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INVESTIGATION OF THE REACTIVITY AND TAUTOMERISM OF AZOLIDINES.

41.* REACTION OF 5-BENZYLIDENE-2,4-THIAZOLIDINEDIONES WITH FORMALDEHYDE

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The reaction of 5-benzylidene-2,4-thiazolidinediones with formaldehyde leads to the formation of only 3-hydroxymethyl-5-benzylidene-2,4-thiazolidenediones in high yields. The structures of the compounds obtained were confirmed by the IR and UV spectra and the results of elementary analysis.

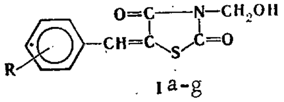
2,4-Thiazolidinediones are ambident compounds that display dual reactivity in reactions with electrophilic reagents [2]. In the alkylation of salts of 2,4-thiazolidinediones in low-polarity solvents the addition of an alkyl group takes place at the N^3 center of the $O{-}C_2{-}N_3{-}C_4{-}O$ ambident system. An increase in the polarity of the solvent and the hardness of the alkylating agent leads to reaction at the harder center of the ambident system, viz., the oxygen atom.

Alkylation in an alkaline medium proceeds through a step involving the formation of stable salts, the negative charge in the anions of which is delocalized on the oxygen atoms [3]. An investigation of the crystal structure of 2,4-thiazolinedione by x-ray diffraction analysis indicates primary localization of the charge on the oxygen atom bonded to the C_2 atom of the thiazolidine ring [4].

The indicated peculiarities of the distribution of the negative charge in the 2,4-thiazolidinedione anion promote reactions with a hard electrophilic reagent at the oxygen atom attached to the C_2 atom of the thiazolidine ring [2]. Considering the information set forth above, it seemed of interest to continue our study of the dual reactivity of 2,4-thiazolidinediones with formaldehyde as the hard electrophile [5].

The reaction of formaldehyde with 5-benzylidene-2,4-thiazolidinedione was carried out in an organic solvent. The reaction was monitored by thin-layer chromatography (TLC). According to the results of TLC, the formation of only one reaction product is observed in the reaction mixture 2-3 h after the reagents are mixed. The polarity of the solvent has a substantial effect on the reaction rate. The yield of the reaction product increases markedly when the polarity of the solvent is increased, and the reaction time is shortened. Thus the time required to achieve an 80% yield is 2 h when acetone is used as the solvent.

On the basis of the dual reactivity of 2,4-thiazolidinediones in reactions with electrophilic reagents [2], structure I, II, or III can be assigned to the product of the reaction with formaldehyde.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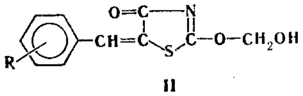
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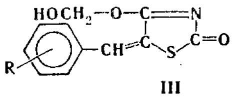
III

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*See [1] for Communication 40.

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TABLE 1. Characteristics of 3-Hydroxymethyl-5-benzylidene-2,4-thiazolidinediones

Compound	R	mp, °C	UV spectrum, λ_{max}, nm (log ε)	N found, %	Empirical formula	N calc., %	Yield, %
Ia	H	251	230 (4,15), 325 (4,30)	6,0	$C_{11}H_4NO_3S$	5,9	80,9
Ib	*o*-OH	235	236 (3,83), 280 (3,66), 365 (4,06)	5,1	$C_{11}H_9NO_4S$	5,6	79,5
Ic	*p*-OCH_3	220	240 (4,19), 280 (4,25), 340 (4,54)	5,5	$C_{12}H_4NO_4S$	5,3	70,8
Id	*p*-Br	261	245 (4,22), 280 (4,40), 335 (4,38)	4,4	$C_{12}H_8NO_3S$	4,5	81,3
Ie	*p*-Cl	247	240 (4,14), 280 (4,29), 335 (4,34)	5,1	$C_{11}H_8NO_3S$	5,2	78,2
If	*p*-$(CH_3)_2N$	254	245 (4,06), 335 (5,13), 450 (4,37)	10,2	$C_{12}H_{14}N_2O_3S$	10,1	65,2
Ig	*p*-NO_2	246	255 (4,11), 320 (4,23)	9,8	$C_{11}H_9N_2O_5S$	10,0	71,6

The UV spectra of hydroxymethyl-5-benzylidene-2,4-thiazolidinediones coincide almost completely with the spectra of model 3-alkyl-5-benzylidene-2,4-thiazolidinediones, which have a diketo structure [6]. The IR spectra of the synthesized compounds contain absorption bands with maxima at 1680-1700 and 1710-1740 cm^{-1}, which were assigned to the stretching vibrations of unconjugated $\nu C_4=O$ and $\nu C_2=O$ groups, respectively [3].

The fact of the addition of the hard electrophilic reagent formaldehyde to the more polarizable center of the ambident system, viz., the nitrogen atom, is evidently due to one of the following reasons: either thermodynamic control of the reaction at the oxygen atom, which is characteristic for most thiazolidones [2], or the peculiarities of the reaction mechanism, viz., addition of formadehyde at the site of location of the proton in the 3 position of the thiazolidine ring [2, 3], which exists in the diketone form in solution. The possibility of the occurrence of the reaction through a step involving the dissociation of 2,4-thiazolidinediones cannot be verified because of rapid hydrolysis of 3-hydroxymethyl-2,4-thiazolidinediones in an alkaline medium with the formation of the starting compounds.

EXPERIMENTAL

The course of the reaction and the purity of the compounds were monitored by TLC on Silufol UV-254 plates. The IR spectra were recorded with an IKS-29 spectrometer. The UV spectra of solutions in ethanol were recorded with an SF-16 spectrophotometer.

3-Hydroxymethyl-5-benzylidene-2,4-thiazolidinedione (Ia). A solution of 2.05 g (0.01 mole) of 5-benzylidene-2,4-thiazolidinedione in 20 ml of acetone was treated at room temperature with 1.3 ml (0.05 mole) of formalin, and the mixture was stirred for 2 h. The completion of the reaction was judged from the disappearance of the spot of the starting 2,4-thiazolidinedione on the thin-layer chromatogram [in an acetone—hexane system (2:1)]. The precipitate that formed after evaporation of two-thirds of the solvent was removed by filtration, washed with a pure solvent, and dried in vacuo. Recrystallization from dioxane gave 1.9 g (80.9) of a product with mp 250-251°C. Compounds Ib-g were similarly obtained (Table 1).

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