CONDENSATION OF SALTS OF 2-AMINO-1,3,4-THIADIAZOLES WITH UNSYMMETRICAL β-DIKETONES

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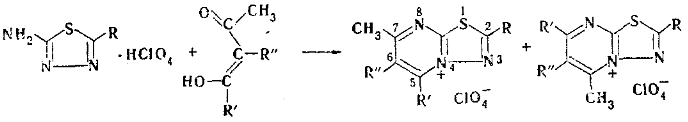
The condensation of acetyl ketones with salts of 2-amino-1,3,4-thiadiazoles generally leads to a mixture of isomeric 1,3,4-thiadiazolo[3,2-*a*]pyrimidinium salts. The structures of the condensation products and the isomer ratios were determined by means of the PMR spectra.

The reaction of salts of 2-amino-1,3,4-thiadiazoles with symmetrical β-diketones [1], β-chlorovinyl ketones, and β-chlorovinyl aldehydes [2], as a result of which 1,3,4-thiadiazolo[3,2-*a*]pyrimidinium derivatives are formed, has been described. It seemed of interest to study the trend of this reaction with unsymmetrical β-diketones, which may give isomeric reaction products. The following unsymmetrical β-diketones were used for this end in the present study: benzoylacetone, propionylacetone, 1-ethoxyacetylacetone, methylbenzoyl acetone, chlorobenzoylacetone, and 1-cyclopropyl-1,2-butanedione. Isomeric 1,3,4-thiadiazolo[3,2-*a*]pyrimidinium salts with a methyl group in either the 5 position (II) or in the 7 position (I) are formed as a result of the condensation of these β-diketones with salts of 2-amino-1,3,4-thiadiazoles.



I II

The condensation was carried out by refluxing the components in alcohol solution. The formation of a red or violet dye on reaction of a sample of the reaction mixture with p-dimethylaminobenzaldehyde in acetic anhydride served as a qualitative sign that the reaction had occurred. This qualitative reaction attests to closing of the pyrimidine ring, in which the methyl group in the 5 or 7 position relative to the bridge quaternary nitrogen atom is active, as a result of which a styryl dye is formed.

The reaction products are pure isomers in only four cases – IIe, Io, Ip, and Iu. In the remaining cases, mixtures of isomers I and II are obtained, and the 7-CH_3 isomer (I) almost always predominates. The ratios of the isomers formed, which were determined from the intensities of the signals of the corresponding methyl groups in the PMR spectra of the crude condensation products, are presented in Table 1.

To assign the condensation product to the I or II type, it is sufficient to know the chemical shift of the methyl group bonded to the pyrimidine ring. As previously demonstrated [1], $\delta_{5\text{-}CH_3}$ is found between 2.75-2.88 ppm and is always greater than $\delta_{7\text{-}CH_3}$ (2.55-2.65 ppm) in a series of 1,3,4-thiadiazolo[3,2-*a*]-pyrimidinium salts. The assignment of the signals of the methyl groups for these salts was similar in communication [2] (with allowance for the difference of about 0.45 ppm in trifluoroacetic acid between the chemical shifts of hexamethyldisiloxane and tetramethylsilane, with respect to which the chemical shifts in [3] were apparently presented). The chemical shifts of the 5- and 7-methyl groups are somewhat shifted only for the 2-amino derivatives and amount to 2.55-2.67 and 2.42-2.44 ppm, respectively. The character of the phenyl signal serves as an additional confirmation of the structures of the products of condensation with benzoylacetone. Regardless of the position of the phenyl group in the examined thiazolopyrimidinium salts, its signal in the PMR spectra is split into two groups of bands with an intensity ratio of two (at weak

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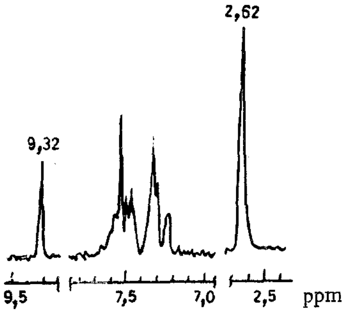
TABLE 1. 1,3,4-Thiadiazolo[3,2-*a*]pyrimidinium Salts

Comp.	R	R′	R″	Reaction time, h	mp, °C	Empirical formula	S, %		δ_{CH_3}, ppm		II/I ratio, %		Yield of crude product, %
							found	calc.	5—	7—	crude product	analyzed sample	
I a	H	C_6H_5	H	1,0	215—216	$C_{13}H_{11}ClN_3O_4S$	9,7	9,8	2,80	2,64	14 : 86	1	46
I, II b	H	C_2H_5	H	3,0		$C_9H_{11}ClN_3O_4S$	11,3	11,4	2,72	2,55	33 : 67	30 : 70	58
I c	H	$C_2H_5OCH_2$	H	4,0	174—175	$C_9H_{12}ClN_3O_5S$	10,3	10,3	2,84	2,65	20 : 80	1	72
I d	H	C_3H_5*	H	0,5	244—245	$C_9H_{10}ClN_3O_4S$	11,1	11,0	2,68	2,48	22 : 78	1	87
II e	H	C_6H_5	CH_3	5,0	143—145	$C_{13}H_{12}ClN_3O_4S$	9,7	9,4	2,86	—	11	11	36
I, II f	CH_3	C_6H_5	H	3,8	—	$C_{13}H_{12}ClN_3O_4S$	9,4	9,4	2,75	2,58	10 : 90	12 : 88	77
I, II g	CH_3	C_2H_5	H	4,0	—	$C_9H_{12}ClN_3O_4S$	10,7	10,9	2,72	2,55	43 : 57	20 : 80	88
I, II h	CH_3	$C_2H_5OCH_2$	H	0,7	—	$C_{10}H_{14}ClN_3O_5S$	9,8	9,9	2,76	2,58	31 : 69	41 : 59	78
II i	C_2H_5	C_6H_5	H	4,0	195—199	$C_{14}H_{14}ClN_3O_4S$	8,9	9,0	2,75	2,60	57 : 33	11	77
I, II j	C_2H_5	C_2H_5	H	4,0	—	—	—	—	2,78	2,60	75 : 25	50 : 50	56
I, II k	*n*-C_3H_7	C_6H_5	H	5,0	—	$C_{15}H_{16}ClN_3O_4S$	8,6	8,7	2,75	2,61	44 : 56	50 : 50	57
I l	CF_3	C_6H_5	H	0,2	253—255	$C_{13}H_9ClF_3N_3O_4S$	8,2	8,1	2,82	2,65	4 : 96	1	49
I m	CH_3S	C_6H_5	H	2,2	220—221	$C_{13}H_{12}ClN_3O_4S_2$	17,0	17,1	2,72	2,55	11 : 89	1	70
I n	$C_6H_5CH_2S$	C_6H_5	H	1,0	168—170	$C_{19}H_{16}ClN_3O_4S_2$	14,2	14,2	2,72	2,55	11 : 89	1	77
I o	NH_2	C_6H_5	H	3,0	220—223	$C_{12}H_{11}ClN_4O_4S$	9,2	9,3	—	2,48	1	1	78
I p	NH_2	C_2H_5	H	5,0	217—220	$C_8H_{11}ClN_4O_4S$	11,0	10,8	—	2,44	1	1	50
I q	C_6H_5	C_6H_5	H	0,4	244—247	$C_{17}H_{14}ClN_3O_4S$	8,1	7,9	2,80	2,61	24 : 76	1	72
I, II r	C_6H_5	C_2H_5	H	0,5	—	$C_{14}H_{14}ClN_3O_4S$	9,2	9,0	2,78	2,55	31 : 69	30 : 70	66
I, II s	C_6H_5	$C_2H_5OCH_2$	H	1,5	—	$C_{15}H_{16}HIN_3O_5S$	8,2	8,3	2,84	2,60	32 : 68	14 : 86	81
I, II t	C_6H_5	C_6H_5	CH_3	5,0	—	$C_{19}H_{16}ClN_3O_4S$	7,6	7,7	2,88	2,57	—	50 : 50	61
I u	C_6H_5	C_6H_5	Cl	2,5	201—205	$C_{17}H_{13}Cl_2N_3O_4S$	7,3	7,3	—	2,61	1	1	57

*Cyclopropyl.



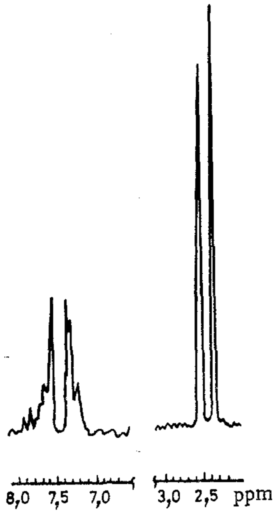


Fig. 1. PMR spectrum of 5-methyl-7-phenyl-1,3,4-thiadiazolo[3,2-*a*]pyrimidinium perchlorate (Ia).

Fig. 2. PMR spectrum of 2-methylmercapto-5-methyl-7-phenyl-1,3,4-thiadiazolo-[3,2-*a*]pyrimidinium perchlorate (Im).

field) to three (at strong field) [2]. However, the difference between the centers of these bands is not identical: 0.2-0.3 ppm for the 5-phenyl group and substantially greater for the 7-phenyl group. The PMR spectra for the products of condensation with benzoylacetone, which confirm the structure of isomer I by the value of the chemical shifts of the methyl groups and by the character of the signal of the phenyl groups, are shown in Figs. 1 and 2.

Chlorobenzoylacetone (2-chloro-1-phenyl-1,3-butanedione) behaves like a β-diketone in this reaction to give a thiadiazolopyrimidinium salt with a chlorine atom in the pyrimidine ring; the Chichibabin reaction does not occur under the given conditions.

EXPERIMENTAL

The PMR spectra of trifluoroacetic acid solutions were obtained with a Varian A-60A spectrometer, and the chemical shifts are presented on the δ scale with respect to hexamethyldisiloxane as the internal standard.

Condensation of 2-Amino-1,3,4-thiadiazole Perchlorates with Unsymmetrical β-Diketones. A mixture of 2-amino-1,3,4-thiadiazole perchlorate and a 10-20% excess of the appropriate β-diketone was refluxed in ethanol. In many cases the reaction product precipitated from the refluxing solution. The mixture was cooled, ether was added, and the precipitate was removed by filtration, washed repeatedly with ether, dried, and crystallized from alcohol. Data on the heating time and properties of the products are presented in Table 1. In four cases (see Table 1), one isomer was formed; in the remaining cases, mixtures of isomers were obtained, from which isomer I could be isolated in pure form in some cases by crystallization from alcohol. The ratios of isomers in the mixtures and the purities of the products were determined from the PMR spectra (Table 1).

LITERATURE CITED

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2. H. Hartmann, Z. Chem., 11, 460 (1971).