CYCLIZATION OF SOME SUBSTITUTED 2-(N-ACYLTHIOUREIDO)-3-CARBETHOXYTHIOPHENES

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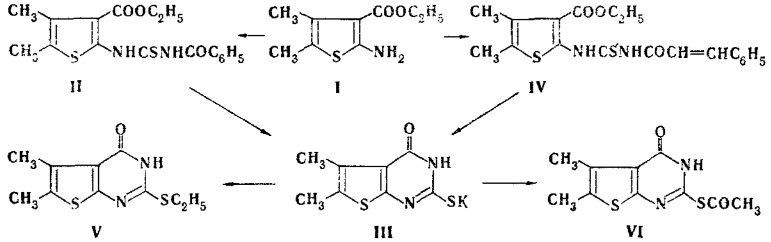
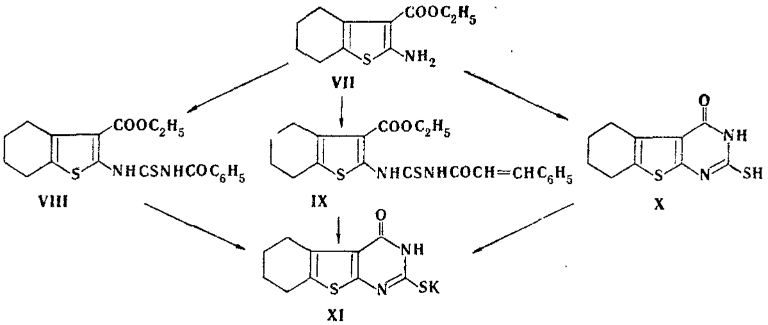
The intramolecular cyclization of 2-(N-acylthioureido)-3-carbethoxy-4,5-R,R'-thiophenes with the formation of potassium salts of 2-thio-4-oxo-5,6-R,R'-3,4-dihydrothieno[2,3-d] pyrimidine was studied, and some of their S-derivatives were obtained.

The intramolecular cyclization of thiophenes containing a 2-N-R-thioureido group, namely, 2-(N-acylthioureido)-3-carbethoxy-4,5-R,R'-thiophenes (AT), leads to pyrimidinothiophenes. The AT were obtained by reaction of 2-amino-3-carbethoxy-4,5-dimethylthiophene [1] (I) and 2-amino-3-carbethoxy-4,5,6,7-tetrahydrobenzo[d]thiophene [1] (VII) with benzoyl and cinnamoyl isothiocyanates (II, IV, VIII, and IX).



Heating II and IV in alkali solution gives potassium salt III, which reacts readily with some halo derivatives to give S-derivatives V and VI.

Similarly, potassium salt XI was obtained from VIII, IX, and X [2].



The cyclization of AT under the influence of alkali takes place with splitting out of acyl groups and formation of condensed pyrimidinothiophenes that do not contain a substituent in the 3-position of the pyrimidine ring.

It might have been assumed that the cyclization of AT would give 3-N-acyl derivatives of the pyrimidine ring, which are hydrolyzed with splitting out of acyl groups by the action of excess alkali. To verify this assumption, we carried out the cyclization of AT with a two-fold amount and equimolecular amounts of alkali. In the first case, III and XI were formed, while in the second case a mixture from which ~38%

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of cyclic products III and XI and $\sim$42% of starting AT were isolated is formed. Thus, the cyclization of AT with alkali is accompanied by simultaneous splitting out of acyl groups and is not accompanied by hydrolysis of 3-N-acyl derivatives of the pyrimidine ring.

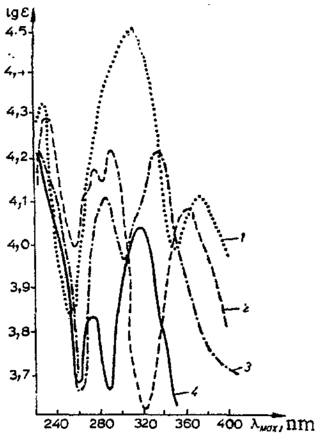

Fig. 1. UV spectra: 1) 2-(N-cinnamoylthioureido)-3-carbethoxy-4,5-dimethylthiophene (IV); 2) 2-(N-benzoylthioureido)-3-carbethoxy-4,5-dimethylthiophene (II); 3) potassium salt of 2-thio-4-oxo-5,6-dimethyl-3,4-dihydrothieno[2,3-d]pyrimidine (III); 4) 2-ethylthio-4-oxo-5,6-dimethyl-3,4-dihydrothieno[2,3-d]pyrimidine (V).

Four absorption maxima are observed in the UV spectra of II and VIII, while three absorption maxima are observed in the UV spectra of IV and IX. The intense absorption band at 230-240 nm (log ε 4.0-4.3) is associated with the fact that these compounds exist in the thione form in alcohol solution (Fig. 1).

The UV spectra of S-derivatives V and VI are similar, and inasmuch as these compounds exist in the thiol form, the absorption band at 230-240 nm is absent in their spectra; this is in agreement with the data in [3, 4]. Potassium salt XI has two absorption maxima at 285 and 335 (log ε 4.20, 4.36).

The absorption band at 355-370 nm of II, IV, VIII, and IX corresponds to the absorption of the acylthioureido chromophore. The intense absorption bands at 260-340 nm are due to absorption of the aromatic systems.

The UV spectroscopic data, a number of alternative syntheses, and the results of elementary analysis confirm the correctness of the schemes presented above.

EXPERIMENTAL

The UV spectra of alcohol solutions (c $1 \cdot 10^{-5}$ to $1 \cdot 10^{-2}$ M) were recorded with an SF-4 A spectrophotometer.

2-(N-Benzoylthioureido)-3-carbethoxy-4,5-dimethylthiophene (II). A 2-g (0.01 mole) sample of I and 1.6 g (0.01 mole) of benzoyl isothiocyanate were heated in ethanol for 30 min on a boiling-water bath. Workup of the mixture gave 3.4 g (94%) of a product with mp 195-197° (from benzene). Found: C 56.3; N 7.8; S 17.8%. $C_{17}H_{18}N_2O_3S_2$. Calculated: C 56.3; N 7.7; S 17.7%.

2-(N-Cinnamoylthioureido)-3-carbethoxy-4,5-dimethylthiophene (IV). A 2-g (0.01 mole) sample of I and 1.9 g (0.01 mole) of cinnamoyl isothiocyanate were heated in benzene on a boiling-water bath for 1 h. Workup of the mixture gave 3.4 g (87%) of a product with mp 191-193° [from dimethyl sulfoxide (DMSO)]. Found: N 7.3%. $C_{19}H_{20}N_2O_3S_2$. Calculated: N 7.2%.

Potassium Salt of 2-Thio-4-oxo-5,6-dimethyl-3,4-dihydrothieno[2,3-d]pyrimidine (III). A mixture of 3.6 g (0.01 mole) of II or 3.9 g (0.01 mole) of IV and 1.1 g (0.02 mole) of potassium hydroxide in aqueous alcohol solution was heated on a boiling-water bath for 2 h. Workup of the mixture gave 1.9 and 1.8 g (75 and 72%, respectively) of products with mp > 350° (from aqueous ethanol). Found: C 38.6; N 11.2%. $C_8H_7KN_2OS_2$. Calculated: C 38.6; N 11.2%. No melting-point depression was observed for mixtures of the products.

2-Ethylthio-4-oxo-5,6-dimethyl-3,4-dihydrothieno[2,3-d]pyrimidine (V). A mixture of 2.5 g (0.01 mole) of III and 1.1 g (0.01 mole) of ethyl bromide in ethanol was heated for 1 h at 50-60°. Workup gave 1.8 g (76%) of a product with mp 230-231° (from methanol). Found: N 11.8%. $C_{10}H_{12}N_2OS_2$. Calculated N 11.7%.

2-Acetylthio-4-oxo-5,6-dimethyl-3,4-dihydrothieno[2,3-d]pyrimidine (VI). A mixture of 2.5 g (0.01 mole) of III and 0.8 g (0.01 mole) of acetyl chloride was heated in benzene at 50-60° for 30 min. Workup gave 2.2 g (87%) of a product with mp 272° (decomp., from DMSO). Found: N 11.0%. $C_{10}H_{10}N_2O_2S_2$. Calculated: N 11.0%.

2-(N-Benzoylthioureido)-3-carbethoxy-4,5,6,7-tetrahydrobenzo[d]thiophene (VIII). A 1.65-g (0.01 mole) sample of benzoyl isothiocyanate was added to 2.25 g (0.01 mole) of VII, which dissolved with the evolution of a considerabel amount of heat. The melt began to crystallize on cooling. Workup gave 3.7 g (95%) of a product with mp 163-164° (from methanol). Found: N 7.3%. $C_{19}H_{20}N_2O_3S_2$. Calculated: N 7.2%.

2-(N-Cinnamoylthioureido)-3-carbethoxy-4,5,6,7-tetrahydrobenzo[b]thiophene (IX). This compound was obtained from VII by the method used to obtain IV. Workup gave 78% of a product with mp 202-204° (from benzene). Found: N 6.8%. $C_{21}H_{22}N_2O_3S_2$. Calculated: N 6.8%.

Potassium Salt of 2-Thio-4-oxo-3,4,5,6,7,8-hexahydrobenzo[b]thieno[2,3-d]pyrimidine (XI). This compound was similarly obtained from VIII and IX by the method used to obtain III. An equimolecular amount of potassium hydroxide was used in the preparation of XI from X [2]. The yields were 80, 74, and 69% from VIII, IX, and X, respectively; mp 345° (decomp., from aqueous ethanol). Found: N 10.2%. $C_{10}H_9KN_2OS_2$. Calculated: N 10.1%. No melting-point depression was observed for mixtures of the products.

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