INVESTIGATION OF THE REACTIVITIES AND TAUTOMERISM OF AZOLIDINES.

53.* SYNTHESIS OF 5-ARYLIDENE-2-ALLYLAMINO-Δ^2-THIAZOLIN-4-ONES AND 5-ARYLIDENE-2-IMINO-3-ALLYLTHIAZOLIDIN-4-ONES

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Depending on the reaction conditions, 2-allylamino-5-arylidene-Δ^2-thiazolin-4-ones, 2-imino-3-allyl-5-arylidenethiazolin-4-ones, and 3-allyl-5-arylidenethiazolidine-2,4-diones are obtained by condensation of 2-allylamino-Δ^2-thiazolin-4-one and 2-imino-3-allylthiazolidin-4-one with aromatic aldehydes.

Compounds that have valuable pharmacological properties have been detected among N-allyl derivatives of thiazolidin-4-one [2-4]. In this connection, it seemed of interest to obtain products of condensation of 2-allylamino-Δ^2-thiazolin-4-one (I) and 2-imino-3-allylthiazolidin-4-one (II) with aromatic aldehydes at the active methylene group.

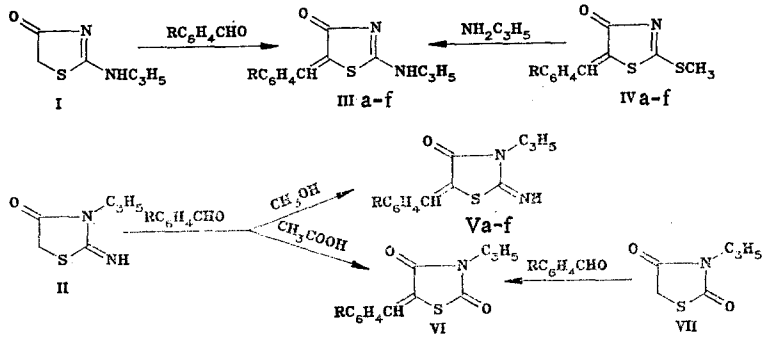
We have observed that the reaction of I with aromatic aldehydes proceeds via a general scheme [6-8].

The structures of IIIa-f were confirmed by alternative synthesis from the corresponding methylmercapto-5-arylidene-Δ^2-thiazolin-4-ones (IVa-f) and allylamine.

2-Imino-3-allyl-5-arylidenethiazolidin-4-ones Va-f were synthesized by condensation of II with aromatic aldehydes.

The introduction of an arylidene grouping stabilizes the structure of Va-f to a significant degree. Thus prolonged refluxing with concentrated HCl did not lead to either hydrolysis of the amino group in the 2 position of the ring or to conversion of the allyl group in the 3 position of the ring.

The hydrolysis of IIa-f to give the corresponding 3-allyl-5-arylidenethiazolidine-2,4-diones (VIa-f) proceeded with ease.



III—V a R=H, b R=p-Br, c R=p-OCH_3, d R=p-$N(CH_3)_2$, e R=p-NO_2, f R=*m*-NO_2

In the reaction of II with aromatic aldehydes in acetic acid hydrolysis of the exocyclic imino group competes with the condensation reaction, and we therefore isolated only 5-arylidenethiazolidine-2,4-diones VIa-f, the structure of which was confirmed by alternative synthesis, viz., by condensation of 3-allylthiazolidine-2,4-dione (VII) with the corresponding aldehydes.

*See [1] for communication 52.

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TABLE 1. 2-Allylamino-5-arylidene-Δ^2-thiazolin-4-ones IIIa-f, 2-Imino-3-allyl-5-arylidenethiazolidin-4-ones Va-f, and 3-Allyl-5-arylidenethiazolidine-2,4-diones VIa-f

Compound	mp,* °C	UV spectrum, λ_{max}, nm (log ε)	IR spectrum, cm^{-1}		Found, %		Empirical formula	Calc., %		Yield, % (method)
			$C_{(4)}=O$	$C_{(2)}=N(O)$	N	S		N	S	
IIIa	164—165 [15]	242 (3,92); 336 (4,39)	1686	1622	11,6	13,0	$C_{13}H_{12}N_2OS$	11,5	13,1	90 (A), 74 (B)
IIIb	236—237	250 (4,00); 340 (4,48)	1688	1628	8,8	9,9	$C_{13}H_{11}BrN_2OS$	8,7	9,9	87 (A), 80 (B)
IIIc	179—180	254 (4,00); 298 (3,96); 355 (4,43)	1680	1625	10,2	11,8	$C_{14}H_{14}N_2O_2S$	10,2	11,7	81 (A), 76 (B)
IIId	209—210	272 (4,18); 330 (3,56); 413 (4,52)	1658	1628	14,5	11,2	$C_{15}H_{17}N_3OS$	14,6	11,2	86 (A), 73 (B)
IIIe	270—271	230 (4,10); 357 (4,38)	1688	1626	14,5	11,1	$C_{13}H_{11}N_3O_3S$	14,5	11,1	92 (A), 78 (B)
IIIf	206—207	235 (4,23); 290 plateau 4,32); 330 (4,39)	1690	1630	14,5	11,1	$C_{13}H_{11}N_3O_3S$	14,5	11,1	85 (A), 72 (B)
Va	93—94	237 (3,94); 256 (3,79); 328 (4,41)	1698	1628	11,6	13,1	$C_{13}H_{12}N_2OS$	11,5	13,1	77 (A), —
Vb	119—120	239 (3,91); 260 (3,71); 334 (4,38)	1703	1620	8,7	9,8	$C_{13}H_{11}BrN_2OS$	8,7	9,9	82 (A), —
Vc	114—115	242 (3,99); 348 (4,13)	1692	1626	10,1	11,8	$C_{14}H_{14}N_2O_2S$	10,2	11,7	83 (A), —
Vd	139—140	260 (3,04); 330 (3,53); 417 (4,33)	1688	1620	14,6	11,3	$C_{15}H_{17}N_3OS$	14,6	11,2	81 (A), —
Ve	163—164	267 (4,16); 357 (4,22)	1710	1640	14,6	11,0	$C_{13}H_{11}N_3O_3S$	14,5	11,1	78 (A),
Vf	132—133	280 (3,78); 323 (4,16)	1699	1632	14,5	11,0	$C_{13}H_{11}N_3O_3S$	14,5	11,1	81 (A), —
VIa	88—89 [13]	220 (3,86); 330 (4,05)	1678	1740	5,7	13,0	$C_{13}H_{11}NO_2S$	5,7	13,1	73 (A), 68 (B)
VIb	165—166	218 (3,94); 332 (3,98)	1680	1748	4,3	9,8	$C_{13}H_{10}BrNO_2S$	4,3	9,9	74 (A), 76 (B)
VIc	86—87	239 (4,01); 342 (4,31)	1680	1743	5,1	11,7	$C_{14}H_{13}NO_3S$	5,1	11,6	81 (A), 72 (B)
VId	130—131 [13]	240 (3,86); 326 (3,55); 425 (4,36)	1678	1745	9,7	11,3	$C_{15}H_{16}N_2O_2S$	9,7	11,1	73 (A), 68 (B)
VIe	160—161 [13, 14]	243 (3,96); 265 (3,95); 345 (4,28)	1675	1740	13,8	10,4	$C_{13}H_{10}N_3O_4S$	13,8	10,5	71 (A), 61 (B)
VIf	150—151 [13]	229 (4,14); 269 (4,17); 321 (4,26)	1670	1740	13,7	10,7	$C_{13}H_{10}N_3O_4S$	13,8	10,5	69 (A), 68 (B)

*The compounds were crystallized: IIIa-f from acetic acid, Va-f from ethanol, and VIa-f from heptane.

The appearance of a high-intensity absorption band with a maximum at 320-417 nm, which is associated with $\pi-\pi^*$ transition of the electrons of the carbonyl group conjugated with an arylidene ring [9, 10], is characteristic for the UV spectra of 5-arylidenethiazolidin-4-ones III-VI.

The IR spectra of I and IIa-f in the high-frequency region contain NH absorption bands at 3060-3290 cm^{-1} and $C_{(4)}=O$ absorption bands at 1658-1710 cm^{-1}, as well as bands at 1622-1640 cm^{-1} (C=N) and 1580-1615 cm^{-1} (C=C), which are related to the stretching vibrations of multiple bonds. Two intense bands of stretching vibrations of a carbonyl group at 1678-1706 cm^{-1} [$C_{(4)}=O$] and 1735-1748 cm^{-1} [$C_{(2)}=O$] and stretching vibrations of an aromatic ring at 1580-1610 cm^{-1} are observed in the IR spectra of VIa-f, but vibrations of an NH group are absent in the high-frequency region of the spectrum [11, 12].

EXPERIMENTAL

The UV spectra of 10^{-5} M solutions of the compounds were recorded with a Hitachi EPS-3T spectrometer. The IR spectra of mineral oil suspensions and KBr pellets of the compounds were recorded with a Perkin-Elmer 283 spectrometer. The compounds were purified by two recrystallizations from suitable solvents, and their individuality was confirmed by chromatography on Silufol-254 plates in an acetone-hexane system (1:1).

3-Allylthiazolidin-2,4-dione (IV) was obtained by the method in [1]. Its condensation with aromatic aldehydes by the method in [8] gave 3-allyl-5-arylidenethiazolidine-2,4-diones VIa-f [13, 14].

The characteristics of II, V, and VI are presented in Table 1. 2-Methylmercapto-5-arylidene-Δ^2-thiazolin-4-ones Va-f [15] were obtained by condensation of 2-methylmercapto-Δ^2-thiazolin-4-one with aromatic aldehydes by the method in [8].

2-Allylamino-5-benzylidene-Δ^2-thiazolin-4-one (IIa). A) A 1.0-g (10 mmole) sample of benzaldehyde and two drops of 25% aqueous methylamine solution were added to 1.5 g (10 mmole) of I in 10 ml of acetic acid, and the mixture was heated on an oil bath at 115°C for 15 min with constant stirring. It was then cooled, and the precipitate was removed by filtration, washed with ether, and purified by cyrstallization from acetic acid to give 2.1 g (90%) of a product with mp 164-165°C (mp 165°C [16]).

The other 5-arylidene derivatives IIIb-f were similarly obtained.

B) A 0.6-g (10 mmole) sample of allylamine was added to 2.5 g (10 mmole) of IVa in 30 ml of chloroform, and the mixture was heated at 50°C for 2 h. The solvent was removed by distillation *in vacuo*, and the residue was crystallized from acetic acid to give 3.0 g (73%) of IIa with mp 164-165°C.

2-Imino-3-allyl-5-benzylidenethiazolidin-4-one (Va). A 1.23-g (15 mmole) sample of sodium acetate, 1.0 g (10 mmole) of benzaldehyde, and one drop of 25% aqueous methylamine solution were added to 1.5 g (10 mmole) of II in 10 ml of methanol, and the mixture was heated at 55°C and stirred for 1 h. The solvent was then removed by distillation *in vacuo* until crystallization commenced, 20 ml of distilled water was added to the precipitate, and the solid material was removed by filtration, washed on the filter with petroleum ether, and purified by crystallization from ethanol to give 1.9 g (77%) of a product with mp 93-94°C.

5-Arylidene derivatives Vb-f were similarly obtained.

3-Allyl-5-benzylidenethiazolidine-2,4-dione (VIa). A) A 1.23-g (15 mmole) sample of sodium acetate, 1.0 g (10 mmole) of benzaldehyde, and one drop of 25% aqueous methylamine solution were added to 1.5 g (10 mmole) of II in 10 ml of acetic acid, and the mixture was heated on a water bath with stirring at 95°C for 0.5 h. It was then poured into 50 ml of ice water, and the aqueous mixture was filtered. The product was purified by crystallization from heptane.

5-Arylidene derivatives VIb-f were similarly obtained.

B) A 10-ml sample of concentrated HCl was added to 1.2 g (5 mmole) of Va, and the mixture was refluxed for 15 min. The precipitate was removed by filtration and purified by recrystallization from heptane to give 0.8 g (79%) of a product with mp 88-89°C.

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CONDENSED HETEROCYCLES WITH A THIAZOLE RING.

10.* THIAZOLO[3,4-b][1,2,4]TRIAZINES

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Derivatives of a new heterocyclic system, viz., the thiazolo[3,4-b][1,2,4]triazinium ion, were obtained by condensation of cyanobenzyl benzenesulfonate with substituted N-dithiocarboxyhydrazones of 1,2-diketones and α-isonitroso ketones.

A number of valuable physiologically active substances [4-6] have been found among previously synthesized [2, 3] derivatives of condensed heterocycles with an angular nitrogen atom constructed on the basis of thiazole and 1,2,4-triazine rings (thiazolo[2,3-c]- and thiazolo[3,2-b][1,2,4]triazine). It seemed of interest to synthesize derivatives of heterocyclic compounds of the indicated type with a new orientation of the thiazole and triazine rings, viz., thiazolo[3,4-b][1,2,4]triazine.

With this end in mind, we studied the reaction of methyl dithiohydrazonate Ia [7] with α-cyanobenzyl benzenesulfonate (II). Since it is known [8] that sulfonate II reacts with methyl dithiocarbamate to give 4-amino-2-methylthiothiazolium salts, in our case we might have expected thiazolium salts with structure III. However, an investigation of the isolated product showed that, in the case of direct heating of a mixture of Ia and II, the reaction does not stop at this stage — condensation to the desired product occurs immediately to give the corresponding thiazolotriazinium salts IVa and Va. The structures of the synthesized compounds were confirmed by data from the PMR spectra (Table 1) and the IR spectra (Table 2). In fact, the IR spectrum of perchlorate Va does not contain absorption bands corresponding to the stretching vibrations of the C=O and N–H bonds of starting hydrazone Ia (1640 and 3210 cm^{-1}) but does contain a band of vibrations of a C=N bond (1590 cm^{-1}).

*See [1] for communication 9.

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