385. Isotropic full-matrix least-squares refinement reduced this value to 0·154 and subsequent full-matrix least-squares anisotropic refinements gave $R = 0{\cdot}070$. The positions of the hydrogen atoms were derived from a difference synthesis. Refinement of all atoms was continued with the hydrogen atoms treated isotropically and all other atoms anisotropically. The weights

Table 3. *Some least-squares planes through parts of the molecule*

All deviations from the planes are in Å with estimated standard deviations of 0·002–0·003 Å. Only the atoms with the largest deviations from the planes are shown in this list.

| | Plane 1 C(1)–C(9), N(10), C(11)–C(14) | Plane 2 C(5)–C(8), C(12), C(14) | Plane 3 C(9), N(10), C(11)–C(14) | Plane 4 C(1)–C(4), C(11), C(13) |
|---|---|---|---|---|
| Cl(1) | −1·492 | −1·446 | −1·544 | −1·529 |
| Cl(2) | 0·801 | 0·716 | 0·836 | 0·820 |
| C(15) | 0·155 | 0·190 | 0·111 | 0·122 |
| C(3) | −0·016 | −0·074 | −0·015 | 0·003 |
| C(4) | −0·012 | −0·071 | −0·005 | 0·003 |
| C(7) | −0·032 | −0·006 | −0·054 | −0·072 |
| C(8) | −0·032 | −0·003 | −0·061 | −0·070 |
| C(9) | 0·049 | 0·058 | 0·021 | 0·027 |
| N(10) | 0·011 | −0·026 | 0·014 | 0·009 |
| Maximum deviation from plane* | 0·049 | −0·074 | −0·061 | −0·072 |
| R.m.s. deviation from plane of atoms calculated in the plane | 0·021 | 0·006 | 0·014 | 0·005 |

Plane equations

1 $8{\cdot}15045x - 2{\cdot}77034y - 6{\cdot}90365z = 0{\cdot}96003$
2 $8{\cdot}07020x - 2{\cdot}87749y - 6{\cdot}88047z = 0{\cdot}88877$
3 $8{\cdot}20900x - 2{\cdot}74186y - 6{\cdot}89458z = 1{\cdot}01584$
4 $8{\cdot}17807x - 2{\cdot}69474y - 6{\cdot}92895z = 1{\cdot}01676$

where $x$, $y$ and $z$ are fractional coordinates.

* Excluding H, Cl, C(15).

used in the refinement were $1/[\sigma^2(F_o)]$ with reflections below observational threshold assigned zero weight. The quantity minimized was $\sum\omega\{|F_o|-|F_c|\}^2$. The final refinement converged with $R=0.049$ and a weighted $R$ value of 0·051.*

The atomic scattering factors used for chlorine, oxygen, nitrogen and carbon atoms are those listed by Cromer & Mann (1968) and for hydrogen atoms those of Stewart, Davidson & Simpson (1965). The real component of the anomalous dispersion correction for chlorine, $\Delta f'=0.348$, is that listed by Cromer & Liberman (1970). Computer programs used in this determination were the X-RAY 72 system (Stewart, 1972), and *UCLALS*4 (full-matrix least-squares) (Gantzel, Sparks, Long & Trueblood, 1969), modified by H. L. Carrell.

The final atomic parameters are presented in Table 2. A view perpendicular to the least-squares plane through the acridine portion of the cation is illustrated together with thermal ellipsoids in Fig. 1 (Johnson, 1965).

## Discussion

The interatomic distances and interbond angles are shown in Fig. 2. They do not differ significantly from those found for acridine (Phillips, 1956; Phillips, Ahmed & Barnes, 1960). For the chloromethyl group, however, the C–C bond [1·502 (3) Å] is slightly longer than values for chloromethylanthracenes [1·485 (2), 1·493 (2) Å] (Gabe & Glusker, 1971; Chomyn, Glusker, Berman & Carrell, 1972) while the C–Cl bond [1·795 (1) Å] is slightly shorter than those for the chloromethylanthracene derivatives [1·810 (2), 1·806 (2) Å]. If shorter C–C distances and longer C–Cl distances (suggesting some contribution to the structure from the resonance form $C=C^+H_2Cl^-$) are indicators of good alkylating agents, then the distances listed above might indicate that the chloromethylacridinium ion is not such a good alkylating agent as the corresponding anthracene derivative.

The chloromethylacridinium cation is nearly planar. The angle between the planes of the two outer rings (*i.e.*, between planes 2 and 4 in Table 3) is 1·62° with values 1·68° and 0·36° for the interplanar angles for 2–3 and 3–4 respectively. Distances from some planes are given in Table 3 and Fig. 1. As in chloromethylanthracenes the methylene carbon atom, C(15), lies out of the plane of the acridine system (0·155 Å) to the opposite side of the plane from that of the chlorine atom (+1·492 Å). The ring atoms deviating most from the molecular plane (1) are C(3), C(4), C(7), C(8), C(9) and N(10), and their deviations, which are significant, are listed in Table 3. This shows that the two ends of the molecule lie below the plane to give a bowed molecule.

The packing of the molecule in the unit cell is shown in Fig. 3. The chloromethylacridinium cations form hydrogen bonds to chloride ions with N(10)···Cl(2), 2·991 (1) Å, H(N10)···Cl(2) 1·91 (2) Å and the angle N(10)–H(N10)···Cl(2) 171 (2)°. The other closest approaches to the chloride ion are two methylene groups of molecules v and vi with distances from Cl(2) of 2·69 (3) Å for H(152$^{v}$), 2·71 (2) Å for H(151$^{vi}$) and 2·73 (2) Å for a ring hydrogen atom H(2$^{vii}$).

The vertical overlap of acridine rings as they stack in the crystal is illustrated in Fig. 4 in which three

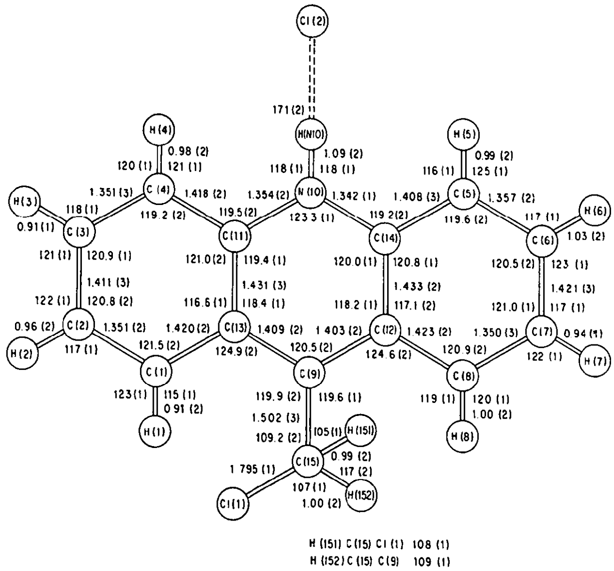



Fig. 2. Interatomic distances and interbond angles. Estimated standard deviations, with respect to the last digit listed, are given in parentheses.

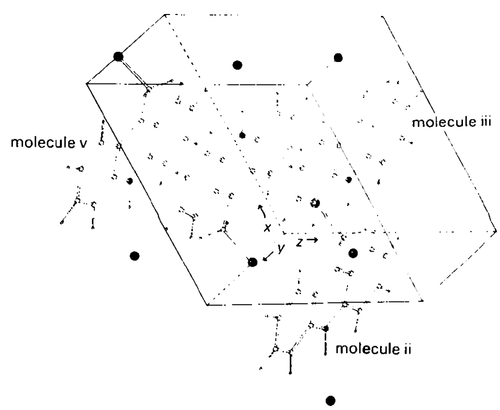



Fig. 3. Packing of molecules in the unit cell showing the anti-parallel stacking of the cations, and the hydrogen bonds to chloride ions. Only four ion-pairs are shown here. Symmetry code: none $x,y,z$; i $x-1,y,z-1$; ii $-x,-y,-z$; iii $1-x,1-y,1-z$; iv $-x,1-y,-z$; v $1-x,1-y,-z$; vi $1+x,1+y,1+z$; vii $1+x,y,1+z$.

* The structure-factor list has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 30423 (15 pp., 1 microfiche). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

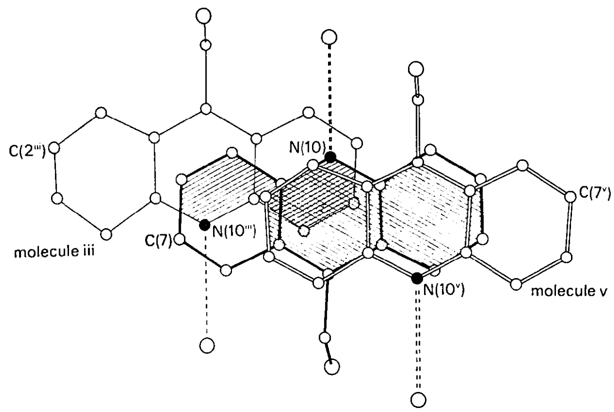



Fig. 4. Overlap of molecules in parallel planes 3·4 Å apart. The vertical overlap of molecule v with the central molecule is shown by shading \ and the vertical overlap of the central molecule with molecule iii is shown by shading /. The cross-hatched area represents an area in which the central molecule is sandwiched between molecules iii and v.

molecules in planes 3·4 Å apart are shown and the extent of vertical stacking is indicated by the shading. The overlap of one chloromethylacridinium ion with another at $1-x, 1-y, 1-z$ (molecule iii) is almost identical with the overlap of pairs of molecules of 10-chloromethyl-2,3,9-trimethylanthracene related by a center of symmetry (Chomyn *et al.*, 1972).

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### References

CHOMYN, A., GLUSKER, J. P., BERMAN, H. M. & CARRELL, H. L. (1972). *Acta Cryst.* B**28**, 3512–3517.
CROMER, D. T. & LIBERMAN, D. (1970). *J. Chem. Phys.* **53**, 1891–1898.
CROMER, D. T. & MANN, J. (1968). *Acta Cryst.* A**24**, 321–324.
DAUDEL, P., GACHELIN, F., DELCEY, M. C., JACQUIGNON, P., BUU HOI, N. P. & QUEVAL, P. (1971/1972). *Chem.-Biol. Interact.* **4**, 223–231.
GABE, E. J. & GLUSKER, J. P. (1971). *Acta Cryst.* B**27**, 1925–1930.
GANTZEL, P. K., SPARKS, R. A., LONG, R. E. & TRUEBLOOD, K. N. (1969). *UCLALS*4. Program in Fortran IV.
GLUSKER, J. P., BERMAN, H. M. & CARRELL, H. L. (1972). *Acta Cryst.* A**28**, S44.
JOHNSON, C. K. (1963). 1620 Programs from I.C.R., *ICR* 10. *Absorption Factors for a Crystal Ground as an Ellipsoid of Revolution.*
JOHNSON, C. K. (1965). *ORTEP.* Report ORNL-3794, Oak Ridge National Laboratory, Oak Ridge, Tennessee.
LERMAN, L. S. (1964). *J. Cell Comp. Physiol.* **64** Suppl., 1.
PHILLIPS, D. C. (1956). *Acta Cryst.* **9**, 237–250.
PHILLIPS, D. C., AHMED, F. R. & BARNES, W. H. (1960). *Acta Cryst.* **13**, 365–377.
STEWART, J. M. (1972). The X-RAY system, version of 1972. Technical Report TR-192 of the Computer Science Center, Univ. of Maryland, June 1972.
STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.
ZACHARIASEN, W. H. (1963). *Acta Cryst.* **16**, 1139–1144.

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# Structure Cristalline du Fluorobéryllate de Potassium–Holmium $KHoBeF_6$. Caractéristiques Cristallographiques des Composés Isotypes

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The fluoroberyllate $KHoBeF_6$ crystallizes in the monoclinic system, space group $P2_1/m$, with $a=7{\cdot}414$ (1), $b=5{\cdot}826$ (3), $c=6{\cdot}356$ (2) Å, $\beta=119{\cdot}12°$, $Z=2$. The crystal structure has been determined from single-crystal diffractometer measurements using Patterson and Fourier syntheses and refined by a least-squares method. The final $R$ value is 0·053. $BeF_4$ tetrahedra connect chains of $HoF_8$ antiprisms which propagate along the **b** direction. Lattice parameters of isotypic compounds are given.

## Préparation et caractéristiques du composé $KHoBeF_6$

Le fluorobéryllate de potassium–holmium a été obtenu à partir de deux préparations différentes:

– En chauffant sous atmosphère d'azote, à 550°C et pendant 24 h, le résidu obtenu par évaporation d'une solution fluorhydrique de $BeF_2$, KF et $HoCl_3$.

– En maintenant à 650°C pendant 48 h en tube scellé de platine, le mélange $KHoF_4 + BeF_2$.

Ce composé cristallise sous forme de petits octaèdres assez réguliers aux sommets tronqués, après fusion à 650°C suivie d'un refroidissement lent ($3\,°h^{-1}$).

Le dosage du potassium et du béryllium, réalisé au Laboratoire d'analyses, de recherches et d'essais chi-