RECYCLIZATION REACTIONS.
30.* INTERACTION OF 3-ACETONYL-2,4-THIAZOLIDINEDIONE WITH NUCLEOPHILES

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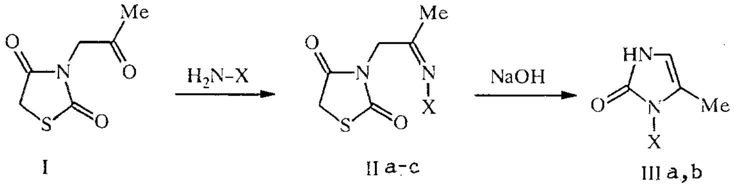
3-Acetonyl-2,4-thiazolidinedione, upon interaction with phenylhydrazine or benzoylhydrazine, forms anti-hydrazones that are recyclized in an alkaline medium to 1-aminoimidazol-2-ones.

It was established in [2] that aromatic derivatives of 3-acylmethyl-2,4-thiazolidinediones react with phenylhydrazine to form syn and anti (relative to the azolidone ring) isomeric hydrazones, which, upon heating in an alkaline medium, are recyclized to 1,2,4-triazin-3-ones and 1-aminoimidazol-2-ones, respectively. With hydrazine hydrate, all of the indicated 3-acylmethyl-2,4-thiazolidinediones are recyclized preferentially to 1,2,4-triazin-3-ones, the intermediates of which, of course, are syn-hydrazones.

In the work reported here, we established that 3-acetonyl-2,4-thiazolidinedione (I), upon interaction with phenylhydrazine, benzoylhydrazine, or hydroxylamine, forms mainly anti-isomer hydrazones (IIa,b) or an oxime (IIc), respectively.



II-IIIa) X = NHPh; b) X = NHCOPh; IIc) X = OH

The action of alkali on the hydrazones IIa,b results in their recyclization to 1-aminoimidazol-2-ones (IIIa,b). The oxime IIc under the same conditions gives a resinous reaction product, from which we were unable to isolate any individual substances.

The composition and structure of compounds II-III were confirmed by elemental analyses and by their IR and PMR spectra; their individuality was confirmed by TLC (Tables 1 and 2).

Thus, in the PMR spectra of the azolidones IIa-c, there are signals of protons of the CH_2 group of the thiazolidinone ring and the exocyclic methylene group (4.2-4.3 ppm), signals of aromatic protons (6.9-7.5 ppm), and also signals of NH or OH groups that are specific for each compound (8.8-10.8 ppm). In the PMR spectra of the imidazolones IIIa,b there are characteristic signals of protons of the CH and NH groups of the imidazole ring (6.1 ppm and 9.8-9.9 ppm, respectively), aromatic protons (6.8-7.5 ppm), and protons of the exocyclic NH group (8.5-11.0 ppm).

In the IR spectra of the azolidones IIa-c, the observed bands correspond to absorption of C=O (1660-1740 cm^{-1}), C=N (1530-1580 cm^{-1}), and NH or OH (3215-3355 cm^{-1}). In the IR spectra of the imidazolones IIIa,b, characteristic bands are observed for C=O (1660-1740 cm^{-1}) and NH (3130-3280 cm^{-1}).

Thus, the results that we obtained in the present work, in combination with those reported in [1], represent a rather well-integrated picture of the recyclization conversions of N-acylmethyl derivatives of 2,4-thiazolidinedione under the influence

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*For Communication 29, see [11].

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TABLE 1. Characteristics of Synthesized Compounds IIa-c and IIIa, b

Compound	Empirical formula	R_f	mp, °C (and solvent)	Yield, %
IIa	$C_{12}H_{13}N_3O_2S$	0,75	172-173 (ethanol)	94
IIb	$C_{13}H_{13}N_3O_3S$	0,72	149-151 (ethanol)	96
IIc	$C_6H_8N_2O_3S$	0,70	158-159 (isopropanol)	38
IIIa	$C_{10}H_{11}N_3O$	0,65	242-244 (ethanol)	73
IIIb	$C_{11}H_{11}N_3O_2$	0,58	204-205 (dioxane)	94

TABLE 2. Spectral Characteristics of Synthesized Compounds IIa-c and IIIa, b

Compound	IR spectrum (in Nujol) ν, cm^{-1}			PMR spectra, ppm*		
	C=O	C=N	other bands	CH_2 (CH_3)	CH_{arom} (CH_{imide})	NH (OH)
IIa	1655 s, 1729 s	1584 m	3355 w (N—H)	4,26 s	6,86 m	8,86 s
IIb	1683 s, 1744 s	1530 m	3244 w, 3270 w (N—H)	(4,33 s, 1,83 s)	7,52 m, 7,71 m	10,64 s
IIc	1675 s, 1742 s	1545 m	3215 w (O—H)	(4,31 s, 1,76 s)	—	(11,41 s)
IIIa	1695 s	—	3127 w (C—H imide), 3190 w (N—H)	—	8,82 m (6,09 s)	8,45 s, 9,83 s
IIIb	1662 s, 1742 s	—	3128 w (C—H imide), 3283 w (N—H)	—	7,52 m, 7,92 m (6,09 s)	9,91 s

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*PMR spectra of compounds IIa and IIIa, b were taken in DMSO, compounds IIb, c in DMSO-d_6.

of various nucleophiles. The thiazolidinedione I, in contrast to its analogs with an aromatic fragment (Ar instead of CH_3 in the side chain) [2], manifests for the most part a tendency to form anti-hydrazones and oximes. We may assume that the unsubstituted hydrazone (IId, X = NH_2) and the oxime (IIc, X = OH), having a low energy barrier to isomerization, can be isomerized to the syn form, the content of which is small. However, in view of the considerably higher reactivity of the NH_2 group of the hydrazone Id in comparison with its enamine tautomer (CH=C—NH), the predominant direction of cyclization in the case of the reaction with hydrazine hydrate, as was shown experimentally in [2], will be the triazine direction.

The conversion of the oxime IIc under the action of caustic proceeds ambiguously, probably because of the lower nucleophilic reactivity of the OH fragment. For the N-substituted hydrazones IIa, b, in view of the higher barrier to isomerization in comparison with the unsubstituted compounds, hardly any syn-isomer species are formed, and the cyclization leads only to the imidazolone derivatives IIIa, b.

EXPERIMENTAL

The PMR spectra were recorded in a Tesla BS-467C spectrometer (Czechoslovakia) with HMDS internal standard. The IR spectra were recorded in a UR-20 spectrometer (East Germany), slit program 4, registration rate 160 cm^{-1}/min. Thin-layer chromatography was performed on Silufol plates (Czechoslovakia), eluent chloroform/methanol 10/1, developer iodine vapor.

The results of elemental analysis of the synthesized compounds for C, H, N, and S were in agreement with the calculated values.

Anti-(E)phenylhydrazone of 3-Acetonyl-2,4-thiazolidinedione (IIa). To a suspension of 2.59 g (15 mmoles) of 3-acetonyl-2,4-thiazolidinedione in 2 ml of methanol, 1.77 g (15 mmoles) of phenylhydrazine was added slowly (dropwise). The reaction mixture was held for 0.5 h at 50°C. The resulting precipitate of IIa was filtered off and dried (see Table 1).

Anti-(E)benzoylhydrazone of 3-Acetonyl-2,4-thiazolidinedione (IIb). To a mixture of 1.73 g (10 mmoles) of 3-acetonyl-2,4-thiazolidinedione and 1.36 g (10 mmoles) of benzoylhydrazine, 10 ml of methanol and 2 drops of concentrated HCl were added, and the mixture was refluxed for 2 h. After cooling, the precipitate of IIb was filtered off and dried.

Anti-(E)oxime of 3-Acetonyl-2,4-thiazolidinedione (IIc). To a suspension of 0.33 g (10 mmoles) of hydroxylamine hydrochloride in 0.5 ml of water, a 40-50% NaOH solution was added to bring the pH to 7. To this solution, 1.73 g (10 mmoles) of 3-acetonyl-2,4-thiazolidinedione and 2 ml of methanol were added. The resulting solution was refluxed for 2 h. After cooling, the precipitate of IIc was filtered off and dried.

3-Phenylamino-4-methylimidazol-2-one (IIIa). To 2 g (8.4 mmoles) of the (E)phenylhydrazone of 3-acetonyl-2,4-thiazolidinedione, a solution of 0.34 g (8.4 mmoles) of NaOH in 3 ml of water was added, and also 4 ml of ethanol. The reaction mixture was held at 90°C for 1 h, cooled, and neutralized with concentrated HCl (pH 7). The resulting precipitate of IIIa was filtered off and dried.

3-Benzoylamino-4-methylimidazol-2-one (IIIb). To 2 g (6.88 mmoles) of the (E)benzoylhydrazone of 3-acetonyl-2,4-thiazolidinedione, a solution of 0.28 g (6.88 mmoles) of NaOH in 3 ml of water was added, and also 2.5 ml of ethanol; the mixture was held at 90°C for 1 h. The solution was cooled and neutralized with concentrated HCl (pH 7), after which it was evaporated to dryness. The residue was taken up with 5 ml of water and allowed to stand for 1 h at 25°C. The precipitate of IIIb was filtered off and dried.

REFERENCES

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