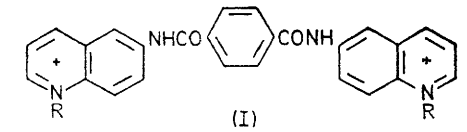
Crystal and Molecular Structure of 4′-(Acridin-9-ylamino)methanesulphonanilide Hydrochloride, a Compound showing Antileukemic Activity

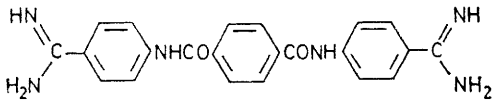
By **David Hall, David A. Swann,** and **T. Neil Waters,*** Department of Chemistry, University of Auckland, New Zealand

The title compound (VI) has antileukemic properties. An *X*-ray analysis shows it to be triclinic, $a = 14{\cdot}074(1)$, $b = 6{\cdot}864(1)$, $c = 10{\cdot}166(1)$ Å, $\alpha = 105{\cdot}40(3)$, $\beta = 101{\cdot}60(2)$, $\gamma = 86{\cdot}07(3)°$, $Z = 2$, space group $P\bar{1}$. The structure was solved by Patterson and Fourier methods. Refinement of 2070 diffractometer data reduced the *R* factor to 0·046. The acridine ring is slightly non-planar and the phenyl ring makes an angle of 77° with it. This latter appears to be a feature of the molecule rather than a crystal-packing requirement.

THE life extension promoted by antileukemic agents derived from bisimidazoles [1] and quaternary ammonium compounds [2] has been paralleled recently in a series of bisquinolinium salts [3] (I). Testing of homologues and

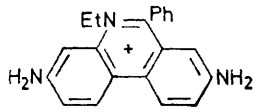


(I)

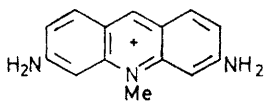


(II)

closely related molecules has led to the conclusions that among the parameters determining activity are the lipid–water partition coefficient, charge separation, and, to a certain extent, the degree of planarity of the system. Thus, members of the bisquaternary series, and also of the phthalanides (II), which exhibit activity, have in common three co-planar rings between two basic functions. When the linear charge separations recorded for activity (these fall into four categories: 8—9, 12·5—14, 18·5—21·5, and 23·5—26·5 Å) were also taken into account, it was suggested that the compounds could bind to an ordered polynucleotide, *i.e.* that the drugs bind in the minor groove of a polynucleotide double helix and then subsequently intercalate between adjacent base pairs.[4] Such intercalation is established for ethidium (III) and trypaflavin (IV).[5-7]

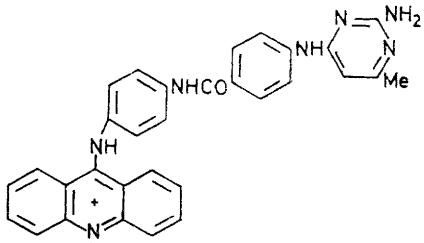


(III)

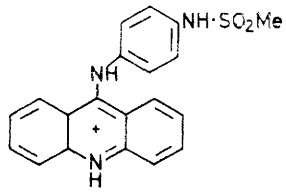


(IV)

In an endeavour to prepare agents with better distributive powers, but which would retain the high activity of bisquaternary salts, Cain and his co-workers have developed a series of 9-(substituted anilino)acridine complexes which remain active. With regard for the criteria already established, and to the likely importance of intercalation, derivatives of the parent compound (V) have been prepared. One structure–activity relationship comes to the fore in this series,[8] namely that a strong electron-donating substituent on the anilino-group, preferably at the 4′-position, is mandatory. A compound which meets this need and also the requirement for significant cellular distribution is the 4′-sulphonamido-derivative (VI), for which an *X*-ray structural analysis, undertaken to elucidate molecular details, is now reported.



(V)



(VI)

EXPERIMENTAL

Pale yellow platelets of 4′-(acridin-9-ylamino)methanesulphonanilide hydrochloride were prepared by Dr. B. F. Cain.

Crystal Data.—$C_{20}H_{17}N_3O_2S,HCl$, $M = 399{\cdot}9$. Triclinic, $a = 14{\cdot}074(1)$, $b = 6{\cdot}864(1)$, $c = 10{\cdot}166(1)$ Å, $\alpha = 105{\cdot}40(3)$, $\beta = 101{\cdot}60(2)$, $\gamma = 86{\cdot}07(3)°$ (obtained by a least-squares fit to 12 reflexions located by four-circle diffractometry), $U = 927$ Å^3, $D_m = 1{\cdot}42$, $Z = 2$, $D_c = 1{\cdot}43$. Space group $P\bar{1}$ (as confirmed by the subsequent analysis). Cu-K_α radiation, $\lambda = 1{\cdot}5418$ Å; μ(Cu-K_α) = 30·0 cm^{-1}.

Intensity data were collected on a Hilger and Watts automatic diffractometer by use of the θ—ω scan technique and corrected for absorption effects to give a total of 2079 independent reflexions for which $F_o^2 > 3\sigma(F_o^2)$.

A sharpened Patterson synthesis, with origin removal, was computed after the $|F_o|^2$ data had been put on an absolute scale. Positions for chlorine and sulphur were obtained from the map and were used (*R* then 0·59) to phase an electron-density computation. With the aid of model-building procedures the remaining non-hydrogen

[1] R. Hirt and R. Berchtold, *Experientia*, 1961, **17**, 418.
[2] L. P. Walls, *Progr. Medicin. Chem.*, 1963, **3**, 52.
[3] G. J. Atwell and B. F. Cain, *J. Medicin. Chem.*, 1967, **10**, 706.
[4] B. F. Cain, G. Atwell, and R. N. Seelye, *J. Medicin. Chem.*, 1969, **12**, 199.
[5] M. J. Waring, *J. Mol. Biol.*, 1965, **13**, 269.
[6] L. Lehman, *J. Mol. Biol.*, 1961, **3**, 18.
[7] J. B. LePecq and C. Paoletti, *J. Mol. Biol.*, 1967, **27**, 87.
[8] B. F. Cain, G. J. Atwell, and R. N. Seelye, personal communication.

atoms were eventually located and after a verifying structure-factor calculation (R 0·253) the twenty-seven atoms were subjected to block-diagonal least-squares refinement. A weighting scheme of the form $w = 4F_o^2/\sigma^2(F_o^2)$ was employed. With the atoms described by individual, but isotropic, thermal parameters, refinement converged at R 0·120, at which stage the twelve hydrogen

TABLE 1

Atom positions

Atom	x/a	y/b	z/c
S	0·34654(6)	0·47302(14)	0·61247(9)
Cl	0·22709(5)	0·11633(14)	0·82271(9)
O(1)	0·2427(2)	0·4786(5)	0·5821(3)
O(2)	0·4005(2)	0·6530(4)	0·6398(3)
C(1)	0·7685(3)	0·1764(5)	0·7049(4)
C(2)	0·7836(3)	0·1429(6)	0·5728(4)
C(3)	0·8777(3)	0·1470(6)	0·5473(4)
C(4)	0·9547(3)	0·1774(5)	0·6542(4)
C(5)	1·1020(2)	0·2730(5)	1·1309(4)
C(6)	1·0977(3)	0·3063(5)	1·2664(4)
C(7)	1·0070(3)	0·3244(5)	1·3089(4)
C(8)	0·9231(3)	0·3044(5)	1·2123(4)
C(9)	0·8381(2)	0·2367(5)	0·9630(3)
N(10)	1·0213(2)	0·2280(4)	0·8947(3)
C(11)	0·8463(2)	0·2140(5)	0·8223(3)
C(12)	0·9411(2)	0·2100(5)	0·7913(3)
C(13)	0·9246(2)	0·2637(5)	1·0694(3)
C(14)	1·0161(2)	0·2551(5)	1·0300(3)
N(15)	0·7542(2)	0·2184(5)	1·0038(3)
C(21)	0·6580(2)	0·2583(5)	0·9368(4)
C(22)	0·6354(2)	0·4447(5)	0·9094(4)
C(23)	0·5424(3)	0·4856(5)	0·8443(4)
C(24)	0·4724(2)	0·3356(5)	0·8063(4)
C(25)	0·4948(3)	0·1519(6)	0·8373(4)
C(26)	0·5873(3)	0·1130(6)	0·9042(4)
N(16)	0·3755(2)	0·3758(5)	0·7429(3)
C(17)	0·3865(4)	0·3059(9)	0·4720(5)
H(1)	0·703(3)	0·168(6)	0·722(4)
H(2)	0·726(3)	0·117(6)	0·490(4)
H(3)	0·888(3)	0·117(6)	0·451(4)
H(4)	1·024(3)	0·181(6)	0·640(4)
H(5)	1·163(3)	0·253(6)	1·093(4)
H(6)	1·156(3)	0·323(6)	1·338(4)
H(7)	1·007(3)	0·360(6)	1·417(4)
H(8)	0·861(3)	0·322(6)	1·240(4)
H(11)	0·365(3)	0·169(6)	0·457(4)
H(12)	0·448(3)	0·259(6)	0·502(4)
H(13)	0·373(3)	0·376(6)	0·411(4)
H(15)	0·759(3)	0·180(6)	1·088(4)
H(16)	0·330(3)	0·284(6)	0·750(4)
H(22)	0·686(3)	0·555(6)	0·937(4)
H(23)	0·527(3)	0·614(6)	0·827(4)
H(25)	0·445(3)	0·050(6)	0·813(4)
H(26)	0·604(3)	−0·022(6)	0·927(4)

atoms of the aromatic rings were included in the model at calculated positions (B for all hydrogen atoms 4·0 Å^2). With all but the hydrogen, methyl carbon, and nitrogen atoms ascribed anisotropic thermal parameters, R was reduced to 0·067 and an electron-density map allowed the placing of the methyl hydrogen atoms and those on the two non-ring nitrogens. The remaining hydrogen atom could not be located. Final refinement cycles allowed adjustments to all positional parameters, including those for hydrogen atoms, and to non-hydrogen thermal parameters. The final R was 0·046.

Final atom co-ordinates and thermal parameters are in Tables 1 and 2, bond lengths and bond angles in Tables 3 and 4. The numbering scheme is that of Figure 1. Observed and calculated structure factor data are deposited in Supplementary Publication No. SUP 21042 (14 pp., 1 microfiche).†

DISCUSSION

The acridine system is slightly, but significantly, non-planar, the outer rings being tipped in opposite directions so that each makes an angle of *ca.* 3° with the

TABLE 2

Thermal parameters * $\times 10^4$

Atom	b_{11}	b_{22}	b_{33}	b_{12}	b_{13}	b_{23}
S	37·2(5)	278(3)	94(1)	−22(2)	5(1)	130(3)
Cl	30·1(4)	270(3)	109(1)	−26(2)	37(1)	123(3)
O(1)	33(2)	464(11)	140(4)	6(6)	−8(4)	235(11)
O(2)	62(2)	282(8)	177(5)	−69(6)	−32(5)	232(10)
C(1)	38(2)	204(10)	75(4)	−4(7)	15(5)	71(10)
C(2)	50(2)	219(10)	76(4)	10(8)	1(5)	72(10)
C(3)	59(3)	224(10)	75(4)	31(8)	40(5)	95(11)
C(4)	45(2)	176(9)	90(4)	20(7)	54(5)	93(10)
C(5)	28(2)	153(9)	102(5)	0(6)	7(5)	70(10)
C(6)	40(2)	167(9)	97(5)	−21(7)	−23(5)	50(10)
C(7)	53(2)	190(9)	76(4)	−27(7)	7(5)	57(10)
C(8)	40(2)	173(9)	78(4)	−9(7)	24(5)	64(10)
C(9)	29(2)	130(8)	75(4)	11(6)	22(4)	64(9)
N(10)	31(2)	154(7)	83(3)	11(5)	23(4)	81(8)
C(11)	30(2)	137(8)	73(4)	2(6)	18(4)	60(9)
C(12)	36(2)	115(8)	83(4)	5(6)	25(4)	73(9)
C(13)	31(2)	120(8)	71(4)	2(6)	18(4)	55(8)
C(14)	33(2)	110(8)	78(4)	7(6)	17(4)	63(9)
N(15)	28(2)	275(9)	81(4)	−3(6)	19(4)	142(9)
C(21)	27(2)	242(10)	74(4)	4(7)	21(4)	96(10)
C(22)	30(2)	225(10)	85(4)	−38(7)	18(5)	65(10)
C(23)	34(2)	201(9)	92(4)	2(7)	23(5)	99(10)
C(24)	27(2)	239(10)	78(4)	−10(7)	18(4)	90(10)
C(25)	32(2)	235(10)	113(5)	−49(7)	17(5)	117(11)
C(26)	34(2)	223(10)	114(5)	−4(7)	28(5)	143(11)
N(16)	26(2)	330(10)	108(4)	−29(6)	13(4)	180(10)
C(17)	77(4)	471(18)	135(7)	−81(12)	67(8)	63(17)

* The scattering factor is expressed as: $f = f_0\exp-(b_{11}h^2 + b_{22}k^2 + b_{33}l^2 + b_{12}hk + b_{13}hl + b_{23}kl)$.

TABLE 3

Bond lengths (Å)

S–O(1)	1·431(3)	C(22)–C(23)	1·388(5)
S–O(2)	1·429(3)	C(23)–C(24)	1·398(5)
S–C(17)	1·743(6)	C(24)–C(25)	1·380(6)
S–N(16)	1·606(3)	C(25)–C(26)	1·385(5)
C(1)–C(2)	1·358(5)	C(26)–C(21)	1·385(5)
C(1)–C(11)	1·427(5)	C(24)–N(16)	1·428(5)
C(2)–C(3)	1·404(6)	C(1)–H(1)	0·99(4)
C(3)–C(4)	1·353(5)	C(2)–H(2)	1·03(4)
C(4)–C(12)	1·401(5)	C(3)–H(3)	0·98(4)
C(5)–C(6)	1·349(5)	C(4)–H(4)	1·02(4)
C(5)–C(14)	1·406(5)	C(5)–H(5)	1·00(4)
C(6)–C(7)	1·416(6)	C(6)–H(6)	0·97(4)
C(7)–C(8)	1·363(5)	C(7)–H(7)	1·06(4)
C(8)–C(13)	1·408(5)	C(8)–H(8)	0·97(4)
C(9)–C(11)	1·424(5)	N(15)–H(15)	0·95(4)
C(9)–C(13)	1·441(5)	C(22)–H(22)	1·01(4)
C(9)–N(15)	1·353(4)	C(23)–H(23)	0·95(4)
N(10)–C(12)	1·365(4)	C(25)–H(25)	0·97(4)
N(10)–C(14)	1·355(4)	C(26)–H(26)	1·01(4)
C(11)–C(12)	1·429(5)	N(16)–H(16)	0·96(4)
C(13)–C(14)	1·418(5)	C(17)–H(11)	0·97(4)
N(15)–C(21)	1·430(5)	C(17)–H(12)	0·92(4)
C(21)–C(22)	1·384(5)	C(17)–H(13)	0·87(4)

central plane. The phenyl ring is planar within the limits of accuracy. Table 5 lists the planes of best fit and deviations therefrom. Substituted hydrogens and exocyclic atoms expected to be coplanar with their rings are invariably so.

The geometry at N(16) is unusual and contrasts with

† See Notice to Authors No. 7 in *J.C.S. Perkin II*, 1973, Index issue.

TABLE 4

Bond angles (deg.)

C(1)–C(2)–C(3)	120·5(6)	N(16)–S–C(17)	107·4(5)
C(1)–C(11)–C(9)	126·0(6)	O(1)–S–O(2)	120·6(4)
C(1)–C(11)–C(12)	115·4(5)	O(1)–S–C(17)	108·1(5)
C(2)–C(3)–C(4)	120·1(6)	O(2)–S–C(17)	105·3(5)
C(2)–C(1)–C(11)	122·2(6)	H(1)–C(1)–C(2)	120(1·6)
C(3)–C(4)–C(12)	120·5(6)	H(1)–C(1)–C(11)	118(1·6)
C(4)–C(12)–N(10)	118·3(6)	H(2)–C(2)–C(1)	121(1·5)
C(4)–C(12)–C(11)	121·3(6)	H(2)–C(2)–C(3)	119(1·5)
C(5)–C(6)–C(7)	120·6(6)	H(3)–C(3)–C(2)	119(1·6)
C(5)–C(14)–N(10)	119·6(5)	H(3)–C(3)–C(4)	120(1·6)
C(5)–C(14)–C(13)	120·2(6)	H(4)–C(4)–C(3)	122(1·5)
C(6)–C(7)–C(8)	120·0(6)	H(4)–C(4)–C(12)	117(1·5)
C(6)–C(5)–C(14)	120·2(6)	H(5)–C(5)–C(6)	125(1·6)
C(7)–C(8)–C(13)	121·2(6)	H(5)–C(5)–C(14)	115(1·6)
C(8)–C(13)–C(9)	123·4(5)	H(6)–C(6)–C(5)	121(1·6)
C(8)–C(13)–C(14)	117·7(5)	H(6)–C(6)–C(7)	118(1·6)
C(9)–C(11)–C(12)	118·3(5)	H(7)–C(7)–C(6)	118(1·5)
C(9)–C(13)–C(14)	118·9(5)	H(7)–C(7)–C(8)	122(1·5)
C(9)–N(15)–C(21)	127·2(5)	H(8)–C(8)–C(7)	121(1·6)
N(10)–C(12)–C(11)	120·4(5)	H(8)–C(8)–C(13)	118(1·6)
N(10)–C(14)–C(13)	120·1(5)	H(15)–N(15)–C(9)	117(1·6)
C(11)–C(9)–C(13)	119·3(5)	H(15)–N(15)–C(21)	116(1·6)
C(11)–C(9)–N(15)	124·1(5)	H(22)–C(22)–C(21)	121(1·6)
C(12)–N(10)–C(14)	122·9(5)	H(22)–C(22)–C(23)	119(1·6)
C(13)–C(9)–N(15)	116·3(5)	H(23)–C(23)–C(22)	120(1·6)
N(15)–C(21)–C(22)	119·6(6)	H(23)–C(23)–C(24)	120(1·6)
N(15)–C(21)–C(26)	120·0(6)	H(25)–C(25)–C(24)	120(1·6)
C(21)–C(22)–C(23)	120·3(6)	H(25)–C(25)–C(26)	120(1·6)
C(21)–C(26)–C(25)	119·5(6)	H(26)–C(26)–C(21)	120(1·5)
C(22)–C(23)–C(24)	119·1(6)	H(26)–C(26)–C(25)	121(1·5)
C(23)–C(24)–C(25)	120·3(6)	H(16)–N(16)–S	116(1·5)
C(23)–C(24)–N(16)	120·1(6)	H(16)–N(16)–C(24)	113(1·6)
C(24)–C(25)–C(26)	120·4(6)	H(11)–C(17)–S	112(1·6)
C(24)–N(16)–S	125·0(5)	H(11)–C(17)–H(12)	87(2)
C(25)–C(24)–N(16)	119·5(6)	H(11)–C(17)–H(13)	125(2)
C(26)–C(21)–C(22)	120·4(6)	H(12)–C(17)–S	109(1·6)
N(16)–S–O(1)	105·5(4)	H(12)–C(17)–H(13)	124(2)
N(16)–S–O(2)	105·3(5)	H(13)–C(17)–S	100(1·8)

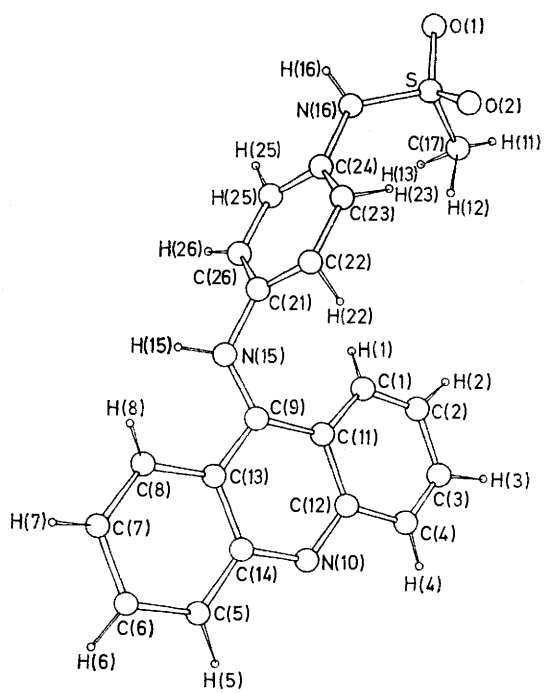


FIGURE 1 Atom numbering for X-ray analysis

the normal trigonal arrangement of N(15). A pyramidal distortion is apparent in that H(16) is displaced 0·44(5) Å away from the trigonal plane towards the chloride anion. Similar effects are seen at the amine centres of the related compound 3,8-diamino-5-ethyl-6-phenylphenanthridinium (III) bromide [9] where one nitrogen has the expected planar configuration but the second is markedly pyramidal. It was suggested that a small energy separation between trigonal and pyramidal geometries may allow hydrogen bonding to stabilise the latter

TABLE 5

Equations of planes of best fit, in the form $AX + BY + CY + D = 0$.* Displacements (Å) of atoms from the planes are given in square brackets

Plane (1): acridine plane, C(1)—(14)

$-0·0051X + 0·9946Y + 0·1038Z - 0·0890 = 0$

[C(1) −0·03, C(2) −0·06, C(3) 0, C(4) 0·04, C(5) −0·05, C(6) −0·04, C(7) 0·03, C(8) 0·05, C(9) −0·02, N(10) 0·01, C(11) 0·04, C(12) 0·05, C(13) −0·01, C(14) −0·01, N(15) −0·20]

Plane (2): C(9)—(14)

$-0·0084X + 0·9917Y + 0·1286Z - 0·2847 = 0$

[C(1) −0·09, C(2) −0·15, C(3) −0·10, C(4) −0·04, C(5) −0·02, C(6) 0·03, C(7) 0·11, C(8) 0·11, C(9), C(9) −0·02, N(10) −0·01, C(11) 0·01, C(12) 0·01, C(13) 0·02, C(14) 0, N(15) −0·19, H(15) 0·56, C(21) −0·18, C(22) −1·49, C(26) 0·75]

Plane (3): Ph ring, C(21)—(26)

$0·4358X - 0·1344Y - 0·8899Z + 4·7036 = 0$

[C(9) 0·90, N(15) 0·03, N(16) −0·03, C(21) 0·02, C(22) 0, C(23) −0·01, C(24) 0·01, C(25) 0, C(26) −0·02, S 0·91]

* X, Y, and Z are orthogonal co-ordinates in Å related to the crystal axes by:

$$\begin{vmatrix} X \\ Y \\ Z \end{vmatrix} = \begin{vmatrix} 1 & \cos\gamma & \cos\beta \\ 0 & \sin\gamma & \cos\psi \\ 0 & 0 & \cos\rho \end{vmatrix} \begin{vmatrix} a \\ b \\ c \end{vmatrix}$$

$\cos\psi = (\sin\gamma)^{-1}(\cos\alpha - \cos\beta\cos\gamma)$

$\cos\rho = (\sin\gamma)^{-1}(1 + 2\cos\alpha\cos\beta\cos\gamma - \cos^2\alpha - \cos^2\beta - \cos^2\gamma)^{\frac{1}{2}}$

arrangement, an argument equally appropriate in the present instance.

The short bond lengths observed for N(10)–C(12) (1·365 Å) and N(10)–C(14) (1·355 Å) when compared with the longer carbon–carbon bonds of the central ring indicate a large degree of double-bond character. There are four short carbon–carbon bonds in the acridine group (1·349—1·363 Å) and ten longer bonds (1·401—1·449 Å) arranged in long–short–long–short–long sequences spreading from N(10)–C(12) and N(10)–C(14).

The opening of the angle N(15)–C(9)–C(11) (124·1°) at the expense of N(15)–C(9)–C(13) (116·3°) almost certainly results from intramolecular steric interactions. There are a number of close approaches between H(1) of the acridine ring and C(21) and C(22) of the phenyl group (Table 6). These interactions could, in principle, be avoided if there were a 90° rotation about the C(9)–N(15) bond and if the phenyl group were then disposed at right-angles to the acridine. The angle of rotation about C(9)–N(15) is, however, only 24° and it will be noted that the bond length of 1·353 Å presupposes considerable double-bond character. The rotation about the N(15)–C(21) bond is 55° (the length of 1·430 Å is as expected for a nitrogen exocyclic to an aromatic ring) bringing the overall dihedral angle between phenyl and

[9] E. Subramanian, J. Trotter, and C. E. Bugg, *J. Cryst. Mol. Struct.*, 1971, **1**, 3.

acridine to 77°. We believe that this conformation is a feature of the compound and not a consequence of the packing in the solid state. If the molecule is imagined to be initially planar (see Figure 1) a number of steric

TABLE 6

Significant geometrical details

C(1) · · · C(21)	2·99 Å	N(16) · · · Cl	3·19 Å
C(1) · · · C(22)	3·21	N(16)–H(16)	1·0
C(21) · · · N(1)	2·3	H(16) · · · Cl	2·3
C(22) · · · H(1)	2·6	N(16)–H(16)–Cl	166°
N(10) · · · Cl′	3·12		
N(10)–H(X)–Cl′	162°		

H(X) not detected but position assumed. Cl′ is at $x-1, y, z$.

difficulties become apparent. That between H(8) and H(15) can be relieved on a model by a rotation of *ca.* 25° about C(9)–N(15), but further twisting will be increasingly resisted by the conjugation with the acridine ring. Close approaches involving H(1) and the phenyl ring remain, however, and these can then be removed by a rotation of *ca.* 60° around the N(15)–C(21) bond. Because of the initial twist about C(9)–N(15) a rotation beyond 60° brings renewed contacts, this time with C(25) and H(25). The overall conformation is therefore uniquely determined by the intermolecular steric effects and the rotational constraint about one of the exocyclic bonds.

The question then arising is whether or not this fixed orientation of the two rings is of significance in determining activity. On the one hand may be cited the similarity of the molecule to ethidium bromide [3,8-diamino-5-ethyl-6-phenylphenanthridinium (III) bromide], in which the phenyl ring makes an angle of 83° with the phenanthridine system;[9] on the other, our preliminary *X*-ray examination of another drug, also showing antileukemic properties, does not reveal such a marked deviation from overall planarity. All we can suggest is that the phenyl group may have a role in orientating the planar acridine section of the molecule during its initial binding to nucleic acid or in the subsequent intercalation step.

The molecular packing within the crystal (Figure 2) gives one indication of the position of the missing hydrogen atom in that the close approach (3·12 Å) of a chloride ion to N(10) suggests a hydrogen bonding

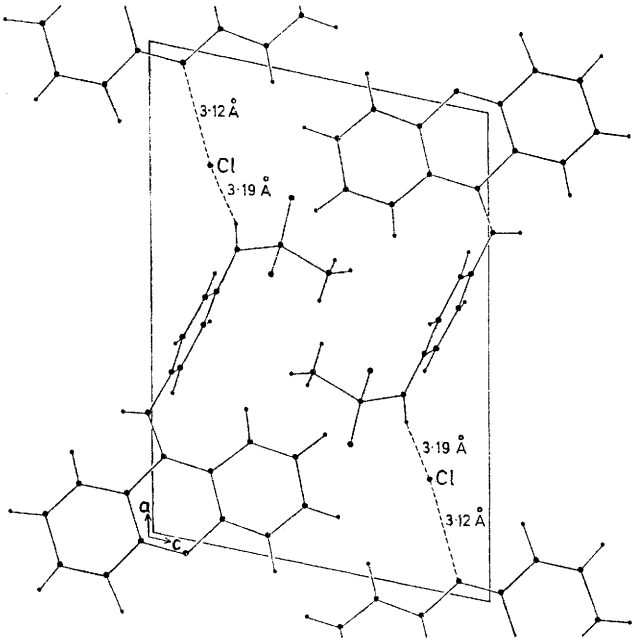


FIGURE 2 Cell contents projected on (010); hydrogen bonds are shown dotted

interaction. The other requirements for such bonding would also be met by a hydrogen on N(10) (see Table 6). There is, however, no crystallographic evidence for the presence of the missing atom at this nitrogen and chemical considerations suggest N(16) as a more likely centre for the positive charge. The existence of a second hydrogen bond can be demonstrated with more certainty, linking N(16) with the chloride. There are no other intermolecular approaches less than expected van der Waals distances.

We thank Dr. B. F. Cain, of the Cancer Chemotherapy Laboratory, Auckland, for supplying crystals and for his interest in this work.

[3/2433 *Received, 27th November,* 1973]