Hydrolysis of Methylthiazolopyridines. X-ray Crystal Structure of 3-Acetamido-2(1*H*)-pyridinethione

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Hydrolysis of 2-methylthiazolo[5,4-*b*]pyridine resulted in ring opening of the thiazole and formation of 3-acetamido-2(1*H*)-pyridinethione whose X-ray crystal structure has been determined.

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Introduction.

Thiazole derivatives have received and continue to receive considerable attention [1-4]. One interesting aspect of their chemistry concerns their photochemical reactions [5]. Another area of interest is the use of isothiazole dioxides as chiral auxilliaries in the stereoselective synthesis as well as their use as sweetening agents [6,7]. In addition, furanosylisothiazoles are involved in the chemistry of nucleic acids [8]. Isothiazole derivatives exhibit biological activities against wide classes of fungi and bacteria [9]. They can also act as inhibitors of blood platelet aggregations [10] and can have other important pharmacological properties, such as antiviral and anti HIV-1 activity [11].

For some years we have been developing a research project aimed at the synthesis and structural characterization of heterocyclic isomers formed by a pyridine ring fused with a five-membered ring [12,13]. In this project the eight members of 3-methyl-1,2- and 2-methyl-1,3-oxazolopyridines have been synthesized and characterized [14-16].

Recently our interest has been focused on thiazoles. We have synthesized and characterized all the members of the two classes of 3-methyl-1,2- and 2-methyl-1,3-thiazolopyridine isomers [17]. We report here the crystal and molecular structure of 3-acetamido-2(1*H*)-pyridinethione [18] obtained as hydrolysis product of 2-methyl-1,3-thiazolo[5,4-*b*]pyridine (Scheme 1).

Results and Discussion.

Among different reaction products possible, the addition of a water molecule to the 2-methylthiazolo[5,4-*b*]pyridine results in thiazole ring opening and the formation of 3-acetamido-2(1*H*)-pyridinethione. Crystal data are given in Table 1. Atomic coordinates and equivalent isotropic thermal parameters, as determined by X-ray crystallography, are reported in Table 2. The molecular structure is depicted in Figure 1, while geometrical parameters are given in Table 3.

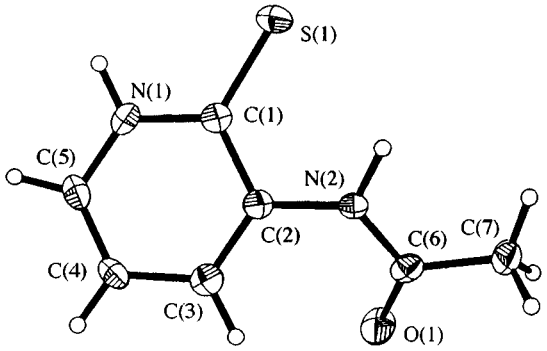

Figure 1. Molecular structure of 3-acetamido-2(1*H*)-pyridinethione. Thermal ellipsoids enclose 50% probability.

The C(1)=S(1) bond length is equal to 1.690(4) Å. This distance reflects the influence of substitution in position 3 as well as that on N(1). In different structure determina-

Scheme 1

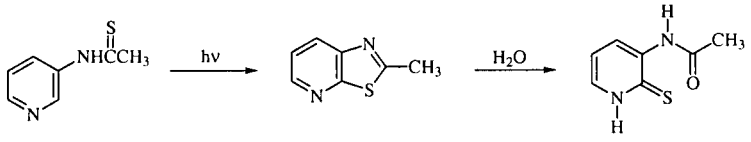

Table 1
Crystal Data for 3-Acetamido-2(1*H*)-pyridinethione

Formula	$C_7H_8N_2OS$
M	168.2
Crystal size/(mm)	0.3 x 0.2 x 0.2
Crystal System	Orthorhombic
Space Group	$Pna2_1$ (n. 33)
a/Å	7.000(1)
b/Å	11.166(1)
c/Å	9.770 (1)
U/Å^3	763.6(1)
Z	4
F(000)	352
D_c/g cm^{-3}	1.46
μ(Mo-Kα)/cm^{-1}	0.361
Radiation	graphite monochr. MoKα (λ = 0.71073 Å)
Scan mode	ω
Scan range/°	2.8 ≤ θ ≤ 25.0
Scan width/°	0.90
Scan speed/° min^{-1}	3.0
Temperature /°C	-93
Unique reflections	825 (R_{int} = 0.02)
Refinement Method	full-matrix anisotropic least squares on F^2 for all reflections
No. parameters refined	108
$R_1(F^2>2\sigma(F^2))$	0.036
$wR_2(F^2>2\sigma(F^2))$	0.063

Table 2
Atom Coordinates and Equivalent Isotropic Thermal Parameters (Å^2) for Non-hydrogen Atoms for 3-Acetamido-2(1*H*)-pyridinethione

Atom	x/a	y/b	z/c	U_{eq}
S(1)	0.07302(16)	-0.00573(8)	0.51758(16)	0.0300(3)
C(1)	0.1068(6)	0.1237(3)	0.6040(4)	0.0190(9)
N(1)	0.1713(5)	0.1221(3)	0.7371(3)	0.0222(9)
C(2)	0.0728(6)	0.2403(3)	0.5489(4)	0.0185(10)
C(3)	0.1035(6)	0.3410(4)	0.6250(4)	0.0234(10)
C(4)	0.1673(6)	0.3312(4)	0.7625(4)	0.0243(11)
C(5)	0.2004(6)	0.2205(3)	0.8136(4)	0.0246(10)
N(2)	0.0042(5)	0.2441(3)	0.4130(3)	0.0201(7)
C(6)	0.0316(6)	0.3344(4)	0.3231(4)	0.0216(10)
O(1)	0.1267(5)	0.4240(2)	0.3496(3)	0.0353(8)
C(7)	-0.0634(7)	0.3187(4)	0.1859(4)	0.0307(12)

Table 3
Bond Lengths (Å) and Angles (°) for 3-Acetamido-2(1*H*)-pyridinethione

S(1)-C(1)	1.690(4)
C(1)-N(1)	1.377(5)
C(1)-C(2)	1.429(5)
C(2)-C(3)	1.365(6)
C(3)-C(4)	1.420(6)
C(4)-C(5)	1.353(6)
C(5)-N(1)	1.344(5)
C(2)-N(2)	1.412(5)
N(2)-C(6)	1.351(5)
C(6)-O(1)	1.229(5)
C(6)-C(7)	1.507(6)
S(1)-C(1)-N(1)	120.4(3)
S(1)-C(1)-C(2)	124.6(3)
N(1)-C(1)-C(2)	115.0(3)
C(1)-C(2)-C(3)	121.3(3)
C(2)-C(3)-C(4)	120.1(4)
C(3)-C(4)-C(5)	118.2(4)
C(4)-C(5)-N(1)	121.0(3)
C(5)-N(1)-C(1)	124.3(3)
C(1)-C(2)-N(2)	116.0(3)
C(3)-C(2)-N(2)	122.7(3)
C(2)-N(2)-C(6)	125.8(3)
N(2)-C(6)-O(1)	123.2(4)
N(2)-C(6)-C(7)	115.4(3)
O(1)-C(6)-C(7)	121.4(4)

tions of pyridine-2(1*H*)-thione this value ranges from 1.672 [19] to 1.700 Å [20], the last structure has been obtained at 116 K. In structures of substituted pyridine-2(1*H*)-thione derivatives, the lowest value determined for the C=S bond length is 1.660 Å found in 5-ethoxycarbonyl-6-methyl-4-(4-fluorophenyl)-3-cyano-2(1*H*)-pyridinethione [21], while the highest value is 1.719(6) Å found in the fused system *N*-{2-[5-methyl-1,3,4-thiadiazolo[3,2-*a*]pyridinio]} acetamidate [22].

The C(1)-N(1) and N(1)-C(5) bond lengths are 1.377(5) and 1.344(5) Å, respectively, in agreement with the mean values of 1.378 (σ_{mean} = 0.004) and 1.355 Å (σ_{mean} = 0.002) obtained for 11 X-ray structures of 3-substituted pyridine-2(1*H*)-thiones found from a search at the Cambridge Structural Database v. 5.16. The other C-C bond lengths in the pyridine ring are similar to those found in analogous structures. The C(2)-N(2) bond length is equal to 1.412(5) Å, while in the acetamido moiety the bond distances N(2)-C(6), C(6)-O(1) and C(6)-C(7) are equal to 1.351(5), 1.229(5), and 1.507(6) Å, respectively.

The S(1)-C(1)-N(1) and N(1)-C(1)-C(2) bond angles are equal to 120.4(3) and 115.0(3)°, respectively, in agreement with analogous structures. The exocyclic bond angle C(1)-C(2)-N(2) is equal to 116.0(3)°.

The pyridine ring is planar with atom deviations less than 0.008 Å from its least squares plane. The sulfur atom is almost coplanar with the heterocyclic system with a deviation of -0.015(1) Å from its least squares plane. The substituent in position 3 is also planar. The least squares plane defined by N(2), C(6), O(1) and C(7) forms a dihedral angle with the pyridine equal to 29.8(1)°. The torsion angle C(1)-C(2)-N(2)-C(6) is equal to -152.2(4)°.

Intramolecular interactions occur between the sulfur and H(N) atoms with S...H(N(1)) and S...H(N(2)) distances equal to 2.688(2) and 2.508(1) Å, respectively. Stacking interactions occur between molecules related by *x+1/2, -y+1/2, z* whose pyridine rings are almost parallel with intermolecular distances in the range 3.2-3.5 Å (Figure 2). The pyridine rings of adjacent molecules in the crystal form a dihedral angle equal to 38°. Intermolecular hydrogen bonds are also present in the crystal structure involving O(*x, y, z*)...H(N(1))(*-x+1/2, y+1/2, z-1/2*) and O(*x, y, z*)...H(N(2))(*x+1/2, -y+1/2, z*) with distances equal to 2.037(3) and 2.525(3) Å, respectively (Figure 2).

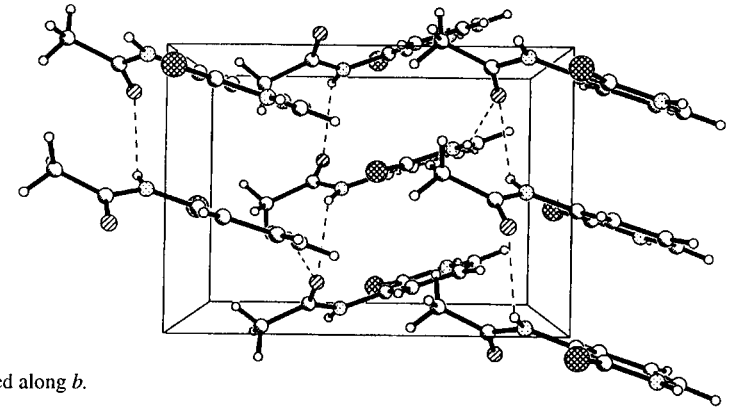

Figure 2. Crystal packing viewed along *b*.

EXPERIMENTAL

2-Methylthiazolo[5,4-*b*]pyridine was synthesized by photocyclization of 3-thioacetamidopyridine in hexane [23]. The addition of water yielded 3-acetamido-2(1*H*)-pyridinethione; m.p. 196-197° C.

Anal. Calcd. for $C_7H_8N_2OS$: C, 49.98; H, 4.79; N, 16.65; Found: C, 49.60; H, 4.42; N, 15.80.

Crystallographic data were collected on a Siemens P4 four-circle diffractometer with graphite monochromated Mo-Kα radiation (λ = 0.71069 Å) in the range $-3 \le h \le 8$, $-13 \le k \le 1$, $-11 \le l \le 11$, ω scan mode for $2.8 \le \theta \le 25.0°$ scan range, scan width 0.90°, constant scan speed 3.0°min^{-1}. The data collection was performed at -93° C by using a Siemens LT-2A low temperature device. The temperature measured by a thermocouple was constant within ±1° C. Three standard reflections measured every 97 reflections showed no variations. 1042 total reflections (R_{int} = 0.02) were collected. Absorption correction was not applied.

The structure was solved by direct methods implemented in SHELX-97 [24]. The refinement was carried out by full-matrix anisotropic least-squares on F^2 for all reflections for all non-H atoms by using SHELX-97 [24]. The hydrogen atoms were localized in the Fourier map and included in the structure-factor calculations.

Final refinement of 108 parameters gave R_1 = 0.036 and wR_2 = 0.063 for $F^2 > 2\sigma(F^2)$. Weighting scheme was $w = 1/[\sigma^2(Fo)^2+0.0288P^2+0.1243P]$, where $P=(Fo^2+2Fc^2)/3$. Minimum and maximum height in last Δρ map were -0.20 and 0.22 eÅ^{-3}, respectively. Atomic scattering factors including f ' and f " were taken from reference 24. Geometrical calculations and molecular graphics were performed by using PARST [25] and SHELXTL [26] packages, respectively.

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