

CONDENSATION OF SALTS OF 2-AMINO-1,3,4-THIADIAZOLES  
WITH  $\beta$ -CHLOROVINYL KETONES,  $\beta$ -CHLOROVINYL  
ALDEHYDES, AND 1,1,3,3-TETRAETHOXYPROPANE

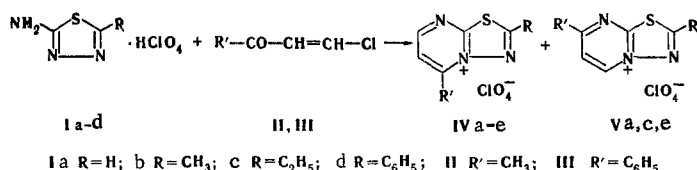
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The condensation of 2-amino-1,3,4-thiadiazole perchlorates with  $\beta$ -chlorovinyl ketones,  $\beta$ -chlorovinyl aldehydes, and 1,1,3,3-tetraethoxypropane has given 1,3,4-thiadiazolo[3,2-*a*]pyrimidinium salts. The structure of the reaction products and the ratio of the isomers formed has been established by PMR spectroscopy.

2-Amino-1,3,4-thiadiazole salts react with  $\beta$ -diketones to form 1,3,4-thiadiazolo[3,2-*a*]pyrimidinium compounds [1].

With methyl and phenyl  $\beta$ -chlorovinyl ketones (II and III, respectively), 2-amino-1,3,4-thiadiazole perchlorates, just like the 2-aminopyridine [2] and 2-aminothiazole [3] salts, form in alcoholic solution the corresponding pyrimidinium compounds - 1,3,4-thiadiazolo[3,2-*a*]pyrimidinium salts (IV) or (V) or mixtures of them.



The reaction of (Ia) with (II) gave a mixture of (IVa) and (Va) in a ratio of 1:1.6 in the crude product; in the analytically pure product, this ratio had become 1:4. It was impossible to isolate the two isomers individually by fractional crystallization; the salt (IVa) was obtained in the pure state in the reaction with the corresponding  $\beta$ -chlorovinyl aldehyde (see below). The ratio of the isomers in the mixture was determined from the PMR spectra of the reaction products (Fig. 1). The assignment of the signals was made on

TABLE 1. Characteristics of the Compounds Obtained

Comp.	R	R'	R''	mp, °C	Empirical formula	S, %		Yield, %
						found	calc.	
IV a	H	CH <sub>3</sub>	—	222	C <sub>6</sub> H <sub>6</sub> ClN <sub>3</sub> O <sub>4</sub> S*	—	—	50†
IV b	CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub>	—	230—234	C <sub>12</sub> H <sub>10</sub> ClN <sub>3</sub> O <sub>4</sub> S	9.5	9.8	45
IV c	C <sub>2</sub> H <sub>5</sub>	CH <sub>3</sub>	—	200—201	C <sub>8</sub> H <sub>10</sub> ClN <sub>3</sub> O <sub>4</sub> S	11.4	11.4	46
IV d	C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	—	226—228	C <sub>17</sub> H <sub>12</sub> ClN <sub>3</sub> O <sub>4</sub> S	8.2	8.2	82
V c	C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub>	—	186—189	C <sub>12</sub> H <sub>10</sub> ClN <sub>3</sub> O <sub>4</sub> S	9.4	9.8	100
VIII a	H	CH <sub>3</sub>	CH <sub>3</sub>	178	C <sub>7</sub> H <sub>8</sub> ClN <sub>3</sub> O <sub>4</sub> S	13.1	13.3	54
VIII c	C <sub>2</sub> H <sub>5</sub>	CH <sub>3</sub>	CH <sub>3</sub>	240—242	C <sub>9</sub> H <sub>12</sub> ClN <sub>3</sub> O <sub>4</sub> S	10.9	10.9	66
IX a	H	—(CH <sub>2</sub> ) <sub>4</sub> —	—	239—240	C <sub>9</sub> H <sub>10</sub> ClN <sub>3</sub> O <sub>4</sub> S	10.9	10.9	20
IX c	C <sub>2</sub> H <sub>5</sub>	—(CH <sub>2</sub> ) <sub>4</sub> —	—	172—174	C <sub>11</sub> H <sub>14</sub> ClN <sub>3</sub> O <sub>4</sub> S	10.1	10.0	36
IX f	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> S	—(CH <sub>2</sub> ) <sub>4</sub> —	—	175—176	C <sub>16</sub> H <sub>16</sub> ClN <sub>3</sub> O <sub>4</sub> S <sub>2</sub>	15.5	15.4	90
X a	H	—	—	220—221	C <sub>5</sub> H <sub>6</sub> ClN <sub>3</sub> O <sub>4</sub> S	11.6	11.6	29
X d	C <sub>6</sub> H <sub>5</sub>	—	—	234—235	C <sub>11</sub> H <sub>8</sub> ClN <sub>3</sub> O <sub>4</sub> S	10.2	10.2	62

\* Found, %: Cl 13.9. Calculated, %: Cl 14.1.

† In the reaction with  $\beta$ -chlorovinyl aldehyde.

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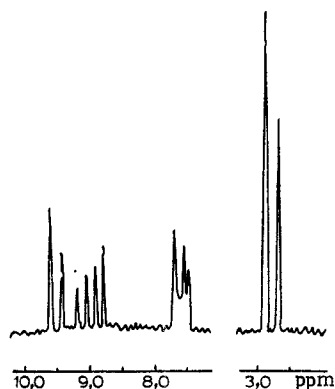


Fig. 1. PMR spectrum of a mixture of 5-methyl- and 7-methyl-1,3,4-thiadiazolo[3,2-a]pyrimidinium perchlorates (IVa and Va, respectively).

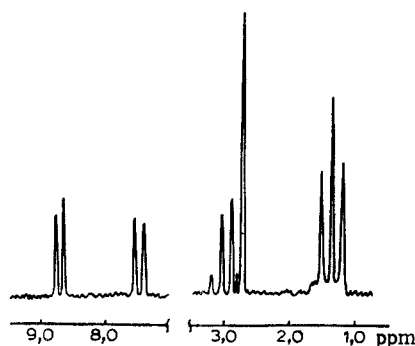


Fig. 2. PMR spectrum of 2-ethyl-5-methyl-1,3,4-thiadiazolo[3,2-a]pyrimidinium perchlorate (IVc).

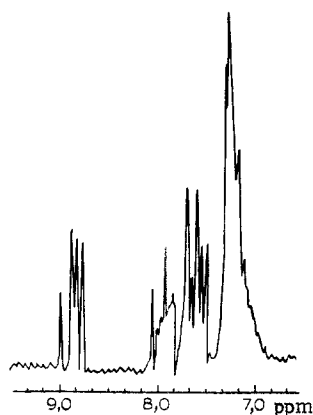
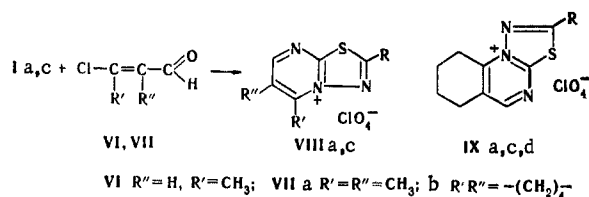


Fig. 3. PMR spectrum of a mixture of 2-ethyl-5-phenyl- and 2-ethyl-7-phenyl-1,3,4-thiadiazolo[3,2-a]pyrimidinium perchlorates (IVe and Ve, respectively) in a ratio of 1:1.

2.3 ppm region. The structure of the products of the condensation of (I) with (VIIb) was determined from the chemical shifts of the most highly descreened ethylene groups, which are at positions 5 or 7 in the pyrimidine ring. The values of 3.05-3.12 ppm (centers of multiplets) for these groups permit the assumption [7] that the products of the reaction of (I) with 2-chloro-1-formylcyclohexene have the structure of 6,7,8,9-tetrahydro[1,3,4]thiadiazolo[3,2-a]quinazolinium perchlorates (IX).

the basis that  $\delta_5\text{-CH}_3 > \delta_7\text{-CH}_3$  in the 1,3,4-thiadiazolo[3,2-a]pyrimidinium salts and other similar pyrimidinium compounds [3,4]. With methyl  $\beta$ -chlorovinyl ketone, (Ic) forms only the corresponding salt (IVc) (PMR spectrum in Fig. 2). Likewise, only one isomer (Vd) was obtained in the reaction of (Id) with methyl  $\beta$ -chlorovinyl ketone; in the PMR spectrum of this compound,  $\delta_7\text{-CH}_3 = 2.65$  ppm and  $J_{5-6} = 7$  Hz. When compounds (Ib and d) were condensed with phenyl  $\beta$ -chlorovinyl ketone the salts (IVb and d) were isolated in the pure state. A proof of their structure was the J value of the pyrimidine protons, of 5 Hz. For (IVb) an additional confirmation of the structure is the nature of the signal of the phenyl group in the PMR spectrum, which is split into two bands with an intensity ratio of 2 (in the weak field): 3 (in the strong field), the distance between the centers of these bands being approximately 0.3 ppm. The signal of the phenyl group in position 7 would also be split into two bands with an intensity ratio of 2:3 in the PMR spectrum, but in this case the distance between the centers of the bands would be about 0.5 ppm or greater [5]. In the PMR spectrum of a mixture of (IVe) and (Ve) (Fig. 3; only the aromatic protons are shown), in addition to the pyrimidine protons of the isomeric products with spin-spin coupling constants of 7 and 5 Hz, the double splitting of the signals of the phenyl radicals is clearly observed with distances between the centers of the corresponding bands of about 0.35 and 0.65 ppm, in agreement with a position of the phenyl radical in position 5 in the isomer (IVe) and in position 7 in the isomer (Ve).

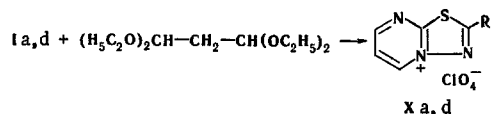
The reaction of (I) with  $\beta$ -chlorovinyl aldehydes also led to 1,3,4-thiadiazolo[3,2-a]pyrimidinium salts.



In contrast to the reaction with  $\beta$ -chlorovinyl ketones, in this case a single isomer (VIII) is formed, just as in the case of other heterocycles [6]. With 2-amino-1,3,4-thiadiazole perchlorate, 3-chlorobut-2-enal (VI), which is isomeric with methyl  $\beta$ -chlorovinyl ketone, gives the salt (VIIIa), identical with one of the condensation products, (IVa), of (Ia) with methyl  $\beta$ -chlorovinyl ketone.

The direction of the reaction with  $\beta$ -chlorovinyl aldehydes was determined from the PMR spectra of the crude condensation products. For (VIII), the chemical shift of the methyl group in position 5 is found in the 2.7-2.8 ppm region, which corresponds to the location of this group in the  $\alpha$  position to the bridge nitrogen atom in the pyrimidine ring; a methyl group in position 6 gives signals in the 2.2-

The acetal of malonaldehyde reacts with the salts (I) to form thiadiazolopyrimidinium salts unsubstituted in the pyrimidine ring (X).



The salts (IVa,c; Vc; VIIa,c; and IXa,c,f) with methyl or methylene groups in position 5 or 7 give polymethine dyes; for example, when they are heated with p-dimethylaminobenzaldehyde in acetic anhydride red or violet styryl dyes are formed (as has been shown previously for 5,7-dimethyl-1,3,4-thiadiazolo[3,2-a]pyrimidinium derivatives [1]), which serves as a qualitative test for the occurrence of condensation reactions.

## EXPERIMENTAL

The PMR spectra were recorded on a Varian A-60A instrument in trifluoroacetic acid, and the chemical shifts are given in the  $\delta$  scale with respect to hexamethyldisiloxane as internal standard.

Condensation of 2-Amino-1,3,4-thiadiazole Perchlorates with  $\beta$ -Chlorovinyl Ketones and  $\beta$ -Chlorovinyl Aldehydes. A 10-50% excess of the chloro carbonyl compound was added to an ethanolic solution of 2-amino-1,3,4-thiadiazole perchlorate, and the solution was left for several hours. Instead of the perchlorate, the free base can be used and 57% perchloric acid be added in 2- to 3-fold excess; for better dissolution, the mixture may be gently heated in the water bath. The precipitate of the reaction product that separated out was filtered off, washed with ether, and crystallized from ethanol (compounds IV, V, VIII, and IX; Table 1).

Condensation of 2-Amino-1,3,4-thiadiazole Perchlorates with 1,1,3,3-Tetraethoxypropane. The tetraethoxypropane (in 5-10% excess) was added to a hot concentrated ethanolic solution of the salt. After a few minutes, the reaction product (X) precipitated from the boiling solution, and after cooling it was filtered off, washed with ether, and crystallized from ethanol (Table 1).

Mixture of 5-Methyl-1,3,4-thiadiazolo[3,2-a]pyrimidinium Perchlorate (IVa) and 7-Methyl-1,3,4-thiadiazolo[3,2-a]pyrimidinium Perchlorate (Va). This was obtained by the general method from methyl  $\beta$ -chlorovinyl ketone and 2-amino-1,3,4-thiadiazole perchlorate with a yield of 82%. The crude product was triturated several times with ethanol and was analyzed. Found, %: S 12.0.  $C_6H_6ClN_3O_4S$ . Calculated, %: S 12.1. Judging from the PMR spectrum (from the intensities of the peaks of the methyl groups at 2.86 and 2.65 ppm) the product consisted of a mixture of (IVa) and (Va) in a ratio of 1:4; mp of this mixture 200-208°C. After several recrystallizations from ethanol, a 2:1 mixture was obtained with mp about 219°C.

Mixture of 2-Ethyl-5-phenyl-1,3,4-thiadiazolo[3,2-a]pyrimidinium Perchlorate (IVe) and 2-Ethyl-7-phenyl-1,3,4-thiadiazolo[3,2-a]pyrimidinium Perchlorate (Ve). This was obtained by heating 2-amino-5-ethyl-1,3,4-thiadiazole perchlorate with a 15% excess of phenyl  $\beta$ -chlorovinyl ketone in ethanolic solution on the water bath for 4 h. After cooling, ether was added, and the precipitate was filtered off and was washed with ethanol and ether. Pink crystals, yield 45%. The product consisted of a mixture of (IVe) and (Ve) in a ratio of 1:1.3. After recrystallization from ethanol, this ratio had become 1:1, mp 166-168°C. Found, %: S 9.4.  $C_{13}H_{12}ClN_3O_4S$ . Calculated, %: S 9.4.

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