SYNTHESIS AND REACTIONS OF 3-AMINO THIAZOLIDINE-2-THION-4-ONE DERIVATIVES.

1. CONVERSION OF 3-AMINO THIAZOLIDINE-2-THION-4-ONE DERIVATIVES TO SUBSTITUTED MERCAPTO-1,3,4-THIADIAZOLES

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The corresponding carboxymethylthiothiadiazoles are formed by the action of formic acid on 3-aminorhodanine and 3-(3-phenylthioureido)rhodanine, and the action of rhodaninemine on 3-(3-phenylthioureido)rhodanine leads to 2-anilino-5-carboxymethylthiothiadiazole anilide, whereas similar treatment of 3-ureidorhodanine leads to a semicarbazide derivative.

Continuing our investigation [1] of the reactions of derivatives of 3-aminothiazolidine-2-thion-4-one (I), we repeated its treatment with formic acid [2]. It has been proposed [3] that 3-formamidorhodanine (II) is formed in this case.

However, the properties of the compound that we obtained, the melting point of which was in agreement with the value presented in [2], were not in agreement with structure II. In contrast to ordinary 3-substituted rhodanines [4], this compound did not react with p-dimethylaminobenzaldehyde, although it did contain a methylene group according to the PMR spectral data (a signal at 4.0 ppm). The expected dye (III) was obtained by the action of formic acid on 3-amino-5-(p-dimethylamino)benzylidenethiazolidine-2-thion-4-one (IV). The structure of III was confirmed by data from the PMR spectrum, in which signals of protons of a phenyl ring and a dimethylamino group with chemical shifts of 7.45 and 3.08 ppm, as well as signals of C–H protons of methylidyne (7.58 ppm) and formamido (8.18 ppm) groups, are observed. The absorption maxima of solutions of dyes III and IV (470 and 472 nm) virtually coincide. One's attention is drawn to the fact that the chemical shifts of the C–H bond of the formamido group in III and of the C–H bond in the compound to which structure II was assigned (9.87 ppm) differ markedly, which indicates the absence of a formamido group in the latter. On the basis of the UV spectra it may be concluded that the product of the reaction of thiazolidine with formic acid also does not contain a rhodanine ring, since the absorption maximum of its solution (265 nm) is considerably higher than in the case of the corresponding solution of aminorhodanine (295 nm) [5].
Taking into account the data on the recyclization of some 3-acylaminothiazolidine-2-thion-4-ones to carboxymethylthio-1,3,4-thiadiazoles under the influence of hydrochloric acid and the absence of an analogous reaction for the compound with hypothetical structure II [6], we arrived at the conclusion that the initially formed formamido rhodanine II undergoes isomerization to carboxymethylthio-1,3,4-thiadiazole (V) during the reaction. In fact, V, which was synthesized from monochloroacetic acid and 2-mercapto-1,3,4-thiadiazole, was found to be identical to the product of the reaction of formic acid with rhodanine I according to the data from thin-layer chromatography (TLC) and the UV and PMR spectra and the melting point.

Similar transformations occur in the case of the action of aqueous solutions of acids also on other 3-aminorhodanine derivatives. For example, from 3-(3-phenylthioureido)thiazolidine-2-thion-4-one (VI) we obtained acid VII, the structure of which was also confirmed by data from the UV and PMR spectra and by alternative synthesis.

The formation of acids V and VII evidently may proceed either through a step involving opening of the thiazolidine ring (A) or through the formation of a triazolothiadiazole (B) with subsequent hydrolysis.

One might have assumed that other agents such as amines would also be capable of similarly opening the thiazolidine ring of 3-aminorhodanine derivatives, since it is apparent from the scheme presented above that the hydroxide ion (and, consequently, possibly other nucleophilic agents also) should participate in the indicated transformations. In fact, we found that the expected anilide (VIII) is formed by the action of aniline on rhodanine VI; however, X was obtained from 3-ureidothiazolidine-2-thion-4-one (IX).

The structures of the isolated products were confirmed by alternative synthesis; thus, for example, derivative VIII was synthesized from monochloroacetic acid anilide and 2-anilino-5-mercapto-1,3,4-thiadiazole.

The data obtained indicate that of the three electrophilic centers of the VI and VIII molecules, the electrophilicity of the carbon atom of the substituent in the 3 position of the thiazolidine ring has a substantial effect on the direction of the reactions.

EXPERIMENTAL

The PMR spectra of solutions of the compounds in CF₃COOH were measured with a Tesla BS-467 spectrometer (60 MHz) with hexamethyldisiloxane as the standard. The UV spectra of solutions of the compounds in CH₃OH were recorded with an SF-8 spectrophotometer.

3-Formamido-5-(p-dimethylaminobenzylidene)thiazolidine-2-thion-4-one (III). A mixture of 0.55 g (2 mmole) of benzylidene derivative IV and 5 ml of formic acid was refluxed for 2 h. The precipitate that formed after partial evaporation of the formic acid was removed by filtration and crystallized from alcohol to give 0.45 g of product (Table 1).

2-Anilino-5-carboxymethylthio-1,3,4-thiadiazole (VII). A) A mixture of 0.28 g (1 mmole) of rhodanine VI and 5 ml of 50% formic acid was heated at 100°C for 2 h, after which the solution was evaporated, and the residue was triturated with water. The product was removed by filtration and recrystallized.