

9-(2-Chloroethylamino)acridine monohydrate and its precursor 9-phenoxyacridine

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Received 6 August 2004

Accepted 5 October 2004

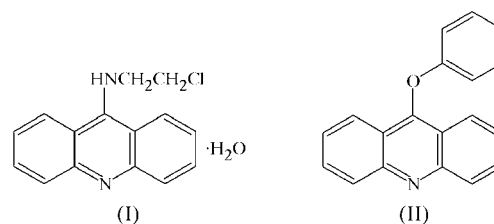
Online 15 January 2005

The title compounds, C₁₅H₁₃ClN₂·H₂O, (I), and C₁₉H₁₃NO, (II), form monoclinic crystals. Arranged in a ‘head-to-tail’ manner, the molecules of the amine form (I) lie along the *b* axis in layers that are linked by a network of hydrogen bonds involving the endocyclic N atom, the H atom at the exocyclic N atom and all the atoms of the solvent water molecule. Molecules of (II), with the phenoxy group nearly perpendicular to the acridine moiety, are arranged in pairs related by a center of symmetry and stabilized *via* two C—H···N contacts; the latter are linked *via* a network of further C—H···N contacts and non-specific dispersive interactions.

Comment

The practically and cognitively interesting 9-aminoacridine molecule has the potential to co-exist, in the liquid and gas phases, in the amine and imine tautomeric forms (Rak *et al.*, 1997), even though it has been established that only the amine tautomer is present in the crystalline phase (Chaudhuri, 1983). It has recently been found that the electron-withdrawing and -donating substituents at the exocyclic N atom have a greater affinity for, respectively, the imine and amine forms of 9-aminoacridines (Wróblewska *et al.*, 2004). Two examples confirm this rule: molecules of the imine form are present in crystals of 9-(trichloroacetylmino)acridine (Meszko *et al.*, 2002) and 9-(phenylsulfonylimino)acridine (Kuz'mina & Struchkov, 1981), both of which contain strongly electron-attracting substituents at the exocyclic N atom (the former compound crystallizes as a monohydrate). In order to obtain more evidence supporting the expected regularity, further 9-aminoacridine derivatives need to be synthesized and their structures and properties determined. This publication focuses on the refinement of the structure of 9-(2-chloroethylamino)acridine monohydrate, (I), in which 9-aminoacridine is substituted at the exocyclic N atom with CH₂CH₂Cl, a substituent that, according to our recent work (Wróblewska *et*

al., 2004), should display an affinity for the imine form of 9-aminoacridine (the logarithm of the equilibrium constant for the amine–imine tautomerization and the mean charge of CH₂CH₂Cl predicted for the gas phase are 1.59 and 0.14, respectively). The other compound investigated here, 9-phenoxyacridine, (II), serves as an intermediate in the syntheses of numerous acridine derivatives, among them 9-aminoacridines (Albert, 1966). Their biological relevance is well established, and 9-aminoacridines are capable of interacting specifically with adjacent molecules. The mechanisms of these interactions undoubtedly depend on the form in which the 9-aminoacridines occur (Barbe *et al.*, 1996; Wróblewska *et al.*, 2004). The present work was undertaken in order to discover the tautomeric form of compound (I) in the crystalline phase and the crystal structure of its precursor (II).



Crystals of (I) contain molecules of the amine form (Fig. 1), eight of which occupy the unit cell (Fig. 2). The acridine moiety is nearly planar in the crystalline phase (Table 1), with atoms C9, N10 and N15 arranged almost linearly [N10···C9—N15 = 176.7 (2)°]. The NCH₂CH₂Cl group is twisted relative to the acridine skeleton, at an angle of 22.8 (1)° (this is the angle between the plane containing atoms N15, C16 and C17, and the mean plane delineated by all the non-H atoms of the acridine nucleus). The value of the N15—C16—C17—C18 torsion angle (Table 1) indicates that the conformation of the NCH₂CH₂Cl substituent is of the *s-cis* type. Molecules of (I) are arranged ‘head-to-tail’ in layers along the *b* axis. Molecules of (I) and water are linked by a network of hydrogen bonds involving the endocyclic N atom, the H atom at the exocyclic N atom and all three water atoms (Fig. 2 and

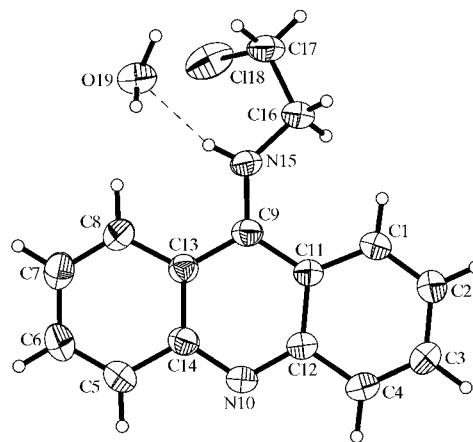


Figure 1
The molecular structure of (I), showing the atom-labeling scheme and 50% probability displacement ellipsoids. H atoms are shown as small spheres of arbitrary radii. The N15—H15···O19 hydrogen bond is represented by a dashed line.

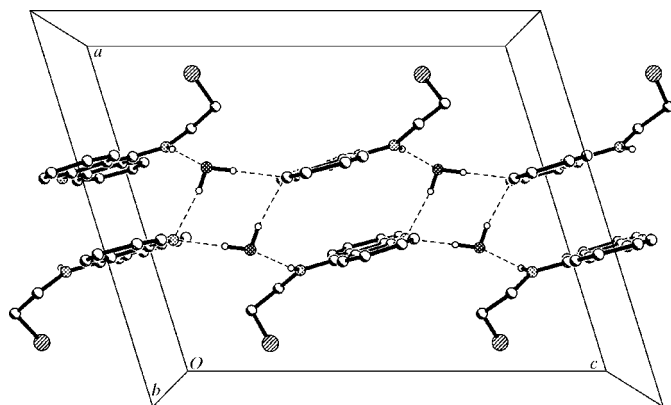


Figure 2
The arrangement of the molecules of (I) in the unit cell, viewed along the *b* axis. H atoms not involved in hydrogen bonds have been omitted. Hydrogen bonds are represented by dashed lines. Symmetry codes are as given in Table 2.

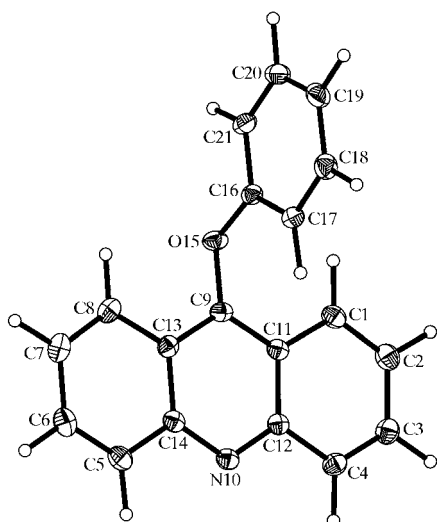


Figure 3
The molecular structure of (II), showing the atom-labeling scheme and 50% probability displacement ellipsoids. H atoms are shown as small spheres of arbitrary radii.

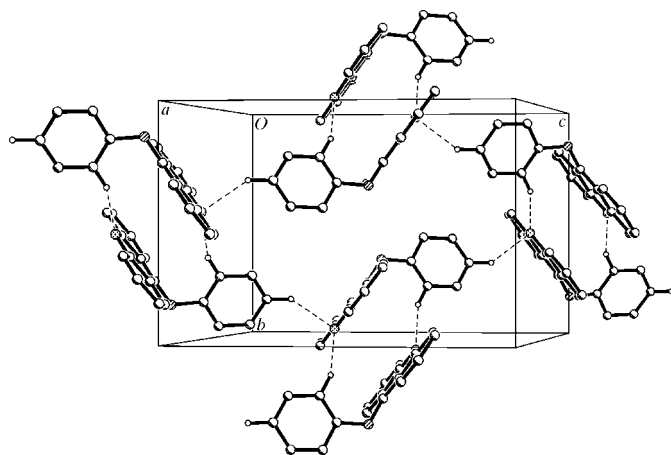


Figure 4
The arrangement of the molecules of (II) in the unit cell, viewed along the *a* axis. H atoms not involved in C—H...N interactions have been omitted. The C—H...N interactions are represented by dashed lines. Symmetry codes are as given in Table 4.

Table 2). These multidirectional hydrogen bonds are the principal factor in stabilizing the lattice and, most probably, in forcing the introduction of (I) into the lattice in the amine tautomeric form.

Four molecules of (II) (Fig. 3) occupy the unit cell (Fig. 4). The acridine moiety is nearly planar in the crystalline phase (Table 3), with atoms C9, N10 and O15 arranged almost linearly [$\text{N10}\cdots\text{C9}-\text{O15} = 176.0(2)^\circ$]. The values of the $\text{C11}-\text{C9}-\text{O15}-\text{C16}$ and $\text{C13}-\text{C9}-\text{O15}-\text{C16}$ angles (Table 3), and the angle between the mean planes delineated by all the non-H atoms of the acridine and the phenyl nuclei [$85.2(1)^\circ$], testify to the almost perpendicular arrangement of the two fragments. Molecules of (II) are arranged in pairs stabilized by two $\text{C17}-\text{H17}\cdots\text{N10}$ contacts (Table 4). Adjacent pairs, which form a herringbone pattern in the crystal [the angle between these pairs – *i.e.* the mean planes delineated by the respective non-H atoms of the acridine nuclei – is $40.1(2)^\circ$], are linked through a network of $\text{C19}-\text{H19}\cdots\text{N10}$ contacts (Table 4) and non-specific dispersive interactions.

Experimental

9-(2-Chloroethylamino)acridine was obtained by heating (1.5 h at 373 K) a mixture of 9-phenoxyacridine and 2-chloroethylamine in phenol (Dupre & Robinson, 1945). The product was purified chromatographically (silica gel 60, toluene/diethylamine, 10:1 *v/v*). Analysis found: C 65.56, H 5.32, N 10.22%; calculated: C 65.45, H 5.45, N 10.18%. Yellow crystals suitable for X-ray analysis were grown from cyclohexane (m.p. 348–350 K). 9-Phenoxyacridine was synthesized according to the procedure described by Albert (1966). The product was purified chromatographically (silica gel 60, toluene/methanol, 10:1 *v/v*) and yellow crystals suitable for X-ray investigation were grown from toluene (m.p. 398–399 K).

Compound (I)

Crystal data

$\text{C}_{15}\text{H}_{13}\text{ClN}_2\cdot\text{H}_2\text{O}$
 $M_r = 274.74$
Monoclinic, $C2/c$
 $a = 14.052(3) \text{ \AA}$
 $b = 11.330(2) \text{ \AA}$
 $c = 17.283(3) \text{ \AA}$
 $\beta = 107.20(3)^\circ$
 $V = 2628.6(10) \text{ \AA}^3$
 $Z = 8$

$D_x = 1.388 \text{ Mg m}^{-3}$
Cu $K\alpha$ radiation
Cell parameters from 25 reflections
 $\theta = 5-25^\circ$
 $\mu = 2.51 \text{ mm}^{-1}$
 $T = 293(2) \text{ K}$
Prism, yellow
 $0.40 \times 0.40 \times 0.35 \text{ mm}$

Data collection

Kuma KM-4 diffractometer
 $\theta/2\theta$ scans
5227 measured reflections
2909 independent reflections
1793 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.038$
 $\theta_{\text{max}} = 81.1^\circ$

$h = -18 \rightarrow 8$
 $k = -10 \rightarrow 14$
 $l = -21 \rightarrow 22$
3 standard reflections
every 200 reflections
intensity decay: 2.5%

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.045$
 $wR(F^2) = 0.136$
 $S = 1.04$
2909 reflections
228 parameters
All H-atom parameters refined

$w = 1/[\sigma^2(F_o^2) + (0.0538P)^2 + 2.9481P]$
where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\text{max}} < 0.001$
 $\Delta\rho_{\text{max}} = 0.34 \text{ e \AA}^{-3}$
 $\Delta\rho_{\text{min}} = -0.37 \text{ e \AA}^{-3}$
Extinction correction: *SHELXL97*
Extinction coefficient: 0.00079 (10)

Table 1
Selected geometric parameters (Å, °) for (I).

C9—C11	1.425 (3)	N10—C14	1.353 (3)
C9—C13	1.427 (3)	N15—C16	1.443 (3)
C9—N15	1.352 (3)	C16—C17	1.504 (3)
N10—C12	1.345 (3)	C17—C18	1.773 (3)
C9—N15—H15	117 (2)	C12—N10—C14	117.4 (2)
C9—N15—C16	129.2 (2)	C13—C9—N15	118.5 (2)
C11—C9—C13	117.6 (2)	N15—C16—C17	110.7 (2)
C11—C9—N15	123.9 (2)	C16—C17—C18	112.2 (2)
C9—N15—H15—C16	−172 (2)	C11—C9—N15—C16	26.9 (4)
C9—N15—C16—C17	149.7 (3)	C12—N10—C14—C13	0.8 (3)
C11—C9—C13—C14	−0.4 (3)	N15—C16—C17—C18	−59.9 (3)
C11—C9—N15—H15	−163 (2)		

Table 2
Hydrogen-bonding geometry (Å, °) for (I).

<i>D</i> —H... <i>A</i>	<i>D</i> —H	H... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> —H... <i>A</i>
N15—H15...O19	0.84 (3)	2.21 (3)	2.996 (3)	157 (3)
O19—H19A...N10 ⁱ	1.00 (4)	1.93 (4)	2.908 (3)	166 (3)
O19—H19B...N10 ⁱⁱ	0.90 (4)	2.07 (4)	2.957 (3)	169 (3)

Symmetry codes: (i) $x, 1 - y, z - \frac{1}{2}$; (ii) $1 - x, 1 - y, 1 - z$.**Compound (II)***Crystal data*

C ₁₉ H ₁₃ NO	$D_x = 1.301 \text{ Mg m}^{-3}$
$M_r = 271.30$	Mo $K\alpha$ radiation
Monoclinic, $P2_1/n$	Cell parameters from 8411 reflections
$a = 9.400 (3) \text{ \AA}$	$\theta = 3.7\text{--}29.0^\circ$
$b = 10.301 (3) \text{ \AA}$	$\mu = 0.08 \text{ mm}^{-1}$
$c = 14.955 (4) \text{ \AA}$	$T = 100 (2) \text{ K}$
$\beta = 106.89 (3)^\circ$	Prism, yellow
$V = 1385.6 (7) \text{ \AA}^3$	$0.5 \times 0.5 \times 0.2 \text{ mm}$
$Z = 4$	

Data collection

Kuma KM-4 CCD diffractometer	$R_{\text{int}} = 0.038$
ω scans	$\theta_{\text{max}} = 29.0^\circ$
17 261 measured reflections	$h = -12 \rightarrow 12$
3641 independent reflections	$k = -12 \rightarrow 14$
3308 reflections with $I > 2\sigma(I)$	$l = -20 \rightarrow 20$

Table 3
Selected geometric parameters (Å, °) for (II).

C9—C11	1.3966 (14)	N10—C12	1.3490 (13)
C9—C13	1.3969 (14)	N10—C14	1.3502 (13)
C9—O15	1.3854 (11)	O15—C16	1.3907 (12)
C9—O15—C16	118.11 (7)	C12—N10—C14	117.93 (8)
C11—C9—C13	121.15 (9)	C13—C9—O15	118.97 (9)
C11—C9—O15	119.76 (8)	O15—C16—C17	123.08 (8)
C9—O15—C16—C17	−1.67 (13)	C12—N10—C14—C13	0.21 (13)
C11—C9—C13—C14	−0.54 (13)	C13—C9—O15—C16	99.06 (10)
C11—C9—O15—C16	−84.92 (11)	O15—C16—C17—C18	−177.76 (9)

Table 4
Hydrogen-bonding geometry (Å, °) for (II).

<i>D</i> —H... <i>A</i>	<i>D</i> —H	H... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> —H... <i>A</i>
C17—H17...N10 ⁱⁱⁱ	1.08	2.40	3.430 (2)	159
C19—H19...N10 ^{iv}	1.08	2.48	3.422 (2)	145

Symmetry codes: (iii) $1 - x, -y, 1 - z$; (iv) $\frac{1}{2} + x, \frac{1}{2} - y, z - \frac{1}{2}$.*Refinement*

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0595P)^2 + 0.4293P]$
$R[F^2 > 2\sigma(F^2)] = 0.043$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.115$	$(\Delta/\sigma)_{\text{max}} = 0.001$
$S = 1.07$	$\Delta\rho_{\text{max}} = 0.33 \text{ e \AA}^{-3}$
3641 reflections	$\Delta\rho_{\text{min}} = -0.24 \text{ e \AA}^{-3}$
242 parameters	
All H-atom parameters refined	

All H atoms were found in difference Fourier maps and were refined without constraints [C—H = 0.92 (4)–0.98 (3) Å in (I) and 0.955 (15)–1.016 (15) Å in (II)]. Parameters of C—H...N contacts in (II) were calculated assuming a C—H bond length of 1.08 Å (Steiner, 1997).

For (I), data collection: *KM-4 Software* (Kuma, 1989); cell refinement: *KM-4 Software*; data reduction: *KM-4 Software*. For (II), data collection: *KM4CCD Software* (Kuma, 1995–1999); cell refinement: *KM4CCD Software*; data reduction: *KM4CCD Software*. For both compounds: program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEPII* (Johnson, 1976); software used to prepare material for publication: *SHELXL97*.

The authors thank the Polish State Committee for Scientific Research (KBN) for financial support through grant No. BW/8000-4-0026-4.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: AV1203). Services for accessing these data are described at the back of the journal.

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