Instrumental Achievements

Crystal Structure of 3-Amino-1,2,4-triazin-5(2*H*)-one

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The 1,2,4-triazine ring system had been suggested for study because of various interesting biological activities.[1] The tautomeric proton is highly effective at making strong intermolecular hydrogen binding with other heteroatoms of molecules involved with biological activity. The title compound 3-amino-1,2,4-triazin-5(2*H*)-one (6-azaisocytosine, Fig. 1), an isosteric isomer of isocytosine, can exist in several tautomeric forms, which have been discussed in earlier reports.[2-4] Ueda and Furukawa[2] concluded that the imino-oxo form is predominant, as shown by infrared spectra. Sasaki and Minamoto[3] used ultraviolet and infrared spectra to show that amino-oxo form (4*H*-tautomer) to be predominant. Pitha *et al*.[4] compared ultraviolet spectra and ionization constants to reveal the relative abundances as 100:1, in favor of the amino-oxo form (2*H*-tautomer). There is a need to obtain more precise information about the most contributed prototropic tautomerism of the title molecule and to confirm the assigned structure. So we have undertaken a critical use of X-ray crystallographic analysis.

The title compound was prepared by the method of Sasaki and Minamoto.[3] The physical properties of 3-amino-1,2,4-triazin-5-one had been reported: mp,[4-6] IR,[2,3,5] UV,[3-5] NMR,[5,6] and dissociation exponent.[4] A colorless crystal of dimensions 0.35 × 0.50 × 0.55 mm^3 suitable for single-crystal X-ray diffraction measurements was obtained by recrystallization from H_2O solution. The results of the X-ray structure determination are given in Tables 1 – 3. The ORTEP diagram for the title compound is shown in Fig. 2.

Data from the X-ray structure reveal that the oxidation site is at C-5 position and that the predominant tautomeric structure is amino-oxo form 2*H*-tautomer (3-amino-1,2,4-triazin-5(2*H*)-one). This analysis reveals that the 1,2,4-triazine ring structure of 3-amino-1,2,4-triazin-5(2*H*)-one is slightly distorted due to the asymmetry of the electronegativity of nitrogen. Obviously, the tautomeric proton 2-H is located at N-2 (N2) with 0.885(20)Å bond distance shorter than the bond length of H–N(3) 1.009 Å,[7] which means the H2–N2 single bond is strongly attracted by the greater π-deficiency triazine ring. The same reason also explains the result that the bond distance 0.966(19)Å of C3–H1 is shorter than the bond length 1.083 Å of C*ar*–H.[7] On the other hand, because of the π-electron resonance effect in the triazine ring, the C1–O bond length 1.2413(18)Å is nearly the same as the bond length 1.240 Å of C*sp*^{2} = O(1) in δ-lactams, and the N2–N3 bond length 1.3565(18)Å is longer than the 1.304 Å of N=N (aromatic) in pyridazine.[7] The short bonds 1.3328(18)Å (C2–N1) and 1.2829(20)Å (C3–N3) in the ring have an appreciable double-bond character, and the latter may be the pathway of 2-H to resonate with 5-O. It is interesting to

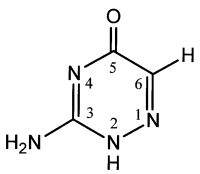

Fig. 1 Chemical structure of 3-amino-1,2,4-triazin-5(2*H*)-one and atom-numbering scheme.

Table 1 Crystal and experimental data

Formula: $C_3H_4N_4O$
Formula weight = 112.09
Crystal system: monoclinic
Space group: $P2_1/c$ $Z = 4$
a = 3.8404(4)Å
b = 9.6713(9)Å β = 97.270(14)°
c = 12.1444(20)Å
V = 447.44(10)Å^3
D_{calc} = 1.664 g/cm^3
μ(Mo K$_\alpha$) = 1.238 cm^{-1}
F(0 0 0) = 232
$2\theta_{max}$: 55.0°
h k l range: –4/4, 0/12, 0/15
λ(Mo K$_\alpha$) = 0.7107 Å
T = 298 K
No. of unique reflections measured = 1016
No. of observed reflections = 878 [$I > 2.0\sigma(I)$]
R = 0.033
Rw = 0.032
Goodness-of-fit = 1.87
No. of refined parameters = 90
$(\Delta/\sigma)_{max}$ = 0.0004
$(\Delta\rho)_{max}$ = 0.200 eÅ^{-3}
$(\Delta\rho)_{min}$ = –0.190 eÅ^{-3}
Measurement: Enraf-Nonius CAD4
Program system: NRCVAX
Structure determination: direct method
Refinement: full-matrix least-squares

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Table 2 Atomic parameters *x*, *y*, *z* and B_{eq}

Atom	*x*	*y*	*z*	B_{eq}
O	0.7956(3)	0.29777(12)	0.26074(09)	3.29(5)
N1	0.4946(3)	0.34662(12)	0.09245(10)	2.15(5)
N2	0.1680(4)	0.16436(13)	0.00245(11)	2.40(5)
N3	0.2612(4)	0.07167(13)	0.08475(11)	2.49(5)
N4	0.1748(4)	0.37651(15)	– 0.07993(11)	2.79(5)
C1	0.5965(4)	0.25964(15)	0.17776(12)	2.21(6)
C2	0.2826(4)	0.29716(14)	0.00607(12)	2.01(5)
C3	0.4669(4)	0.11661(15)	0.16858(13)	2.48(6)
H1	0.536 (5)	0.0518 (20)	0.2278 (15)	3.5 (4)
H2	0.038 (5)	0.1319 (21)	– 0.0573 (17)	3.9 (4)
H3	0.035 (5)	0.3391 (20)	– 0.1390 (16)	3.6 (4)
H4	0.266 (5)	0.4640 (22)	– 0.0819 (16)	4.1 (5)

Estimated standard errors refer to the last digit printed.
B_{eq} is the mean of the principal axes of the thermal ellipsoid.

Table 3 Selected bond distances (Å) and bond angles (°)

O-C1	1.2413(18)	N2-C2	1.3565(18)
N1-C1	1.3534(18)	N3-C3	1.2829(20)
N1-C2	1.3328(18)	N4-C2	1.3196(19)
N2-N3	1.3565(18)	C1-C3	1.4696(21)
C1-N1-C2	117.92(12)	N1-C1-C3	117.68(12)
N3-N2-C2	123.20(12)	N1-C2-N2	121.92(13)
N2-N3-C3	116.06(12)	N1-C2-N4	120.89(13)
O-C1-N1	121.70(13)	N2-C2-N4	117.20(13)
O-C1-C3	120.61(13)	N3-C3-C1	123.22(13)

note that the bond distance 1.3196(19)Å between C2–N4 is shorter than the bond length 1.355 Å of C*ar*-NH_2 (Nsp^2: planar),[7] even shorter than those of C1–N1, C2–N1, C2–N2 and N2–N3 in the triazine ring. Evidently, the 3-amino group strongly donates the unpaired electrons and resonates with the 1,2,4-triazine ring.

This X-ray analysis has clarified that the prototropic tautomerism of 3-amino-1,2,4-triazin-5(2*H*)-one has the long distance resonance, which also serves as the mechanism of the conclusion from our previous X-ray crystallographic analysis study[8] that the site of *N*-glycosylation of 3-amino-1,2,4-triazin-5(2*H*)-one is at N-2 (N2).

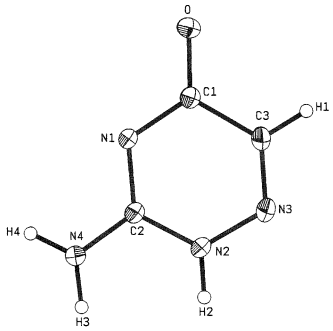

Fig. 2 ORTEP drawing of 3-amino-1,2,4-triazin-5(2*H*)-one.

Acknowledgements

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