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REACTIONS OF 3,4-DICHLORO-N-R-MALEIMIDES WITH SUBSTITUTED 2-THIOURACILS

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Reactions of 3,4-dichloro-N-R-maleimides with substituted thiouracils at 40°C gave a 1:1 mixture of isomers of pyrrolothiazolopyrimidinetriones. Under conditions of thermodynamic control (100°C, 5 h) only pyrrolo[3',4':4,5]thiazolo[3,2-a]pyrimidine-4,6,8-triones were formed, hydrolysis of which followed by decarboxylation gave 5-oxo-5H-thiazolo[3,2-a]pyrimidine-2-carboxamide. The structure of N^2-phenyl-6-methyl-5-oxo-5H-thiazolo[3,2-a]pyrimidine-2-carboxamide was confirmed by X-ray crystallography. Analogous cyclization of 3,4-dichloro-N-R-maleimides with 2-thioxoquinazol-4-one also gave a mixture of two isomers which were successfully separated by fractional crystallization.

Keywords: 7-R-2-R^2-3-R^1-7,8-dihydro-4H,6H-pyrrolo[3',4':4.5][1,3]thiazolo[3,2-*a*]pyrimidine-4,6,8-triones, N^2-R-6-R^1-5-oxo-5H[1,3]thiazolo[3,2-*a*]pyrimidine-2-carboxamide, nucleophilic substitution in 3,4-dichloro-N-R-maleimides.

In 1989-1990 Katritzky [1,2] described the formation of the pyrrolo-[3,4-*d*]thiazole ring as a result of the reaction 3,4-dichloro-N-phenylmaleimide with thioamides (thiourea, thoacetamide, dithiooxamide). Japanese authors later reported other products from the reaction of substituted maleimides with dithiooxamide – tetrahydro-1H,5H-[1,4]dithiino[2,3-*b*:6,5-*b′*]dipyrrole [3], but in 1993 Katritzky showed that pyrrolo[3,4-*d*]-thiazoles were only obtained in negligible quantities from the maleimides with thioamides, while the main products of the reactions are tetrahydro-1H,5H-[1,4]dithiino[2,3-*b*;6,5-*b′*]dipyrroles [4].

In the present work we have studied the interaction of 3,4-dichloro-N-R-maleimides **1** with 2-thiouracils **2** which contain three nucleophilic centers: the sulfur atom and the nitrogen atoms at positions 1 and 3.

In mild conditions (30-40°C) the reaction did not stop at the replacement of just one chlorine atom of the imide **1** but proceeded to cyclization as a result of which a mixture of the isomers **3** and **4** was formed in approximately equal amounts (to judge from the ^{1}H NMR spectrum) (Scheme 1).

When the reactions were carried out under more vigorous conditions (100°C, 5 h) only the isomers **3a-m** were formed. We did not succeed to isolate isomers **4** in pure form. Calculation of the energies of the isomers with structures **3** and **4** was carried out using the AM1 method (Hyper Chem 5.0, grad = 0.01 kcal/mol, suite of programs) showed that isomer **3** has a lower energy than isomer **4** (ΔE = 7-10 kcal/mol). Evidently in the boiling reaction mixture isomers **4** are converted to the more thermodynamically stable isomers **3** which is similar to what occurs in the Dimroth rearrangement [5].

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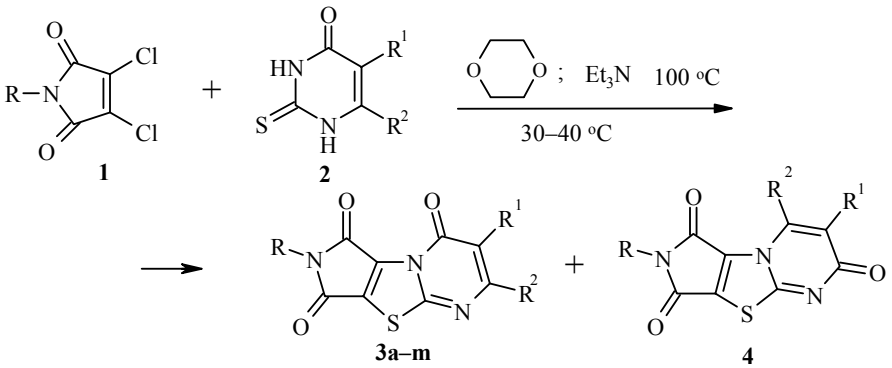
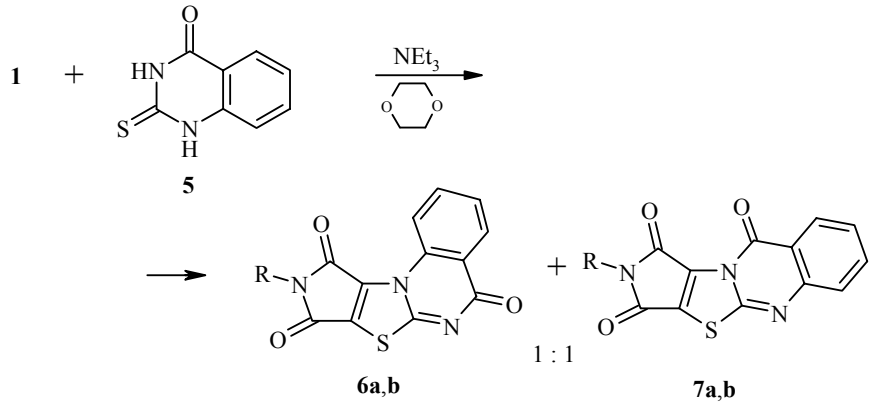
Scheme 1



R = CH_2Ph, Ar; R^1 = H, Me, R^1, R^2 = CH_2–CH_2–CH_2 ; R^2 = H, Me, *n*-Pr

The IR spectra of compounds **3a-m** contain two carbonyl stretching bands of the maleimide ring at 1785-1775 (*as*) and 1730-1715 (*s*) cm^{-1}. The carbonyl stretching vibration of the pyrimidine ring is observed at 1715-1685 cm^{-1}, which corresponds to data [6] characteristic for isomers of type **3**.

2-Thioxo-1,2,3,4-tetrahydro-4-quinazolone (**5**), a benzo-annelated derivative of 2-thiouracil, also reacted with dichloromaleimides **1** (R = 4-MeC_6H_4 or 4-$MeOC_6H_4$) under mild conditions to form a mixture of isomers **6** and **7** in equal amounts (according to the ^{1}H NMR spectra).

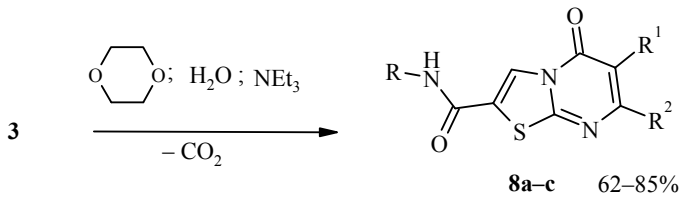


6, **7** **a** R = 4-MeC_6H_4; **b** R = 4-$MeOC_6H_4$

However in this case heating the reaction mixture at 100°C for 5h gave only a negligible increase in the quantity of isomer **7**. Compounds **6b**, **7a,b** were isolated in pure form by fractional crystallization. The ^{1}H NMR spectrum of isomer **6b** permitted the elucidation of the positions of the resonances of the protons of isomer **6a** by difference from the ^{1}H NMR spectra of the mixture of isomers (Table 1). Isomers **6a,b** are less soluble in dioxane than isomers **7a,b**, they are higher melting, and are chromatographically less mobile (R_f (**6**) = 7.8; R_f (**7**) = 8.8).

As a result of the angular structure of the planar molecules of isomers **6a,b**, the proton in position 1 is in the same plane as the carbonyl groups of the maleimide ring. In the ^{1}H NMR spectra of compounds **6a,b** the deshielding effect of the carbonyl groups cause a considerable shift of the proton of this signal to weak field: 9.11 (**6a**) and 9.08 ppm (**6b**) (1H, d). In the ^{1}H NMR spectra compounds **7a,b** the proton at position 9 appears at weakest field at 8.31 and 8.29 ppm (1H, d). In the IR spectra of compounds **6b, 7a,b** the two bands corresponding to the carbonyl groups of the maleimide ring are observed at 1785-1770 (*as*) and

1720-1715 (*s*) cm^{-1}. Vibrations of the carbonyl group of the quinazoline nucleus were observed at 1700 for isomers **7a,b** and at 1650 cm^{-1} for isomer **6b**. Refluxing compounds **3** in aqueous dioxane in he presence of an equimolar amount of triethylamine led to hydrolysis and opening of the maleimide ring with subsequent decarboxylation to give compounds **8a-c**.



8a–c 62–85%

The ^{1}HNMR spectra of **8a-c** include a singlet for the proton of the thiazole ring in the region of 8.99-9.14 ppm. The signal of the amide proton, which disappears on the addition of D_2O, is observed in the 10.39-10.71 ppm region. The signals of the protons of the substituents R, R^1, and R^2 are cited in Table 1.

The carbonyl stretching frequencies of the maleimide ring are absent from the IR spectra of compounds **8a-c.** The stretching vibrations of the amide carbonyl group and the carbonyl group of the pyrimidine ring appear in the 1650-1640 cm^{-1} region. The N–H stretching vibrations are in the region of 3290-3280 $cm^{-1}$and the band for the C–H bond of the thiazole ring is in the 3080-3060 cm^{-1} region.

The structure of compound **8b** was confirmed by X-ray crystallography (Fig. 1, Table 2) using the CAMERON method [7]. The bicyclic system $S_{(1)}N_{(1)}N_{(2)}C_{(1-6)}$ is planar within 0.026 A, and the interfacial angle between the $S_{(1)}N_{(1)}C_{(1-3)}$ and $N_{(1)}N_{(2)}C_{(3-6)}$ rings is only 1.9°. The geometric parameters of the cyclic systems indicate considerable electron density delocalization [8,9]. The exocyclic carboxamide fragment $C_{(1)}C_{(8)}O_{(2)}N_{(3)}C_{(9)}$ is also almost planar (torsion angles $C_{(1)}$-$C_{(8)}$-$N_{(3)}$-$C_{(9)}$ and $O_{(2)}$–$C_{(8)}$–$N_{(3)}$–$C_{(9)}$ are 174.5 and 4.2°) and forms an interfacial angle with the bicyclic plane $S_{(1)}N_{(1)}N_{(2)}C_{(1-6)}$ of 7.8°Atom $N_{(3)}$ has a planar trigonal configuration of bonds: the sum of the angles is 360°. The benzene ring $C_{(9-14)}$ is rotated relative to the plane $C_{(1)}C_{(8)}O_{(2)}N_{(3)}C_{(9)}$ by 28.1°. The molecules of compound **8b** are connected into a zigzag chain in the crystal and form intermolecular bonds $N_{(3)}$–$H_{(3)}$···$O_{(1)}$ with the following parameters: $N_{(3)}$···$O_{(1)}$ 2.877(3), $H_{(3)}$···$O_{(1)}$ 2.12(3), $N_{(3)}$–$H_{(3)}$ 0.81(3) A, $N_{(3)}H_{(3)}O_{(1)}$ 157(2)°.

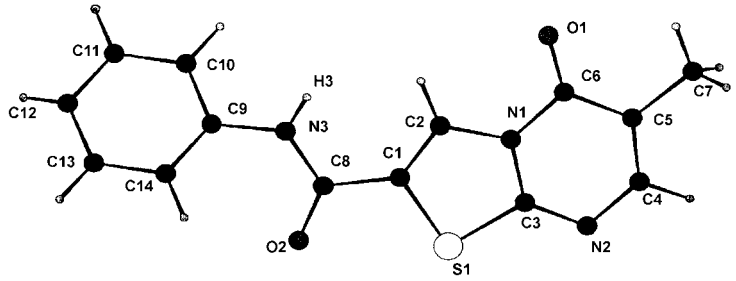


Fig. 1. Molecular structure of compound **8b**.

TABLE 1. Characteristics of Compounds **3a-m**, **6a**,**b**, **7a**,**b**, **8a-c**

Compound	R*	Empirical formula	Found, % / Calculated, %		^{1}H NMR spectrum, δ, ppm (*J*, Hz)	mp, °C	Yield, %
			N	S			
1	2	3	4	5	6	7	8
3a	CH_2Ph	$C_{15}H_9N_3O_3S$	13.42 / 13.50	10.23 / 10.30	4.78 (2H, s, CH_2); 6.42 (1H, d, *J* = 6.0, C(3)-H); 7.22-7.39 (5H, m, H_{Ar}); 8.03 (1H, d, *J* = 6.0, C(2)-H)	179-180	65
3b	3-MeC_6H_4	$C_{15}H_9N_3O_3S$	13.59 / 13.50	10.10 / 10.30	2.38 (3H, s, CH_3); 6.50 (1H, d, *J* = 6.0, C(3)-H); 7.19-7.22 (2H, m, 2'- and 4'-H_{Ar}); 7.30 (1H, d, *J* = 9.0, 6'-H_{Ar}); 7.44 (1H, t, *J* = 7.8, 5'-H_{Ar}); 8.04 (1H, d, *J* = 6.0, C(2)-H)	212-213	58
3c	4-$MeOC_6H_4$	$C_{15}H_9N_3O_4S$	13.07 / 12.84	9.56 / 9.79	3.80 (3H, s, OCH_3); 6.43 (1H, d, *J* = 6.0, C(3)-H); 7.08 (2H, d, *J* = 8.7, 3'- and 5'-H_{Ar}); 7.32 (2H, d, *J* = 8.7, 2'- and 6'-H_{Ar}); 8.05 (1H, d, *J* = 6.0, C(2)-H)	189-190	60
3d	CH_2Ph	$C_{16}H_{11}N_3O_3S$	13.04 / 12.92	9.99 / 9.85	2.30 (3H, s, CH_3); 4.78 (2H, s, CH_2); 6.32 (1H, s, C(3)-H); 7.2-7.3 (5H, m, H_{Ar})	185-186	61
3e	Ph	$C_{15}H_9N_3O_3S$	13.32 / 13.50	10.17 / 10.30	2.19 (3H, s, CH_3); 7.2-7.4 (3H, m, 3'-, 4'- and 5'-H_{Ar}); 7.72 (2H, d, *J* = 7.5, 2'- and 6'-H_{Ar}); 8.03 (1H, s, C(2)-H)	193-194	53
3f	Ph	$C_{17}H_{13}N_3O_3S$	12.50 / 12.38	9.37 / 9.45	0.95 (3H, t, *J* = 7.2, CH_3); 1.68 (2H, m, CH_2-$\underline{CH_2}$-CH_3); 2.58 (2H, t, *J* = 7.2, $\underline{CH_2}$-CH_2-CH_3); 6.36 (1H, s, C(3)-H); 7.3–7.6 (5H, m, H_{Ar})	191-192	62
3g	CH_2Ph	$C_{18}H_{15}N_3O_3S$	12.09 / 11.89	9.28 / 9.07	0.93 (3H, t, *J* = 7.2, CH_3); 1.65 (2H, m, CH_2-$\underline{CH_2}$-CH_3); 2.53 (2H, t, *J* = 7.0, $\underline{CH_2}$-CH_2-CH_3); 4.78 (2H, s, $C_6H_5\underline{CH_2}$); 6.30 (1H, s, C(3)-H); 7.2-7.4 (5H, m, H_{Ar})	151-152	58
3h	2-MeC_6H_4	$C_{18}H_{15}N_3O_3S$	12.12 / 11.89	9.31 / 9.07	0.92 (3H, t, *J* = 7.3, CH_3); 1.67 (2H, m, CH_2-$\underline{CH_2}$-CH_3); 2.19 (3H, s, CH_3); 2.58 (2H, t, *J* = 7.2, $\underline{CH_2}$-CH_2-CH_3); 6.38 (1H, s, C(3)-H); 7.30-7.45 (4H, m, H_{Ar})	214-215	59
3i	Ph	$C_{17}H_{11}N_3O_3S$	12.38 / 12.46	9.48 / 9.50	2.08 (2H, m, C(7)-H); 2.76 (2H, t, *J* = 7.6, C(6)-H); 2.90 (2H, t, *J* = 7.6, C(8)-H); 7.4-7.55 (5H, m, H_{Ar})	233–234	69
3j	2-MeC_6H_4	$C_{18}H_{13}N_3O_3S$	12.05 / 11.96	9.18 / 9.12	2.09 (2H, m, C(7)-H); 2.18 (3H, s, CH_3); 2.76 (2H, t, *J* = 7.5, C(6)-H); 2.91 (2H, t, *J* = 7.5, C(8)-H); 7.3-7.45 (4H, m, H_{Ar})	222-223	55
3k	4-MeC_6H_4	$C_{18}H_{13}N_3O_3S$	11.88 / 11.96	9.15 / 9.12	2.08 (2H, m, C(7)-H); 2.37 (3H, s, CH_3); 2.75 (2H, t, *J* = 7.6, C(6)-H), 2.90 (2H, t, *J* = 7.6, C(8)-H); 7.26 (2H, d, *J* = 8.4, 3'- and 5'-H_{Ar}); 7.34 (2H, d, *J* = 8.4, 2'- and 6'-H_{Ar})	209-210	67

TABLE 1 (continued)

1	2	3	4	5	6	7	8
3l*[2]	4-ClC_6H_4	$C_{17}H_{10}ClN_3O_3S$	11.44 / 11.30	8.70 / 8.62	2.08 (2H, m, C(7)-H); 2.75 (2H, t, *J* = 7.6, C(6)-H); 2.90 (2H, t, *J* = 7.6, C(8)-H); 7.43 (2H, d, *J* = 8.7, 3'- and 5'-H_{Ar}); 7.61 (2H, d, *J* = 8.7, 2'- and 6'-H_{Ar})	228-29	53
3m*[3]	2,3-$Cl_2C_6H_3$	$C_{17}H_9Cl_2N_3O_3S$	10.42 / 10.34	8.08 / 7.89	2.10 (2H, m, C(7)-H); 2.77 (2H, t, *J* = 7.6, C(6)-H); 2.91 (2H, t, *J* = 7.6, C(8)-H); 7.58 (2H, m, 4'- and 5'-H_{Ar}); 7.87 (1H, d, *J* = 9.0, 6'-H_{Ar})	232-233	58
6a	4-MeC_6H_4	$C_{19}H_{11}N_3O_3S$	11.63	8.87	2.40 (3H, s, CH_3); 7.26 (2H, d, *J* = 8.2, 3'- and 5'-H_{Ar}); 7.37 (2H, d, *J* = 7.8, 2'- and 6'-H_{Ar}); 7.75 (1H, t, *J* = 8.1, C(3)-H); 8.0 (1H, t, *J* = 8.1, C(2)-H); 8.26 (1H, d, *J* = 7.8, C(4)-H); 9.11 (1H, d, *J* = 9.0, C(1)-H)		
6b	4-$MeOC_6H_4$	$C_{19}H_{11}N_3O_4S$	11.19 / 11.13	8.54 / 8.50	3.82 (3H, s, OCH_3); 7.13 (2H, d, *J* = 8.4, 3'- and 5'-H); 7.39 (2H, d, *J* = 7.8, 2'- and 6'-H_{Ar}); 7.72 (1H, t, *J* = 8.1, C(3)-H); 7.98 (1H, t, *J* = 8.4, C(2)-H); 8.22 (1H, d, *J* = 8.1, C(4)-H); 9.08 (1H, d, *J* = 8.1, C(1)-H)	279-280	11
7a	4-MeC_6H_4	$C_{19}H_{11}N_3O_3S$	11.57 / 11.63	8.68 / 8.87	2.38 (3H, s, CH_3); 7.29 (2H, d, *J* = 8.1, 3'- and 5'-H_{Ar}); 7.35 (2H, d, *J* = 7.8, 2'- and 6'-H_{Ar}); 7.62 (1H, t, *J* = 8.1, C(8)-H); 7.72 (1H, d, *J* = 8.1, C(6)-H); 7.95 (1H, t, *J* = 8.1, C(7)-H); 8.31 (1H, d, *J* = 8.1, C(9)-H)	245-246	23
7b	4-$MeOC_6H_4$	$C_{19}H_{11}N_3O_4S$	11.25 / 11.13	8.46 / 8.50	3.82 (3H, s, OCH_3); 7.09 (2H, d, *J* = 9.0, 3'- and 5'-H_{Ar}); 7.34 (2H, d, *J* = 8.7, 2'- and 6'-H_{Ar}); 7.61 (1H, t, *J* = 8.1, C(8)-H); 7.70 (1H, d, *J* = 7.8, C(6)-H); 7.94 (1H, t, *J* = 7.8, C(7)-H); 8.29 (1H, d, *J* = 8.1, C(9)-H)	234-235	26
8a	4-$MeOC_6H_4$	$C_{14}H_{11}N_3O_3S$	14.05 / 13.95	10.57 / 10.64	3.75 (3H, s, OCH_3); 6.33 (1H, d, *J* = 6.0, C(6)-H); 6.95 (2H, d, *J* = 8.0, 3'- and 5'-H_{Ar}); 7.61 (2H, d, *J* = 8.0, 2'- and 6'-H_{Ar}); 8.06 (1H, d, *J* = 6.0, C(7)-H); 9.09 (1H, s, C(3)-H); 10.57 (1H, s, NH)	276-277	77
8b	Ph	$C_{14}H_{11}N_3O_2S$	14.81 / 14.73	11.10 / 11.24	2.06 (3H, s, CH_3); 7.16 (1H, t, *J* = 7.5, 4'-H_{Ar}); 7.39 (2H, t, 3'- and 5'-H_{Ar}); 7.71 (2H, d, *J* = 7.3, 2'- and 6'-H_{Ar}); 8.02 (1H, s, C(7)-H); 9.14 (1H, s, C(3)-H); 10.71 (1H, s, NH)	242-243	85
8c	4-MeC_6H_4	$C_{17}H_{15}N_3O_2S$	13.08 / 2.91	10.00 / 9.85	2.03 (2H, m, C(7)-H); 2.28 (3H, s, CH_3); 2.75 (2H, t, *J* = 7.8, C(8)-H); 2.85 (2H, t, *J* = 7.8, C(6)-H); 7.17 (2H, d, *J* = 8.4, 3'- and 5'-H_{Ar}); 7.54 (2H, d, *J* = 8.4, 2'- and 6'-H_{Ar}); 8.99 (1H, s, C(3)-H); 10.39 (1H, s, NH)	253-254	62

* **3a-d**,**f-h**, **8a** R^1 = H; **3e**, **8b** R^1 = Me; **3i-m**, **8c** $R^1+R^2 = (CH_2)_3$; **3a-s,e**, **8a,b** R^2 = H; **3d** R^2 = Me; **3f-h** R^2 = *n*-Pr.

*[2] Found, %: Cl 9.62; calculated, %: Cl 9.54

*[3] Found, %: Cl 17.42; calculated, %: Cl 17.45.

TABLE 2. Bond Lengths (*d*) and Bond Angles (ω) in the Molecule of Compound **8b**

Bond	*d*, Å	Angle	ω, deg.
$S_{(1)}$–$C_{(1)}$	1.740(3)	$S_{(1)}$–$C_{(3)}$–$N_{(1)}$	110.7(2)
$S_{(1)}$–$C_{(3)}$	1.731(3)	$N_{(1)}$–$C_{(3)}$–$N_{(2)}$	124.7(3)
$O_{(1)}$–$C_{(6)}$	1.226(3)	$N_{(2)}$–$C_{(4)}$–$C_{(5)}$	126.5(3)
$O_{(2)}$–$C_{(8)}$	1.220(3)	$C_{(4)}$–$C_{(5)}$–$C_{(6)}$	119.4(3)
$N_{(1)}$–$C_{(2)}$	1.395(3)	$N_{(1)}$–$C_{(6)}$–$C_{(5)}$	113.0(2)
$N_{(1)}$–$C_{(3)}$	1.373(3)	$O_{(2)}$–$C_{(8)}$–$N_{(3)}$	125.9(3)
$N_{(1)}$–$C_{(6)}$	1.413(3)	$O_{(2)}$–$C_{(8)}$–$C_{(1)}$	118.6(2)
$N_{(2)}$–$C_{(3)}$	1.304(4)	$N_{(3)}$–$C_{(8)}$–$C_{(1)}$	115.4(2)
$N_{(2)}$–$C_{(4)}$	1.362(4)	$N_{(1)}$–$C_{(2)}$–$C_{(1)}$	112.5(2)
$C_{(1)}$–$C_{(2)}$	1.337(4)	$C_{(3)}$–$N_{(1)}$–$C_{(6)}$	122.1(2)
$C_{(1)}$–$C_{(8)}$	1.491(4)	$C_{(3)}$–$N_{(2)}$–$C_{(4)}$	114.3(2)
$C_{(4)}$–$C_{(5)}$	1.354(4)	$C_{(8)}$–$N_{(3)}$–$C_{(9)}$	127.2(2)
$C_{(5)}$–$C_{(6)}$	1.428(4)	$C_{(2)}$–$N_{(1)}$–$C_{(3)}$	113.8(2)
$N_{(3)}$–$C_{(9)}$	1.419(4)	$C_{(1)}$–$S_{(1)}$–$C_{(3)}$	90.31(14)
$N_{(3)}$–$C_{(8)}$	1.341(4)	$S_{(1)}$–$C_{(1)}$–$C_{(2)}$	112.6(2)

EXPERIMENTAL

The course of reactions and the purity of the synthesized compounds were monitored by TLC (Silufol UV-254m eluent 9:1 chloroform–methanol). IR spectra of KBr discs were recorded with UR-20, Specord IR-75, and Pye-Unicam instruments, ^{1}H NMR spectra of DMSO-d_6 solutions with TMS as internal standard were recorded with a Varian machine (300 MHz).

The X-ray Crystallographic Study of a monocrystal (0.25 × 0.31 × 0.59 mm) of compound **8b** was carried out at room temperature with an automatic four circle Enraf-Nonius CAD-4 diffractometer (Mo*K*α radiation, relative rate of scanning $2\theta/\omega = 1.2$, $\theta_{max} = 65°$, segment of the sphere $0 < h < 12$, $0 < k < 8$, $-17 < l < 17$). 2306 reflexions were collected of which 2006 were symmetrically independent ($R_{int} = 0.015$). Crystals of compound **8b** are monoclinic, $C_{14}H_{11}N_3O_2S$; M = 285.32; $a = 11.476(4)$, $b = 7.471(4)$, $c = 15.395(7)$ Å; $\beta = 100.62(3)°$; $V = 1297.3$ Å^3; $Z = 4$; $d = 1.46$ g/cm^3; space group $P2_1/n$; $\mu = 2.42$ cm^{-1}; $F(000) = 593$. The structure was solved by direct methods and refined by least squares in the complete matrix anisotropic approximation with the CRYSTALS suite of programs [10]. For the refinement 1748 reflexions with $I > 3\sigma(I)$ were used. All hydrogen atoms were found from difference syntheses of the electron density and were included in the conclusion in fixed positions and thermal parameters (only atom $H_{(3)}$ was refined isotropically). Calculation of absorption in the crystal was carried out using azimuthal scanning [11]. The Chebyshev weighting scheme [12] with parameters of 1.61, 0.90, 1.51, -0.22, and 0.38 was used in the refinement. The final residual factors were $R = 0.041$, $R_w = 0.046$, GoF 1.137. The complete set of crystallographic data, including atomic coordinates and their anisotropic thermal parameters have been deposited in the Cambridge Crystal Structure Bank (CCDC 155191).

7-R-2-R^2-3-R^1-7,8-Dihydro-4H,6H-pyrrolo[3',4':4,5]thiazolo[3,2-*a*]pyrimidine-1,3,9-triones 3i-m. A solution of the corresponding dichloromaleimide **1** (10 mmol) (R = 4-MeC_6H_4, 4-MeOC_6H_4) and 2-thioquinazolone **2** (1.78 g, 10 mmol), and triethylamine (1.52 g, 15 mmol) in dry dioxane (20 ml) was refluxed for 5h. Ethanol (10 ml) was added to the cooled solution. The precipitate was filtered off, washed with ethanol, and recrystallized from dry dioxane.

Mixtures of isomers **3** and **4** were prepared in milder conditions analogous to the method used to prepare the mixtures of isomers **6a** + **7a** and **6b** + **7b.**

9-R,9,10-Dihydro-5H,8H-pyrrolo[3',4':4,5]thiazolo[3,2-*a*]quinazoline-5,8,10-triones 6a,b; 2-R-2,3-Dihydro-1H,10H-pyrrolo[3',4':4,5]thiazolo[2,3-*b*]quinazoline-1,3,10-triones 7a,b. To a solution of the corresponding dichloromaleimide **1** (10 mmol) (R = 4-MeC_6H_4, 4-$MeOC_6H_4$) and 2-thioquinazolone **2** (1.78 g, 10 mmol) in dry dioxane (25 ml), triethylamine (1.52 g, 15 mmol) was added dropwise at 30-40°C. The mixture was then stirred for 4 h at 35-45°C and then kept at room temperature for 8h. The precipitate was filtered off and washed with a small amount of dioxane and water. The precipitate was a mixture of approximately equal amounts of isomers **6** and **7**. The overall yields of the mixtures of isomers were 55 (**6a** + **7a**) and 67% (**6b** + **7b**). Compounds **6b** (11%), **7a** (23%), and **6a** (26%) were obtained in pure form by fractional crystallization from dry dioxane.

N^2-R-6-R^1-5-Oxo-5H-thiazolo[3,2-*a*]pyrimidine-2-carboxamides 8a,b; N^2(4-methylphenyl-5-oxo-5,6,7,8-tetrahydrocyclopenta[*f*]thiazolo[3,2-*a*]pyrimidine-2-carboxamide (8c) (Table 1). A solution of the corresponding compound **3** (3 mmol), triethylamine (0.303 g, 3 mmol), and water (1 ml) in dioxane (10 ml) was boiled for 1 h and then the reaction mixture was kept at room temperature for 8 h. The precipitate was filtered off and washed with a small amount of dioxane and water. It was recrystallized from DMF.

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