INVESTIGATION OF THE REACTIVITY AND TAUTOMERISM OF AZOLIDINES

X.* SYNTHESIS OF 2-IMINO-4-THIAZOLIDONES

S. M. Ramsh, K. A. V'yunov,
A. I. Ginak, and E. G. Sochilin

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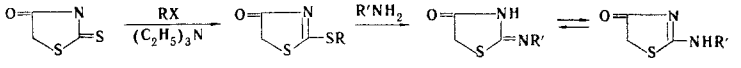
The reaction of 2-alkylrhodanines and aromatic amines was studied, and 2-(alkylimino)- and 2-(arylimino)-4-thiazolidones were obtained. It was shown by means of IR spectroscopy that the investigated compounds exist primarily in the imino form; the amino form predominates only for compounds with strong electron-donor substituents.

The existing methods for the preparation of substituted 2-imino-4-thiazolidones have a number of disadvantages. The severe conditions used to carry out the reactions cause considerable destruction of the thiazolidine ring [2,3] or the formation of isomeric compounds [4,5].

In an investigation of the amination of 2-alkylrhodanines, we have shown that substitution of an alkylmercapto group by an amino group proceeds under mild conditions to give high yields of 2-imino-4-thiazolidones (I-XI). In the course of a subsequent investigation, it was established that the S-alkyl derivatives can be aminated without isolating them from the reaction mixture.



Ia XIa Ib XIb

R=CH_3, C_2H_5; X=Br, I; I R′=H; II R′=C_2H_5; III R′=n-C_4H_9; IV R′=p-$(CH_3)_2NC_6H_4$; V R′=p-HOC_6H_4; VI R′=p-$CH_3OC_6H_4$; VII R′=p-$CH_3C_6H_4$; VIII R′=C_6H_5; IX R′=p-BrC_6H_4; X R′=p-ClC_6H_4; XI R′=m-$O_2NC_6H_4$

Compounds I-XI were identified by mixed-melting-point determinations with substances obtained by alternative synthesis [5].

2-(Arylimino)-4-thiazolidones (IV-XI) are potentially tautomeric substances, and the prototropic equilibrium A⇌B is possible in solutions of them.

The introduction of substituents into the phenyl ring of IV-XI has a considerable effect on the position of the tautomeric equilibrium, the constants of which were calculated from the deviation from the linear dependence of pK_a on σ^0. The method of calculation is described in greater detail in [6]. Predominance of the amino form is observed in 70% dioxane only for IV and VI, which have strong electron-donor substituents. However, it was necessary to confirm the results of the sort of analysis by some independent method, for example, a spectral method.

It has been shown [7,8] that compounds with aliphatic substituents (R′) are found exclusively in the amino form (B), while the tautomeric equilibrium of 2-(arylimino)-4-thiazolidones remains virtually uninvestigated. There is only some information that VII and VIII exist primarily in the imino form [9] in the crystalline state and in solutions.

*See [1] for communication IX.

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TABLE 1. Characteristic Frequencies in the IR Spectra of 2-Imino-4-thiazolidones

Compound	$\nu_{C=O}$, cm^{-1}			$\nu_{C=N}$, cm^{-1}		
	in the crystalline state	in chloroform	in tetrahydrofuran	in the crystalline state	in chloroform	in tetrahydrofuran
III	—	—	1732	—	—	1651
IV	1695 1743	1687 1735 (shoulder)	1708 1732	1614 1650 (shoulder)	1607 1647	1607 1648
V	1695 —	1691 1724 1692	1705 1712 1700 (shoulder)	1612 1658 1604	1610 1643 1610	1608 1647 1605 (shoulder)
VI	1735 1708	1739 (shoulder) 1711	1725 (superimp.)	1655 1601	1650 1610 1650	1657 1610 1650
VII	1674	1730 1691	1724 1711 (shoulder)	1636	1610	1610
VIII	1720 1675	1736 1700	1728 —	1638 1609	1649 1610	1655 —
IX	1721 1700	1742 1695	1732 —	1640 1610	1651 1610	1648 —
X	1730 1702	1724 1695	1732 —	1640 1613	1653 1610	1654 —
XI	1696	1740 1710	1728 —	1605	1655 1610	1652 1606

TABLE 2. 2-Iminothiazolidones

Compound	Synthetic conditions		mp, °C (literature data)*	Yield, %
	amine : rhodanine molar ratio	amination time, h		
I	53	2	240 (241)[13]	85
II	3	3,5	147 (144)[14]	84
III	3	3	103†	81
IV	2,5	3	236 (222)[15]	90
V	1	6	249 (251)[16]	92
VI	3	6	180 (184)[17]	87
VII	3	7	183 (183)[18]	89
VIII	2,5	7	176 (179)[19]	75
IX	2	9	222 (224)[20]	70
X	3	9	180 (180)[2]	82
XI	2	10	203 (200)[21]	71

*Compounds I and V were recrystallized from ethanol, while the remaining compounds were recrystallized from acetone.

†Found: N 16.8; S 18.3%. $C_7H_{12}N_2OS$. Calculated: N 16.3; S 18.6%.

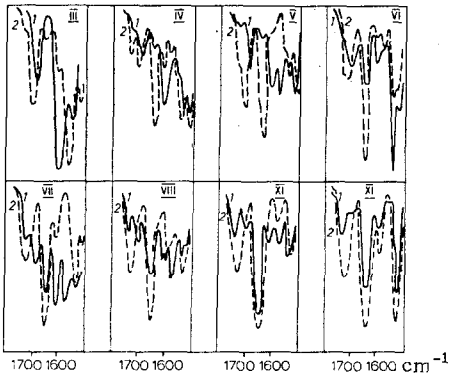

Fig. 1. IR spectra of 2-imino-4-thiazolidones: 1) in chloroform; 2) in tetrahydrofuran (the symbols are the same as in Table 2).

The low solubility of the investigated substances in 70% aqueous dioxane made it impossible to study the tautomeric equilibrium by spectroscopy under conditions similar to those of the potentiometric method [6].

We investigated principally the high-intensity bands in the IR spectra of III-IX in chloroform at 1600-1750 cm^{-1} (Fig. 1), where the $\nu_{C=O}$ and $\nu_{C=N}$ valence vibrations, which make it possible to judge the position of the tautomeric equilibrium, are situated. As should have been expected, two groups of $\nu_{C=O}$ and $\nu_{C=N}$ absorption bands are observed, which indicates the presence of a prototropic equilibrium in the investigated series. The assignment of the absorption bands of the carbonyl group was based on the fact [10] that a decrease in the absorption frequency of the carbonyl group itself is observed when it is conjugated with a C=N bond [11]. This sort of decrease was also previously observed for S-alkylrhodanines [12], and the bands at 1687-1711 cm^{-1} were therefore as-

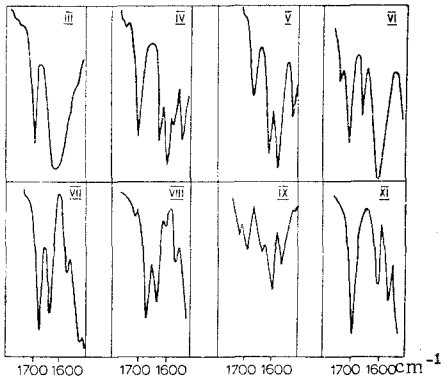

Fig. 2. IR spectra of 2-imino-4-thiazolidones in the solid state (the symbols are the same as in Table 2).

signed to $\nu_{C=O}$ of amino form B (Fig. 1), while the bands at 1712-1742 cm^{-1} were assigned to $\nu_{C=O}$ of imino form A. The intensity of the $\nu_{C=O}$ bands varies as a function of the substituent in the phenyl ring and decreases at 1712-1742 cm^{-1} and increases at 1687-1711 cm^{-1} as its electron-donor properties increase. This sort of assignment is in agreement with the results of correlation analysis [6]. The $\nu_{C=N}$ bands are situated at 1601-1658 cm^{-1} (Fig. 1) and are also divided into two groups: we assigned the 1601-1614 cm^{-1} region to the amino form and the 1638-1658 cm^{-1} region to the imino form. This assignment is a consequence of an examination of the spectra, in which the $\nu_{C=N}$ bands at 1601-1614 cm^{-1} are combined with $\nu_{C=O}$ of the amino form (1687-1711 cm^{-1}), while the $\nu_{C=N}$ bands at 1638-1658 cm^{-1} are combined with $\nu_{C=O}$ of the imino form (1712-1742 cm^{-1}) (Table 1). The maximum intensity of the stretching vibrations for the exocyclic C=N bond in solutions in chloroform is observed for IX-XI, which have strong electron-acceptor substituents, while the intensity of the stretching vibrations of the ring C=N bonds, which are affiliated with form B, is higher for IV-VI. This assignment of the C=N bands is in agreement with the observations regarding the relationship between the frequencies of the ring and exocyclic bonds in 2-(acetylimino)thiazolidines [11]. At the same time, there is another interpretation of the spectra of VII and VIII [9]. The spectrum of thiazolidone III, which is a model of the amino form [7,8], which has only two absorption bands $\nu_{C=O}$ 1687 cm^{-1} and $\nu_{C=N}$ 1607 cm^{-1} in the examined region, should be considered to be a confirmation of our point of view.

The IR spectra of III-IX in tetrahydrofuran (THF) are practically the same as the spectra of these compounds in chloroform. There is only an increase in the intensity of the $\nu_{C=O}$ 1712-1742 cm^{-1} and $\nu_{C=N}$ 1638-1658 cm^{-1} bands, which is caused by a shift in the prototropic equilibrium to favor the imino form, which is apparently explained by the higher polarity of THF as compared with chloroform.

The lack of spectra of the methylated compounds, which might have served as models of the tautomeric forms, makes it impossible to quantitatively calculate the equilibrium constants from the IR spectra.

An examination of the IR spectra of III-IX in the crystalline state demonstrated that III, IV, VII, and XI exist in the amino form, while VI and VIII-X exist as a mixture of two tautomeric forms (Fig. 2), which differs substantially from the tautomeric equilibrium of the synthesized substances in solutions and demonstrates that the nature of the substituent in the phenyl ring has little effect on the ratio of the tautomeric forms during crystallization.

In contrast to the spectra of solutions, the spectrum of crystalline 2-(p-hydroxyphenylimino)-4-thiazolidone (V) does not contain $\nu_{C=O}$ absorption, which is apparently due to the strong intermolecular hydrogen bonds of the hydroxyl group in the phenyl ring with the carbonyl group of the thiazolidine ring.

We will continue our investigation of the position of the tautomeric equilibrium. We thank N. A. Smorygo for his useful discussions of the IR spectra.

EXPERIMENTAL

2-Methylrhodanine. A suspension of 1.33 g (0.01 mole) of rhodanine in 50 ml of chloroform was heated with stirring to 40-50°, and 2 ml of methyl iodide and 1.01 g (0.01 mole) of triethylamine were added. The reaction mixture was stirred for 2 h, cooled to room temperature, and washed with water. The chloroform layer was dried with calcined Na_2SO_4, and the solvent was removed by vacuum distillation to give 1.35 g (93%) of a product with mp 82° (from ethanol). Found: N 10.6; S 43.4%. $C_4H_5NOS_2$. Calculated: N 10.9; S 43.6%.

2-Imino-4-thiazolidone (I). A total of 15 ml of 25% ammonium hydroxide was added to a solution of 1.47 g (0.01 mole) of 2-methylrhodanine in 20 ml of alcohol, and the mixture was stirred at 40-50° for 1 h. Another 15 ml of ammonium hydroxide was added, and the mixture was stirred for another hour. Three-fourths of the solvent was removed by vacuum distillation, and the precipitate was removed by filtration and washed with chloroform to give 0.98 g (85%) of a product with mp 240°. Found: N 24.0; S 27.8%. $C_3H_4N_2OS$. Calculated: N 24.1; S 27.6%.

2-(Phenylimino)-4-thiazolidone (VIII). A 1.01-g (0.01 mole) sample of triethylamine was added dropwise with vigorous stirring to a suspension of 1.33 g (0.01 mole) of rhodanine in ether, and the precipitated salt was removed by filtration, washed with ether, and dissolved in chloroform. A 7.1-ml sample of ethyl bromide was added to the solution, and the mixture was stirred at 40° for 4 h, after which 2.3 g (0.025 mole) of aniline was added. The reaction mass was then stirred at 50° for 3 h, cooled, washed with water, and dried with calcined Na_2SO_4. Half of the solvent was removed by distillation, and the addition of ether to the residue precipitated 1.44 g (75%) of cream-colored crystals with mp 176° (from acetone). Found: N 14.4; S 16.4%. $C_9H_8N_2OS$. Calculated: N 14.6; S 16.7%. Compounds II-VII and IX-XI were similarly obtained (Table 2).

The IR spectra of III-XI in the crystalline state in mineral oil were recorded with a UR-20 spectrophotometer, while the spectra of $3 \cdot 10^{-2}$ -$5 \cdot 10^{-4}$ solutions were recorded with an IKS-14A spectrophotometer with a NaCl prism.

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