Structure and Reactions of a Thiazolino[3,2-*a*]pyrimidine Carbinolamine (1)

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Ethyl 4-chloroacetoacetate condenses with 4-amino-6-hydroxy-2-pyrimidinethiol to yield ethyl 3-hydroxy-5-oxo-7-aminothiazolino[3,2-*a*]pyrimidin-3-acetate (**3**), and not ethyl 3-hydroxy-5-amino-7-oxothiazolino[3,2-*a*]-pyrimidin-3-acetate, as previously reported. This compound reacts with ammonia to produce ethyl 4-(6′-amino-4′-oxo-2′-pyrimidinethiol)-3-aminocrotonate (**8**), the open chain structure of which accounts for the cyclization of **3** to the poly-cyclic lactam, 6a-hydroxy-5,6,6a,7-tetrahydro-8-thia-1,4-diazacycl[3.3.2]azine-2,5-dione, rather than the sterically more favorable lactone, when **3** was treated with triethylamine. Some other reactions of **3** are described, and the structures of **3** and **8** were comfirmed by single crystal X-ray diffraction analysis.

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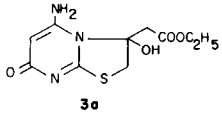
We have shown (2-4) that ethyl 4-chloroacetoacetate (**1**), when reacted with "thiocarbamate containing" compounds, is a versatile reagent for the formation of sulfur-nitrogen containing heterocycles. We recently reported the cyclizations of ester **1** with pyrimidine-2-thiols (3,4), including the reaction of 4-amino-6-hydroxy-2-pyrimidinethiol **2** with **1** to yield a covalently hydrated thiazoloino-[3,2-*a*]pyrimidin-3-acetate to which we assigned structure **3a** (4). This assignment was based on the principal of least



3a

distortion, and depended on the observation that the acetate side chain could be caused to condense with the amine group to form lactam **9** (Scheme 1) by treatment with concentrated hydrochloric acid, or with triethylamine in boiling ethanol (4). The structure of **9** was confirmed by X-ray crystal diffraction analysis.

In the course of studying the chemistry of compound **3**, it was observed that treatment with ammonia in alcohol opened the thiazoline ring, to form the β-aminocrotonate **8** (Scheme 1). The structure of this crystalline derivative was established also by X-ray crystal diffraction analysis. Since treatment with base in alcohol opened the ring, a method which was useful in converting **3** to the free base of **9** (4), the principal of least distortion was no longer valid and structure **3a** became suspect. Indeed, X-ray crystal diffraction analysis proved that **3** had the isomeric structure of ethyl 3-hydroxy-5-oxo-7-aminothiazolino[3,2-*a*]-pyrimidine-3-acetate, shown in Scheme 1. The details of single crystal structure analysis of compounds **3** and **8** are reported here (*vide infra*).

Compound **3**, which contains a carbinolamine moiety, underwent a variety of reactions; however, efforts to replace the hydroxy group of the carbinolamine function were unsuccessful. Dehydration of **3** to ethyl 7-amino-5-oxothiazolo[3,2-*a*]pyrimidin-3-acetate (**4**) was achieved by warming in concentrated sulfuric acid (Scheme 1). An unconjugated carbonyl band at 1725 cm^{-1} in the ir (potassium bromide) indicated that **4** eliminated water in the 2-3 position to generate the double bond in the triazole ring as opposed to formation of an α,β-unsaturated ester by exocyclic dehydration. Two one proton singlets came at δ 6.90 (C-2) and 4.95 (C-6) in the pmr (hexadeuteriodimethyl sulfoxide).

Solution in concentrated hydrochloric acid resulted in hydrolysis of **4** to 7-amino-5-oxothiazolo[3,2-*a*]pyrimidin-3-acetic acid hydrochloride (**5**) (Scheme 1). Protonation on the C-7 amino group was indicated by the broad three proton singlet at δ 8.55 in hexadeuteriodimethyl sulfoxide. The thiazole C-2 proton appeared as a sharp singlet at δ 6.90 and the pyrimidine C-6 hydrogen gave a broad singlet at δ 5.05. A typical salt stretch (3200-2400 cm^{-1}) was visible in the ir (potassium bromide).

Nitrosating **3** at 0° yielded a mixture of two products: ethyl 3-hydroxy-5-oxo-7-iminothiazolino[3,2-*a*]pyrimidin-3-acetate-6-oxime (**6**) (Scheme 1), the main component, and impure 4-amino-6-hydroxy-5-nitroso-2-thiopyrimidine (**7**). At room temperature, the major product was **7**. The two compounds were easily separated on basis of solubility. Violet crystals of **6** were precipitated from acetone solution. Compound **7** was identified by spectral comparison with a commercial sample (Aldrich). Nitrogen-hydrogen and oxygen-hydrogen stretching absorbed between 3300 and 2700 cm^{-1} and carbonyl bands in the range 1725-1690 cm^{-1} in the ir spectrum (potassium bromide) of **6**. Broad singlets at δ 7.85, 9.15 and 11.15 appeared in the pmr (hexadeuteriodimethyl sulfoxide) and were assigned to the hydroxyl, imino and oxime protons, respectively; a complex multiplet occurred between δ 3.25 and 4.30 (-$COCH_2$-, -SCH_2-, and -CH_2CO-). Bright blue solutions were formed

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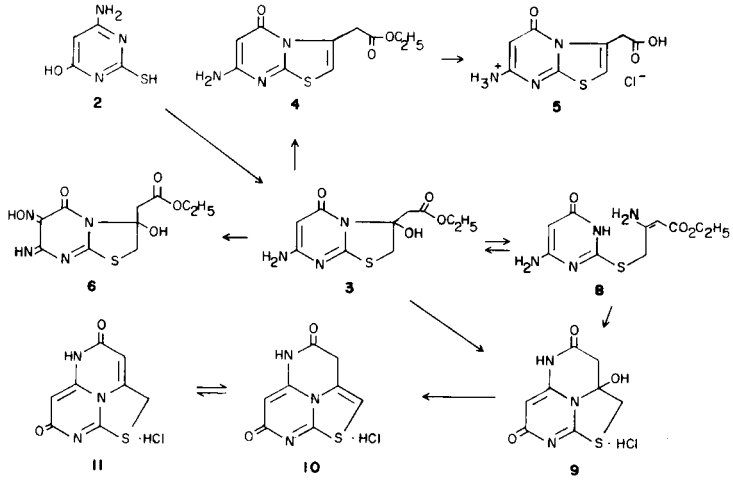
SCHEME I



after dissolving **6** in several neutral organic and aqueous solvents.

Stirring **3** in saturated methanolic ammonia yielded the open chain β-amino-α,β-unsaturated ester, ethyl 4-(6′-amino-4′-oxo-2′-pyrimidinethio)-3-aminocrotonate (**8**). The conjugated ester carbonyl came at extremely long wavelength, 1675 cm^{-1} in the ir (potassium bromide). Absorptions from the amine hydrogens occurred at δ 6.70 (singlet, 2H), 7.50 (singlet, 1H), and 8.60 (broad singlet) and ring NH resonated at δ 11.50 as a broad singlet in the pmr (hexadeuteriodimethyl sulfoxide). The enamine vinylic proton came at δ 4.55 (singlet).

Conversion of **8** back to **3** was brought about by stirring in acetic acid, and transformation of **8** to tricyclic 6a-hydroxy-5,6,6a,7-tetrahydro-8-thia-1,4-diazacycl[3.3.2]-azine-2,5-dione hydrochloride (**9**) resulted after treatment with concentrated hydrochloric acid at room temperature, as previously reported (4). It is pertinent to note that when **1** was allowed to react with 4,6-diaminopyrimidine-2-thiol, the cyclization to form the cyclazine analogous to **9** occurred directly, and no intermediate analogous to **3** was isolated (3). This observation supports the structural assignment of **3**, since more vigorous treatment is required to convert **3** to **9**.

Elimination of water from **9** to yield a mixture of 5,6-dihydro-4*H*-8-thia-1,4-diazacycl[3.3.2]azine-2,5-dione hydrochloride (**10**) and 5,7-dihydro-4*H*-8-thia-1,4-diazacycl[3.3.2]azine-2,5-dione (**11**) was accomplished by heating in concentrated hydrochloric acid (Scheme 1). A high frequency carbonyl band came at 1720 cm^{-1} in the vibrational spectrum along with numerous absorptions (HNC=O, C=N) between 1700 and 1450 cm^{-1}. In hexadeuteriodimethyl sulfoxide, pmr absorptions were observed from both **10** and **11**: a doublet at δ 4.15 (C-6 methylene protons, J = 2 Hz), a singlet at δ 6.35 (C-3 proton) and a triplet at δ 7.20 (C-7 proton, J = 2 Hz) were assigned to tautomer **10** (65%), while **11** (35%) gave peaks at δ 4.65 (doublet, J = 2 Hz, C-7 methylene protons), 5.50 (singlet, C-3 proton), and 6.05 (triplet, J = 2 Hz, C-6 proton). On the other hand, only absorptions from **10** appeared in trifluoroacetic acid: singlets at δ 7.50 (broad, C-7 proton), 6.65 (C-3 proton), and 4.40 (broad, C-6 methylene protons). Recrystallization did not change the mixture's spectral characteristics. A similar tautomeric mixture has also been previously observed with a related 8-thia-1,4-diazacycl[3.3.2]azine analogue (3).

Singlet Crystal X-Ray Structures of **3** and **8**.

The single crystal X-ray structures of **3** and **8** (see Figures 1 and 2) confirm the assigned structures. All crystallographic data for **3** and **8** were obtained at low temperature using a gaseous nitrogen cooling system and

Table 1

Crystal Data

Compound No.	**3**	**8**
Formula	$C_{10}H_{13}N_3O_4S$	$C_{10}H_{14}N_4O_3S{\cdot}CH_3OH$
Color	yellowish-clear	clear
Crystal dimensions	0.2 x 0.3 x .0.5	0.3 x 0.3 x 0.4 mm
Space Group	P1	$P2_1/c$
Temperature	−170 ± 5°	−170 ± 5°
a	12.738(6)	9.606(4)
b	8.986(4)	9.197(4)
c	7.679(3)	15.893(7)
α	119.69(4)	-
β	63.08(4)	94.87(4) (6)
γ	130.56(3)	-
Z	2	4
Volume	568.68 Å³	1399.01 Å³
D_c	1.585	1.436 g. cm^{-1}
Linear Absorption Coefficient	2.829	2.391 cm^{-1}
No. of Unique Intensities	1503	1836
No. of I ≥ σ(I)	1472	1644
R(F)	0.030	0.072
Rw(F)	0.043	0.094

locally modified Picker diffractometer. Complete details of the experimental setup, data reduction formula and computer system have been described elsewhere (5a). Crystal data are presented in Table 1. Both structures were solved by direct methods and refined by full-matrix least squares, using isotropic thermal parameters for hydrogens and anisotropic thermal parameters for all other atoms. Fractional coordinates and thermal parameters for **3** and **8** are given in Tables 2 and 3, respectively, and bond distances and angles for all non-hydrogen atoms are given in Tables 4 and 5. All hydrogen distances and angles appear normal.

Table 2

Fractional Coordinates and Isotropic Thermal Parameters for **3** (a)

Atom	x	y	z	10 B_{iso}
S(1)	−114.7(5)	7573.9(7)	3310.2(7)	11
C(2)	663(2)	6360(3)	3081(3)	11
C(3)	2158(2)	7337(3)	1814(3)	11
N(4)	2074(1)	7929(2)	389(2)	9
C(5)	3160(2)	8597(3)	−1301(3)	10
C(6)	2920(2)	9287(3)	−2276(3)	12
C(7)	1807(2)	9521(3)	−1494(3)	11
N(8)	850(2)	9024(2)	262(2)	11
C(8A)	1028(2)	8260(3)	1083(3)	10
C(9)	2635(2)	5843(3)	665(3)	13
C(10)	2744(2)	5339(3)	2148(3)	13
O(11)	1787(2)	4593(2)	3472(2)	23
O(12)	4040(1)	5846(2)	1836(2)	14
C(13)	4327(2)	5556(3)	3248(3)	18
C(14)	3725(2)	3350(3)	2845(3)	15
O(15)	4205(1)	8538(2)	−1751(2)	12
N(16)	1593(2)	10266(3)	−2349(3)	13
O(17)	3042(2)	9109(2)	3155(2)	10
H(1)	13(2)	503(3)	241(3)	0(3)
H(2)	67(2)	659(3)	435(3)	2(3)
H(3)	358(2)	964(3)	−349(3)	8(4)
H(4)	349(2)	630(3)	−25(3)	10(4)
H(5)	201(2)	473(3)	−4(3)	5(4)
H(6)	398(2)	623(3)	461(4)	18(4)
H(7)	541(3)	646(4)	301(3)	22(5)
H(8)	270(3)	264(4)	318(3)	23(5)
H(9)	405(2)	279(3)	144(4)	15(4)
H(10)	402(3)	323(4)	368(4)	33(5)
H(11)	379(3)	951(4)	260(4)	23(6)
H(12)	96(2)	1026(3)	−193(3)	6(5)
H(13)	199(2)	1016(3)	−366(4)	19(5)

(a) Coordinates are x 10^4 for non-hydrogen atoms and x 10^3 for hydrogens.

The numbering scheme used in the tables are given on the ORTEP drawings (5b) in Figures 1 and 2. Complete crystallographic data for **3** and **8** are available, including anisotropic thermal parameters and observed and calculated structure amplitudes (6).

Table 3

Fractional Coordinates and Isotropic Thermal Parameters for **8** (a)

Atom	x	y	z	10 B_{iso}
C(1)	5922(5)	−1128(6)	3337(4)	18
N(2)	6828(5)	−2077(5)	3104(3)	19
C(3)	7648(5)	−2751(6)	3743(3)	18
C(4)	7534(6)	−2453(6)	4591(3)	16
C(5)	6537(5)	−1457(6)	4812(3)	16
N(6)	5730(5)	−819(5)	4148(3)	17
S(7)	4856(1)	−110(2)	2619(1)	20
C(8)	5273(5)	−796(7)	1596(3)	18
C(9)	6556(5)	−183(6)	1269(3)	17
C(10)	6444(5)	858(6)	658(3)	18
C(11)	7630(6)	1416(6)	273(3)	20
O(12)	7278(4)	2452(5)	−301(3)	29
C(13)	8378(7)	3055(9)	−775(4)	34
C(14)	8147(9)	2685(9)	−1672(5)	40
N(15)	8560(5)	−3693(5)	3468(4)	22
O(16)	6317(4)	−1106(4)	5558(2)	20
N(17)	7769(5)	−747(6)	1591(3)	19
O(18)	8850(4)	1015(4)	425(2)	22
O(19)	1348(5)	829(5)	3325(3)	24
C(20)	939(7)	−593(7)	3500(4)	28
H(1)	809(8)	−286(9)	496(6)	48(20)
H(2)	501(7)	−27(7)	425(4)	22(13)
H(3)	453(6)	−45(6)	117(4)	15(11)
H(4)	521(5)	−173(7)	166(3)	3(12)
H(5)	543(7)	136(8)	39(4)	39(15)
H(6)	710(8)	321(9)	−183(5)	55(18)
H(7)	859(9)	411(11)	−57(6)	65(24)
H(8)	886(9)	321(10)	−206(6)	64(21)
H(9)	841(10)	149(12)	−150(6)	90(27)
H(10)	939(5)	294(5)	−52(3)	8(9)
H(11)	856(5)	−386(6)	285(4)	16(11)
H(12)	913(6)	−395(6)	378(4)	10(13)
H(13)	857(6)	−36(6)	143(4)	13(11)
H(14)	776(5)	−137(6)	198(4)	8(11)
H(15)	199(7)	98(7)	345(4)	11(16)
H(16)	190(6)	−132(7)	335(4)	28(14)
H(17)	68(7)	−67(8)	426(5)	35(15)
H(18)	8(7)	−92(7)	320(4)	32(15)

(a) Coordinates are x 10^4 for non-hydrogens and x 10^3 for hydrogen atoms.

The pyrimidine rings in both **3** and **8** are structurally similar, as seen in the bond distances and angles in Tables 4-7. Both show considerable ring conjugation. The C(3)-N(4) bond length of 1.500(2) Å in **3** (see Figure 1) in somewhat longer than the "normal" C-N bond length of 1.479 Å (7).

EXPERIMENTAL

Melting points were taken on a Mel-Temp melting point apparatus and are uncorrected. Infrared spectra were determined on a Perkin-Elmer Model 137-B infrared spectrometer using potassium bromide pellets

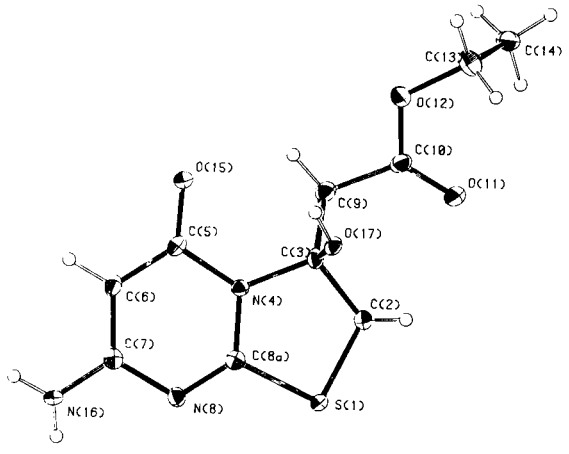


Figure 1. ORTEP drawing of **3**. All thermal ellipsoids are shown at the 50% probability level except hydrogens, which have been given an isotropic value of 0.5 for artistic purposes.

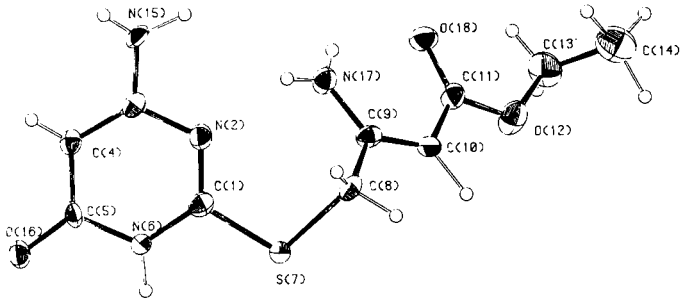


Figure 2. ORTEP drawing of **8**. All thermal ellipsoids are shown at the 50% probability level except hydrogens, which have been given an isotropic value of 0.5 for artistic purposes.

unless stated otherwise. With hexadeuteriodimethyl sulfoxide as solvent, nuclear magnetic resonance spectra were determined on a Varian Associates Model EM-360 spectrometer and the high resolution experiment was performed on a Varian HR 220 MHz High Resolution spectrometer. At 70 eV, a Varian Mat CH-7 spectrometer recorded the mass spectra. Elemental analysis were performed at Midwest Micro Labs Inc., indianapolis, Indiana. Usually based on the first crystallization, the percent yields are not considered optimum.

Ethyl 7-Amino-5-oxothiazolo[3,2-*a*]pyrimidin-3-acetate (**4**).

A clear yellow solution was gradually formed when 5.0 g. (18.5 mmoles) of the covalently hydrated **3** (4) was warmed 5 minutes in 25 mo. of concentrated sulfuric acid. After pouring over ice and diluting with water (100 ml.), the chilled aqueous mixture was slowly neutralized with saturated potassium carbonate solution. Several chloroform extracts (75 ml., 5X) of the aqueous suspension were combined, washed with water (150 ml., 2X), dried (magnesium sulfate) and concentrated under reduced pressure. Slow addition of ethyl ether precipitated 2.0 g. (43%) of yellow tinted thiazolopyrimidine **4**. Colorless crystals of **4** melted at 171-173° after crystallizing from 2-propanol; ir (potassium bromide): 3500-3100 (NH), 1725 (C=O), 1675-1570, 1550-1530; (=NC=O, C=N) cm^{-1}; pmr

Table 4

Bond Distances and Angles for **3**

(a) Bond Distances in Angstroms

A	B	Distance
S(1)	C(2)	1.806(2)
S(1)	C(8A)	1.745(2)
O(11)	C(10)	1.208(2)
O(12)	C(10)	1.328(2)
O(12)	C(13)	1.463(2)
O(15)	C(5)	1.245(2)
O(17)	C(3)	1.399(2)
N(4)	C(3)	1.500(2)
N(4)	C(5)	1.424(3)
N(4)	C(8A)	1.365(3)
N(8)	C(7)	1.381(3)
N(8)	C(8A)	1.297(3)
N(16)	C(7)	1.337(3)
C(2)	C(3)	1.529(3)
C(3)	C(9)	1.533(3)
C(5)	C(6)	1.398(3)
C(6)	C(7)	1.380(3)
C(9)	C(10)	1.502(3)
C(13)	C(14)	1.497(3)

(b) Angles in Degrees

A	B	C	Angle
C(2)	S(1)	C(8A)	90.9(1)
C(10)	O(12)	C(13)	117.3(1)
C(3)	N(4)	C(5)	124.2(1)
C(3)	N(4)	C(8A)	114.7(1)
C(5)	N(4)	C(8A)	119.4(2)
C(7)	N(8)	C(8A)	116.2(2)
S(1)	C(2)	C(3)	107.9(1)
O(17)	C(3)	N(4)	109.3(1)
O(17)	C(3)	C(2)	107.3(2)
O(17)	C(3)	C(9)	111.7(2)
N(4)	C(3)	C(2)	104.3(1)
N(4)	C(3)	C(9)	112.3(1)
C(2)	C(3)	C(9)	111.5(2)
O(15)	C(5)	N(4)	118.9(2)
O(15)	C(5)	C(6)	126.9(2)
N(4)	C(5)	C(6)	114.2(2)
C(5)	C(6)	C(7)	121.9(2)
N(8)	C(7)	N(16)	115.6(2)
N(8)	C(7)	C(6)	121.5(2)
N(16)	C(7)	C(6)	122.9(2)
S(1)	C(8A)	N(4)	113.3(1)
S(1)	C(8A)	N(8)	120.4(1)
N(4)	C(8A)	N(8)	126.2(2)
C(3)	C(9)	C(10)	110.5(2)
O(11)	C(10)	O(12)	124.0(2)
O(11)	C(10)	C(9)	124.8(2)
O(12)	C(10)	C(9)	111.2(2)
O(12)	C(13)	C(14)	112.5(2)

Table 5

Bond Distances and Angles for **8**

(a) Bond Distances in Angstroms

A	B	Distance
S(7)	C(1)	1.741(6)
S(7)	C(8)	1.820(6)
O(12)	C(11)	1.342(7)
O(12)	C(13)	1.459(7)
O(16)	C(5)	1.264(6)
O(18)	C(11)	1.233(7)
O(19)	C(20)	1.400(8)
N(2)	C(1)	1.309(7)
N(2)	C(3)	1.379(7)
N(6)	C(1)	1.348(7)
N(6)	C(5)	1.385(7)
N(15)	C(3)	1.332(7)
N(17)	C(9)	1.337(7)
C(3)	C(4)	1.388(8)
C(4)	C(5)	1.392(8)
C(8)	C(9)	1.489(8)
C(9)	C(10)	1.361(8)
C(10)	C(11)	1.432(8)
C(13)	C(14)	1.464(11)

(b) Angles in Degrees

A	B	C	Angle
C(1)	S(7)	C(8)	103.8(3)
C(11)	O(12)	C(13)	118.0(5)
C(1)	N(2)	C(3)	116.3(5)
C(1)	N(6)	C(5)	121.7(5)
S(7)	C(1)	N(2)	122.7(4)
S(7)	C(1)	N(6)	113.2(4)
N(2)	C(1)	N(6)	124.1(5)
N(2)	C(3)	N(15)	113.6(5)
N(2)	C(3)	C(4)	122.7(5)
N(15)	C(3)	C(4)	123.7(5)
C(3)	C(4)	C(5)	119.2(5)
O(16)	C(5)	N(6)	118.6(5)
O(16)	C(5)	C(4)	125.3(5)
N(6)	C(5)	C(4)	116.1(5)
S(7)	C(8)	C(9)	115.6(4)
N(17)	C(9)	C(8)	116.1(5)
N(17)	C(9)	C(10)	124.0(5)
C(8)	C(9)	C(10)	119.9(5)
C(9)	C(10)	C(11)	122.6(5)
O(12)	C(11)	O(18)	121.7(5)
O(12)	C(11)	C(10)	112.4(5)
O(18)	C(11)	C(10)	125.9(5)
O(12)	C(13)	C(14)	111.0(6)

(DMSO-d_6): δ 1.15 (t, 3H, -CH_3), 3.70-4.20 (m, 4H, -CH_2CO-, OCH_2-), 4.90 (s, 1H, pyrimidine vinylic proton), 6.50 (broad s, 2H, -NH_2, 6.90 (s, 1H, thiazole vinylic proton).

Anal. Calcd. for $C_{10}H_{11}N_3O_3S$: C, 47.41; H, 4.39; N, 16.59; S, 12.64; m.w. 253. Found: C, 47.35; H, 4.33; N, 16.55; S, 12.65; M^+ 253.

Ethyl 7-Amino-5-oxothiazolo[3,2-*a*]pyrimidin-3-acetic Acid Hydrochloride (**5**).

Ester **4** (2.0 g., 7.90 mmoles) in 30 ml. of concentrated hydrochloric acid was stirred 12 hours at room temperature. Ethyl ether was added, the mixture stirred and then the ether decanted after setting for 10 minutes. This was repeated several times. Triturating the slurry with hot ethanol (40 ml.) gave 1.80 g. (87%) of the crystalline hydrochloride **5** collected after cooling. Recrystallized from hot methanol, **5** melted at 213-215°; ir (potassium bromide): 3500-2500 (NH^+, -CO_2H), 1725-1600 (C=O, =NC=O), 1500 (C=N cm^{-1}; pmr (DMSO-d_6): δ 4.00 (s, 2H, -CH_2CO-), 5.05 (broad s, 1H, pyrimidine vinylic proton), 6.90 (s, 1H, thiazole vinylic proton), 8.60 (broad s, 3H, -NH_3^+).

Anal. Calcd. for $C_8H_8ClN_3O_3S$: C, 36.71; H, 3.09; N, 16.06; S, 12.24; m.w. -HCl, 225. Found: C, 37.05; H, 3.30; N, 16.16; S, 12.02; M^+ 225.

Ethyl 3-Hydroxy-7-imino-5-oxothiazolino[3,2-*a*]pyrimidin-3-acetate-6-oxime (**6**).

Compound **3** (7.0 g., 25.8 mmoles) and sodium nitrite (1.78 g., 25.8 mmoles) were added to 250 ml. of water in a 500 ml. RB flask and placed in an ice bath. With constant stirring, 40 ml. of 0.6*N* hydrochloric acid was added dropwise over a period of one hour. Gradually turning maroon in color, the initially off-white suspension was stirred 15 hours at 0° and then 5 hours at room temperature as a suspension. The insoluble maroon material (7.0 g.) was filtered, washed with water, and dried. The filtrate was bright blue. When crystallizing from acetone, 1.5 g. of insoluble **7** was filtered. Bright violet crystals of **6** (4.5 g., 58%) separated from the cooled concentrated acetone filtrate; slow addition of ethyl ether enhanced precipitation; m.p. 153-155° (dec., acetone); ir (potassium bromide): 3300-2700 (-NH, -OH, hydrogen bonded), 1725-1690, 1650-1600, 1500 (C=O, C=N) cm^{-1}; pmr (DMSO-d_6): δ 1.15 (t, 3H, -CH_3), 3.25-4.30 (m, 6H, -OCH_2-, -CH_2CO-, -SCH_2-), 7.85 (broad s, 1H, -OH), 9.15 (broad s, 1H, =NH), 11.15 (broad s, 1H, =NOH).

Anal. Calcd. for $C_{10}H_{12}N_4O_5S$: C, 39.98; H, 4.04; N, 18.86; S, 10.66; m.w. 300. Found: C, 39.89; H, 4.22; N, 18.54; S, 10.35; M^+ 300.

Ethyl 4-(6′-Amino-4′-oxo-2′-pyrimidinethio)-3-aminocrotonate (**8**).

To 250 ml. of saturated methanolic ammonia solution, 6.0 g. (22.1 mmoles) of **3** was added and stirred 10 days at room temperature. The initially bright yellow reaction mixture (a suspension throughout) gradually turned dark yellow. After concentrating under reduced pressure, slow addition of ethyl ether enhanced precipitation of product. Filtering and drying yield 5.0 g. (84%) of **8**; m.p. 182-185° (dec., methanol); ir (potassium bromide): 3500-2600 (-NH_2, -OH, hydrogen bonded), 1675-1500, 1450, (C=O, C=N) cm^{-1}; pmr (220 MHz, DMSO-d_6): δ 1.14 (t, 3H, -CH_3), 2.95 (q, 2H, -OCH_2-), 3.77 (s, 2H, -SCH_2-), 4.55 (s, 1H, exocyclic vinylic proton), 5.05 (s, 1H, C-6 pyrimidine proton), 6.70 (broad s, 2H, -NH_2), 7.50 (broad s, 1H, -NH), 8.60 (broad s, 1H, NH), 11.50 (broad s, 1H, NH).

Anal. Calcd. for $C_{10}H_{14}N_4O_3S$: C, 44.42; H, 5.23; N, 20.74; S, 11.85; m.w. 270. Found: C, 44.44; H, 5.42; N, 21.12; S, 11.45; M^+ 270.

5,6-Dihydro-4*H*-8-thia-1,4-diazacycl[3.3.2]azine-2,5-dione Hydrochloride (**10**) and 5,7-Dihydro-4*H*-8-thia-1,4-diazacycl[3.3.2]azine-2,5-dione Hydrochloride (**11**).

In 35 ml. of concentrated hydrochloric acid, 8.0 g. (35.5 mmoles) of covalently hydrated **9** (4) was heated as a heterogeneous mixture for 15 hours. At room temperature, an excess of 2-propanol was added. The mixture was stirred several minutes, allowed to settle, and the clear supernatant liquid decanted. Methanol (30 ml.) was then added and the mixture stirred 30 minutes. Filtering, washing with methanol, and drying yielded 8.0 g. (93%) of hydrochloride (**10** and **11**); decomposition > 300° (water, 2-propanol, hydrochloric acid); ir (potassium bromide): 3100-2400 (NH^+), 1720-1450 (HNC=O, C=N) cm^{-1}; pmr (DMSO-d_6): (**10**) δ 4.15 (d, 1.30 H, C-6 methylene protons, J = 2 Hz), 6.35 (s, 0.65 H, C-3 proton), 7.20 (t, 0.65 H, C-7 proton, J = 2 Hz); (**11**) δ 4.65 (d, 0.70 H, C-7 methylene protons, J = 2 Hz), 5.50 (s, 0.35 H, C-3 proton),

6.05 (t, 0.35 H, C-6 proton, J = 2 Hz).

Anal. Calcd. for $C_8H_5ClN_3O_2S$: C, 39.43; H, 2.48; Cl, 14.56; N, 17.25; S, 13.14; m.w. -HCl = 207. Found: C, 39.41; H, 2.78; Cl, 14.35; N, 17.09; S, 13.00; M^+ 207.

REFERENCES AND NOTES

(1) Contribution No. 3562. Taken in part from a thesis submitted by T. P. S. for the degree Doctor of Philosophy to Indiana University, February 1979.

(2) E. Campaigne and T. P. Selby, *J. Heterocyclic Chem.*, **15**, 401 (1978).

(3) E. Campaigne and T. P. Selby, *ibid.*, **16**, 151 (1979).

(4) E. Campaigne and T. P. Selby, *ibid.*, **16**, 725 (1979).

(5a) J. C. Huffman, L. N. Lewis and K. G. Caulton, *Inorg. Chem.*, **19**, 2755 (1980); (5b) C. K. Johnson, ORTEP. Report ORNL-3794, Oak Ridge National Laboratories, Tennessee, 1965.

(6) Complete crystallographic data for **3** and **8** are avilable from the Indiana University Chemistry Department Library. Request M. S. C. Report 7924 for **3** and 7918 for **8**.

(7) International Distances Supplement, *Chem. Soc. Spec. Publ.*, No. 18 (L. D. Sutton, Ed.), Chemical Society, London, 1965.