INVESTIGATION OF THE REACTIVITIES AND TAUTOMERISM OF AZOLIDINES.

40.* 2-IMINOTHIAZOLIDIN-4-ONE IN THE MANNICH REACTION

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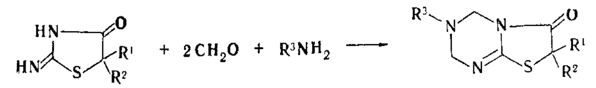
It is shown that the aminomethylation of 2-iminothiazolidin-4-one and its 5-methyl and 5-arylidene derivatives in an alcohol medium leads to the formation of 6-oxo-2,3,4,5,6,7-hexahydrothiazolo[3,2-a]-1,3,5-triazines. The structures of the compounds obtained were confirmed by their IR, PMR, and UV spectra.

Despite the fact that 2-iminothiazolidin-4-one (Ia) has four nucleophilic reaction centers, viz., the nitrogen, oxygen, and C_5 atoms, its aminomethylation usually takes place only at the ring nitrogen atom [2, 3] or, if it is substituted, at the exocyclic nitrogen atom [4, 5].

Our attempts to obtain aminomethyl derivatives of Ia by the method in [2] by the use of aromatic amines were unsuccessful. An aminomethylation product is formed in appreciable amounts only 24 h after mixing the reagents; however, its purification to remove the side product and the unchanged starting compound leads to great losses, and the yield of the recrystallized reaction product does not exceed 10-20%. We isolated a chromatographically pure aminomethylation product from the reaction mixture only when we used a 2.5-fold to threefold excess of formaldehyde and increased the reaction time to 20-24 h. As in [2], the reaction was carried out in methanol at room temperature. The yield decreased substantially at higher temperatures. We used the described method to obtain a number of Mannich bases (IIb-i)(see Table 1), of which IIb, c, e had melting points and UV spectral characteristics that were in agreement with those observed for the compounds obtained in [2] when similar aromatic amines were used. However, the results of elementary analysis and the data from the IR and PMR spectra of these compounds do not confirm the 3-aminomethyl derivative structure proposed for them. The absence in the IR spectra of bands of vibrations of an NH bond and the presence in the PMR spectra of signals of protons of three methylene groups constitute primary evidence in favor of two-ring structure II. The formation of thiazolo-[3,2-a]-1,3,5-triazine derivatives is not unexpected, since the reaction of thioureas with primary amines and formaldehyde, which leads to the formation of substituted perhydro-sym-triazines, is well known [6]. It is clear that only 50% conversion of Ia can be achieved in the ideal case at a reagent ratio of 1:1:1.



I a-f

II a-o

I a $R^1=R^2=H$; b $R^1=H$, $R^2=CH_3$; c $R^1R^2=CHC_6H_5$; d $R^1R^2=CHC_6H_4Cl$-*p*;
e $R^1R^2=CHC_6H_4F$-*p*; f $R^1R^2=CHC_6H_4Br$-*p*

It is known that 2-iminothiazolidin-4-one (Ia) is a very weak acid with a pK_a value in water of 11.7 [7]. When aromatic amines are used, as a consequence of the low concentration of substrate anions, the rate of aminomethylation is evidently comparable to the rate of the side reaction, viz., the formation of anhydroformaldehydeaniline [8], which, inasmuch as it exists in equilibrium with the aminomethylating particle and thus has aminomethylating activity, is gradually consumed with the formation of principal products IIb-i.

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*See [1] for Communication 39.

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TABLE 1. 6-Oxo-2,3,4,5,6,7-hexahydrothiazolo[3,2-a]-1,3,5-triazines

Compound	R^1	R^2	R^3	mp, °C	UV spectrum, λ_{max}, nm (log ε)	IR spectrum, cm^{-1}		PMR spectrum,[a] δ, ppm		Found, %		Empirical formula	Calc., %		Yield, %
						C=O	C=N	2-H	4-H	N	S		N	S	
IIa	H	H	CH_3	112	215 (4,34)	1725	1660	4,59	4,21	24,7	18,6	$C_6H_9N_3OS$	24,5	18,7	65
IIb	H	H	C_6H_5	142 (140 [2])	237 (4,21)	1725	1642	5,23	4,90	17,7	13,4	$C_{11}H_{11}N_3OS$	18,0	13,7	89
IIc	H	H	*p*-$CH_3C_6H_4$	126 (127 [2])	237 (4,27)	1700	1620	5,12	4,85	17,2	12,4	$C_{12}H_{13}N_3OS$	17,0	13,0	89
IId	H	H	*m*-$CH_3C_6H_4$	129	238 (4,12)	1710	1640	5,15	4,93	17,2	12,4	$C_{12}H_{13}N_3OS$	17,0	13,0	84
IIe	H	H	*p*-$CH_3OC_6H_4$	129 (128 [2])	238 (4,22)	1705	1625	5,05	4,78	15,9	11,8	$C_{12}H_{13}N_3O_2S$	16,0	12,2	90
IIf	H	H	*m*-ClC_6H_4	148	211 (4,56) 240 (4,17) 280 (3,02)	1742	1687	5,19	4,86	15,6	12,1	$C_{11}H_{10}ClN_3OS$ [b]	15,7	12,0	90
IIg	H	H	*m*-BrC_6H_4	151	211 (4,58) 242 (4,18) 282 (3,16)	1741	1687	5,20	4,87	13,7	10,4	$C_{11}H_{10}BrN_3OS$ [c]	13,5	10,3	88
IIh	H	H	*m*-$NO_2C_6H_4$	191	238 (4,34)	1717	1620	5,23	4,90	20,6	10,9	$C_{11}H_{10}N_4O_3S$	20,1	11,5	42
IIi	H	H	β-Naphthyl	182	214 (4,58) 241 (4,69)	1725	1630	5,32	5,05	14,8	10,8	$C_{15}H_{13}N_3OS$	14,8	11,3	89
IIj	H	CH_3	β-Naphthyl	144	240 (4,71)	1725	1635	5,22	4,98	14,2	10,7	$C_{16}H_{15}N_3OS$	14,1	10,8	69
IIk	CHC_6H_5		CH_3	142	232 (3,90) 254 (3,79) 329 (4,42)	1720	1650	4,80	4,38	16,2	12,3	$C_{13}H_{13}N_3OS$	16,2	12,4	59
II*l*	CHC_6H_4Cl-*p*		CH_3	170	233 (3,98) 333 (4,41)	1710	1635	4,70	4,40	15,1	10,8	$C_{13}H_{12}ClN_3OS$ [d]	14,3	10,9	52
IIm	CHC_6H_4F-*p*		CH_3	159	235 (3,92) 330 (4,38)	1725	1650	4,71	4,40	15,4	12,2	$C_{13}H_{12}FN_3OS$ [e]	15,2	11,6	65
IIn	CHC_6H_4Br-*p*		CH_3	163	235 (3,94) 335 (4,45)	1720	1650	4,70	4,40	12,8	9,4	$C_{13}H_{12}BrN_3OS$ [f]	12,4	9,5	68
IIo	CHC_6H_5		C_6H_5	180	235 (4,18) 265 (4,41)	1690	1650	5,30	5,02	13,6	10,3	$C_{18}H_{15}N_3OS$	13,1	10,0	56

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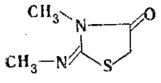
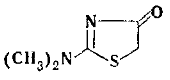
[a] The PMR spectra of IIa, b, d, f-h, k were recorded in d_6-DMSO, while the PMR spectra of IIc, e, i, j, *l*-o were recorded in $CDCl_3$. [b] Found: Cl 13.1%. Calculated: Cl 13.2%. [c] Found: Br 25.3%. Calculated: Br 25.6%. [d] Found: Cl 12.4%. Calculated: Cl 12.0%. [e] Found: F 7.5%. Calculated: F 6.8%. [f] Found: Br 23.7%. Calculated: Br 23.6%.

2-Imino-5-methylthiazolidin-4-one (Ib) and 2-imino-5-arylidenethiazolidin-4-ones (Ic-f) behave like Ia in aminomethylation and give the corresponding thiazolo[3,2-*a*]-1,3,5-triazines (IIj-o). The molecular masses of IIa and IIk determined by mass spectrometry correspond to their empirical formulas.

Aminomethylation does not involve the other nucleophilic O_4 and C_5 atoms. This is confirmed unambiguously by the presence of a band of carbonyl absorption in the IR spectra and the signal of methylene protons attached to the C_5 atom in the PMR spectra of all of the Mannich bases obtained. The single absorption maximum at 215 nm in the UV spectrum of Mannich base IIa coincides in its position with the absorption maximum of 2-methylimino-3-methylthiazolidin-4-one (III, imino structure) and differs from the absorption of IV (241 nm) [7], and this confirms proposed structure II.



III



IV

The UV spectra of IIb-i, which are derivatives of aromatic amines, contain three absorption maxima. The short-wave band with $\lambda_{max} \leqslant$ 200-211 nm is due to the absorption of a heterocyclic imino structure upon which is superimposed the absorption of the aromatic ring, which leads to an increase in its intensity as compared with the intensity of the corresponding band of methyl analog IIa. The two other absorption maxima at 237-242 and 270-290 nm are characteristic for aromatic amines. If the C=N bond were situated in the thiazole ring, the intensity of the absorption at 237-242 nm would be considerably greater, since the absorption of the amino structure of the heterocycle would be superimposed on the absorption of the aromatic amines here.

The IR spectrum of IIa at 1500-1750 cm^{-1}, in which region the characteristic frequencies of the vibrations of 2-iminothiazolidin-4-one are located, resembles the IR spectrum of III with a fixed imino structure (1720, 1696, and 1652 cm^{-1}) and differs from the IR spectrum of IV with a fixed amino structure (1689, 1593, 1565 cm^{-1}). Bands of vibrations of an aromatic ring are observed in the IR spectra of IIb-o in the same region.

EXPERIMENTAL

The PMR spectra of the compounds were recorded with Perkin—Elmer R-12 and Tesla BS-467 spectrometers (60 MHz) with hexamethyldisiloxane as the internal standard. The IR spectra of suspensions of the compounds in mineral and perfluorinated mineral oils were recorded with an IKS-29 spectrometer. The UV spectra of solutions of the compounds in ethanol were recorded with an SF-16 spectrophotometer. The molecular masses were determined with an MKh-1303 spectrometer with a system for direct introduction of the samples; the temperature of the admission system were 70°C (IIa) and 135°C (IIk) (lower than the melting points of the samples), and the ionizing voltages were 15 and 70 eV. Thin-layer chromatography (TLC) was carried out on Silufol UV-254 plates with ethanol—chloroform (1:4) (IIa-h, j) and acetone—hexane (1:2) (IIi, k-o) as the eluents. The following solvents were used to recrystallize the compounds obtained: benzene (IIh), hexane (IIk, m, n), and benzene—hexane [2:1 (IIb-g, i, j), 1:5 (IIa), and 1:9 (II*l*-o)].

3-Methyl-6-oxo-2,3,4,5,6,7-hexahydrothiazolo[3,2-*a*]-1,3,5-triazine (IIa). A 5.0-g (0.04 mole) sample of a 25% aqueous solution of methylamine was added dropwise with stirring to 4.6 g (0.04 mole) of 2-iminothiazolidin-4-one (Ia) in 9.6 ml (∿0.12 mole) of formalin while maintaining the temperature between 0 to 5°C. After the addition was complete, the reaction mixture was stirred without cooling for another 15 min, after which it was treated with warm (30-40°C) benzene (four 20-ml portions). The benzene layer was dried with magnesium sulfate, the benzene was removed by distillation to one fifth of the original volume, and IIa was precipitated with hexane.

3-Phenyl-6-oxo-2,3,4,5,6,7-hexahydrothiazolo[3,2-*a*]-1,3,5-triazine (IIb). A 9.6-ml (∿0.12 mole) sample of formalin and 3.7 g (0.04 mole) of aniline were added to a suspension of 4.6 g (0.04 mole) of 2-imino-thiazolidin-4-one (Ia) in 60 ml of methanol. After 20 h, IIb was removed by filtration. Compounds IIc-j were similarly obtained.

3-Methyl-6-oxo-7-benzylidene-2,3,4,5,6,7-hexahydrothiazolo[3,2-*a*]-1,3,5-triazine (IIk). A 2.4-ml (∿0.03 mole) sample of formalin and 1.2 g (0.01 mole) of a 25% aqueous solution of methylamine were added to 1.8 g (0.01 mole) of 2-imino-5-benzylidenethiazolidin-4-one (Ic) in 30 ml of ethanol, and the mixture was stirred at 60-70°C for 10-15 min until starting Ic dissolved completely. The IIk that precipitated after the reaction mixture was cooled was removed by filtration. Compounds II*l*-o were similarly obtained.

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MESOIONIC COMPOUNDS WITH A BRIDGED NITROGEN ATOM.

6.* POLYMETHINE DYES OF THE THIAZOLO[3,2-*a*]QUINOLINIUM 1-OXIDE SERIES

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Mesoionic compounds formed from (2-quinolylthio)acetic acids readily give polymethine dyes. The structures of the synthesized compounds were confirmed by data from the PMR spectra and the results of elementary analysis.

It has been assumed [2, 3] that the reaction of acetic anhydride with (4-methyl-2-quinolylthio)acetic acid (Ib) gives 5-methylthiazolo[3,2-*a*]quinolinium 1-oxide (IIb), which reacts with the intermediates used for the synthesis of cyanine dyes [for example, with 3-ethyl-2-(2-acetanilidovinyl)benzothiazolium iodide] to give compounds of the III type [4]. Products of the latter condensation with precisely this structure have been patented [5] as spectral sensitizers of silver halide emulsions. However, spectral characteristics of such dyes have not been presented in the literature, analytical data are not available for a number of compounds, and half a molecule of methanol has been assigned to the empirical formulas in some cases to obtain satisfactory analytical data [5].

We have established that the primary product obtained from acid Ib under the conditions indicated in the literature is not oxide IIb, as was previously assumed, but rather its acetyl derivative (IV); the latter itself also gives dyes, which up until now have been assumed to be derivatives of 2-unsubstituted thiazoloquinolinium 1-oxide. For example, a dye with the V structure is formed with 3-methyl-2-methylthiobenzothiazolium salts [7].

Further studies showed that the reaction of (2-quinolylthio)acetic acids Ia, b with a mixture of acetic anhydride and pyridine at room temperature gives the previously unknown thiazolo[3,2-*a*]quinolinium 1-oxides (IIa, b) [6]. The latter readily undergo reaction in

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*See [1] for Communication 5.

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