New Heterocyclic Structures. [1,2,5]Thiadiazolo[3',4':4,5]pyrimido-[2,1-*b*][1,3]thiazine and Thiazolo[3,2-*a*][1,2,5]thiadiazolo[3,4-*d*]pyrimidine

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Derivatives of two new molecular structures, namely, 7,8-dihydro-6*H*,10*H*-[1,2,5]thiadiazolo[3',4':4,5]pyrimido[2,1-*b*][1,3]thiazin-10-one and 6,7-dihydro-9*H*-thiazolo[3,2-*a*][1,2,5]thiadiazolo[3,4-*d*]pyrimidin-9-one, and derivatives of *N*-substituted sulfamic acid, namely, (8-amino-3,4-dihydro-2*H*,6*H*-pyrimido[2,1-*b*][1,3]thiazin-6-on-7-yl)sulfamic acid and (7-amino-2,3-dihydro-5*H*-thiazolo[3,2-*a*]pyrimidin-5-on-6-yl)sulfamic acid, were separated out as by-products in the reduction reaction of 8-amino-3,4-dihydro-7-nitroso-2*H*,6*H*-pyrimido[2,1-*b*][1,3]thiazin-6-one and 7-amino-2,3-dihydro-6-nitroso-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one derivatives, respectively, with sodium hydrosulfite.

A mechanism of reaction, which hypothesizes the action of sodium hydrosulfite in an asymmetic form, is proposed.

The results of single-crystal X-ray investigation on 7,8-dihydro-6*H*,10*H*-[1,2,5]thiadiazolo[3',4':4,5]pyrimido[2,1-*b*][1,3]thiazin-10-one (R = 0.032 for 863 reflections) and (8-amino-3,4-dihydro-2*H*,6*H*-pyrimido[2,1-*b*]-[1,3]thiazin-6-on-7-yl)sulfamic acid, sodium salt (R = 0.028 for 3507 reflections) are reported.

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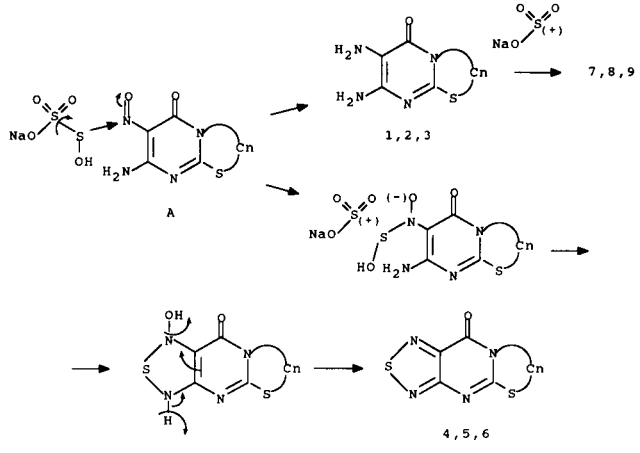
During preceding research [1,2] it was noted that reduction of 8-amino-3,4-dihydro-7-nitroso-2*H*,6*H*-pyrimido[2,1-*b*][1,3]thiazin-6-one [Scheme 1 **A**, Cn = CH_2-CH_2-CH_2], of its 3-methyl derivative [**A**, Cn = CH_2-$CH(CH_3)$-CH_2] and of 7-amino-2,3-dihydro-6-nitroso-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one [**A**, Cn = CH_2-CH_2] with sodium hydrosulfite yielded the relative diamino-derivatives, namely, 7,8-diamino-3,4-dihydro-2*H*,6*H*-pyrimido[2,1-*b*][1,3]thiazin-6-one (**1**), its 3-methyl derivative **2** and 6,7-diamino-2,3-dihydro-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**3**), respectively, together with other unknown compounds. In particular, a strongly fluorescent compound with higher Rf than the relative diamino-derivative [the solvent system was the heavy fraction of the mixture formed by chloroform-methanol-water (5:5:3 v/v/v)] was separated out in each reaction, by thin-layer chromatography.

Scheme 1

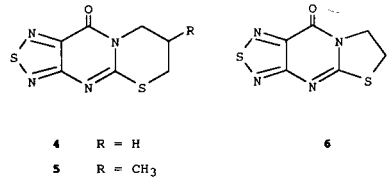


The same behaviour occurred in the reduction reaction of 6-amino-5-nitroso-3-methyl-2-methylthio-4(3*H*)pyrimidinone with sodium hydrosulfite to 5,6-diamino-3-methyl-2-methylthio-4(3*H*)pyrimidinone (**10**) [3].

The high fluorescent power of all the above-mentioned compounds, and the fact that the yield in fluorescent compound in every reaction was higher when sodium hydrosulfite purchased many years before was used, prompted us to isolate and study the structure of the fluorescent compound and of another unknown compound, obtained in moderate yield, and to investigate the reaction mechanism involved.

The fluorescent compound was separated out from the relative diamino-derivative and from another unknown compound by either fractionating the reaction solution or extracting the crude with an appropriate solvent or using thin-layer chromatography.

Fluorescent compounds, derived from nitrosopyrimidothiazinone and nitrosothiazolopyrimidinone derivatives, are found to have the following structures as determined



by elemental analysis and confirmed by uv and ^{1}H-nmr data, and, in the case of **4**, by single-crystal X-ray analysis.

The uv spectrum of the fluorescent compound obtained by reaction of 6-amino-5-nitroso-3-methyl-2-methylthio-4(3*H*)-pyrimidinone and sodium hydrosulfite is very

Table 1

Crystallographic Data

	Compound **4**	Compound **7**
Formula	$C_7H_6N_4OS_2$	$C_7H_9N_4O_4S_2^- \cdot Na^+ \cdot 3H_2O$
Molecular Weight	214.26	354.33
Crystal System	orthorhombic	triclinic
Space Group	Pbcn (No. 60)	$P\bar{1}$ (No. 2)
a, Å	8.860(2)	7.289(1)
b, Å	14.158(3)	10.127(1)
c, Å	14.034(3)	10.480(1)
α, deg	90	72.02(1)
β, deg	90	72.68(1)
γ, deg	90	79.36(1)
V, Å^3	1760.4(6)	699(1)
Z	8	2
D_{calcd}, g·cm^{-3}	1.617	1.684
D_{obsd}, g·cm^{-3}	1.60	1.70
F(000)	928	368
Radiation (λ, Å)	graphite monochromated MoKα (0.71069)	
Reflections measured	+h, +k, +l	±h, ±k, +l
Scan Type	ω - 2θ	ω - 2θ
θ Limits, deg	1.0-25.0	1.5-30.0
Scan Width, deg	0.75 + 0.35tan θ	0.60 + 0.35tanθ
Scan Speed Limits, deg·min^{-1}	1.03-2.75	0.92-8.24
Standard Reflections	2 every 1 hour (no changes)	2 every 1 hour (no changes)
No. of measured Reflections	1733	4050
No. of observed Reflections	863 with I > 2σ (I)	3507 with I > 3σ (I)
Crystal Dimensions, mm	0.32 x 0.14 x 0.14	0.40 x 0.35 x 0.30
μ, cm^{-1}	5.1	3.9
Transmission, max-min	0.991-0.936	0.999-0.946
No. of Varied Parameters	128	248
R	0.032	0.028
R_w	0.034	0.033
w	$0.85/(\sigma^2(F)+0.00095F_o^2)$	$1.0/(\sigma^2(F)+0.00205F_o^2)$
Δ ρ: max-min, e·Å^{-3}	+0.27 -0.16	+0.25 -0.19

Unit cell parameters were derived from least-squares fit to the setting angles of 25 intense reflections from various regions of reciprocal space.

similar to that of **4** and **5**; but because of its low yield, it was not subjected to elemental and ^{1}H-nmr analysis.

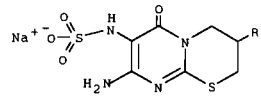
Compound **4** was also obtained by reacting 8-amino-3,4-dihydro-7-nitroso-2*H*,6*H*-pyrimido[2,1-*b*][1,3]thiazin-6-one with thiourea, following the method used for synthesizing [1,2,5]thiadiazolo[3,4-*d*]pyrimidine derivatives [4].

The mechanism of reduction of nitroso-derivatives by sodium hydrosulfite in its classical symmetrical form, Na O_2S-SO_2H, is reportedly due to the weak, easily oxidizable S-S bond [5,6], but the same symmetrical form does not afford an explanation for the cyclization process. The process could be explained if sodium hydrosulfite were assumed to be asymmetric or if decomposition products were to form during the reaction.

As reported in Scheme 1, the asymmetric molecule Na O_3S-SOH allows an electronically-correct cyclization mechanism to be described. This molecule, which is probably formed by slow dismutation of symmetric sodium hydrosulfite, has a nucleophilic functional group, -SOH, able to initiate the cyclization process.

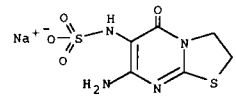
The participation of decomposition products generated during the reaction has not been taken into account, as the yield of fluorescent product varies greatly according to whether old or recently-purchased sodium hydrosulfite is used.

That the cyclization mechanism could be considered correct is supported by the fact that, together with **4**, **5** and **6** and the relative diamino compounds **1**, **2** and **3**, molecules **7**, **8** and **9** were also separated out. Moreover, by reacting 6-amino-5-nitroso-3-methyl-2-methylthio-4(3*H*)-pyrimidinone and sodium hydrosulfite, (6-amino-3-methyl-2-methylthio-4(3*H*)pyrimidinon-5-yl)sulfamic acid monosodium salt (**11**) was obtained.



7 R = H

8 R = CH_3



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The X-ray crystal structure of (8-amino-3,4-dihydro-2*H*, 6*H*-pyrimido[2,1-*b*][1,3]thiazin-6-on-7-yl)sulfamic acid, sodium salt (**7**) trihydrate, is described in this paper; that of (7-amino-2,3-dihydro-5*H*-thiazolo[3,2-*a*]pyrimidin-5-on-6-yl)sulfamic acid, sodium salt (**9**) trihydrate, will be published elsewhere [7].

The likeness between the uv spectra of **7** and **8** and that of **11**, as well as the ^{1}H-nmr data and elemental analysis, confirm that molecule **11** is a sulfamate.

The structures of **7**, **8**, **9** and **11** seem to confirm the proposed mechanism; *i.e.* the asymmetric molecule, Na O_3S-SOH, with its nucleophilic site, attacks the nitroso group, thus releasing the positive leaving group, $NaO_3S^{(+)}$, which reacts with the amine group of **1**, **2**, **3** and **10** to give **7**, **8**, **9** and **11**. However, the asymmetric structure of sodium hydrosulfite samples was studied by ir and powder X-ray analysis, without result [8].

The fact that sodium hydrosulfite stored for many years at room temperature gives a higher yield of cyclized compound leads one to hypothesize that sodium hydrosulfite changes partially into an asymmetric form, probably Na O_3S-SOH, which in turn transforms nitroamino derivatives into thiadiazolo derivatives.

Description of the Structures **4** and **7**.

Figure 1 shows the molecular structure of compound **4**, whose bond distances and bond angles are reported in Table 4, along with those of compound **7**. As previously found for other pyrimidothiazine derivatives [9,10,11], the thiazine ring of **4** exhibits half-chair conformation, the

Table 2
Final Fractional Coordinates and Equivalent Isotropic Thermal Parameters for Compound **4**

$B_{eq} = 1/3\Sigma_i\Sigma_j B_{ij}\, \alpha_i^* \alpha_j^*\, a_i \cdot a_j$

Atom	x	y	z	Beq,Å^2
S(1)	0.6468(1)	0.02891(7)	0.07247(8)	3.40(4)
C(1)	0.5736(5)	0.1480(3)	0.0787(4)	4.0(2)
C(2)	0.6690(5)	0.2088(3)	0.1421(3)	4.0(2)
C(3)	0.8260(5)	0.2155(3)	0.1057(3)	3.9(2)
N(1)	0.9084(3)	0.1241(2)	0.1147(2)	2.5(1)
C(4)	0.8379(4)	0.0378(3)	0.1004(2)	2.4(1)
N(2)	0.9021(3)	-0.0445(2)	0.1052(2)	2.7(1)
C(5)	1.0504(4)	-0.0439(2)	0.1308(3)	2.4(1)
N(3)	1.1308(4)	-0.1225(2)	0.1434(3)	3.1(1)
S(2)	1.2966(1)	-0.08865(7)	0.17698(8)	3.22(4)
N(4)	1.2751(3)	0.0250(2)	0.1751(2)	3.0(1)
C(6)	1.1336(4)	0.0389(3)	0.1487(3)	2.4(1)
C(7)	1.0627(4)	0.1313(3)	0.1351(3)	2.7(1)
O(1)	1.1260(3)	0.2062(2)	0.1422(2)	4.4(1)
H(C1a)	0.5754	0.1789	0.0158	3.9
H(C1b)	0.4800	0.1425	0.1079	3.9
H(C2a)	0.6719	0.1816	0.2102	3.9
H(C2b)	0.6315	0.2701	0.1370	3.9
H(C3a)	0.8792	0.2555	0.1376	3.9
H(C3b)	0.8272	0.2392	0.0395	3.9

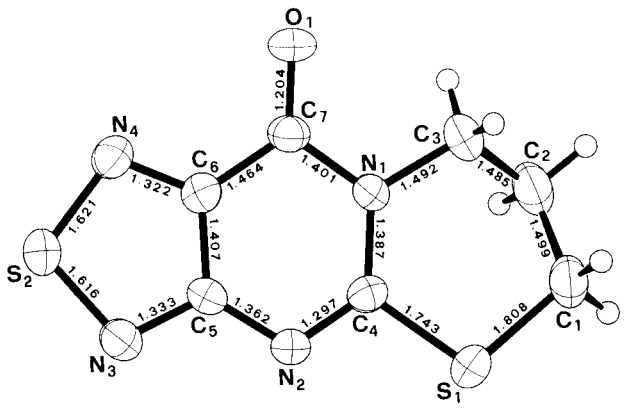

Figure 1. ORTEP [18] drawing showing atom numbering scheme, thermal motion ellipsoids (50%), and bond distances (Å) of compound **4**.

Table 3
Final Fractional Coordinates and Equivalent Isotropic Thermal Parameters for Compound **7**

$B_{eq} = 1/3\Sigma_i\Sigma_j B_{ij}\, \alpha_i^* \alpha_j^*\, a_i \cdot a_j$

Atom	x	y	z	B_{eq}, Å^2
S(1)	0.29969(5)	-0.04146(3)	0.29622(3)	2.67(1)
C(1)	0.3628(2)	0.0940(2)	0.1363(1)	3.26(5)
C(2)	0.2831(2)	0.2366(2)	0.1566(1)	3.12(5)
C(3)	0.3551(2)	0.2701(1)	0.2626(1)	2.45(4)
N(1)	0.2975(1)	0.17378(9)	0.40293(9)	1.70(3)
C(4)	0.2763(1)	0.0372(1)	0.4271(1)	1.76(3)
N(2)	0.2319(1)	-0.04992(9)	0.5512(1)	2.02(3)
C(5)	0.2040(1)	-0.0004(1)	0.6637(1)	1.75(3)
N(3)	0.1658(2)	-0.0936(1)	0.7881(1)	2.55(3)
C(6)	0.2177(1)	0.1391(1)	0.6490(1)	1.65(3)
N(4)	0.1937(1)	0.18649(9)	0.76845(9)	1.81(3)
S(2)	-0.02496(3)	0.25631(3)	0.83610(2)	1.744(8)
O(2)	-0.1020(1)	0.3559(1)	0.72644(9)	3.06(3)
0(3)	0.0139(1)	0.3221(1)	0.93011(9)	2.86(3)
0(4)	-0.1426(1)	0.1420(1)	0.90829(9)	2.77(3)
C(7)	0.2703(1)	0.23012(9)	0.5159(1)	1.55(3)
O(1)	0.2952(1)	0.35561(7)	0.48958(8)	2.00(2)
Na(1)	0.5	0.5	0.5	2.44(2)
Na(2)	0.0	0.5	0.5	2.56(2)
O(w1)	0.4957(1)	0.3768(1)	0.7380(1)	2.83(3)
O(w2)	0.8164(2)	0.3567(1)	0.4261(1)	3.59(4)
O(w3)	0.7984(2)	0.4411(1)	0.1397(1)	3.48(4)
H(1C1)	0.510(3)	0.085(2)	0.111(2)	4.8(3)
H(2C1)	0.301(3)	0.076(3)	0.079(2)	4.8(3)
H(1C2)	0.135(3)	0.241(2)	0.193(2)	4.2(3)
H(2C2)	0.323(3)	0.304(2)	0.069(2)	4.2(3)
H(1C3)	0.501(3)	0.267(2)	0.235(2)	3.6(3)
H(2C3)	0.297(3)	0.360(2)	0.266(2)	3.6(3)
H(1N3)	0.144(3)	-0.064(2)	0.848(2)	3.8(3)
H(2N3)	0.162(3)	-0.178(2)	0.783(2)	3.8(3)
H(N4)	0.273(3)	0.237(2)	0.761(2)	3.2(3)
H(1w1)	0.606(4)	0.362(2)	0.749(2)	4.7(3)
H(2w1)	0.448(3)	0.438(2)	0.781(2)	4.7(3)
H(1w2)	0.807(4)	0.385(3)	0.334(3)	6.4(4)
H(2w2)	0.821(4)	0.270(3)	0.449(3)	6.4(4)
H(1w3)	0.831(3)	0.416(3)	0.073(3)	4.8(3)
H(2w3)	0.862(3)	0.515(3)	0.155(2)	4.8(3)

Table 4

Bond Distances (Å) and Bond Angles (deg)

Bonds	Compound **4**	Compound **7**
C(1)-S(1)	1.808(4)	1.805(1)
C(4)-S(1)	1.743(4)	1.741(1)
C(2)-C(1)	1.499(6)	1.508(2)
C(3)-C(2)	1.485(6)	1.507(2)
N(1)-C(3)	1.492(5)	1.480(1)
C(4)-N(1)	1.387(4)	1.357(1)
C(7)-N(1)	1.401(5)	1.414(1)
N(2)-C(4)	1.297(5)	1.312(1)
C(5)-N(2)	1.362(4)	1.367(1)
N(3)-C(5)	1.333(4)	1.338(1)
C(6)-C(5)	1.407(5)	1.392(1)
S(2)-N(3)	1.616(4)	
N(4)-S(2)	1.621(3)	1.662(1)
C(6)-N(4)	1.322(5)	1.427(1)
C(7)-C(6)	1.464(5)	1.401(1)
O(1)-C(7)	1.204(4)	1.250(1)
O(2)-S(2)		1.454(1)
O(3)-S(2)		1.462(1)
O(4)-S(2)		1.445(1)
C(4)-S(1)-C(1)	105.7(2)	105.09(7)
C(2)-C(1)-S(1)	111.2(3)	111.45(9)
C(3)-C(2)-C(1)	111.1(4)	112.9(1)
N(1)-C(3)-C(2)	111.9(3)	113.0(1)
C(4)-N(1)-C(3)	122.1(3)	123.9(1)
C(7)-N(1)-C(3)	115.6(3)	116.29(9)
C(7)-N(1)-C(4)	122.2(3)	119.82(8)
N(1)-C(4)-S(1)	122.2(3)	123.58(7)
N(2)-C(4)-S(1)	111.9(3)	112.26(8)
N(2)-C(4)-N(1)	125.9(3)	124.1(1)
C(5)-N(2)-C(4)	115.5(3)	118.2(1)
N(3)-C(5)-N/(2)	123.1(3)	116.3(1)
C(6)-C(5)-N(2)	123.9(3)	121.63(8)
C(6)-C(5)-N(3)	113.1(3)	122.0(1)
S(2)-N(3)-C(5)	106.1(2)	
N(4)-S(2)-N(3)	100.5(2)	
C(6)-N(4)-S(2)	105.3(3)	117.33(8)
N(4)-C(6)-C(5)	115.1(3)	120.17(8)
C(7)-C(6)-C(5)	119.7(3)	119.5(1)
C(7)-C(6)-N(4)	125.2(3)	120.12(9)
C(6)-C(7)-N(1)	112.4(3)	116.59(9)
O(1)-C(7)-N(1)	122.4(4)	118.06(8)
O(1)-C(7)-C(6)	125.3(4)	125.3(1)
O(2)-S(2)-N(4)		109.85(6)
O(3)-S(2)-N(4)		102.18(5)
O(3)-S(2)-O(2)		112.90(6)
O(4)-S(2)-N(4)		106.57(5)
O(4)-S(2)-O(2)		111.85(6)
O(4)-S(2)-O(3)		112.83(5)

C(2) atom being displaced 0.713 Å out of the mean plane through the other five-ring atoms (planar within ±0.050 Å). The pyrimidinone ring of **4** shows significant distortion from planarity in the pattern of atomic deviations ranging from +0.030 to −0.040 Å, with torsion angles between +6.7 and −5.8°. These are markedly greater than those previously observed [9,10,11], and may be related to a marked decrease in the double-bond character of the C(6)-C(7) bond [1.464(5) Å]. Corresponding values ranging from 1.392(2) [10] to 1.449(5) Å [9] were previously observed. The geometrical features of the [1,2,5]thiadiazole moiety, which is planar within the bounds of experimental incertainty [max. atomic deviation = 0.007 Å],

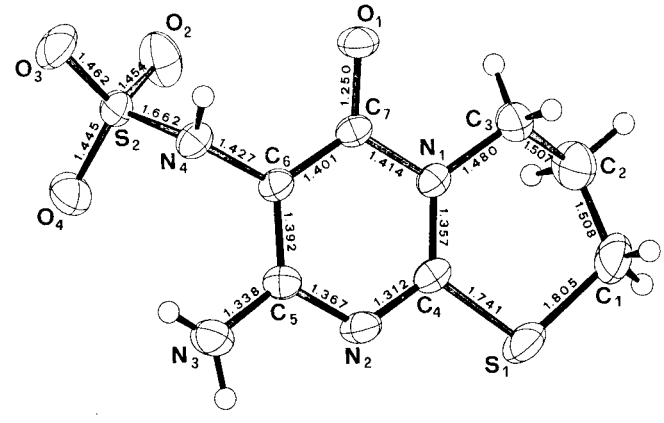

Figure 2. ORTEP view of the anionic moiety of compound **7** with atom numbering scheme and bond distances (Å). Thermal ellipsoids enclose 60% probability.

compare well with those reported for other derivatives as determined by means of X-ray [12,13] or electron diffraction [14] methods. The thiadiazole and the planar moiety of the thiazine ring are slightly tilted from coplanarity with the inner pyrimidine ring by rotation about their common bonds. Dihedral angles of 2.8° and 4.6°, respectively, are formed between their mean planes. The molecular packing in compound **4** is mainly determined by aromatic ring-stacking interactions along the *c* axis [Figure 4], and is characterized by many (twenty) short van der Waals contacts. The shortest one [3.023(3) Å] occurs between the S(2) and O(1) atoms.

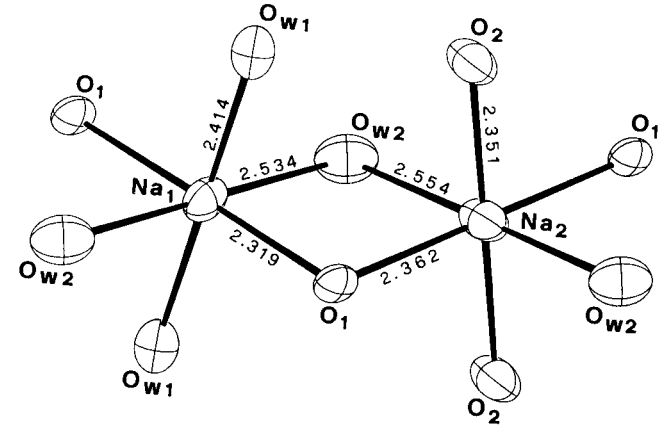

Figure 3. The Na(+) coordination spheres in **7** with bond distances (Å, e.s.d.'s +0.001).

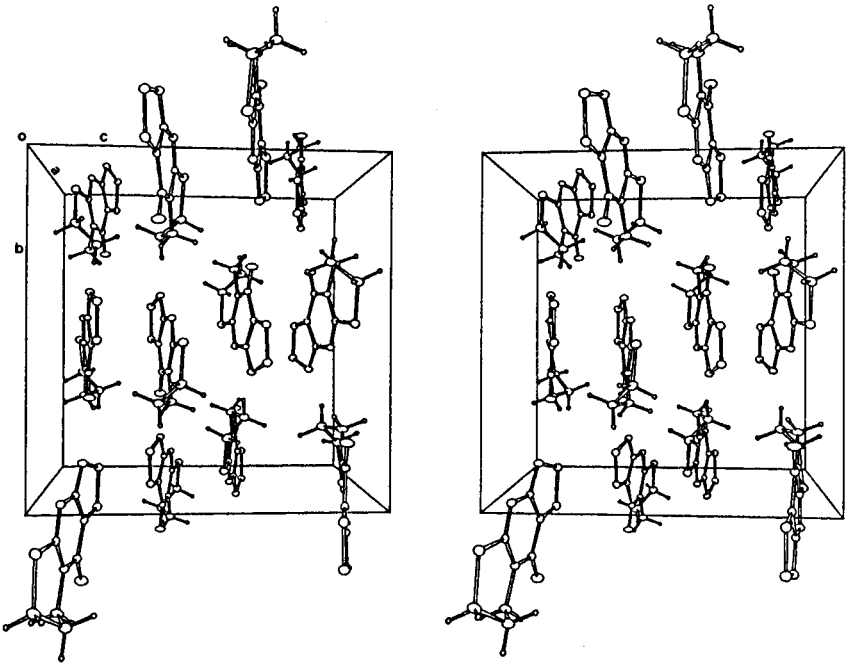

Figure 4. Stereoview of the molecular packing of compound **4**.

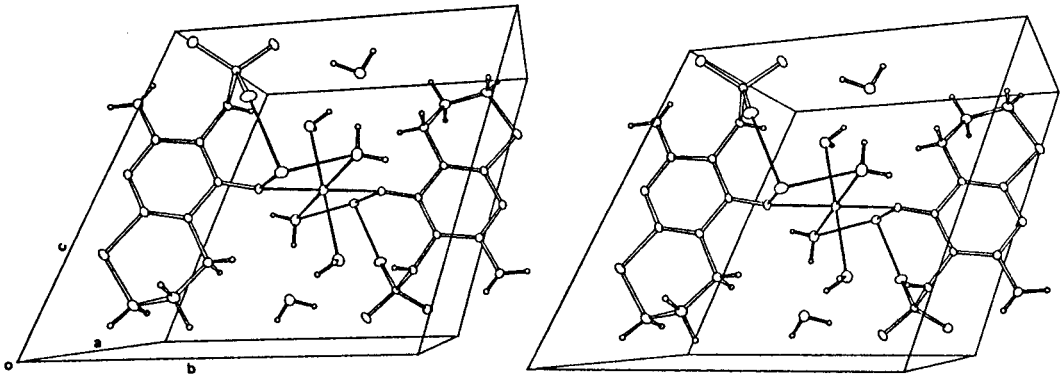

Figure 5. Stereoview of the unit cell contents of compound **7**.

The structure of compound **7** is built up of one sulfamate anion [Figure 2], two crystallographically-independent $Na^{(+)}$ cations, both lying on an inversion centre, of two water molecules bonded to $Na^{(+)}$ ions, and of one lattice water molecule. Both $Na^{(+)}$ ions show octahedral six-coordination, and their coordination polyhedra share two opposite edges [Figure 3], so determining a linear chain structure parallel to the *a* cell axis. The carbonyl O(1) atom and one water oxygen act as bridging atoms. Two water molecules complete the six-coordination about the Na(1) ion, whereas two sulfonic O(2) atoms are bonded to the Na(2) cation, with formation of seven-membered chelate rings. It is worth noting that compounds **7** and **9** [7] are isostructural. The dimensions of the half-chair shaped thiazine ring of **7** compare very well those of **4**. The C(2) atom is displaced 0.664 Å out of the mean plane through the other ring atoms, which are planar within 0.021 Å. Comparison of the corresponding bond distances in the pyrimidinone moieties of compounds **4** and **7** reveals two noteworthy differences: firstly, a relevant lengthening of the C(7)-O(1) bond [from 1.204(4) to 1.250(1) Å] when the carbonyl oxygen is involved in metal ion binding; secondly, a stronger-double bond character of the C(6)-C(7) bond in compound **7** [1.401(1) *vs.* 1.464(5) Å]. As a consequence, the pyrimidine ring of compound **7** exhibits less distortion from planarity: the atomic deviations from the mean plane are within ±0.016 Å, and the torsion angles range from −3.1 to 3.0°. The dihedral angle between the mean planes through the pyrimidine and thiazine rings is 1.9°. As in compound **9**, the -$NHSO_3^-$ group of **7** is bonded to the ring

in antiperiplanar conformation and there is good agreement between C-N and N-S bond distances [1.667(1) and 1.424(2) Å, respectively, in **9**; 1.662(1) and 1.427(1) Å in **7**]. In spite of these rather short bond distances, the nitrogen atom shows fundamental sp^3 configuration, being displaced 0.302 Å from the CHS plane [0.303 Å in compound **9**].

Coordination to the $Na^{(+)}$ ions appears to be the major contributor to the crystal packing of compound **7** [Figure 5] but there is also an extensive network of strong hydrogen bond interactions (nine crystallographically independent) which involve mainly water or aminic hydrogens and sulfonic or water oxygens.

EXPERIMENTAL

Nitroso derivatives [Scheme 1 **A**] were prepared according to the literature [1,2,3].

The old sodium hydrosulfite was purchased from C. Erba many years ago and kept at room temperature. The new sodium hydrosulfite was recently purchased from Aldrich Co. and refrigerated at +4°. All chromatographic solvents of analytical-reagent grade were obtained from Merck. The samples, dissolved in suitable solvent and spotted on 10 x 20 cm precoated silica gel F_{254} plates (Merck), were developed at room temperature, using as solvent system the heavy fraction formed by chloroform-methanol-water (5:5:3 v/v/v). Melting points were determined on a Buchi 510 apparatus and are uncorrected. The uv spectra were obtained with a Perkin-Elmer Spectrophotometer model Lambda 15, using 1 cm quartz cells in 10^{-5} *M* ethanol or aqueous solution. The wavelength absorption maxima are reported in nanometers. The ^{1}H-nmr spectra were recorded with a Varian spectrometer model XL 200 (Centro Interdipartimentale Grandi Strumenti, Modena University) in DMSO-d_6 solution. Chemical shifts are reported in ppm from tetramethylsilane used as internal standard, and are given in δ units. The following abbreviations are used to designate the multiplicity of individual signals: s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet.

Microanalyses were carried out by Miss S. Selmi in the Microanalysis Laboratory of the Dipartimento di Scienze Farmaceutiche, Modena University.

Crystallography.

Suitable crystals for the diffraction studies of **4** and **7** were obtained by slow evaporation from aqueous solution. All measurements were carried out on an Enraf-Nonius CAD4 diffractometer, at room temperature, under the conditions listed in Table 1. Data reduction included Lp and absorption (based on empirical Ψ scan) corrections.

Both structures were solved by direct methods with the program SHELX86 [15], and were refined through full-matrix least-squares calculations (SHELX76 [16]) minimizing $\Sigma w (| F_o | - | F_c |)^2$. In both cases, all non-H atoms were refined anisotropically. The H atoms of **7** were refined isotropically, whereas those of **4** were refined isotropically but with a common temperature factor, through some least-squares cycles, and then kept fixed because of the low parameter/reflection ratio. In the case of **7**, a secondary extinction x parameter was applied and refined, its final value being $6.1(4)\cdot10^{-6}$. In addition, zero weight was assigned to four strong low-order reflections with F_o deviating markedly from F_c. In both cases. the weighting scheme, reported in Table 1, gave satisfactory agreement analyses.

Complex neutral atom (except $Na^{(+)}$) scattering factors, including anomalous dispersion terms for non-H atoms, were taken from ref [17]. Major calculations were carried out on a VAX 6310 computer.

Final atomic coordinates are given in Tables 2 and 3, and selected bond distances in Table 4. Lists of anisotropic temperature factors, complete bond distances and bond angles, hydrogen-bonding interactions, torsion angles, shortest van der Waals contacts, selected least-squares planes, and observed and calculated structure factors are available on request from the Author **.

7,8-Dihydro-6*H*,10*H*-[1,2,5]thiadiazolo[3',4':4,5]pyrimido[2,1-*b*]-[1,3]thiazin-10-one (**4**), its 3-Methyl-derivative **5**, 6,7-Dihydro-9*H*-thiazolo[3,2-*a*][1,2,5]thiadiazolo[3,4-*d*]pyrimidin-9-one (**6**); (8-Amino-3,4-dihydro-2*H*,6*H*-pyrimido[2,1-*b*][1,3]thiazin-6-on-7-yl)sulfamic Acid, Sodium Salt (**7**), its 3-Methyl-derivative **8**, (7-Amino-2,3-dihydro-5*H*-thiazolo[3,2-*a*]pyrimidin-5-on-6-yl)sulfamic Acid, Sodium Salt (**9**) and (6-Amino-3-methyl-2-methylthio-4(3*H*)pyrimidinon-5-yl)sulfamic Acid, Sodium Salt (**11**).

Old sodium hydrosulfite was added slowly to a suspension of either 8-amino-3,4-dihydro-7-nitroso-2*H*,6*H*-pyrimido[2,1-*b*][1,3]-thiazin-6-one [1] (1.0 g, 4.7 mmoles) or its 3-methyl-derivative [2] (1.5 g, 6.6 mmoles) or 7-amino-2,3-dihydro-6-nitroso-5*H*-thiazolo-[3,2-*a*]pyrimidin-5-one [1] (1.0 g, 5.0 mmoles) or 6-amino-5-nitroso-3-methyl-2-methylthio-4(3*H*)pyrimidinone [3] (0.7 g, 3.5 mmoles) in boiling water (25 ml) until the blue colour completely disappeared. The pale-yellow solution was refluxed for 4-5 minutes and then refrigerated for 2-4 hours. In the first three reactions the first precipitate consists of the slightly impure thiadiazole derivatives **4, 5,** and **6**, respectively. In the last reaction an unknown fluorescent compound was formed in very low yield; therefore it was not separated out.

By concentrating the mother liquors, 7,8-diamino-3,4-dihydro-2*H*,6*H*-pyrimido[2,1-*b*][1,3]thiazin-6-one (**1**), or the 3-methyl-derivative (**2**), or 6,7-diamino-2,3-dihydro-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**3**) or 5,6-diamino-3-methyl-2-methylthio-4(3*H*)-pyrimidinone (**10**) [3] precipitates, in low yield, together with a residual part of **4, 5** and **6**, and of the unknown fluorescent compound, respectively. When recently-purchased sodium hydrosulfite was used, only a small fraction of thiadiazolo derivatives are revealed by thin-layer chromatography analysis.

Further concentration of mother waters yielded **7, 8, 9** and **11** in crystalline form; they are soluble in water and have Rf values that are practically zero in the above-mentioned solvent system.

Compound **4** was obtained in a yield of 11% (0.116 g), mp 218-220° (water); uv (ethanol): λ max (nm) (log ϵ) 340 (3.94), 260 (sh) (4.10), 245 (4.18); ^{1}H-nmr (DMSO-d_6): δ 4.06 (t, 2H, NCH_2), 3.24 (t, 2H, SCH_2), 2.20 (m, 2H, CCH_2C).

Anal. Calcd. for $C_7H_6N_4OS_2$: C, 37.16; H, 2.67; N, 24.76; S, 28.34. Found: C, 36.95; H, 2.53; N, 24.75; S, 27.96.

Compound **4** was also obtained, in low yield, following this method: thiourea (0.2 g) (2,6 mmoles) and 8-amino-3,4-dihydro-7-nitroso-2*H*,6*H*-pyrimido[2,1-*b*][1,3]thiazin-6-one (0.3 g, 1.4 mmoles) were mixed and heated in a bath at 160-170°. The reaction was completed in 10 minutes, the melt was triturated with water and the solid extracted with chloroform. The soluble frac-

tion consists of **4**.

Compound **5** was obtained in a yield of 13% (0.2 g), mp 200° (water); uv (ethanol): λ max nm (log ε) 340 (3.98), 257 (sh) (4.12) 244 (4.21); ^{1}H-nmr (DMSO-d_6): δ 4.34 (dq, 1H, CH), 3.50 (q, 1H, CH), 3.24 (dq, 1H, CH), 3.03 (q, 1H, CH), 2.33 (m, 1H, 3-H), 1.13 (d, 3H, 3-CH_3).

Anal. Calcd. for $C_8H_8N_4OS_2$: C, 39.99; H, 3.36; N, 23.32. Found: C, 39.63; H, 3.68; N, 23.04.

Compound **6** was obtained in a yield of 5% (0.055 g), mp 198-200° (water); uv (ethanol): λ max nm (log ε) 328 (4.00), 257.5 (4.12), 236.5 (4.10); ^{1}H-nmr (DMSO-d_6): δ 4.41 (t, 2H,NCH_2), 3.61 (t, 2H, SCH_2).

Anal. Calcd. for $C_6H_4N_4OS_2$: C, 33.97; H, 1.90; N, 26.42. Found: C, 33.71; H, 2.05; N, 26.08.

Compound **7** was obtained in a yield of 25% (0.35 g), mp 240° (water); uv (water): λ max nm (log ε) 273 (3.87), 221 (4.20), 203 (4.27); ^{1}H-nmr (DMSO-d_6): δ 6.44 (s, 2H, 8-NH_2), 5.52 (s, 1H, 7-NH), 3.85 (t, 2H, NCH_2), 3.11 (t, 2H, SCH_2), 2.08 (m, 2H, CCH_2C).

Anal. Calcd. for $C_7H_9N_4NaO_4S_2$: C, 28.00; H, 3.02; N, 18.66. Found: C, 27.74; H, 2.99; N, 18.35.

Compound **8** was obtained in a yield of 36% (0.74 g), mp 200° (water); uv (water): λ max nm (log ε) 275 (3.86), 221 (4.20), 203 (4.26); ^{1}H-nmr (DMSO-d_6): δ 6.45 (s, 2H, 8-NH_2), 5.56 (s, 1H, 7-NH), 4.15 (dq, 1H, CH), 3.26 (q, 1H, CH), 3.08 (dq, 1H, CH), 2.90 (q, 1H, CH), 2.17 (m, 1H, 3-H), 1.07 (d, 3H, 3-CH_3).

Anal. Calcd. for $C_8H_{11}N_4NaO_4S_2$: C, 30.57; H, 3.53; N, 17.83. Found: C, 30.35; H, 3.71; N, 17.60.

Compound **9** was obtained in a yield of 16% (0.24 g), mp >300°; uv (water), λ max nm (log ε) 278 (3.82), 220 (4.31); ^{1}H-nmr (DMSO-d_6): δ 6.52 (s, 2H, 7-NH_2), 5.43 (s, 1H, 6-NH), 4.20 (t, 2H, NCH_2), 3.50 (t, 2H, SCH_2).

Anal. Calcd. for $C_6H_7N_4NaO_4S_2 \cdot H_2O$: C, 23.68; H, 2.98; N, 18.41. Found: C, 23.78; H, 2.83; N, 18.47.

Compound **11** was obtained in a yield of 23% (0.247 g), mp >300°; uv (water): λ max nm (log ε) 280 (3.88), 229 (4.21), 216 (4.24); ^{1}H-nmr (DMSO-d_6): δ 6.46 (s, 2H, 6-NH_2), 5.54 (s, 1H, 5-NH), 3.31 (s, 3H, N-CH_3), 2.48 (s, 3H, S-CH_3).

Anal. Calcd. for $C_6H_9N_4NaO_4S_2 \cdot H_2O$: C, 23.53; H, 3.62; N, 18.29. Found: C, 23.30; H, 3.85; N, 18.17.

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