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sym-TRIAZINE DERIVATIVES. 5.* CONVERSION OF 2,4,6-TRIETHOXYCARBONYL-1,3,5-TRIAZINE TO 2-ETHOXYCARBONYL-4-ARYLHYDRAZINO-5-OXOIMIDAZOLES

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The reaction of 2,4,6-triethoxycarbonyl-1,3,5-triazine with arylhydrazines proceeds with rearrangement and leads to the formation of 2-ethoxycarbonyl-4-arylhydrazino-5-oxoimidazoles. The factors that limit the possibility of the occurrence of the reaction are examined from the point of view of the postulated mechanism.

Together with G. M. Vakhatova, we have previously shown [2] that the reaction of 2,4,6-triethoxycarbonyl-1,3,5-triazine (I) with phenylhydrazine (IIa) takes place at the C=N bonds of the heterocyclic system and is accompanied by rearrangement with the formation of 5-oxoimidazole derivative IIIa.

It seemed of interest to determine the limits of this new rearrangement and to evaluate how the structure of the hydrazine component affects the ease with which it occurs. For this we investigated the reaction with ester I of 2- [3] 3- [4] and 4-methyl- [3], 4-chloro- [3], 4-nitro- [5], and 2,4-dinitrophenylhydrazines (IIb-g), as well as hydrazobenzene. In all cases the process was carried out by refluxing triester I with arylhydrazine II in absolute ethanol with monitoring of the course of the reaction by thin-layer chromatography (TLC) on Silufol UV-254.

We found that the introduction of both electron-donor and electron-acceptor substituents in the para position of phenylhydrazine has no effect on the course of the rearrangement. The yields of oxoimidazole derivatives IIId,f were 75 and 78%. In the case of 4-chlorophenylhydrazine (IIe) the yield of IIIe reached 94%. The yields decreased somewhat (to 53% in the case of IIb and to 62% in the case of IIc) on passing from the p- to the m- and o-methyl-substituted compounds.

*See [1] for Communication 4.

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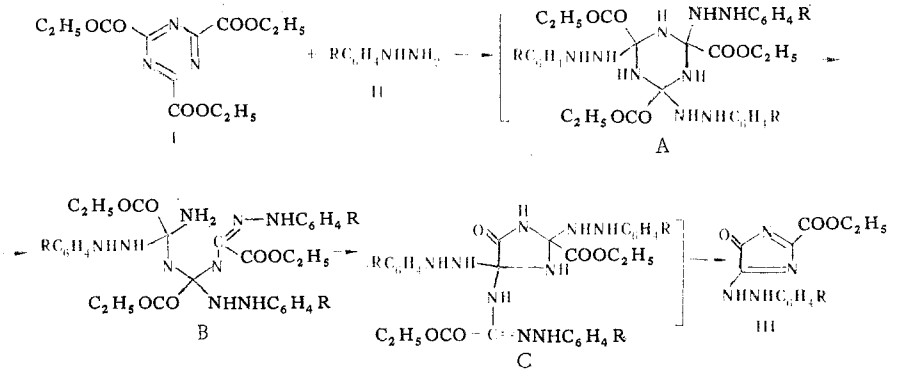
TABLE 1. 2-Ethoxycarbonyl-4-arylhydrazino-5-oxoimidazoles III

Compound	mp, °C	IR spectrum, ν, cm^{-1}	UV spectrum, λ_{max}, nm (log ε)	PMR spectrum, δ, ppm	Mass spectrum, m/z	Found, %			Empirical formula	Calc., %			Yield, %
						C	H	N		C	H	N	
IIIb	194—195	3480, 1710, 1680	206 (4,33), 222 (4,14), 299 (4,16)	1,38 (3H, t, CH_3CH_2); 2,20 (3H, s, CH_3Ph); 4,44 (2H, q, CH_2CH_3); 7,04 (br s, NH); 7,26—7,40 (4H, m, C_6H_4); 8,64 (br s, NH)	274 [M$^+$], 246 [(M$-C_2H_4$)$^+$],	56,6	5,1	20,6	$C_{13}H_{14}N_4O_3$	57,0	5,1	20,4	53
IIIc	167—168	3470, 1740, 1670	206 (4,27), 229 (4,05), 296 (4,08)	1,40 (3H, t, CH_3CH_2); 2,42 (3H, s, CH_3Ph); 4,44 (2H, q, CH_2CH_3); 5,96 (br s, NH); 7,20—7,50 (4H, m, C_6H_4); 7,83 (br s, NH)	229 [(M$-OC_2H_5$)$^+$], 201 [(M$-COOC_2H_5$)$^+$], 133 [(M$-ON_2C_2COOC_2H_5$)$^+$], 105 [(M$-NH_2OC_3N_2COOC_2H_5$)$^+$], 91 [(M$-NHNHOC_3N_2COOC_2H_5$)$^+$]	56,8	5,2	20,4	$C_{13}H_{14}N_4O_3$	57,0	5,1	20,4	62
IIId	252—253	3470, 1740, 1670	205 (4,21), 226 (4,08), 297 (4,04)	1,40 (3H, t, CH_3CH_2); 2,42 (3H, s, CH_3Ph); 4,44 (2H, q, CH_2CH_3); 6,93 (br s, NH); 7,20—7,60 (4H, m, C_6H_4); 7,85 (br s, NH)		57,0	5,1	20,4	$C_{13}H_{14}N_4O_3$	57,0	5,1	20,4	75
IIIe	253—253,5	3485, 1750, 1680	205 (4,11), 227 (4,02), 298 (4,08)	1,40 (3H, t, CH_3CH_2); 4,42 (2H, q, CH_2CH_3); 6,90 (br s, NH); 7,40—7,60 (5H, m, C_6H_4NH)	294, 296 [M$^+$], 266, 268 [(M$-C_2H_4$)$^+$], 249, 251 [(M$-OC_2H_5$)$^+$], 221, 223 [(M$-COOC_2H_5$)$^+$], 153, 155 [(M$-OC_2N_2COOC_2H_5$)$^+$], 111, 113 [(M$-NHNHC_3ON_2COOC_2H_5$)$^+$]	49,1	3,8	18,9	$C_{12}H_{11}ClN_4O_3$	48,9	3,8	19,0	94
IIIf	260—261	3480, 1740, 1680, 1525—1535, 860		1,28 (3H, t, CH_3CH_2); 4,25 (2H, q, CH_2CH_3); 8,24—8,60 (5H, m, NH, C_6H_4); 9,02 (br s, NH)	305 [M$^+$], 277 [(M$-C_2H_4$)$^+$], 260 [(M$-OC_2H_5$)$^+$], 232 [(M$-COOC_2H_5$)$^+$], 164 [(M$-OC_2N_2COOC_2H_5$)$^+$], 136 [(M$-NH_2OC_3N_2COOC_2H_5$)$^+$], 122 [(M$-NHNHOC_3N_2COOC_2H_5$)$^+$]	46,9	3,6	23,1	$C_{12}H_{11}N_5O_5$	47,2	3,6	23,0	78

The basicity of 2,4-dinitrophenylhydrazine (IIg) proved to be insufficiently high, and we were unable to realize the reaction under the indicated conditions. According to data obtained by thin-layer chromatography (TLC), the process also did not take place in more polar solvents, viz., dimethylformamide (DMF) and dimethyl sulfoxide (DMSO), in which both starting I and IIg were soluble. The rearrangement does not occur on passing from monoarylhydrazines IIa-f to disubstituted hydrazobenzene (IIh). Increasing the temperature through the use of o-xylene or benzyl alcohol as the refluxing solvent led only to the starting substances in the first case, according to TLC, whereas in the second case it led to transesterification of ester I to give 2,4,6-tribenzyloxycarbonyl-1,3,5-triazine, which was isolated preparatively (mp 105-106°C; the composition was confirmed by total elementary analysis, while the structure was confirmed by means of the IR and mass spectra).

Thus the conversion of 2,4,6-triethoxycarbonyl-1,3,5-triazine (I) to 2-ethoxycarbonyl-4-arylhydrazino-5-oxoimidazoles (III) by the action of arylhydrazines (II) proceeds via the scheme

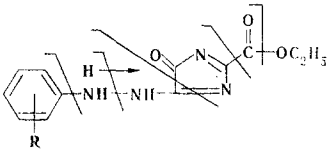


II, III a R=H; b R=2-CH_3; c R=3-CH_3; d R=4-CH_3; e R=4-Cl; f R=4-NO_2

The reaction is general in character if the arylhydrazine has sufficient nucleophilicity for the addition of ester I to the C=N bonds of the triazine ring to give intermediate A. The instability of A leads to its rearrangement to B, which undergoes intramolecular acylation to give oxoimidazoline C, which is stabilized due to splitting out of the arylhydrazine and oxalic acid ethyl ester arylhydrazinylamide with the development of the stable final reaction product, viz., 2-ethoxycarbonyl-4-arylhydrazino-5-oxoimidazole (III). The peculiarities of the effect of the structure of the hydrazine component on the course of the process that are manifested in the reactions are in good agreement with this reaction mechanism.

The structure of oxoimidazole derivatives IIIa-f was confirmed by IR and PMR spectroscopy (see Table 1).

A general type of fragmentation, which can be represented in the following way, is characteristic for the mass spectra of IIIa-f:



EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a Perkin-Elmer 457 spectrometer. The UV spectra of solutions in ethanol were recorded with a Perkin-Elmer 402 spectrophotometer. The PMR spectra were obtained with an XL-100 spectrometer with tetramethylsilane as the internal standard. The mass spectra were obtained with an MAT-112 spectrometer at 70 eV by direct introduction of the samples.* The synthesis and characteristics of IIIa are presented in [2].

*The spectral studies were conducted by K. F. Turchin, O. S. Anisimova, and E. M. Peresleni in the laboratory of physicochemical methods of investigation of the S. Ordzhonikidze All-Union Scientific-Research Institute of Pharmaceutical Chemistry under the supervision of Professor Yu. N. Sheinker.

Reactions of 2,4,6-Triethoxycarbonyl-1,3,5-triazine (I) with Arylhydrazines (II). A solution of 80.6 mmole of arylhydrazine II in 30 ml of absolute ethanol was added to a suspension of 6.15 g (20.6 mmole) of 2,4,6-triethoxycarbonyl-1,3,5-triazine (I) in 20 ml of absolute ethanol, and the reaction mixture was refluxed with stirring for 2 h. It was then cooled, and the precipitated III was removed by filtration, washed with absolute ethanol, and recrystallized from absolute ethanol. The yields and spectral characteristics of III are presented in Table 1. Compounds IIIb-e were obtained as colorless crystals that were soluble in chloroform, acetone, benzene, and ethyl acetate, only slightly soluble in alcohols, and insoluble in water, heptane, and ether. Compound IIf was soluble in DMF, DMSO, and hot ethyl acetate but insoluble in other organic solvents and water.

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