2-(4-Chlorophenyl)-1,3-dicyano-6,7-dihydro-4-imino-9,10-dimethoxy-benzo[a]quinolizine–water (2/5)

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Crystals of the title compound, C_{23}H_{17}ClN_{4}O_{2}·2.5H_{2}O, contain channels filled with highly disordered water molecules. The best structure refinement was obtained by removing the solvent contribution from the intensity data and refining against a solvent-free model. The central six-membered ring of the quinolizine molecule has a slightly distorted screw-boat conformation.

Comment

Fused isoquinoline derivatives are of considerable pharmaceutical and agricultural interest (Kleeman & Engel, 1982; Dannhardt & Sommer, 1985; Fülöp et al., 1990). Compounds with a fused five-membered ring at the original isoquinoline C=N bond can be prepared conveniently by 1,3-dipolar cycloadditions with 3,4-dihydroisoquinolines, (I) (Shawali, 1993). For example, [1,2,4]triazolo[3,4-a]isoquinolines of type (II) were obtained in high yield from cycloadditions with nitrile–imines (cf. Caramella & Grünanger, 1984), which were generated in situ from the corresponding hydrazonoyl halides by elimination of HX on treatment with a base (Dannhardt & Sommer, 1985; Fülöp et al., 1990; Szabó et al., 1992; Abdelhadi et al., 1996; Elwan et al., 1996; Awad et al., 2002). On the other hand, pyrrolo[2,1-a]isoquinoline derivatives were obtained from 1-(cyanomethyl)-3,4-dihydroisoquinolines and hydrazonoyl halides in refluxing tetrahydrofuran in the presence of Et_{3}N (Awad et al., 2002). In none of the reactions was a product with a fused six-membered ring formed (cf. Fülöp et al., 1990; Elwan et al., 1996). However, isoquinolines with a fused six-membered ring at the original C=N bond are attractive targets (Fülöp et al., 1997; Fülöp & Bernáth, 1999; Martinek et al., 2000), and several methods for the preparation of benzo[a]quinolizines have been reported (Kametani, 1978; Bhattacharjya et al., 1983; Maiti & Pakrashi, 1984; Ninomiya et al., 1984; Akhrem & Chernov, 1988).

Recently, we developed a novel and efficient one-pot synthesis for polyfunctional benzo[a]quinolizine derivatives (Awad et al., 2002). The reaction of 1-(cyanomethyl)-6,7-dimethoxy-3,4-dihydroisoquinoline [(I), \( R^1 = CH_2CN \)] with ethyl \( \beta \)-aryl-\( \alpha \)-cyanocinnamates in the presence of piperidine led to 1,3-dicyano-6,7-dihydrobenzo[a]quinolizin-4-ones, (III), in high yield, whereas similar reactions with arylidene-malononitriles gave the corresponding 4-iminoquinolizines,

![Figure 1](https://example.com/figure1.png)

Figure 1
View of the quinolizine molecule of (IVA) showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level. H atoms are represented by circles of arbitrary size. The solvent molecules were not included in the model.
C4 and C5 (Awad et al., 2002). The structures of these products have been established on the basis of their spectroscopic data and elemental analyses. With the aim of proving the structure of the imino compounds of type (IV), the low-temperature crystal structure of the title compound, (IVA) (R = Me, R1 = CN, Ar = 4-ClC6H4), has been determined.

Compound (IVA) crystallizes as a hydrate with approximately 2.5 water molecules for every quinolizine molecule. There are two solvent cavities per unit cell, so that each cavity contains five water molecules. The water molecules appear to be highly disordered and it was difficult to model their positions and distribution reliably. Therefore, the SQUEEZE function of PLATON (van der Sluis & Spek, 1990; Spek, 2001) was used to eliminate the contribution of the electron density in the solvent region from the intensity data, and the solvent-free model was employed for the final refinement. Further details are given in the Experimental section. Due to the omission of the water molecules from the model, it was not possible to analyse the hydrogen-bonding interactions fully. Attempts to model the solvent molecules indicated that they are suitably positioned for a series of water–water hydrogen bonds to exist. The packing diagram (Fig. 2) shows that the solvent cavities are aligned into channels through the structure, so that infinite chains of hydrogen-bonded water molecules are conceivable. Fig. 2 also shows that the imine H atom is far from the solvent channels and is therefore unable to form a hydrogen bond with any of the water molecules. Furthermore, the N2—H2 bond is aligned in the plane of the quinolizine molecule and these molecules are stacked parallel to one another. In this position, the imine H atom does not partake in any hydrogen-bonding interactions.

The central six-membered ring of the quinolizine molecule has a slightly distorted screw-boat conformation (Fig. 1), with puckering parameters (Cremer & Pople, 1975) Q = 0.514 (3) Å, θ = 72.7 (2)° and φ = 263.3 (3)° for the atom sequence N1—C6—C7—C12—C13—C14. For an ideal screw-boat, the nearest ideal values are θ = 67.5° and φ = 270°. Atoms C12 and C13 are 0.409 (4) and 0.887 (4) Å, respectively, from the mean plane defined by atoms N1, C6, C7 and C14, and the r.m.s deviation of these latter four atoms from their plane is 0.035 Å. The r.m.s. deviation of the six atoms of the benzo ring from their mean plane is 0.011 Å, while the cyano-substituted six-membered ring is distorted very slightly from planarity, with an r.m.s. deviation of 0.031 Å; the maximum deviation from this plane is 0.0527 (16) Å for C6. The angle between the mean planes of the benzo and cyano-substituted rings is 29.71 (6)°, while the latter ring makes an angle of 43.25 (6)° with the p-chlorophenyl ring. The bond lengths around the cyano-substituted six-membered ring (Table 1) show that there is significant delocalization of the electron density from the C2=N=N2, C3=C4 and C5=C6 double bonds towards the N1—C2, N1—C6 and C4—C5 bonds. Similar delocalization involving the N1 atom is observed in the structure of the related compound 11,16,16-trimethyl-8-aza-homogona-1,3,5(10),9(11),13,17-hexa-12-one (Lyakhov et al., 1997).

**Experimental**

The title compound, (IVA)-2.5H2O, was obtained in 82% yield by reacting 1-(cyanomethyl)-3,4-dihydro-6,7-dimethoxyisoquinoline [(I), R = Me, R1 = CH2CN; 1.15 g, 5 mmol] with (4-chlorophenyl)-methylidenemalononitrile (0.94 g, 5 mmol) and piperidine (0.5 ml) in refluxing acetonitrile (40 ml) for 3 h. After evaporation of the solvent in vacuo, the residue was triturated with methanol (10 ml) and crystallized from ethanol (m.p. 494–496 K). Suitable single crystals of (IVA)-2.5H2O were obtained by recrystallization from diethyl ether.

**Crystal data**

C23H17ClN4O2·2.5H2O  
Mø = 461.90  
Monoclinic, P21/c  
α = 17.4665 (18) Å  
β = 17.0031 (16) Å  
γ = 7.347 (3) Å  
V = 2175.1 (9) Å³  
Z = 4

**Data collection**

Rigaku AFC-5R diffractometer  
ω-20 scans  
5556 measured reflections  
4982 independent reflections  
Rint = 0.034  
θmax = 27.5°

**Refinement**

Refinement on F²  
R(F²) > 2σ(F²) = 0.051  
wR(F²) = 0.151  
S = 0.97  
4982 reflections  
277 parameters

H atoms treated by a mixture of independent and constrained refinement  
w = 1/[σ²(Fo²) + (0.0795P)²]  
where P = (F² + 2Fo²)/3  
(Δρ)max = 0.31 e Å⁻³  
Δρmin = −0.26 e Å⁻³

There are two cavities of 178 Å³ per unit cell which appear to be filled by rather diffuse water molecules. The symmetry-unique cavity is centred at (0.18, 0.25, −0.03). Satisfactory refinement results were
obtained when two full-occupancy O atoms and one half-occupancy O atom were defined in the asymmetric unit. This yields five water molecules per cavity. However, the anisotropic displacement parameters of these O atoms were very large. Several trials at defining additional sites or using lower site-occupation factors for these O atoms yielded inferior results. Therefore, it was assumed that the additional sites or using lower site-occupation factors for these O atoms were very large. Several trials at defining N1–C2 1.414 (3), C2–C3 1.463 (3), C1–C2 1.374 (3), C1–C14 1.482 (3), C4–C5 1.430 (3), and C5–C6 1.403 (3) selected interatomic distances (Å).

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<tr>
<td>N1–C6</td>
<td>1.363 (3)</td>
<td>C2–C3</td>
<td>1.463 (3)</td>
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<tr>
<td>N1–C2</td>
<td>1.414 (3)</td>
<td>C3–C4</td>
<td>1.374 (3)</td>
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<td>1.430 (3)</td>
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<tr>
<td>N2–C2</td>
<td>1.283 (3)</td>
<td>C5–C6</td>
<td>1.403 (3)</td>
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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1527). Services for accessing these data are described at the back of the journal.

References