LITERATURE CITED

1. I. B. Levshin, I. V. Grigor'eva, A. A. Tsurkan, É. L. Tarasyavichus, K. A. V'yunov, and A. I. Ginak, Khim. Geterotsikl. Soedin., No. 3, 336 (1985).
2. V. G. Zapadnyuk, Farm. Toks., 24, No. 1, 33 (1961).
3. M. Mousseron, French Patent No. 1,412,398; Chem. Abstr., 65, 7391 (1966).
4. A. Serrei, Handbook of Organic Reactions [Russian translation], GITIKhL, Moscow (1962), p. 150.
5. G. Fenech, Atti Convegno Sci. Farmac. Med. Lat., Supp. Lavori Ist. Farmac., Univ. Messina, Vol. 8 (1973), p. 73.
6. F. Brown, Chem. Rev., 61, 463 (1961).
7. S. P. Singh, S. S. Parmar, K. Raman, and V. I. Stenberg, Chem. Rev., 81, 175 (1981).
8. I. B. Levshin, A. A. Tsurkan, K. A. V'yunov, and A. I. Ginak, Zh. Prikl. Khim., No. 7, 1453 (1983).
9. I. M. Turkevich, Zh. Obshch. Khim., 31, 3718 (1961).
10. K. A. V'yunov, A.I. Ginak, and E. G. Sochilin, Zh. Prikl. Spektrosk., 16, 1037 (1972).
11. L. Bellamy, Infrared Spectra of Complex Molecules, Methuen, London (1958).
12. K. A. V'yunov, A. I. Ginak, and E. G. Sochilin, Zh. Prikl. Spektrosk., 25, 865 (1976).
13. E. V. Vladzimirskaya, Zh. Obshch. Khim., 31, 2019 (1962).
14. O. G. Demchuk, Master's Dissertation, Lvov (1973).
15. E. L. Tarasyavichus and R. B. Pyachyura, Summaries of Papers Presented at the Third All-Union Convention of Pharmacists [in Russian], Kishinev (1980), p. 299.
16. H. Schubert, West German Patent No. 929,549; Ref. Zh. Khim., No. 18, 59,384 (1956).

CONDENSED HETEROCYCLES WITH A THIAZOLE RING.

10.* THIAZOLO[3,4-b][1,2,4]TRIAZINES

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Derivatives of a new heterocyclic system, viz., the thiazolo[3,4-b][1,2,4]triazinium ion, were obtained by condensation of cyanobenzyl benzenesulfonate with substituted N-dithiocarboxyhydrazones of 1,2-diketones and α-isonitroso ketones.

A number of valuable physiologically active substances [4-6] have been found among previously synthesized [2, 3] derivatives of condensed heterocycles with an angular nitrogen atom constructed on the basis of thiazole and 1,2,4-triazine rings (thiazolo[2,3-c]- and thiazolo[3,2-b][1,2,4]triazine). It seemed of interest to synthesize derivatives of heterocyclic compounds of the indicated type with a new orientation of the thiazole and triazine rings, viz., thiazolo[3,4-b][1,2,4]triazine.

With this end in mind, we studied the reaction of methyl dithiohydrazonate Ia [7] with α-cyanobenzyl benzenesulfonate (II). Since it is known [8] that sulfonate II reacts with methyl dithiocarbamate to give 4-amino-2-methylthiothiazolium salts, in our case we might have expected thiazolium salts with structure III. However, an investigation of the isolated product showed that, in the case of direct heating of a mixture of Ia and II, the reaction does not stop at this stage — condensation to the desired product occurs immediately to give the corresponding thiazolotriazinium salts IVa and Va. The structures of the synthesized compounds were confirmed by data from the PMR spectra (Table 1) and the IR spectra (Table 2). In fact, the IR spectrum of perchlorate Va does not contain absorption bands corresponding to the stretching vibrations of the C=O and N-H bonds of starting hydrazone Ia (1640 and 3210 cm^{-1}) but does contain a band of vibrations of a C=N bond (1590 cm^{-1}).

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*See [1] for communication 9.

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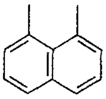
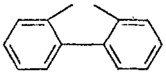
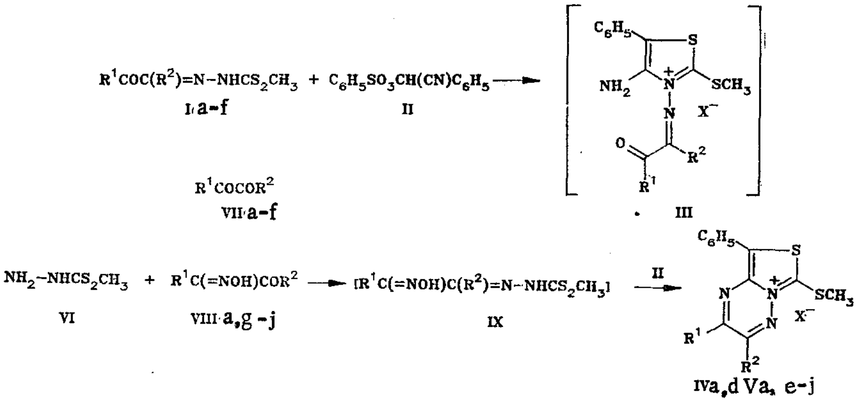
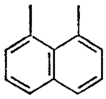
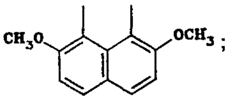
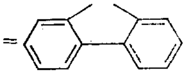
TABLE 1. PMR Spectrum of Thiazolotriazines

Compound	R^1	R^2	Chemical shifts, ppm (relative intensities)					
			SCH_3	Ar—H	R^1		R^2	
					≥C—H	C—CH_3	≥C—H	C—CH_3
IVb			2,49	6,6—7,6 (16)	—	—	—	—
IVd			2,52	6,5—7,9 (18)	—	—	—	—
Va	C_6H_5	C_6H_5	2,53	6,8—7,7 (15)	—	—	—	—
Ve	C_6H_5	H	2,57	6,9—7,9 (10)	—	—	8,67	—
Vf	CH_3	C_6H_5	2,50	6,8—7,8 (10)	—	2,23	—	—
Vg	H	C_6H_5	2,57	6,9—7,9 (10)	8,60	—	—	—
Vh	H	CH_3	2,55	6,9—7,6 (5)	8,06	—	—	2,28
Vi	CH_3	CH_3	2,54	6,9—7,5 (5)	—	2,24	—	2,28
Vj	C_6H_5	CH_3	2,48	6,9—7,6 (10)	—	—	—	2,20



a $R^1=R^2=C_6H_5$; b $R^1—R^2=$  ; c $R^1—R^2=$ 

;

d $R^1—R^2=$  ; e $R^1=C_6H_5$, $R^2=H$; f $R^1=CH_3$, $R^2=C_6H_5$; g $R^1=H$, $R^2=C_6H_5$; h $R^1=H$, $R^2=CH_3$; i $R^1=R^2=CH_3$; j $R^1=C_6H_5$, $R^2=CH_3$; IV $X=C_6H_5SO_3$; V $X=ClO_4$

Further studies showed that methyl dithiocarbazinate (VI) reacts readily not only with benzil (VIIa) [7], but also with other 1,2-diketones (VIIb-f) to give hydrazones Ib-f. Whereas there is no doubt about the structure in the case of symmetrical diketones and phenylglyoxal, in the case of the reaction of hydrazine VI with acetylbenzoyl (methylphenylglyoxal) one might have expected the formation of two isomeric products. However, according to the results of thin-layer chromatography (TLC), we found that this reaction gives only one substance, to which, on the basis of the IR spectra, we assigned structure If. In fact, the frequency of the vibrations of the C=O group of this compound is shifted 15 cm^{-1} to the high-frequency side as compared with its phenyl-substituted analog Ia. It should be noted that monohydrazones with similar structures were also obtained [9, 10] in the reaction of acetylbenzoyl (VIIf) with hydrazine derivatives such as semicarbazide and formylhydrazine. Like many other monosubstituted hydrazones of 1,2-diketones, Ia-f also exist in the syn-s-cis form [11, 12], as indicated by the low values of the frequencies of the stretching vibrations of the C=O groups in their molecules (1620-1655 cm^{-1}).

Hydrazonates Ib-f also react readily with benzenesulfonate II to give the corresponding thiazolotriazines IVb-d and Ve,f. It is possible that the one-step synthesis of the condensed thiazolotriazine is facilitated by the existence of hydrazones Ia-f in the form

TABLE 2. Characteristics of I, IV, and V

Compound	mp,* °C	IR spectrum, cm^{-1}	λ_{max}, nm (lg ε)	Found, %		Empirical formula	Calc., %		Yield, %
				Cl(N)	S		Cl(N)	S	
Ia	109—111 111—113 [7]	1565, 1580, 1640, 2920, 2990, 3020, 3050, 3205	256 (4,15), 334 (4,30)	(8,8)	20,7	$C_{16}H_{14}N_2OS_2$	(8,9)	20,4	80
Ib	210—211	1555, 1595, 1670, 3200	352 (4,01), 482 (4,37)	(9,4)	22,0	$C_{14}H_{10}N_2OS_2$	(9,8)	22,4	77
Ic	216—217	1520, 1600, 1630, 1710, 2850, 2920, 2950, 2990, 3170	362 (4,39)	(8,4)	18,5	$C_{16}H_{14}N_2O_3S_2$	(8,1)	18,5	79
Id	201—202	1505, 1585, 1620, 2915, 3070	420 (4,15), 455 (4,15)	(8,7)	20,1	$C_{16}H_{12}N_2OS_2$	(9,0)	20,5	68
If	130—132	1580, 1600, 1655, 3230	260 (3,85), 329 (4,34)	(11,7)	25,7	$C_{11}H_{12}N_2OS_2$	(11,3)	25,7	85
IV a	209—211	1560, 1575, 1590, 2930, 3015, 3065	339 (4,30), 470 (3,71)	(7,3)	16,5	$C_{30}H_{23}N_3O_3S_3$	(7,4)	16,9	70
IVb	249—250	1525, 1575, 1610, 3020—3060	400 (3,84), 525 (3,26)	(7,5)	17,7	$C_{28}H_{23}N_3O_3S_3$	(7,8)	17,8	77
IVc	265—266	1520, 1575, 1620, 1635, 2850, 2950, 3030, 3080	397 (4,08), 550 (3,44)	(6,9)	15,5	$C_{30}H_{23}N_3O_5S_3$	(6,9)	15,5	64
IVd	266—267	1500, 1550, 1570, 1600, 3000, 3040, 3075	336 (4,67), 615 (3,41)	(7,4)	16,9	$C_{30}H_{21}N_3O_3S_3$	(7,4)	16,9	82
Va	287—290	1550, 1590, 2940, 3075	339 (4,33), 470 (3,69)	7,0	12,5	$C_{24}H_{19}ClN_3O_4S_2$	6,9	12,5	30
Ve	246—247	1560, 1580, 1595, 3025, 3070	333 (4,37), 468 (3,68)	8,1	15,1	$C_{18}H_{14}ClN_3O_4S_2$	8,1	14,7	22
Vf	230—231	1550, 1580, 2930, 3025, 3070	329 (4,27), 468 (3,74)	8,1	14,5	$C_{19}H_{16}ClN_3O_4S_2$	7,9	14,2	60
Vg	227—230	1550, 1560, 1585, 2920, 3015, 3060	303 (4,40), 457 (3,57)	8,4	14,8	$C_{18}H_{14}ClN_3O_4S_2$	8,1	14,7	27
Vh	214—215	1560, 1610, 2935, 3020	324 (3,97), 425 (3,70)	9,6	17,1	$C_{13}H_{12}ClN_3O_4S_2$	9,5	17,1	54
Vi	274—276	1510, 1565, 1585, 1610, 2930, 3025, 3090	324 (3,94), 425 (3,78)	9,3	16,5	$C_{14}H_{14}ClN_3O_4S_2$	9,1	16,5	30
Vj	241—242	1550, 1580, 2930, 3030, 3070	329 (4,24), 447 (3,71)	7,9	14,3	$C_{19}H_{16}ClN_3O_4S_2$	7,9	14,2	30

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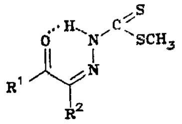
*The compounds were crystallized: Ia,f from isopropyl alcohol, Ib–d and IVb–d from nitromethane, IVa and Va,e–g,j from acetic acid—formic acid (5:1), Vi from acetic acid—formic acid (2:1), and Vh from acetic acid.



It is known that in the reaction of a number of 1,2-diketones, as, for example diacetyl [13], with methyl dithiohydrazinate (VI) monohydrazones of the I type cannot be isolated, since the reaction proceeds further to give bishydrazones. For the synthesis of the corresponding thiazolotriazines we used the ability of nitroso ketones VII to undergo condensation at the carbonyl group with hydrazine, in which the corresponding α-nitrosohydrazones are formed [14]. We found that in the reaction of hydrazine VI with nitroso ketones VIIIa,g-j we also obtained hydrazones of the IX type, which, because of their instability, cannot be isolated from the solutions but are immediately subjected to reaction with benzenesulfonate II. The structure of the thiazolotriazine derivatives was confirmed by data from their IR and PMR spectra.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were obtained with a UR-10 spectrometer. The electronic spectra of solutions in acetonitrile (Ia,f, IVa, and Va-j) and DMF (Ib-d and IVb-d) were recorded with an SF-8 spectrophotometer. The PMR spectra of solutions in trifluoroacetic acid were recorded with a BS-467 spectrometer (60 MHz) with hexamethyldisiloxane (HMDS) as the internal standard. Thin-layer chromatography (TLC) was carried out on Silufol UV-254 in a chloroform—methanol system (9:1).

The characteristics of the synthesized compounds are presented in Table 2.

1,2-Diketone Methyldithiohydrazonates (Ia-d,f). A solution of 1.22 g (10 mmole) of hydrazine VI in 5 ml of acetic acid was added to a solution of 10 mmole of the corresponding diketone VIIa-d,f in 10 ml of acetic acid, and the mixture was maintained at room temperature for 10 min. It was then treated with 15 ml of water, and the product was removed by filtration and crystallized.

Phenylglyoxal Methyldithiohydrazonate (Ie). A 1.22-g (10 mmole) sample of finely ground hydrazine VI was added to a solution of 1.34 g (10 mmole) of phenylglyoxal in 10 ml of water, and the suspension was stirred for 2 h. The precipitate was removed by filtration, dried, and used without further purification.

6-Methylthio-2,3,8-triphenylthiazolo[3,4-b][1,2,4]triazinium Benzenesulfonate (IVa). A mixture of 0.31 g (1 mmole) of hydrazone Ia and 0.30 g (1.1 mmole) of benzenesulfonate II was heated at 90°C for 20 min, after which the melt was triturated with acetone, and the precipitate was removed by filtration and crystallized.

9-Methylthio-11-phenylacenaphtho[1,2-e]thiazolo[3,4-b][1,2,4]triazinium (IVb), 1,6-Dimethoxy-9-methylthio-11-phenylacenaphtho[1,2-e]thiazolo[3,4-b][1,2,4]triazinium (IVc), and 11-Methylthio-13-phenylphenanthro[9,10-e]thiazolo[3,4-b][1,2,4]triazinium (IVd) Benzenesulfonates. These salts were obtained from the corresponding hydrazones Ib-d as in the preceding experiment.

Perchlorates Va,e,f. A mixture of 1 mmole of the corresponding hydrazone Ia,e,f and 0.30 g (1.1 mmole) of benzenesulfonate II was heated at 90°C for 20 min, after which the melt was dissolved in 10 ml of acetic acid, and a solution of 0.12 g (1 mmole) of sodium perchlorate in 5 ml of acetic acid was added. The precipitate was removed by filtration and crystallized.

Thiazolotriazines Va,g-j. A mixture of 1 mmole of the corresponding isonitroso ketone VIIa,g-j, 0.12 g (1 mmole) of hydrazine VI, and 10 ml of acetic acid was heated to the boiling point, 0.4 g (1.5 mmole) of benzenesulfonate II was added, and the mixture was heated for 5 min. It was then treated with 1 ml of 57% perchloric acid and 20 ml of ethyl acetate, and the product was removed by filtration and crystallized.

LITERATURE CITED

1. Yu. P. Kovtun and N. N. Romanov, Khim. Geterotsikl. Soedin., No. 2, 211 (1985).
2. D. L. Trepanier and P. E. Krieger, J. Heterocycl. Chem., 7, 1231 (1970).
3. A. Singh, K. S. Dhaka, U. S. Shaudhari, and U. K. Pujari, Ind. J. Chem., B, 15, 46 (1977).

4. E. S. A. Ibrahim, D. S. A. Shamsel, and F. S. G. Solinan, Pharmazie, 34, 392 (1979).
5. D. L. Trepanier and P. E. Krieger, US Patent No. 3,641,019; Chem. Abstr., 76, 127024k (1972).
6. S. S. Smagin, V. E. Bogachev, A. K. Yakubovskii, S. E. Metkalova, G. P. Privol'neva, V. V. Chugunov, and E. F. Lavretskaya, Khim.-farm. Zh., 9, 11 (1975).
7. J. Korosi, West German Patent No. 1,934,809; Chem. Abstr., 72, 100334s (1970).
8. E. K. Mikitenko and N. N. Romanov, Khim. Geterotsikl. Soedin., No. 5, 634 (1982).
9. C. Alberti, L. Bernardi, and B. Camerio, Gazz. Chim. Ital., 84, 489 (1954).
10. R. Metze, Chem. Ber., 88, 772 (1955).
11. Yu. P. Kitaev and B. I. Buzykin, in: Hydrazones [in Russian], Nauka, Moscow (1974), p. 56.
12. K. N. Zelenin, V. V. Alekseev, and V. A. Khrustalev, Khim. Geterotsikl. Soedin., No. 6, 769 (1983).
13. R. Hull, J. Chem. Soc., 2959 (1952).
14. M. Forster and B. Day, J. Chem. Soc., 101, 2234 (1912).

MESOIONIC COMPOUNDS WITH A BRIDGED NITROGEN ATOM.

13.* THIAZOLOPYRIMIDOINDOLES

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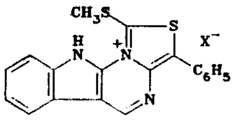
UDC 547.853.3'785.5'789.6

Derivatives of a new heterocyclic system, viz., thiazolo[3',4':3,2]pyrimido-[4,5-b]indole, are formed when 4-amino-2-methylthio-5-phenylthiazolium benzenesulfonate is heated with 3-formyloxindole in phosphorus oxychloride.

It is known that a number of compounds of the indole series, including condensed heterocycles with an indole ring [2], display high physiological activity. In this connection, it seems of interest to search for derivatives of new heterocyclic systems that contain an indole ring.

With this end in mind, we studied the reaction of 4-amino-2-methylthio-5-phenylthiazolium benzenesulfonate (I) with 3-formyloxindole (II). We found that condensation to give thiazopyrimidoindolium salts III and IV occurs upon prolonged heating of a mixture of the starting components in phosphorus oxychloride.



III,IV

III X=ClO$_4$; IV X=BF$_4$

The structures of the synthesized compounds were confirmed by IR and PMR spectral data, their chemical transformations, and alternative synthesis. Thus, for example, the IR spectrum of perchlorate III does not contain bands of the stretching vibrations of a C=O bond, but one does observe bands of the vibrations of C=N and N–H bonds (1525-1590 cm^{-1} and 3270 cm^{-1}); the PMR spectrum contains signals of protons of a methylthio group and aromatic protons with chemical shifts of 2.77 and 7.1-8.0 ppm, respectively. It should be noted that the molecules of the synthesized thiazolopyrimidoindolium salts can exist in the form of the 4H or 10H isomer.

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*See [1] for communication 12.

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