10-Benzyl-4-oxo-2,3,4,10-tetrahydropyrimido[4,5-*b*]quinolin-2-iminium chloride sesquihydrate: a polarized electronic structure within a complex hydrogen-bonded sheet structure

Jorge Trilleras,[a] Luis G. López,[a] Justo Cobo[b] and Christopher Glidewell[c]*

[a]Departamento de Química, Universidad del Atlántico, Km 7 vía antigua Puerto Colombia, Barranquilla, Colombia, [b]Departamento de Química Inorgánica y Orgánica, Universidad de Jaén, 23071 Jaén, Spain, and [c]School of Chemistry, University of St Andrews, Fife KY16 9ST, Scotland

Correspondence e-mail: cg@st-andrews.ac.uk

In the title compound, $C_{18}H_{15}N_4O^+ \cdot Cl^- \cdot 1.5H_2O$, one water site is fully ordered with unit occupancy while the other, which lies close to an inversion centre in the space group $C2/c$, has only 0.5 occupancy. The cation exhibits bond fixation in the fused carbocyclic ring and electronic polarization in the terminal heterocyclic ring. The components are linked into complex sheets by a combination of N—H···O, N—H···Cl, O—H···O, O—H···Cl and C—H···O hydrogen bonds.

Comment

Pyrimido[4,5-*b*]quinolines have been synthesized by a diverse range of procedures which involve the cyclocondensation of 2-aminoquinoline-3-carboxylic acid derivatives with a variety of reagents such as formamide, acetic anhydride, phenyl isocyanate and diethyl carbonate (Taylor & Kalenda, 1956). The Skraup, Dobner von Miller, Friedländer and Combes syntheses are also well known methods for preparing quinolines (Yang *et al.*, 2007). Despite this, the development of simple, general and efficient procedures for the preparation of these important heterocyclic compounds still proves to be demanding. We report here the structure of the title deazaflavine analogue which has been prepared using an intramolecular cyclization of 2-amino-4-[benzyl(phenyl)amino]-6-chloropyrimidine-5-carbaldehyde in acetic acid, mediated by microwave radiation; cyclization of precursor (*A*) (see Scheme) accompanied by hydrolysis at the 6-position yields as the primary product salt (*B*), crystallization of which gave the title compound, (I). We have recently reported the structure of the unsolvated 4-toluenesulfonate salt, (II), of the analogous 10-ethyl cation (Trilleras *et al.*, 2008) prepared in a rather similar way from precursor (*C*) (see Scheme), but here in the

presence of 4-toluenesulfonic acid rather than acetic acid. The molecular and supramolecular structures of compounds (I) and (II) are of interest as they exhibit both similarities and differences. We have not investigated the source of the water which is involved in the formation of compound (I), both in respect of the hydrolysis of the 6-chloro substituent and in the crystallization as a sesquihydrate; however, such hydrolyses appear to be entirely general in syntheses of this type, regardless of the nature of the acid employed (Quiroga *et al.*, 2010), and it seems likely that the acid is the most plausible source of the water component.
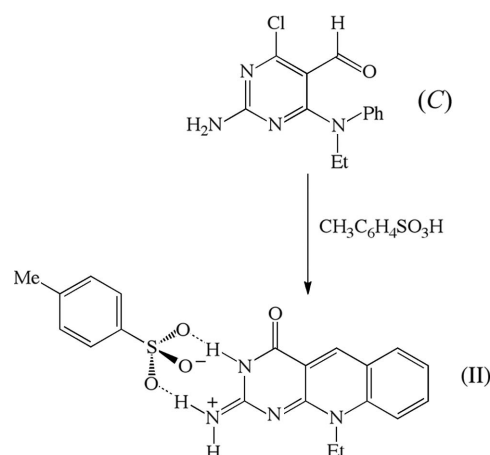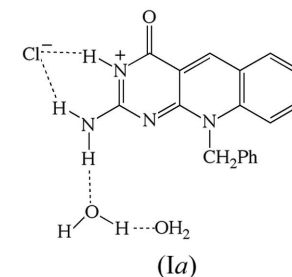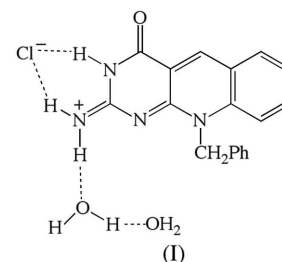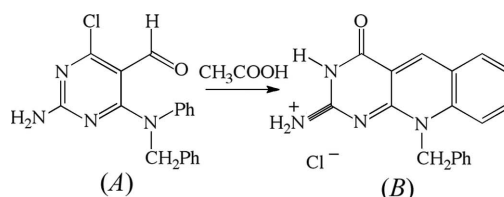
The title compound is a hydrated hydrochloride salt containing 1.5 molecules of water per ion pair (Fig. 1). One of the water molecules, that containing atom O1, is fully ordered with unit occupancy, but the other, containing atom O2, has a

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site occupancy of 0.5; unfortunately it did not prove possible to make reliable identifications of the corresponding H-atom sites. Atom O2 is located close to a centre of inversion such that the distance between the inversion-related pair of sites occupied by atoms of type O2 is only 1.005 (8) Å; consequently, if at the local level one site in such an inversion-related pair is occupied, the other must necessarily be unoccupied, and *vice versa*.

Despite the presence of four independent entities within the structure, it is possible to specify a fairly compact asymmetric unit in which the four components are all linked by hydrogen bonds (Table 2 and Fig. 1). In the selected asymmetric unit, atoms N2 and N3 both act as hydrogen-bond donors to the chloride ion, forming an $R_2^1(6)$ (Bernstein *et al.*, 1995) motif, and atom N2 also acts as hydrogen-bond donor to the full-occupancy water atom O1. The O1 atom in turn acts as hydrogen-bond donor, *via* atom H11, either to water atom O2 within the selected asymmetric unit or to the inversion-related atom O2 at $(1 - x, 1 - y, 1 - z)$, depending upon which of the two alternative O2 sites is occupied. Thus, with the asymmetric unit specified in this manner, the inversion-related pair of O2 sites lies across $(\frac{1}{2}, \frac{1}{2}, \frac{1}{2})$, but no matter which of these two sites is occupied, the O2 atom which is present in one of them always accepts a hydrogen bond from the adjacent O1 atom at (x, y, z).

Within the fused carbocyclic ring, the C—C distances (Table 1) show evidence of some bond fixation, as the C6—C7 and C8—C9 bonds are significantly shorter than the remaining peripheral bonds, while in the central ring of the fused system, the C4A—C5 bond is very much shorter than the C5—C5A bond, indicative of a double bond between atoms C4A and C5. By contrast, in the C111–C116 ring, the C—C distances all lie within a rather narrow range [1.368 (4)–1.380 (3) Å]. The

C—N distances associated with the pyrimidinone ring show some interesting variations: in particular, the exocyclic C2—N2 bond is very short for a single bond [mean value for this type (Allen *et al.*, 1987) = 1.355 (20) Å, lower-quartile value = 1.340 Å, no s.u. cited], while the C2—N3 and N3—C4 bonds differ only slightly in length. These observations indicate that the predominant canonical form (I) (see Scheme) is that having the positive charge localized at atom N2, while form (I*a*), with the charge localized at N3, is less significant. A rather similar pattern of distances was observed in the cation of compound (II), which was described as a protonated iminouracil derivative (Trilleras *et al.*, 2008).

In addition to the four hydrogen bonds within the selected asymmetric unit (Fig. 1), the structure also contains a considerable number of other hydrogen bonds, encompassing N—H⋯O, N—H⋯Cl, O—H⋯O, O—H⋯Cl and C—H⋯O types, which link the four-component aggregates defined by the selected asymmetric unit to form complex sheets. However, the analysis of the sheet formation is very much simplified using the substructure approach (Ferguson *et al.*, 1998*a*,*b*; Gregson *et al.*, 2000), which permits the identification of a one-dimensional substructure in the form of a ribbon of edge-fused rings built from the full-occupancy components only, while the linking of adjacent ribbons of this type straightforwardly leads to the formation of a sheet.

Atoms O1 and N2 in the reference aggregate at (x, y, z) act as hydrogen-bond donors, respectively, *via* atoms H12 and H22, to atoms Cl1 and O4 in the aggregate at $(\frac{1}{2} + x, \frac{1}{2} - y, \frac{1}{2} + z)$, so linking aggregates related by the *n*-glide plane at $y = \frac{1}{4}$ into a ribbon running parallel to the [101] direction and built from edge-fused $R_2^1(6)$ and $R_4^3(10)$ rings (Fig. 2).

The linking of the ribbons depends upon a combination of O—H⋯O and C—H⋯O hydrogen bonds, both having disordered water atom O2 as the acceptor, and it is convenient to consider, in turn, the two cases where the occupancy of an inversion-related pair of sites involves first the O2 site at $(x, y,$
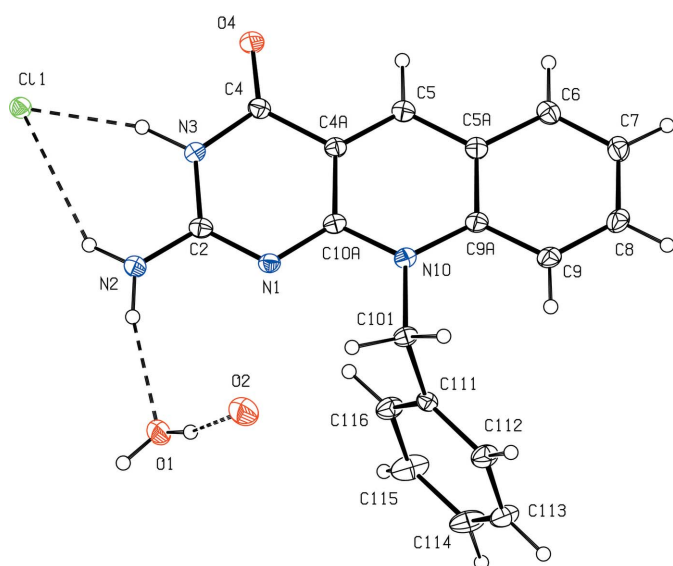

Figure 1
The independent components of compound (I), showing the atom-labelling scheme and the hydrogen bonds within the selected asymmetric unit. Water atom O2 has 0.5 occupancy but the associated H atoms could not be located. Displacement ellipsoids are drawn at the 30% probability level.
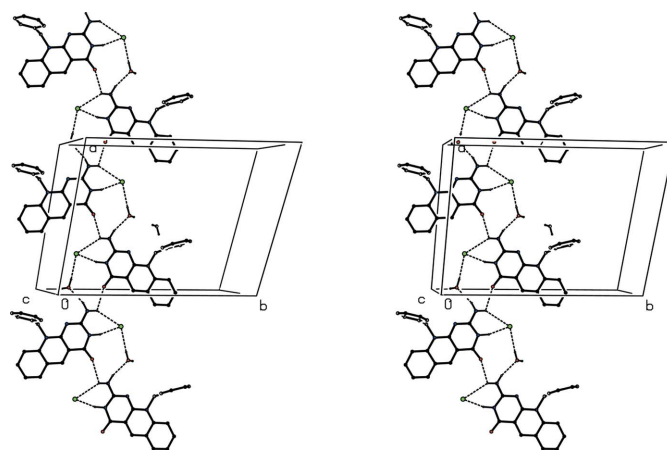

Figure 2
A stereoview of part of the crystal structure of compound (I), showing the formation of a hydrogen-bonded ribbon of $R_2^1(6)$ and $R_4^3(10)$ rings running parallel to [101]. For the sake of clarity, H atoms bonded to C atoms and the partial-occupancy water atom O2 have been omitted.

z) and secondly the O2 site at $(1 - x, 1 - y, 1 - z)$. When the O2 site at (x, y, z) is occupied and that at $(1 - x, 1 - y, 1 - z)$ is vacant, O2 accepts O—H···O hydrogen bonds from O1 at (x, y, z) and $(1 - x, 1 - y, 1 - z)$, and it accepts a C—H···O hydrogen bond from C101 at $(1 - x, 1 - y, 1 - z)$ (Table 2). On the other hand, if the O2 site at $(1 - x, 1 - y, 1 - z)$ is occupied and that at (x, y, z) is vacant, O2 still accepts O—H···O hydrogen bonds from O1 at (x, y, z) and $(1 - x, 1 - y, 1 - z)$, and it accepts a C—H···O hydrogen bond from C101 at (x, y, z). Consequently, regardless of which of the two inversion-related sites in any such pair is occupied, O2 accepts hydrogen bonds from the ordered components at (x, y, z) and $(1 - x, 1 - y, 1 - z)$. The ordered components at (x, y, z) form part of that ribbon along [101] which contains the *n*-glide plane at $y = \frac{1}{4}$, while those at $(1 - x, 1 - y, 1 - z)$ lie in the ribbon containing the *n*-glide plane at $y = \frac{3}{4}$, and propagation of these hydrogen bonds by the space-group symmetry operation links the ribbon along [101] into a complex sheet lying parallel to $(10\bar{1})$. It should be noted here that with the possible exception of the benzyl ring at $(x, 1 - y, \frac{1}{2} + z)$, there are no acceptor sites within plausible hydrogen-bonding range of the O2 site other than the two symmetry-related O1 sites; possibly this absence of available acceptor sites leads to positional disorder of the H atoms bonded to O2.

The structure also contains two C—H···Cl contacts, both of which are nearly linear (Table 2). That involving atom C5 lies within the ribbon along [101] and containing the *n*-glide plane at $y = \frac{1}{4}$, while the contact involving atom C101 is between adjacent ribbons within the $(10\bar{1})$ sheet. Regardless, therefore, of whether these contacts can be regarded as structurally significant (Aakeröy *et al.*, 1999; Brammer *et al.*, 2001; Thallapally & Nangia, 2001), they have no bearing on the overall dimensionality of the hydrogen-bonded structure.

The complex hydrogen-bonded structure of compound (I), dependent on a combination of N—H···O, N—H···Cl, O—H···O, O—H···Cl and C—H···O interactions, may be contrasted with the much simpler supramolecular structure of compound (II) (Trilleras *et al.*, 2008), where three independent N—H···O hydrogen bonds link the ions into centrosymmetric four-ion aggregates, which themselves are linked into sheets by a single, rather strong C—H···O hydrogen bond. The greater complexity in compound (I) is almost certainly a consequence of its crystallization as a hydrate; but why (I) is a hydrate, while (II) is solvent-free cannot readily be explained.

Experimental

A solution of 2-amino-4-[benzyl(phenyl)amino]-6-chloropyrimidine-5-carbaldehyde (1.0 mmol) in glacial acetic acid (1.5 ml) was subjected to microwave irradiation (maximum power 300 W during 15 min at a controlled temperature of 573 K) using a focused microwave reactor (CEM Discover). The resulting solid product was collected by filtration and washed with hot hexane to give a yellow solid that was recrystallized from hexane to afford crystals suitable for single-crystal X-ray diffraction (yield 80%, m.p. > 573 K). MS (70 eV) *m/z* (%): 303 [$(M - \text{Cl} - \text{H}_2\text{O})^+$, 23], 302 (99), 301 (78), 273 (13), 231 (30), 129 (14), 91 (100).

Crystal data

$\text{C}_{18}\text{H}_{15}\text{N}_4\text{O}^+\cdot\text{Cl}^-\cdot1.5\text{H}_2\text{O}$	$V = 3348.2\ (7)$ Å^3
$M_r = 365.82$	$Z = 8$
Monoclinic, $C2/c$	Mo $K\alpha$ radiation
$a = 18.8725\ (10)$ Å	$\mu = 0.25$ mm^{-1}
$b = 18.4777\ (8)$ Å	$T = 120$ K
$c = 13.417\ (2)$ Å	$0.41 \times 0.25 \times 0.22$ mm
$\beta = 134.307\ (7)°$	

Data collection

Bruker–Nonius KappaCCD diffractometer	33176 measured reflections
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)	3122 independent reflections
$T_{\min} = 0.885,\ T_{\max} = 0.936$	2297 reflections with $I > 2\sigma(I)$
	$R_{\text{int}} = 0.085$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.044$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.107$	
$S = 1.06$	
3122 reflections	$\Delta\rho_{\max} = 0.34$ e Å^{-3}
241 parameters	$\Delta\rho_{\min} = -0.27$ e Å^{-3}
3 restraints	

Table 1
Selected bond lengths (Å).

N1—C2	1.330 (3)	C8—C9	1.365 (4)
C2—N3	1.358 (3)	C9—C9A	1.394 (3)
N3—C4	1.367 (3)	C9A—N10	1.384 (3)
C4—C4A	1.459 (3)	N10—C10A	1.354 (3)
C4A—C5	1.342 (3)	C10A—N1	1.321 (3)
C5—C5A	1.405 (3)	C4A—C10A	1.421 (3)
C5A—C6	1.401 (3)	C5A—C9A	1.408 (3)
C6—C7	1.355 (3)	C2—N2	1.304 (3)
C7—C8	1.385 (4)	C4—O4	1.206 (3)

Table 2
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N2—H21···O1	0.86	2.03	2.876 (4)	165
N2—H22···Cl1	0.91	2.71	3.484 (2)	144
N2—H22···O4^i	0.91	2.33	2.745 (3)	108
N3—H3···Cl1	1.00	2.09	3.068 (2)	163
O1—H11···O2	0.83 (4)	1.90 (4)	2.711 (7)	165 (3)
O1—H11···O2^{ii}	0.83 (4)	2.04 (4)	2.847 (6)	165 (3)
O1—H12···Cl1^i	0.81 (3)	2.43 (3)	3.233 (3)	172 (3)
C5—H5···Cl1^{iii}	0.95	2.66	3.570 (3)	161
C101—H10A···O2^{ii}	0.99	2.29	3.112 (6)	139
C101—H10B···Cl1^{iv}	0.99	2.58	3.519 (3)	159

Symmetry codes: (i) $x + \frac{1}{2}, -y + \frac{1}{2}, z + \frac{1}{2}$; (ii) $-x + 1, -y + 1, -z + 2$; (iii) $x - \frac{1}{2}, -y + \frac{1}{2}, z - \frac{1}{2}$; (iv) $-x + \frac{1}{2}, y + \frac{1}{2}, -z + \frac{3}{2}$.

It was apparent from an early stage in the refinement that the atom site designated as O2 (*a*) had only partial occupancy and (*b*) was close to an inversion-related analogue. Refinement of the site occupancy for O2, treated anisotropically, gave an occupancy of 0.494 (7); thereafter the site occupancy was fixed at 0.5. Alternative assignments for this site were discounted on the following grounds: chloride and hydroxide were discounted because difference maps provided no evidence of any further protonation elsewhere in the structure, and in any event this site is too close to O1 for it to be occupied by Cl; NH₃ was discounted because refinement of the site occupancy of N gave a value of 0.591 (7), which is impossible so close to an inversion centre. Although data were collected to $\theta = 27.5°$, the data were very weak

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above $\theta = 25.5°$ with correspondingly rather high values of R_1 and wR_2; accordingly, reflections with $\theta > 25.5°$ were excluded from the final refinements. With the exception of the H atoms bonded to O2, all other H atoms were located in difference maps, but there is no evidence for any degree of protonation at atoms N1 or N10. H atoms bonded to C atoms were then treated as riding atoms in geometrically idealized positions, with C—H distances of 0.95 (ring H atoms) or 0.99 Å (CH$_2$) and with $U_{iso}(H) = 1.2U_{eq}(C)$. H atoms bonded to N atoms were permitted to ride at the positions deduced from the difference maps, with $U_{iso}(H) = 1.2U_{eq}(N)$, giving N—H distances in the range 0.86–1.00 Å. The coordinates of the H atoms bonded to water atom O1 were refined, with $U_{iso}(H) = 1.5U_{eq}(O)$, with restraints of 0.82 (1) and 1.32 (2) Å, respectively, applied to the O—H and H$\cdots$H distances, giving final O—H distances of 0.81 (3) and 0.83 (4) Å.

Data collection: *COLLECT* (Hooft, 1999); cell refinement: *DIRAX/LSQ* (Duisenberg *et al.*, 2000); data reduction: *EVALCCD* (Duisenberg *et al.*, 2003); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *PLATON* (Spek, 2009); software used to prepare material for publication: *SHELXL97* and *PLATON*.

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