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The Crystal Structure of an Analog of a Benzacridine Alkylating Agent, 7-[3-(Ethyl-2-hydroxyethylamino)propylamino]benz[*c*]acridine, ICR-292-OH

BY WILLIAM C. STALLINGS AND JENNY P. GLUSKER

The Institute for Cancer Research, The Fox Chase Cancer Center, Philadelphia, PA 19111, *USA*

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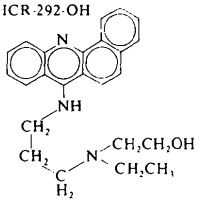
The crystal structure of 7-[3-(ethyl-2-hydroxyethylamino)propylamino]benz[*c*]acridine (ICR-292-OH) has been determined by single-crystal X-ray diffraction with three-dimensional data. When the terminal hydroxyl group is replaced by a Cl atom, the product (ICR-292) is a mutagen for *Salmonella*, an antitumor agent for ascites tumors, a carcinogen, and is believed to intercalate in DNA. The crystals are orthorhombic, space group *Pbca* with $Z = 8$, FW 373·50, cell dimensions $a = 12{\cdot}636$ (2), $b = 20{\cdot}469$, $c = 15{\cdot}612$ (2) Å, $V = 4037{\cdot}8$ (8) Å^3 and observed and calculated densities of 1·22 and 1·23 g cm^{-3} respectively. The structural formula is:

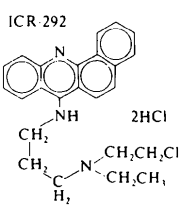


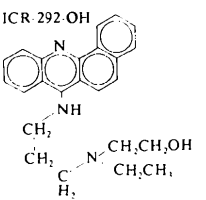
Three-dimensional diffractometer data were collected with graphite-monochromatized Cu $K\alpha$ radiation to a maximum $\sin\theta/\lambda$ value of 0·61 Å^{-1}. Of the 3767 reflections scanned, 1093 were below the threshold of measurement. The structure was solved by direct methods and refined anisotropically by full-matrix least squares to a crystallographic residual of 0·056. The ethyl group of the side chain is disordered; the C–C bond length is affected by this disorder and four of the five H atoms of this group could not be unambiguously located. All other H atoms were located from difference maps and refined isotropically. The acridine portion of the molecule is not planar, the dihedral angle between the planes of the outer rings being 16·7°. The N atom of the ring system forms a hydrogen bond (2·917 Å) with the hydroxyl group of a neighboring molecule. As observed in all other ICR molecules (analogs of acridine alkylating agents) studied to date, the N atoms of the side chain form an intramolecular hydrogen bond (2·884 Å). There is no overlap of the ring systems in planes 3·4 Å apart although such stacking has been observed as a constant feature in other ICR compounds studied.

Introduction

The alkylating agent ICR-292 is a benz[*c*]acridine nitrogen half-mustard which is one of a series of acridine nitrogen half-mustards with varying but well-defined degrees of antitumor and mutagenic activity (Creech, Preston, Peck, O'Connell & Ames, 1972). It is an antitumor agent against ascites tumors, a mutagen for *Salmonella* (Creech *et al.*, 1972) and a carcinogen (Peck, Tan & Peck, 1976). It is believed to intercalate in DNA (Travaglini, 1970).

ICR-292-OH is the hydroxy analog of ICR-292; the molecular formulae of both compounds are illustrated below.





The hydroxy analog was studied crystallographically since this derivative was obtainable in crystalline form.

The crystal structures of five such acridine derivatives, ICR-191-OH (Carrell, 1972), ICR-171-OH (Glusker, Minkin & Orehowsky, 1972), ICR-170-OH (Berman & Glusker, 1972), ICR-449-OH (Glusker, Gallen & Carrell, 1973) and ICR-372-OH (Glusker, Carrell, Berman & Gallen, 1975), have been determined in this laboratory to attempt to correlate their biological activities with their three-dimensional structures. This paper is the first report of a benzacridine derivative in this series of structure determinations. All others studied to date were acridine derivatives except ICR-372-OH, which is an azaacridine derivative.

Experimental

Crystals of ICR-292-OH were provided by Drs R. M. Peck, R. K. Preston and H. J. Creech of this Institute; they exist in the form of yellow-gold rectangular parallelepipeds. Three-dimensional X-ray intensity data were collected on a Syntex automated diffractometer with graphite-monochromatized Cu $K\alpha$ radiation and the θ–2θ scan technique over a dispersion-corrected base width of 2·0°; the scan speed was variable over the range 2–24° min^{-1}. There was no fall-off of intensity as a function of time in periodically measured standard reflections.

The intensity data were converted to structure amplitudes by the application of Lorentz and polarization factors. No absorption correction was applied. Additional crystal data and details of the data collection are summarized in Table 1.

Table 1. *Crystal data and some details of the data collection*

Formula: $C_{24}H_{27}N_3O$	*Pbca*
FW 373·50	$Z = 8$
$a =$ 12·636 (2) Å	$D_c = 1{\cdot}23$ g cm^{-3}
$b =$ 20·469 (3)	$D_o = 1{\cdot}22$ (aqueous KI solution)
$c =$ 15·612 (2)	
$V =$ 4037·8 (8) Å^3	
Crystal size	0·1 × 0·4 × 0·5 mm
Crystal shape	Rectangular parallelepipeds
Crystal color	Gold-yellow
Number of unique reflections measured (excluding those that are systematically absent)	3767
Maximum sin θ/λ	0·61 Å^{-1}
Criterion for threshold value	$I_o = 2{\cdot}33\sigma(I)$
Number of reflections below the threshold value	1093
Criterion for $\sigma(I)$	Counting statistics
Criterion for $\sigma(F)$	$\sigma(F) = (F/2)\{[\sigma^2(I)/I^2] + \delta^2\}^{1/2}$ where δ = instrumental uncertainty = 0·022

Structure determination and refinement

The structure was solved easily by direct methods with *MULTAN* (Main, Woolfson & Germain, 1971); the first E map calculated revealed the positions of all of the non-hydrogen atoms in the molecule except those of the ethyl group [C(27) and C(28)]. These were readily located in the subsequent Fourier map. The structure was refined by the full-matrix least-squares method (Gantzel, Sparks, Long & Trueblood, 1969; Carrell, 1975); the non-hydrogen atoms were assigned anisotropic temperature factors and the H atoms, located from intermediate difference Fourier syntheses, were assigned isotropic temperature factors. As discussed below, four of the five H atoms covalently linked to the ethyl group could not be located well.

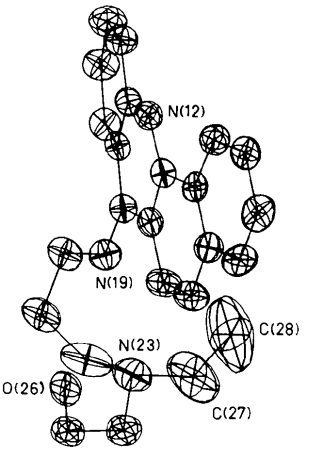


Fig. 1. A view of the molecule illustrating the thermal ellipsoids for C, N and O atoms; note the high thermal motion of the ethyl group [C(27) and C(28)]. This drawing was made with the program *ELLPS2* (Bernstein *et al.*, 1974).

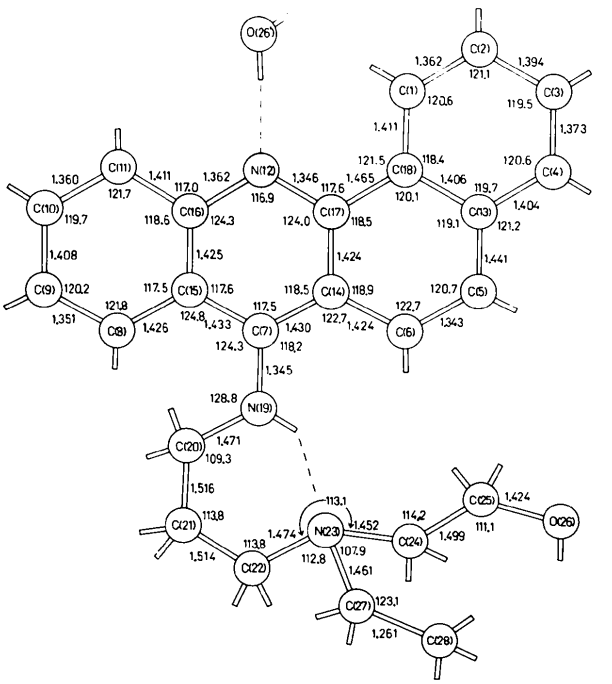


Fig. 2. Bond distances and angles for ICR-292-OH. The estimated standard deviation (e.s.d.) for distances between all C, N, O atoms except C(27) and C(28) is 0·003–0·004 Å. The e.s.d. for bond angles involving all C, N, O atoms except C(28) is 0·2–0·3°. The e.s.d. for the C(27)–C(28) bond length is 0·009 Å; the e.s.d. for other distances involving C(28) is 0·008 Å and the e.s.d. for other distances involving C(27) is 0·005–0·006 Å. The e.s.d. for bond angle N(23)–C(27)–C(28) is 0·5°. The minimum bond lengths between C, N, O atoms and H atoms to which they are bonded are C(27)–H(27*A*), C(9)–H(9), C(11)–H(11) at 0·90, 0·91 and 0·91 Å respectively. The maximum bond length between C, N, O atoms and H atoms to which they are bonded is C(5)–H(5) at 1·19 Å.

The weights, w, for reflections were $1/\sigma^2(F)$ with weights of zero for reflections below the threshold value; the function minimized in the least-squares process was $\Sigma w(|F_o| - |F_c|)^2$. The atomic scattering factors used for C, N and O were from *International Tables for X-ray Crystallography* (1962, pp. 201–207) and those for H atoms from Stewart, Davidson & Simpson (1965). The final R is 0·056 with a weighted R of 0·065.

There is apparently disorder in the ethyl side chain. Of the five H atoms of the ethyl group, only one, H(27*A*), tentatively located in a difference Fourier map, refined in a well-behaved manner. The maximum r.m.s. amplitudes of vibration along the longest axes of the thermal ellipsoids were 0·56 Å for C(27) and 0·64 Å for C(28), an indication of disorder in this portion of the molecule; the final C(27)–C(28) bond length is 1·26 Å, a value much shorter than that expected for a C–C bond in an ethyl group, and another indication of a problem such as disorder. Fig. 1 illustrates the refined thermal ellipsoids for C, N and O atoms. The high thermal motion of C(27) and C(28) is evident in this figure. Attempts to analyze the disorder, including occupancy refinements of C(27) and C(28) disordered such that the centers of half-weighted atoms were displaced to 0·3 Å from either end of their longest axis of thermal motion, were unsuccessful. Therefore, during the final cycles of refinement, H(27*B*) and the H atoms of the methyl group were placed at calculated positions, and assigned isotropic temperature factors of 12 Å^2. The coordinates of these H atoms were not refined. The refined parameters for H(27*A*), although quite reasonable, should be only cautiously considered as valid.

Final refined positional and thermal parameters for ICR-292-OH are listed in Table 2 together with estimated standard deviations. A final difference Fourier map calculated using all of the parameters of Table 2 (including deposited thermal parameters) revealed the presence of no peaks above 0·35 e Å^{-3}.*

Discussion

Bond distances and valence angles are illustrated in Fig. 2. Comparison of these values with those of ICR-449-OH (an acridine derivative lacking the ethyl group at

* Lists of structure factors and anisotropic and isotropic (for H) thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 32362 (19 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 2. *Regional positional parameters for* ICR-292-OH

E.s.d.'s with respect to the last digit reported are in parentheses.

	x	*y*	*z*		*x*	*y*	*z*
C(1)	0·4765 (2)	0·7920 (1)	0·4555 (2)	H(1)	0·459 (2)	0·750 (1)	0·435 (2)
C(2)	0·4008 (2)	0·8283 (1)	0·4953 (2)	H(2)	0·329 (2)	0·810 (1)	0·498 (2)
C(3)	0·4253 (2)	0·8882 (1)	0·5327 (2)	H(3)	0·374 (2)	0·916 (1)	0·564 (2)
C(4)	0·5271 (2)	0·9115 (1)	0·5286 (2)	H(4)	0·549 (2)	0·954 (1)	0·549 (2)
C(5)	0·7126 (2)	0·9004 (1)	0·4791 (2)	H(5)	0·724 (2)	0·956 (1)	0·504 (1)
C(6)	0·7870 (2)	0·8666 (1)	0·4364 (2)	H(6)	0·855 (2)	0·887 (1)	0·431 (2)
C(7)	0·8442 (2)	0·7705 (1)	0·3486 (1)	H(8)	0·938 (2)	0·699 (1)	0·218 (2)
C(8)	0·8701 (2)	0·6808 (1)	0·2388 (2)	H(9)	0·871 (2)	0·606 (1)	0·156 (2)
C(9)	0·8339 (2)	0·6265 (1)	0·1992 (2)	H(10)	0·710 (2)	0·557 (2)	0·193 (2)
C(10)	0·7360 (2)	0·5991 (1)	0·2231 (2)	H(11)	0·614 (2)	0·612 (1)	0·297 (2)
C(11)	0·6758 (2)	0·6291 (1)	0·2837 (2)	H(19)	0·949 (2)	0·836 (1)	0·367 (2)
N(12)	0·6374 (1)	0·7175 (1)	0·3761 (1)	H(20*A*)	1·039 (2)	0·712 (1)	0·336 (2)
C(13)	0·6064 (2)	0·8755 (1)	0·4868 (2)	H(20*B*)	1·048 (2)	0·763 (1)	0·262 (2)
C(14)	0·7661 (2)	0·8054 (1)	0·3966 (1)	H(21*A*)	1·194 (2)	0·764 (1)	0·355 (2)
C(15)	0·8108 (2)	0·7128 (1)	0·3042 (1)	H(21*B*)	1·119 (2)	0·796 (1)	0·430 (2)
C(16)	0·7085 (2)	0·6875 (1)	0·3237 (1)	H(22*A*)	1·155 (3)	0·858 (2)	0·268 (3)
C(17)	0·6639 (2)	0·7770 (1)	0·4060 (1)	H(22*B*)	1·226 (3)	0·879 (2)	0·351 (2)
C(18)	0·5819 (2)	0·8145 (1)	0·4505 (2)	H(24*A*)	1·174 (2)	0·980 (1)	0·400 (2)
N(19)	0·9438 (1)	0·7935 (1)	0·3484 (1)	H(24*B*)	1·040 (3)	0·988 (2)	0·429 (2)
C(20)	1·0420 (2)	0·7600 (1)	0·3233 (2)	H(25*A*)	1·180 (2)	0·888 (1)	0·497 (2)
C(21)	1·1358 (2)	0·7947 (1)	0·3633 (2)	H(25*B*)	1·142 (2)	0·960 (1)	0·546 (2)
C(22)	1·1560 (2)	0·8620 (2)	0·3269 (2)	H(26)	1·052 (3)	0·848 (2)	0·560 (3)
N(23)	1·0726 (2)	0·9099 (1)	0·3473 (2)	*H(27*A*)	1·095 (3)	0·974 (2)	0·235 (2)
C(24)	1·1015 (2)	0·9538 (1)	0·4165 (2)	*H(27*B*)	1·011	1·002	0·286
C(25)	1·1219 (2)	0·9204 (1)	0·5003 (2)	*H(28*A*)	0·944	0·972	0·176
O(26)	1·0306 (1)	0·8861 (1)	0·5290 (1)	*H(28*B*)	0·974	0·888	0·195
C(27)	1·0423 (4)	0·9496 (3)	0·2735 (3)	*H(28*C*)	0·886	0·930	0·265
C(28)	0·9601 (5)	0·9390 (4)	0·2299 (5)				

* Parameters for this atom were not refined.

the more terminal amino group of the side chain; e.s.d.'s 0·003–0·004 Å and 0·2–0·4° for C, N and O atoms) reveals that the major differences, significant at the 4σ level, are effects resulting from the addition of the [*c*] ring and the ethyl group. Significant lengthening of the C(17)–C(18), C(13)–C(18) and C(5)–C(13) bonds and significant shortening of the C(5)–C(6) bond are observed in ICR-292-OH when compared with the corresponding geometry in ICR-449-OH; the C(5)–C(6) bond, which apparently has more double-bond character in ICR-292-OH, is analogous to the so-called '*K* region' of polycyclic aromatic hydrocarbons and its pronounced double-bond character, which has been both experimentally observed and theoretically predicted (Pullman & Pullman, 1963), is often invoked to explain the biological activity of the hydrocarbon. It may also be relevant to the situation in acridine derivatives. The other three bond changes are the consequence of the addition of the [*c*] ring. Significant differences in valence angles occur at C(13)–C(5)–C(6), C(18)–C(13)–C(5), C(25)–C(24)–N(23), C(24)–N(23)–C(22) and N(23)–C(22)–C(21). The first two angles listed occur in the ring system and we attribute these differences (a respective increase and decrease for the case of ICR-292-OH over ICR-449-OH) directly to the addition of the [*c*] ring. An identical pattern of bond lengthening and shortening, and increase and decrease of valence angles is indicated by a comparison of a series of structures of anthracene derivatives with a series of benzanthracene derivatives (Gabe & Glusker, 1971; Chomyn, Glusker, Berman & Carrell, 1972; Glusker & Zacharias, 1972; Lewis, Carrell, Glusker & Sparks, 1976; Glusker, Zacharias & Carrell, 1976; Iball, Morgan & Zacharias, 1975).

Analysis of the differences in valence angles around the terminal amino group [N(23)] indicates that at all of the above-mentioned angles, there is an apparent widening of these angles in the tertiary amine [ICR-292-OH with an ethyl group at N(23)] over the corresponding angles in the secondary amine [ICR-449-OH with a H atom at the equivalent of N(23)]. At this point, it should again be emphasized that the ethyl group is disordered and no H atoms have been located with certainty. Therefore, in ICR-292-OH there is a relatively more bulky substituent at N(23); probably as a result of this, the angles in which this N atom is involved widen. In the case of C(22)–N(23)–C(24), distances between the H substituents of C(22), C(24) and C(27) illustrate this [non-bonded contacts H(24*B*)···H(27*B*), H(22*A*)···H(27*A*) and H(24*A*)···H(22*B*) are 2·21, 2·44 and 2·26 Å respectively]. Were the angle C(24)–N(23)–C(22) smaller, greater interpenetration of the electron clouds of these H atoms would occur.

The alkylating side chain is twisted from full extension by an intramolecular hydrogen bond between N(19) and N(23). This is a feature observed in all ICR compounds (analogs of acridine alkylating agents, see Table 3) studied to date. The torsion angles which define the side-chain conformation in ICR-292-OH as well as in ICR-449-OH and ICR-191-OH (which lack the ethyl group) and ICR-170-OH (in which the side chain is identical with that of ICR-292-OH) are listed in Table 3. Similarities in the conformation begin to break down at C(21)–C(22)–N(23)–C(24). We attribute this divergence to differences in the chemical composition of the side chain itself and to differences in the packing arrangements for the cases of each crystal structure determined.

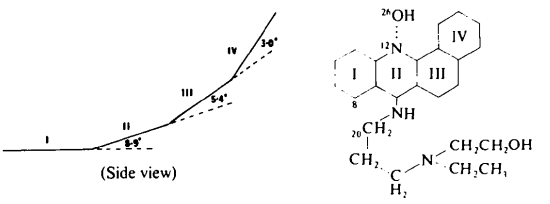
Table 3. *Conformations of the side chains in some ICR compounds*

Torsion angles	ICR-292-OH (this work)	Comparable quantities in ICR-449-OH (Glusker, Gallen & Carrell, 1973)	191-OH (Carrell, 1972)	170-OH (Berman & Glusker, 1972)
C(7)–N(19)–C(20)–C(21)	−159·3 (3)°	−153·9°	−156·1°	−149·0°
N(19)–C(20)–C(21)–C(22)	−68·6 (4)	−53·0	−59·1	−65·0
C(20)–C(21)–C(22)–N(23)	+67·4 (4)	+78·7	+73·3	+75·3
C(21)–C(22)–N(23)–C(24)	+101·6 (4)	+177·9	−169·1	−163·3
C(22)–N(23)–C(24)–C(25)	−61·7 (4)	−170·4	−61·3	+94·3
N(23)–C(24)–C(25)–O(26)	−60·1 (4)	+60·6	−60·2	+73·0
C(22)–N(23)–C(27)–C(28)	+100·9 (8)			+58·0
C(25)–C(24)–N(23)–C(27)	+172·9 (4)			−131·5
C(24)–N(23)–C(27)–C(28)	−133·4 (7)			−73·0
C(21)–C(22)–N(23)–C(27)	−135·6 (4)			+65·0
C(15)–C(7)–N(19)–C(20)	−16·1 (4)	−6·5	−16·6	−17·4
C(14)–C(7)–N(19)–C(20)	+163·5 (3)	+172·7	+163·5	+162·6
R_1*	$-CH_2-CH_2-OH$	$-CH_2-CH_2-OH$	$-CH_2-CH_2-OH$	$-CH_2-CH_2-OH$
R_2*	$-CH_2-CH_3$	−H	−H	$-CH_2-CH_3$

* See Fig. 3.

Interestingly, apart from similarities in the first three torsion angles of Table 3, another feature remains remarkably constant over this series of molecules; the side chain does not extend initially up and away from the plane of the aromatic portion of the molecule, but rather folds over such that the C(14)–C(7)–N(19)–C(20) and C(15)–C(7)–N(19)–C(20) torsion angles in ICR-292-OH are +163·5 and −16·1° (*i.e.* the side chain lies approximately in the plane of the aromatic ring system). This is shown diagrammatically in Fig. 3. In acridine and anthracene derivatives with $-CH_2-X$ as the side chains [where X = Cl (Zacharias & Glusker, 1974; Chomyn, Glusker, Berman & Carrell, 1972) and where $X = -S-CH_2-CH_2-Cl$ (Glusker & Zacharias, 1972; Lewis, Carrell, Glusker & Sparks, 1976)] the side chain X extends up and away approximately perpendicular to the plane of the aromatic ring system. This is also shown diagrammatically in Fig. 3; some torsion angles relevant to these conformations are collected in Tables 3 and 4. In order to test whether the approximate coplanarity of the ring system and the initial portion of the side chain is a result of electronic or steric forces, a potential-energy calculation allowing rotation of the side chain about the C(7)–N(19) vector was carried out. This indicated that considerable geometric freedom exists. The calculation was accomplished with the program *WMIN* (Busing, 1972) with interatomic interaction terms from Hopfinger (1973) in a Lennard–Jones 6–12 nonbonded potential function. Presumably then, the consistency with which these torsion angles are observed is an electronic effect, the stabilizing influence being the large amount of double-bond character localized in the C(7)–N(19) bond. The distance is 1·345 Å, a value similar to that listed (*International Tables for X-ray Crystallography*, 1962, p. 275) for a partial double bond in heterocyclic systems. This implies some conjugation with the ring system, a factor which effectively prevents free rotation about the C–N bond so that the side chain initially lies in the plane of the aromatic system. Since the H atom attached to N(19) also lies approximately in the plane

Table 5. *Planarity in* ICR-292-OH



Angles between planes of the rings

Planes	ICR-292-OH	Equivalent values in ICR-449-OH using the side-chain directionality to distinguish rings I and III
I and IV	16·7°	
I and II	8·9	8·6°
II and III	5·4	4·2°
III and IV	3·0	
I and III	14·1	12·5
II and IV	8·1	

Note: The molecule is bowed as shown schematically above (side view).

Deviations from a least-squares plane calculated with the C and N atoms of the benzacridine ring. Of the 18 atoms used to determine the best plane, the r.m.s. deviation from that plane is 0·164 Å. Of the atoms of the benz[*c*]acridine ring system, C(9) and N(12) show maximum deviations of 0·3 Å.

C(1)*	0·002 Å	C(15)*	0·029 Å
C(2)*	−0·124	C(16)*	0·191
C(3)*	−0·184	C(17)*	0·164
C(4)*	−0·132	C(18)*	0·063
C(5)*	−0·018	N(19)	0·208
C(6)*	0·039	C(20)	0·568
C(7)*	0·110	C(21)	1·040
C(8)*	−0·275	C(22)	−0·056
C(9)*	−0·339	N(23)	−0·576
C(10)*	−0·083	C(24)	−0·049
C(11)*	0·175	C(25)	1·439
N(12)*	0·308	O(26)	1·851
C(13)*	−0·023	C(27)	−2·035
C(14)*	−0·096	C(28)	−2·762

* Used in the calculation of the least-squares plane.

Table 4. *Torsion angles for compounds in which the side chain does not contain an intramolecular* N · · · N *hydrogen bond*

Compound	X	C(14)–C(7)–C(19)–X and C(15)–C(7)–C(19)–X (not distinguishable because of symmetry)
9-Chloromethylacridine hydrochloride (Zacharias & Glusker, 1974)	−Cl	92·4°, −88·4°
10-Chloromethyl-2,3,9-trimethylanthracene (Chomyn, Glusker, Berman & Carrell, 1972)	−Cl	82·4, −95·4
10-Methyl-9{[(2-chloromethyl)thio]methyl}anthracene (Glusker & Zacharias, 1972)	$-S-CH_2-CH_2-Cl$	89·3, −89·0
9-{[(2-Chloroethyl)thio]methyl}anthracene (Lewis, Carrell, Glusker & Sparks, 1976)	$-S-CH_2-CH_2-Cl$	84·3, −93·4

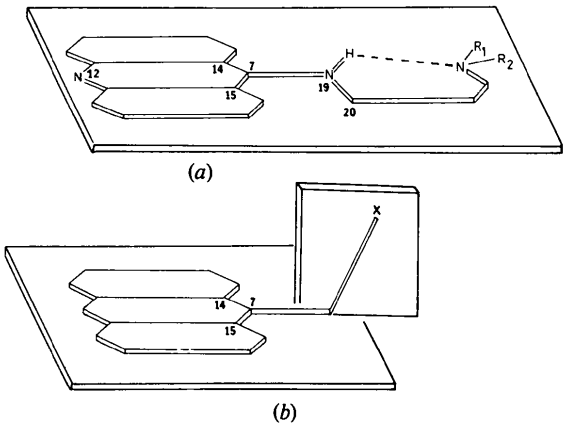


Fig. 3. (*a*) Side chain containing an intramolecular N···N hydrogen bond; it does not initially extend up and away from the plane of the acridine ring system but lies approximately in the acridine plane. See Table 3 for examples. (*b*) Side chain not containing an intramolecular N···N hydrogen bond; it extends up and away from the plane of the aromatic ring system as illustrated. This is also true when the acridine moiety is replaced by anthracene and 10-methylanthracene. For examples see Table 4.

of the rings, N(23) must also lie near this plane in order to form a nearly linear hydrogen bond. It should be noted that if the stabilizing electronic effects described above were removed, the observed conformation, as a result of steric repulsions between H atoms [such as H(6) and H(19)], would be less stable than other conformations obtained by rotation about the C(7)–N(19) bond.

Angles between the rings of the benz[*c*]acridine system are not 0°, but, as shown in Table 5, are very similar to those of ICR-449-OH (using the directionality of the side chain to distinguish rings I and III in the latter); this table also includes information concerning deviations from a least-squares plane calculated with the coordinates of the 18 atoms of the ring system. Most of the buckling occurs between rings I and II to give a butterfly-like structure; this is probably due to non-bonded intramolecular interactions H(8)···H(20*A*) and H(8)···H(20*B*) which are 2·23 (4) and 2·01 (4) Å apart respectively. The buckling between rings II and IV probably results from the close approach to N(12) by O(26) in the intermolecular hydrogen-bonding pattern; the non-bonded contact H(1)···H(26) is 2·27 (5) Å. It is not known whether this buckling persists in solution.

Table 6. *Hydrogen bonding*

Intramolecular		
N(19)–H(19)···N(23)	N(19)–H(19)	0·93 (3) Å
	H(19)···N(23)	2·19 (3)
	N(19)···N(23)	2·884 (3)
	∠N(19)–H(19)···N(23)	131 (2)°
Intermolecular		
O(26)–H(26)···N(12)*	O(26)–H(26)	0·96 (4) Å
	H(26)···N(12)	1·99 (4)
	O(26)···N(12)	2·917 (3)
	∠O(26)–H(26)···N(12)*	163 (4)°

* N(12) related to its coordinates as listed in Table 2 by the following transformation: $\frac{1}{2} + x, \frac{3}{2} - y, 1 - z$.

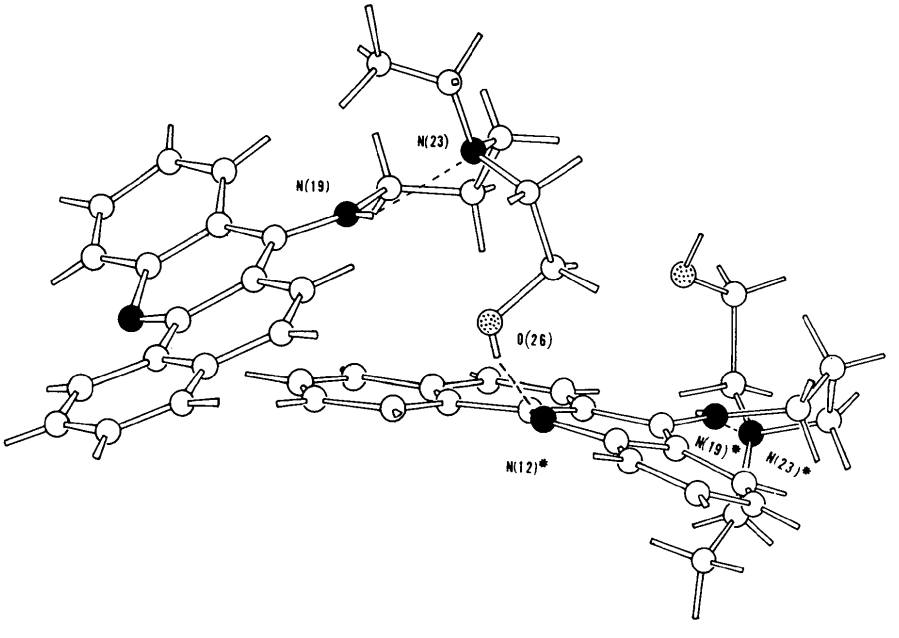


Fig. 4. Hydrogen bonding in ICR-292-OH. Open circles represent C atoms, black circles represent N atoms and stippled circles represent O atoms.

When a group is attached or hydrogen-bonded to an atom in the 12-position, some planarity is observed. For example the planarity of dibenzanthracene, where no such effect occurs, is such that the maximum deviation from the least-squares plane through the molecule is 0·03 Å (Iball, Morgan & Zacharias, 1975). Comparison of planarity in the structures 7-chloromethylbenz[*a*]anthracene and 7-chloromethyl-12-methylbenz[*a*]anthracene (Glusker, Zacharias & Carrell, 1976) is also of interest. The angle between rings II and IV of the former, lacking a bulky substituent in this area, is 1°; in the latter, with a methyl group substituted in the 12-position, this angle is 18°. In ICR-292-OH, the corresponding angle is 8·1°, probably the result of the close intermolecular approach of O(26) to form a hydrogen bond to N(12).

There are two unique hydrogen bonds in this crystal structure as shown in Fig. 4: an intramolecular N(19)—H(19)···N(23) hydrogen bond and an intermolecular O(26)—H(26)···N(12) hydrogen bond. Various parameters which define their geometries are listed in Table 6. It is of interest to note that for other ICR compounds studied, the donor in the intermolecular hydrogen bond involving the aromatic N is approximately positioned in the plane of the rings. In ICR-292-OH, O(26) donating the H atom to N(12) deviates 2·23 Å from the least-squares plane calculated through the benzacridine ring. As mentioned earlier, a

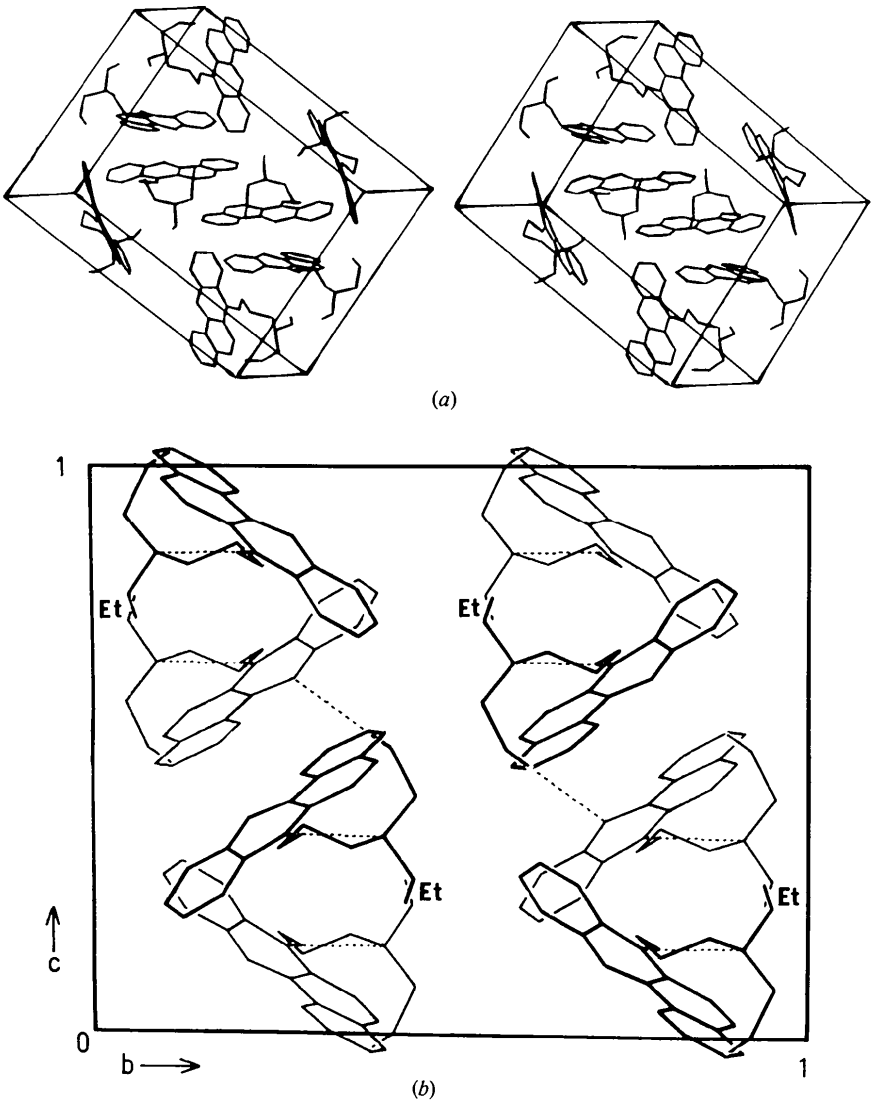


Fig. 5. (*a*) A stereoview of the packing in the unit cell. (*b*) A view of the packing down the *a* axis. Et denotes the side-chain ethyl group. These drawings were created with the aid of the program *PRJCTN* (Bernstein *et al.*, 1974).

coplanar approach is prohibited by steric crowding created by the proximity of H(1). The buckling of the benzacridine moiety is such that if the outer rings are bowed down, the approach of O(26) is from above. This is shown in Fig. 4.

The packing of the molecules in the unit cell is illustrated in Fig. 5(*a*). A dominant feature is the large vacant area (at $y = 0$ and $y = \frac{1}{2}$) occupied by the ethyl group; this is best illustrated in Fig. 5(*b*) (where the ethyl group is marked as Et). The minimum non-hydrogen intermolecular contact for C(28) is C(28)···C(13) at 4·068 (8) Å; this quantity for C(27) is C(27)···C(9) at 3·967 (6) Å. Such lack of restriction explains the disorder of this ethyl group. As illustrated in Fig. 5(*a*) and (*b*), there is no overlap of ring systems of neighboring molecules in planes 3·4 Å apart; the packing is perhaps best described as a herring-bone pattern. This packing has not been observed for any of the acridine members of this series of compounds where the common mode of packing has involved stacking of the rings in planes approximately 3·4 Å apart. Self-stacking in the crystalline state has been previously interpreted as perhaps indicative of the ability of a molecule to intercalate or interact with DNA. To investigate this matter further, we plan to study another analog of a benz[*c*]acridine alkylating agent.

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