CYCLOADDITION OF DIVINYL SULFIDE TO THIOUREA*

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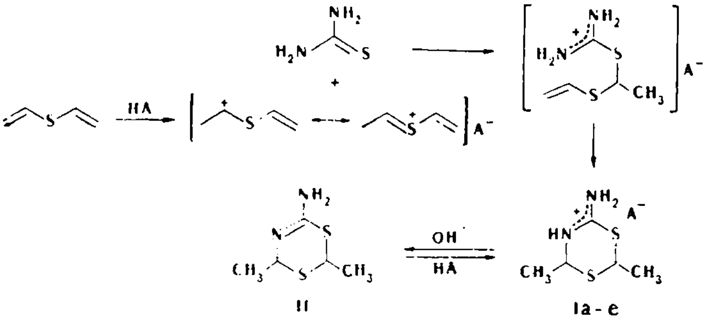
Data on the addition of thiourea to the double bond are limited. The data basically are from papers [2-4] dealing with the addition of thiourea to electrophilic alkenes. The preparation of S-[β-(2- or 4-pyridyl)ethyl]isothiuronium salts by reacting thiourea with 2- or 4-vinylpyridine in the presence of p-toluenesulfonic acid (p-TSA) has been reported [5]. The reactions of thiourea with some α,β-unsaturated carbonyl compounds and divinyl sulfone [6] have been investigated. The addition of thiourea to unsaturated glycidyl ethers in the presence of acids takes place at the epoxide group [7].

The formation of new heterocyclic systems can be expected from the reaction of divinyl sulfide with thiourea. In fact, as our investigations showed [8], divinyl sulfide adds thiourea smoothly in the presence of strong acids forming 2H,6H-2,6-dimethyl-4-amino-1,3,5-dithiazine salts (Ia-e).



Ia A=Cl; b A=Br, c A=ClO_4; d A=NO_3, e A=$O_3SC_6H_4CH_3$-4

Salts Ia-e are obtained by mixing the reagents in equimolar amounts (or with a slight excess of the divinyl sulfide) in aqueous or alcoholic media at 40-50°C; the yield is 70-90%. The use of alcohol instead of water as the solvent permits one to create a homogeneous medium that enables one to increase the yield 10-20%.

The cycloaddition is realized only in the presence of acids. Their nature exerts a controlling effect on the course of the reaction. No cycloadducts can be obtained with such acids as acetic, trifluoroacetic, and dimethyldithiophosphoric acids. The dependence of the course of the reaction on the strength of the acid indicates that the cyclization begins with the protonation of the divinyl sulfide double bond and the formation of a carbosulfonium ion which is further stabilized by the thiourea molecule. The subsequent protonation of the second double bond of the intermediate is completed by the ring closure. In order to initiate the reaction according to this scheme, equilibrium concentrations of the strong acids present in the reaction mixture through the dissociation of the isothiuronium salts are sufficient.

The introduction of an electron-acceptor substituent into the divinyl sulfide molecule affects the process unfavorably; this agrees with the proposed protophilic cyclization scheme. Thus di(β-phenylvinyl) sulfide does not react with thiourea under the same conditions; only the cis-trans isomer ratio changes for it.

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Oxidized divinyl sulfide derivatives also lose their ability to cycloadd thiuronium salts together with their losses in protophilicity. For example, one fails to obtain the analogs of cyclic salts Ia-e from divinyl sulfoxide, which as is known is quite inactive in electrophilic addition reactions. Instead of them, linear bis adducts are formed through a nucleophilic addition mechanism.† Divinyl sulfone yields diethyl sulfone bis(s-isothiuronium)-p-toluenesulfonate [6] with thiourea in the presence of p-TSA.

Free 2H,6H-2,6-dimethyl-4-amino-1,3,5-dithiazine (II) can be obtained by reacting salts I with an alkali; II again forms salts Ia-e with aqueous acid solutions. Neutralization of compound II with acids also permits one to synthesize the salts which cannot be obtained by the direct reaction of divinyl sulfide with thiourea. Thus trifluoroacetate If was obtained for example.

The feasibility of synthesizing the various salts of II by an exchange reaction was demonstrated by reacting hydrochloride Ia with an aqueous lead nitrate solution, which results in nitrate Id.

Two doublets of the CH_3 groups in the 1.58-1.68 ppm region are observed in the PMR spectrum of compounds Ia-f (the chemical shifts of both CH_3 groups coincide in the spectra of Ia, b, e), and accordingly so are two quartets of the methine protons in the $CH-CH_3$ fragments at 4.98-5.20 ppm with a spin-spin coupling constant of 6.5 Hz.

The signals of the methyl (1.48 and 1.50 ppm) and especially of the methine protons (4.49 and 4.66 ppm) are shifted toward the strong field in the spectrum of the free base II; at this time shielding of the remaining NH protons increases by several ppm at once.

The methyl groups of compounds Ia-f and II can have a cis or trans position relative to the plane of the ring. However, the possible doubling of the signals in the PMR spectrum is not observed. Consequently, either the cycloaddition of the isothiuronium salts to divinyl sulfide proceeds stereospecifically with the formation of a single isomer or both isomers for all the compounds have the same chemical shifts of the protons in the PMR spectra: the latter has little probability.

The IR spectra of salts Ia-f contain several maxima in the 3000-3450 cm^{-1} region corresponding to the symmetrical and antisymmetrical NH stretching vibrations. The intense absorption at 1590-1670 cm^{-1} is attributable to the planar NH deformation vibrations; here the absorption of the $C{=}N$ bond decreases. The stretching vibrations of the $C-S$ bond appear in the 600-730 cm^{-1} region. The methyl groups have two bands with frequencies of 1320-1380 and 1450 cm^{-1} (the symmetrical and asymmetrical $C-H$ deformation vibrations) and an absorption in the 2820-2910 cm^{-1} region ($C-H$ stretching vibrations). The bands which characterize the stretching vibrations of the NO_3^- group (1385 cm^{-1}) and the deformation vibrations of the $-O-N-O-$ group (840 cm^{-1}) are clearly expressed in the spectrum of salt Id.

There is an intense band (log ε 3.5-4.4) with a maximum at 210-220 nm, which can be attributed to the $\pi-\pi^*$ transition of the $C{=}N$ bond, in the UV spectrum of adducts Ia, d, e. Thus the absence of the $C{=}S$ group in the adducts is confirmed, since the thione chromophore of the thiourea derivatives absorbs in the longer wave region (225-300 nm), as is known [2].

EXPERIMENTAL

The PMR spectra of 20% solutions of products Ia-f and II in CD_3OD and DMSO-d_6 were run on a Tesla BS-487-C spectrometer (80 MHz); TMS was the internal standard. The IR spectra were run on a UR-20 instrument as KBr pellets.

The Reaction of Divinyl Sulfide with Thiourea in the Presence of Acids (general method). A total of 3.75 g (0.049 mole) of thiourea, 30 ml of alcohol, and an aqueous solution (10-13 ml of H_2O) of 0.049 mole of acid was agitated for 30 min at room temperature. The temperature was increased to 50°C and 5.3 g (0.06 mole) of divinyl sulfide was added. The reaction mixture was stirred for 6 h. The solvents were evaporated in vacuo, the viscous liquid formed was dissolved in a minimum of ethanol, and precipitated in dry ether (the operation was repeated three times). After drying the substance in vacuo (2 mm, 50°C) white hygroscopic powders usually melting at a lower temperature than the crystalline samples were obtained. Nitrate Id was an exception; it crystallized nicely from ethanol. The other salts crystal-

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†These data obtained together with N. K. Gusarova and G. G. Efremova will be discussed separately in more detail.

TABLE 1. 2H,6H-2,6-Dimethyl-4-amino-1,3,5-dithiazine Salts (II)

Compound	mp, °C (ethanol)	Found, %					Empirical formula	Calculated, %				
		C	H	Hal	N	S		C	H	Hal	N	S
Ia	144—145*	—	—	18,2	13,9	32,5	$C_5H_{11}ClN_2S_2$	—	—	17,8	14,1	32,3
Ib	136—137*	—	—	32,9	11,5	26,6	$C_5H_{11}BrN_2S_2$	—	—	32,9	11,5	26,4
Ic	89—91*	—	—	13,3	10,9	24,5	$C_5H_{11}ClN_2O_4S_2$	—	—	13,5	10,7	24,4
Id	135—137*	26,3	4,9	—	18,7	28,4	$C_5H_{11}N_3O_3S_2$	26,6	4,9	—	18,6	28,5
Ie	115—117	43,3	5,5	—	8,6	28,9	$C_{12}H_{18}N_2O_3S_3$	43,1	5,4	—	8,4	28,8
If	125,5—126,5	30,1	4,1	20,2	10,1	23,1	$C_7H_{11}F_3N_2O_2S_2$	30,4	4,0	20,6	10,1	23,2
II	100—101	37,2	6,2	—	17,3	39,2	$C_5H_{10}N_2S_2$	37,0	6,2	—	17,3	39,5

*With decomposition.

lized upon prolonged standing. The physical constants and analytical data of the products obtained are given in Table 1.

2H,6H-2,6-Dimethyl-4-amino-1,3,5-dithiazine (II). To 60 ml of the aqueous nitrate solution (6.5 g, 0.029 mole) was added with stirring 58.2 ml of 0.5 N KOH (0.029 mole); agitation was continued for 4 h at room temperature. Then the mixture was extracted with ether (30 × 4 ml). The ether was evaporated in vacuo. After drying in vacuo (2 mm, 50°C), 4.4 g (95%) of base II was obtained; after recrystallization from ethanol the mp was 100-101°C (Table 1).

Reaction of Dithiazine II with Acids. To 2 g (0.012 mole) of base II in ethanol (20 ml) was added 2.2 ml of 5 N HNO_3 (0.78 g of HNO_3; 0.012 mole); the mixture was kept at room temperature for 6 h. After evaporating the solvent in vacuo, 2.7 g (97%) of a crystalline product was obtained; after recrystallization from ethanol the mp was 135-136°C (with decomp.). A mixed melting point with the sample of Id obtained by the reaction of divinyl sulfide with thiourea and HNO_3 did not yield a melting-point depression. Similarly the salts with HCl (Ia), HBr (Ib), $HClO_4$ (Ic), $4\text{-}MeC_6H_4SO_3H$ (Ie), and CF_3COOH (If) were obtained from base II.

The salts obtained this way (quantitative yield) crystallize better, and have a sharp melting point.

Reaction of 2H,6H-2,6-Dimethyl-4-amino-1,3,5-dithiazine Chloride (Ia) with $Pb(NO_3)_2$. To 30 ml of an aqueous solution (6.8 g, 0.034 mole) of salt Ia with agitation was added 20 ml of an aqueous $Pb(NO_3)_2$ solution (5.7 g, 0.017 mole). A white precipitate immediately became apparent, which within an hour became orange. The precipitate was separated out, washed with ethanol, and ether. White crystals contaminated with the orange precipitate were isolated from the alcohol—ether fraction. After several recrystallizations from ethanol 1 g (13%) of nitrate Id was obtained, mp 135-136°C (with decomp.). The IR spectrum was identical to the spectrum of salt Id synthesized from divinyl sulfide, thiourea, and HNO_3. The orange precipitate was washed with hot water from which white $PbCl_2$ needles precipitated upon cooling.

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