8. A. A. Potekhin, I. G. Zenkevich, V. V. Sokolov, and S. M. Shevchenko, Zh. Org. Khim., 16, 1952 (1980).
9. A. A. Potekhin and E. A. Bogan'kova, Khim. Geterotsikl. Soedin., No. 11, 1461 (1973).

# METHYLATION OF 2-AMINO-$\Delta^2$-THIAZOLIN-4-ONE

Yu. G. Basova, S. M. Ramsh, and A. I. Ginak

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It is shown that the nucleophilicity of the sodium salt of 2-amino-$\Delta^2$-thiazolin-4-one with respect to dimethyl sulfate and methyl iodide is extremely low, regardless of the nature of the solvent. The anomalous (in the 4-thiazolidone series) behavior of this salt in methylation is explained by the low degree of heterolytic dissociation of the O—Na bond. The possible reasons for the inertness of the oxygen atom in the anions of 2-substituted 4-thiazolidones with respect to alkylating agents are discussed.

It is known that 2-substituted 4-thiazolidones are readily alkylated in an alkaline medium to give, as a rule, products of alkylation in the 2 and 3 positions. The ambident character of the anions of 2-oxo- [1], 2-thioxo- [2], and 2-aryliminothiazolidin-4-ones [3] makes it possible to assume that 2-amino-$\Delta^2$-thiazolin-4-one (I) (pseudothiohydantoin) would also display dual reactivity with respect to alkylating agents. The direct alkylation of I has not been reported, although its mono- and dimethyl derivatives, which were obtained from the corresponding thioureas [4], are known.

We were able to obtain the sodium salt (II) of 2-amino-$\Delta^2$-thiazolin-4-one, the IR spectrum of which does not contain carbonyl absorption bands, which constituted evidence for salt formation at the oxygen atom. The signal of the 5-methylene protons of II lies in the same region of the PMR spectrum as in the case of I. This excludes the possible (owing to enolization of the ketomethylene fragment of the molecule) enolate structure of the salt and confirms its lactim structure.

Although the sodium salts of 2-aryliminothiazolidin-4-ones are readily alkylated in ethanol [3], quite unexpectedly the degree of conversion of salt II in the case of methylation with dimethyl sulfate or methyl iodide in various solvents, viz., water, methanol, ethanol, acetone, acetonitrile, dimethylformamide (DMF), and dimethyl sulfoxide (DMSO), turned out to be very low (5-10%). Of course, it must be noted that salt II is virtually insoluble in all of the indicated solvents except water and DMSO. According to data from thin-layer chromatography (TLC), four products, the $R_f$ values of which coincide with the $R_f$ values for 2-methylamino-$\Delta^2$-thiazolin-4-one (III), 2-imino-3-methylthiazolidin-4-one (IV), 2,2-dimethylamino-$\Delta^2$-thiazolin-4-one (V), and 2-methylimino-3-methylthiazolidin-4-one (VI), which were obtained by alternative synthesis [4], are present in the reaction mixture. We were able to isolate the products from the reaction mixture in amounts necessary for identification only by means of column chromatography. These products were found to be identical to III-VI. Similarly, methylated derivatives III-VI can be isolated from the reaction mixture from methylation of I with dimethyl sulfate in methanol in the presence of an equivalent amount of sodium methoxide; in both cases the yields are very low ($\sim$5%) and considerably lower than in the methylation under similar conditions of the oxygen analog of I, viz., 2-amino-$\Delta^2$-oxazolin-4-one [5]. In the presence of dibenzo-18-crown-6-ether salt II dissolves in acetonitrile and is methylated by dimethyl sulfate; however, we were unable to separate the products from the crown ether.

The principal reason for the low nucleophilicity of salt II in reactions with methylating agents consists, in our opinion, either in the essentially covalent character of the

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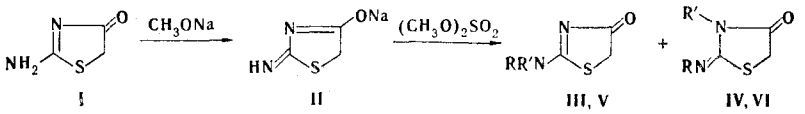

I II III, V IV, VI

III, IV R = H, R′ = $CH_3$; V, VI R = R′ = $CH_3$

O—Na bond [6] or, if charge separation nevertheless occurs, in shielding of the charge on the oxygen atom in the virtually undissociated unreactive Het—$O^-Na^+$ contact ion pair. These same factors are evidently responsible for the extremely low solubility of salt II. Its solubility in water is probably associated with solvation of the II molecule at the imino group (with the formation of an immonium compound), whereas its solubility in DMSO is probably fostered by the ability of this proton-acceptor solvent to form hydrogen bonds with the imino group. It is logical to assume that the degree of heterolytic dissociation of the O—Na bond is also negligibly small in these solvents, and this hinders methylation. If partial dissociation of the dissolved part of the salt at the O—Na bond to give "free" anions nevertheless occurs in hydroxy-containing solvents, as a result of solvolysis their concentration should be extremely low (the $pK_a$ of I in water is 11.7 [4]), especially since the salt is only slightly soluble even in refluxing alcohols. An attempt to methylate I in the presence of a fivefold excess of sodium alkoxide or hydroxide for generation of the anion was unsuccessful — the methylating agent was consumed in competitive alkaline solvolysis.

As in the case of other 4-thiazolidones, we did not observe the formation of O-methylation products. The isolation of products of alkylation at the oxygen atom has also not been reported for the analogous 4-azolidones, viz., 2-oxo- and 2-thioxooxazolidin-4-ones [7] and 2-oxo- [8] and 2-iminoimidazolidin-4-ones [9] (the isolation of O-alkyl derivatives in the alkylation of silver salts of 5,5-disubstituted 2-oxooxazolidin-4-ones in ether [7] constituted an exception). This is all the more surprising, since, judging from the spectral data, the negative charge in mesomeric anions of the corresponding compounds is evidently localized to a significant degree on the oxygen atom [10]; the salts are dissociated substantially in the solvents used for alkylation [11]. The hard-soft acid—base concept does not make it possible to satisfactorily explain this fact, since neither "soft" alkylating agents nor the "hard" proton attack the "hardest" oxygen atom of the ambident anions of 4-azolidones — the existence of 4-OH tautomers has never been reported, and this is evidently a general principle for five-membered heterocycles with similar structures [12]. According to the theory of prototropic tautomerism [13], the instability of the lactim or enol tautomeric forms consists in their greater acidity, which evidently exceeds the acidities of the stable tautomeric forms by several orders of magnitude. In this case neither term, viz., the basicity and the polarizability, in the Edwards nucleophilicity equation [14] will promote O-alkylation; however, the percentages of the alkylation products in kinetically controlled reactions of ambident anions are determined by the relative nucleophilicites of their reaction centers [14], and virtually no O-alkylation products are formed.

An alternative explanation consists in thermodynamic control of the O-alkylation reaction: The O center of the ambident anion is a "poor" nucleophile (the basicity and polarizability are relatively low) but a "good" leaving group [6], i.e., the O-alkyl derivatives of the compounds under consideration are strong alkylating agents, the O-alkylation reaction is reversible, and the thermodynamically more stable products of alkylation in the 2 and (or) 3 positions are formed as a result of alkylation.

The initial alkylation at the two reaction centers indicates the ambident character of the anion of I; however, the subsequent exhaustive methylation of the resulting monomethyl derivatives makes it impossible to study the quantitative characteristics of the dual reaction.

## EXPERIMENTAL

The PMR spectra were recorded with a Tesla BS-467 spectrometer (60 MHz) with hexamethyldisiloxane as the internal standard. The IR spectra were recorded with an IKS-29 spectrometer. The UV spectra of solutions of the compounds in ethanol were recorded with an SF-16 spectrophotometer. Thin-layer chromatography (TLC) was carried out on Silufol UV-254 plates with elution by ethanol—chloroform (1:10).

2-Amino-$\Delta^2$-thiazolin-4-one Sodium Salt (II). A 1.6-g (0.014 mole) sample of finely ground 2-amino-$\Delta^2$-thiazolin-4-one (I) was added to a refluxing solution of sodium ethoxide obtained from 1.5 g (0.065 mole) of sodium and 50 ml of absolute ethanol, after which the insoluble material was removed by rapid filtration. The salt that precipitated when the filtrate was cooled was washed with cold ethanol and dried *in vacuo* (2 mm) at 100°C to give 0.23 g (12%) of a product with mp 208-210°C. IR spectrum (thin layer): 3300, 3275 ($N_2'$—H); 1638 ($C_2$=$N_2'$); 1542, 1500 ($N_3$=$C_4$); 1322 $cm^{-1}$ ($C_4$—O). UV spectrum (in water) [this is actually the UV spectrum of I ($pK_a$ 11.7), since at a concentration of $\sim 10^{-4}$ mole/liter its salt was hydrolyzed completely], $\lambda_{max}$ (log $\varepsilon$): 220 (4.26) and 249 nm (3.88). PMR spectrum (in $d_6$-DMSO): 3.60 (2H, s, $C_5H_2$). Found: N 19.8; S 22.7%. $C_3H_3N_2NaOS$. Calculated: N 20.3, S 23.2%. The purity of samples of the salt was 95% according to the results of potentiometric titration.

Methylation of 2-Amino-$\Delta^2$-thiazolin-4-one (I). A 10-ml (0.10 mole) sample of dimethyl sulfate was added to 11.6 g (0.10 mole) of I in sodium methoxide solution prepared from 100 ml of methanol and 2.5 g (0.11 mole) of sodium, and the reaction mixture was refluxed for 2 h, after which it was cooled and filtered to remove the precipitated sodium methanesulfonate and unchanged I, and the filtrate was evaporated to dryness *in vacuo*. The residue was stirred with 100 ml of a 0.5 N solution of NaOH in 100 ml of methylene chloride, and the organic layer was dried with sodium sulfate for 12 h. The solvent was removed by distillation, and the residue (an oil) was chromatographed with a column (60 × 1.2 cm) filled with silica gel (Silpearl from Czechoslovakia) with elution by chloroform. The mixture was introduced into the column in solution in ethanol mixed with the adsorbent. The fractions were detected by means of TLC. The corresponding eluates were evaporated, and the isolated compounds were crystallized from suitable solvents [4]. No melting-point depressions were observed for mixtures with the previously synthesized compounds, and their UV spectra were also identical [4]. The yields and melting points of the methyl derivatives were as follows: 0.13 g (1.0%) of III with mp 196-198°C; 0.13 g (1.0%) of IV with mp 143-144°C; 0.31 g (1.0%) of IV with mp 143-144°C; 0.31 g (2.2%) of V with mp 77-78°C; 0.12 g (0.8%) of VI with mp 67-69°C.

Methylation of 2-Amino-$\Delta^2$-thiazolin-4-one Sodium Salt (II). A 10-ml (0.10 mole) sample of dimethyl sulfate was added to 13.8 g (0.10 mole) of II in 100 ml of methanol, and the reaction mixture was then treated as in the methylation of I. The yields of the methyl derivatives were as follows: 0.11 g (0.8%) of III, 0.12 g (0.9%) of IV, 0.42 g (2.9%) of V, and 0.15 g (1.0%) of VI. The melting points of the compounds obtained were in agreement with those presented above.

2-Methylamino-$\Delta^2$-thiazolin-4-one (III). A 2-ml sample of a 25% aqueous solution of methylamine was added to 1.0 g (7 mmole) of 2-methylthio-$\Delta^2$-thiazolin-4-one in 15 ml of ethanol, and the reaction mixture was allowed to stand at 20°C for 30 min. The resulting precipitate was removed by filtration and crystallized from water to give 0.72 g (78.5%) of a product with mp 197-198°C (mp 196-199°C [16]). IR spectrum (thin layer): 1630 ($C_2$=$N_3$) and 1695 $cm^{-1}$ ($C_4$=O). UV spectrum (in water), $\lambda_{max}$ (log $\varepsilon$): 229 nm (4.25). PMR spectrum (in $d_6$-DMSO): 9.43, 9.03 (1H, $N_2'$—H); 3.87 (2H, s, $C_5H_2$); 3.10, 2.85 (3H, $N_2'$—$CH_3$). Found: N 21.8; S 24.7%. $C_4H_6N_2OS$. Calculated: N 21.5; S 24.6%.

## LITERATURE CITED


1. K. A. V'yunov, A. I. Ginak, and E. G. Sochilin, Zh. Org. Khim., 14, 1075 (1978).
2. A. Masias, D. Torres, and I. P. Beletskaya, Zh. Org. Khim., 15, 665 (1979).
3. F. C. Brown, Chem. Rev., 61, 463 (1961).
4. S. M. Ramsh, A. I. Ginak, N. A. Smorygo, Yu. G. Basova, and E. G. Sochilin, Zh. Org. Khim., 14, 1327 (1978).
5. C. F. Howell, N. Q. Quinones, and R. A. Hardy, J. Org. Chem., 27, 1686 (1962).
6. H. Becker, Introduction to the Electronic Theory of Organic Reactions [Russian translation], Mir, Moscow (1977), pp. 202, 340.
7. J. B. V. Clark-Lewis, Chem. Rev., 58, 63 (1958).
8. E. Ware, Chem. Rev., 46, 403 (1950).
9. C. Lempert, Chem. Rev., 59, 667 (1959).
10. K. A. V'yunov, A. I. Ginak, and E. G. Sochilin, Zh. Prikl. Spektrosk., 27, 1071 (1977).
11. V. G. Sushchev, S. M. Ramsh, A. I. Ginak, and E. G. Sochilin, Zh. Org. Khim., 15, 1720 (1979).

12. I. D. Blackburne, M. J. Cook, and C. D. Johnson, Ann. Rep. Prog. Chem., B 69, 425 (1972).
13. M. I. Kabachnik, Zh. Vses. Khim. Ova., 7, 263 (1962).
14. J. O. Edwards, J. Am. Chem. Soc., 78, 1819 (1956).
15. S. A. Shevelev, Usp. Khim., 39, 1773 (1970).
16. E. Akerblom, Acta Chem. Scand., 21, 843 (1967).

# INVESTIGATION OF THE STRUCTURE OF 2H,6H-2,6-DIMETHYL-4-AMINO-1,3,5-DITHIAZINE BY IR SPECTROSCOPY

É. I. Kositsyna, B. A. Trofimov, G. M. Gavrilova, S. V. Amosova, and V. I. Gostevskaya

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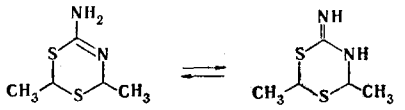
It was established by IR spectroscopy that 2H,6H-2,6-dimethyl-4-amino-1,3,5-dithiazine exists in the amino form in carbon tetrachloride at low concentrations.

Cyclic derivatives of thiourea are interesting subjects for the study of amino-imino tautomerism [1]. 2H,6H-2,6-Dimethyl-4-amino-1,3,5-dithiazine (I), which we synthesized by heterocyclization of divinyl sulfide with thiourea [2, 3], can, in principle, also exist in the II form.



I II

Amino form I with equatorially oriented methyl groups was preferred in an analysis of the PMR spectra of this heterocycle and its derivatives [4]. An independent solution of this problem can be obtained by IR spectroscopy.

In the present research we made a thorough analysis of the IR spectra of I and its 4-dideuteroamino derivative (the degree of deuteration was 70-75%), which were obtained in dilute solutions in carbon tetrachloride and chloroform, as well as in the crystalline state. Each form, i.e., I and II, individually gives two absorption bands in the region of NH stretching vibrations in the IR spectrum, whereas the I $\rightleftarrows$ II amino-imino equilibrium should be characterized by at least three (and possibly four) bands [5].

Two intense bands at 3387 and 3491 $cm^{-1}$, which, on the basis of the information in [5], could be assigned to symmetrical ($\nu_s$) and asymmetrical ($\nu_{as}$) NH vibrations in the $NH_2$ group, appear distinctly in the spectrum recorded in $CCl_4$ at a I concentration of $1 \cdot 10^{-3}$ mole/liter (Fig. 1, spectrum 1).

However, a deviation of 16 $cm^{-1}$ between the experimental $\nu_s$ value and the value calculated from the Bellamy dependence $\nu_s = 345.53 + 0.876\ \nu_{as}$, with a mean square error of 4.8 $cm^{-1}$ [6], is observed. Under the condition of the universality of this dependence, its nonfulfillment could constitute evidence for the erroneous selection of the structure.

However, the equation presented above was obtained for amines [6], and its applicability to thiourea fragments requires special proof. In a special case the bands belonging to structures I and II may overlap, but complete coincidence of the frequencies is unlikely, and the simultaneous existence of the two tautomers should therefore be excluded. The choice between structures I and II was made on the basis of an analysis of the position of the intensity (A) and the half width ($\nu_{1/2}$) of the IR absorption bands (Table 1).

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