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ANOMALOUS HETEROCYCLIZATION OF SULFUR-35 LABELED N-ALLYLTHIOUREAS IN PROTONIC ACID MEDIA

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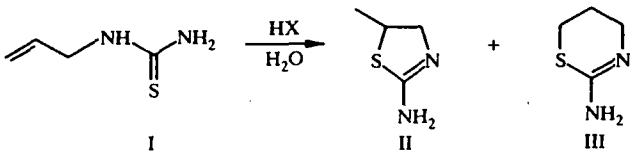
We have previously reported [1] that heterocyclization of sulfur-35 labelled N-allylthiourea (I*) under the influence of protonic acids leads to a whole spectrum of products which confirmed the result of synthetic practice in which this reaction has been used for the quantitative preparation of derivatives of 5-methyl-2-amino-2-thiazoline (II). In this paper we demonstrate that the result of heterocyclization of I under the influence of protonic acids depends substantially on the sulfur isotope in the molecule. We have compared the composition of the reaction products from thiourea I, unlabelled and labelled with sulfur-35.

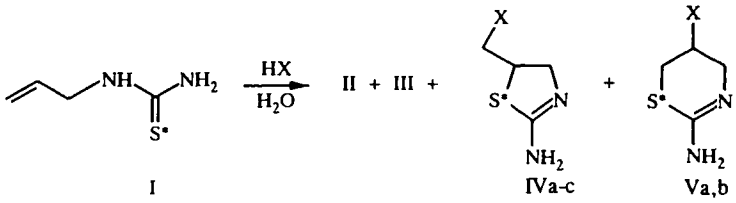
We prepared [^{35}S]-N-allylthiourea (I*) by isotopic exchange with elemental sulfur-35 and studied its cyclization in aqueous solutions of protonic acids by radiochromatography (after careful multistage purification).

As expected, almost the only product of cyclization of unlabelled thiourea I on heating in aqueous solution with protonic acids (HX, X = Cl, Br, HSO_4) is 5-methyl-2-amino-2-thiazoline (II). Formation of traces of the isomeric 2-amino-5,6-dihydro-4H-1,3-thiazine (III) was also observed (not more than 1-1.5% of III when the reaction had gone 100% to completion). The composition of the reaction products was by ^{1}H NMR spectroscopy (after complete removal of the aqueous solutions of the acids in vacuum). In addition, the cyclization of thiourea I in 1.0 mol/liter D_2SO_4 in D_2O at 95°C in an ampule in the cavity of the NMR spectrometer was studied. In this case also, only the formation of heterocycles II and III was observed and the content of the latter did not exceed 1-1.5% even at high degrees of conversion.



I II III

Under the same conditions, cyclization of 35-sulfur labelled I* under the influence of aqueous halogen-containing acids gave not only the thiazoline II and the dihydrothiazine III but also the anomalous reaction products 5-halogenomethyl-2-amino-2-thiazolines (IVa and b) and 5-halogeno-5,6-dihydro-4H-1,3-thiazines (Va and b), and under the influence of sulfuric acid 5-hydroxymethyl-2-amino-2-thiazoline (IVc). In addition, in all cases a considerable increase (compared with cyclization of unlabelled thiourea I) was observed in the content of the dihydrothiazine III in the reaction mixtures, sometimes reaching 20%.



I IVa-c Va,b

IV,Va X = Cl, b X = Br, IVc X = OH

The quantity of anomalous cyclization products in these reactions depends strongly on the following factors: 1) the specific radioactivity of the initial thiourea I; 2) the acid concentration; 3) the content of halogen ions in the solution.

Evidently, the basic cause of these results is radiolysis of the sulfur-35 labeled thiourea (I*) caused by β-decay of the sulfur-35 which generates epithioradicals similar to intermediates formed during the reduction of heterocycles IV and V by metals in acidic media [2].

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