INVESTIGATION OF NITROGEN- AND SULFUR-CONTAINING HETEROCYCLES. 39.* REACTIONS OF 2-MERCAPTO-3-UREIDO- AND 2-MERCAPTO-3-AMINOPYRIDINES WITH β-HALO CARBONYL COMPOUNDS. SYNTHESIS OF 6-OXO DERIVATIVES OF PYRIDO[2,3-b][1,5]THIAZEPINES

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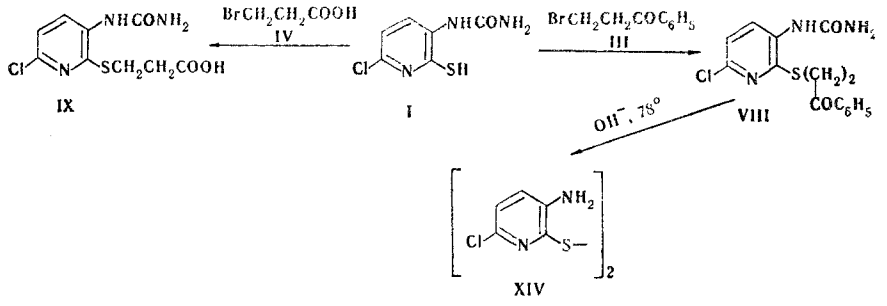
The reaction of 2-mercapto-3-ureido- and 2-mercapto-3-aminopyridines with β-halo derivatives of carbonyl compounds (ketones, acids, and aldehydes) and with acrylonitrile proceeds not only via the mercapto group but also via the amino group, as a result of which S-β-keto(carboxy, cyano)alkyl, N,S-bis(β-ketoalkyl), and N,S-diacyl derivatives of pyridine are formed. The action of acids, alkalis, and dehydrating agents on 2-S-β-keto(carboxy, cyano)ethyl-3-aminoureidopyridines was studied. A method for the preparation of derivatives of a new heterocyclic system, viz., 6-oxopyrido[2,3-b][1,5]thiazepine, by the reaction of 2-mercapto-3-aminopyridines with β-bromopropionic acid and subsequent treatment of 2-(β-carboxyethyl)thio-8-aminopyridines with dicyclohexylcarbodiimide was developed.

In a continuation of our earlier research [1, 2, 5] and on the basis of the interest in 1,5-benzodiazepine derivatives and condensed thiazepine derivatives in connection with the search for biologically active substances we looked into the possibility of the synthesis of similar compounds in the pyrido[2,3-b][1,5]thiazepine series. With this end in mind we investigated the reaction of 2-mercapto-3-amino-6-chloro(methoxy)pyridine (IIa, b) with β-halo carbonyl compounds (III-VI), as well as with acrylonitrile (VII), which readily adds to compounds that have a labile hydrogen atom [3]. We established that in the reaction of 2-mercapto-3-ureidopyridine (I) with β-bromopropiophenone (III) and β-bromopropionic acid (IV) in the presence of an equimolar amount of alkali 2-(β-benzoylethyl)thio-3-ureido-6-chloropyridine (VIII) and 2-(β-carboxyethyl)thio-3-ureido-6-chloropyridine (IX) are formed.

Scheme 1



The reaction of 2-mercapto-3-amino-6-chloropyridine (IIa) with β-bromopropiophenone (III) in the presence of alkali proceeds at both the mercapto and amino groups and leads to 2-(β-benzoylethyl)thio-3-(β-benzoylethyl)amino-6-chloropyridine (X). 2-(β-Benzoylethyl)-thio-3-amino-6-chloropyridine (XI) was obtained when the latter reaction was carried out under milder conditions. In contrast to the spectrum of XI, the absorption band of a primary amino group is absent in the IR spectrum of thio ether X, but the spectrum does contain an NH band (3360 cm^{-1}) and bands of two CO groups (1670, 1680 cm^{-1}) (see Table 1). α-Methyl-β-(3-amino-6-chloro-2-pyridyl)thiobutenal (XII) was obtained in the reaction of

*See [5] for Communication 38.

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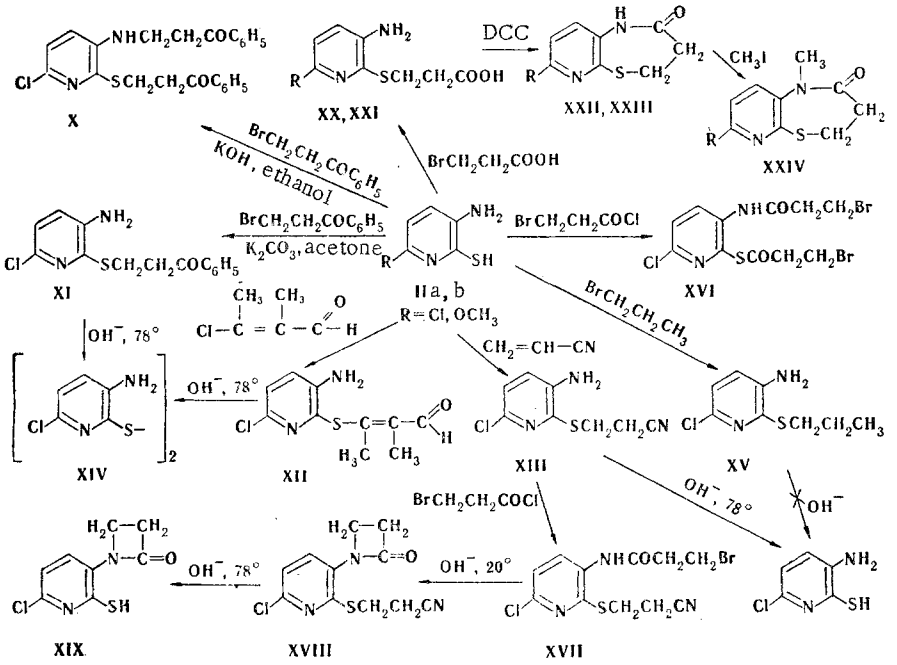
TABLE 1. Analytical and Spectral Data for the Compounds Obtained

Compound	mp, °C	IR spectra, cm^{-1}	UV spectra, λ_{max}, nm (log ε)	PMR spectra, δ, ppm	Found, %					Empirical formula	Calculated, %					Yield, %
					C	H	Cl	N	S		C	H	Cl	N	S	
VIII	172—175	1670 (CO), 1700 (CO), 3320, 3420 (NH, NH_2)	247 (4,28), 310 (3,83)	—	53,9	4,1	10,6	12,5	9,7	$C_{15}H_{14}ClN_3O_2S$	53,7	4,2	10,6	12,5	9,6	76
IX	178—180	1670 (CO), 1720 (CO), 3280, 3450 (NH, NH_2)	—	—	38,9	3,6	12,3	15,3	11,6	$C_9H_{10}ClN_3O_3S$	39,2	3,6	12,4	15,2	11,6	49
X	121—122	1670 (CO), 3360 (NH)	—	3,45, 3,29	65,2	5,0	8,6	6,6	7,4	$C_{23}H_{21}ClN_2O_2S$	65,0	5,2	8,3	6,6	7,5	38
XI	106—107	1680 (CO), 3200, 3300 (NH_2)	245 (4,3), 325 (3,9)	—	57,7	4,4	12,2	9,5	10,9	$C_{14}H_{13}ClN_2OS$	57,4	4,5	12,1	9,6	10,9	66
XII	120—121	1640—1660 (C=C—C=O), 3320, 3420 (NH_2)	—	—	49,3	4,8	14,4	11,6	13,3	$C_{10}H_{11}ClN_2OS$	49,5	4,6	14,6	11,5	13,2	56
XIII	93—95	2260 (CN), 3360, 3340 (NH_2)	—	—	44,9	3,9	16,5	19,9	14,7	$C_8H_8ClN_3S$	44,9	3,7	16,6	19,6	15,0	90
XIV[a]	210—212															
XV[b]	162—165	2500 (NH_3^+)	260 (3,98)	—	40,3	5,1	29,3	11,6	13,7	$C_8H_{12}Cl_2N_2S$	40,1	5,1	29,6	11,7	13,4	98
XVI	122—123	1690—1710 (CO), 3350 (NH)	—	—	31,0	2,4	—	6,5	7,4	$C_{11}H_{11}Br_2ClN_2O_2S$	30,7	2,5	—	6,5	7,4	64
XVII	113—114	2250 (CN), 1660 (CO), 3100, 3250 (NH)	—	—	38,0	3,3	33,0	12,1	9,0	$C_{11}H_{11}BrClN_3OS$	37,9	3,2	33,1	12,1	9,2	81
XVIII	130—132	1750 (CO), 2250 (CN)	—	3,84, 3,4, 3,1, 2,9 (4 CH_2)	49,0	3,6	13,1	15,9	11,6	$C_{11}H_{10}ClN_3OS$	49,3	3,7	13,2	15,7	11,9	87
XIX	185—187	1750 (CO), 3250, 3360 (NH_2)	258 (4,0), 326 (3,89)	—	44,7	3,5	16,8	12,8	14,6	$C_8H_7ClN_2OS$	44,7	3,3	16,5	13,1	14,9	50
XX	130—131	1710 (CO), 3350, 3430 (NH_2)	242 (3,99), 327 (3,9)	—	41,5	4,1	15,1	11,9	14,1	$C_8H_9ClN_2OS$	41,3	3,9	15,2	12,1	13,8	77
XXI	120—121	1700 (CO), 3260, 3310 (NH_2)	250 (3,7), 305 (3,5)	3,56, 2,73 (CH_2)	47,2	5,2	—	12,1	14,3	$C_9H_{12}N_2O_3S$	47,3	5,3	—	12,2	14,1	52
XXII	180—182	1640 (CO), 3310 (NH)	306 (3,47)	—	45,1	3,4	16,6	12,7	15,1	$C_8H_7ClN_2OS$	44,8	3,3	16,5	13,1	14,9	87
XXIII	212—213	1640 (CO), 3310 (NH)	—	—	51,8	5,1	—	13,4	15,5	$C_9H_{10}N_2O_2S$	51,4	4,8	—	13,3	15,2	86
XXIV	121—122	1670 (CO)	—	—	47,0	3,6	15,1	12,4	13,9	$C_9H_9ClN_2OS$	47,2	3,9	15,5	12,2	14,0	81

[a]See [6]. [b]Compound XV was characterized in the form of the hydrochloride. The compounds were crystallized: VIII-X, XIV, XVI, XVIII, XIX, XXII, and XXIII from ethanol, XII, XIII, XVII, and XXI from benzene, XX from water, XI from cyclohexane, XXIV from hexane, and XV from acetone.

pyridine II with β-chlorobutenal (V) in the presence of an equimolar amount of alkali. The reaction of pyridine II with acrylonitrile (VII) in aqueous alkali at room temperature gives 2-(β-cyanoethyl)thio-3-amino-6-chloropyridine (XIII). The structures of thio ethers IX-XIII were confirmed by analytical and spectral data (Table 1).

Scheme 2



We then ascertained the ability of thio ethers IX-XIII to undergo cyclization under the influence of alkaline (NaOH, C_2H_5ONa) and acidic (HCl, $POCl_3$) agents and dehydrating agents (P_2O_5). We noted that thio ethers VIII, IX, and XI, in contrast to the previously obtained 2-phenylacylthio-3-ureido- and 2-phenacylthio-3-aminopyridines [1, 2], are stable substances: They remain unchanged when they are refluxed in high-boiling solvents and do not undergo cyclization to pyridothiazepines when they are treated with alcoholic alkali or sodium ethoxide or in the presence of acids, phosphorus oxychloride, and phosphorus pentoxide. When thio ethers VIII, IX, and XI-XIII are heated with alkali, they are converted to starting pyridines I and II or to bis(3-amino-6-chloro-2-pyridyl) disulfide (XIV). This process is facilitated by the presence in the β position of strong electron-acceptor groups (COOH, CN, CO), which promote detachment of a proton from the adjacent carbon atom, and evidently proceeds via a mechanism of the β-elimination type. This assumption is confirmed by the fact that in compounds that contain an alkyl substituent attached to the sulfur atom, as, for example, in the case of 2-propylthio-3-amino-6-chloropyridine (XV), cleavage of the alkyl group does not occur not only under the conditions indicated above but also under more severe conditions.

We have previously observed that a carbamide residue in 2-phenacylthio-3-ureido- and 2-carboxymethylthio-3-ureidopyridines is split out exceptionally easily in the process of cyclization to pyridothiazines [1]. In contrast to these compounds, the carbamide residue in thio ethers VIII and IX is not split out under rather severe conditions, i.e., when they are heated with alkali.

During a study of the reaction of pyridine II with β-bromopropionyl chloride (VI) we observed that acylation proceeds simultaneously at the amino and mercapto groups and that this leads to the production of an N,S-diacyl derivative (XVI). The structure of XVI is confirmed by the presence in the IR spectrum of NH (3320 cm^{-1}) and CO (an extensive band at 1700-1720 cm^{-1}) absorption bands. In subsequent experiments the mercapto group in II was protected by a cyanoethyl group, which, as we noted above, is readily split out under the influence of alkalis. The reaction of cyanoethyl derivative XIII with acid chloride VI gave 2-(β-cyanoethyl)thio-3-(β-bromopropionyl)amino-6-chloropyridine (XVII). When pyridine XVII was treated with alcoholic alkali even in the cold, instead of the expected cyclization with splitting out of a cyanoethyl residue, we observed splitting out of hydrogen bromide with simultaneous formation of a β-lactam ring, as a result of which 2-β-cyanoethylthio-3-

N-(1'-aza-2'-cyclobutanonyl)-6-chloropyridine (XVIII) was formed. When pyridine XVIII was heated in alcoholic alkali, it was converted to 2-mercapto-3-N-(1'-aza-2'-cyclobutanonyl)-6-chloropyridine (XIX). The structures of lactams XVIII and XIX were confirmed by data from the IR spectra — there is an absorption band of the CO group of a β-lactam (1750 cm^{-1}), whereas signals of protons of methylene groups (3.84, 3.4, 3.15, and 2.9 ppm) are observed in the PMR spectrum of XVIII. Lactam XIX is an unstable substance and undergoes resinification rapidly upon storage in air and when it is heated.

The reaction of pyridines IIa, b with β-bromopropionic acid (IV) was studied. 2-(β-Carboxyethyl)thio-3-amino-6-chloro(methoxy)pyridines (XX, XXI) were obtained in the presence of alkali at room temperature. When we used dicyclohexylcarbodiimide as the dehydrating agent, we were able to convert thio ethers XX and XXI to pyrido[2,3-b][1,5]-thiazepin-6-ones (XXII and XXIII) [4]. The structures of thiazepinones XXII and XXIII were confirmed by the presence in the IR spectra of amide CO (1690 cm^{-1}) and NH (3300 cm^{-1}) absorption bands, while the PMR spectra contained signals of two CH_2 groups (two triplets centered at 3.56 and 2.79 ppm) and singlets of protons of a pyridine ring in the form of two doublets at 7.3-7.4 ppm. An N-alkyl derivative (XXIV) was obtained by the reaction of thiazepinone XXII with methyl iodide.

EXPERIMENTAL

The IR spectra were recorded with a double-beam UR-10 spectrometer and with a Perkin—Elmer spectrometer. The PMR spectra were obtained with a JNM-4H-100 spectrometer with DMSO as the internal standard. Information regarding the synthesized compounds and their spectral characteristics are presented in Table 1.

2-(β-Benzoylethyl)thio-3-ureido-6-chloropyridine (VIII). A solution of 0.42 g (2 mmole) of β-bromopropiophenone (III) in 10 ml of ethanol was added at 0°C to a solution of 0.4 g (2 mmole) of pyridine I in 25 ml of ethanol containing 0.11 g (2 mmole) of KOH, and the mixture was stirred for 1 h. It was then filtered, and the mother liquor was evaporated to dryness. The residue was triturated with water, and the solid substance was removed by filtration to give 0.5 g of VIII.

2-(β-Carboxyethyl)thio-3-ureido-6-chloropyridine (IX). A solution of 0.46 g (2.9 mmole) of β-bromopropionic acid in 10 ml of ethanol containing 0.17 g (2.9 mmole) of KOH was added at 0°C to a solution of 0.6 g (2.9 mmole) of I in 20 ml of ethanol containing 0.17 g (2.9 mmole) of KOH, and the mixture was stirred at 20°C for 3 h, after which the side product, viz., bis(3-amino-6-chloro-2-pyridyl) disulfide (XIV), was removed by filtration, and the alcoholic mother liquor was evaporated to dryness. The residue was triturated with water and acidified with CH_3COOH, and the solid substance was removed by filtration to give 0.4 g of IX.

2-(β-Benzoylethyl)thio-3-(β-benzoylethyl)amino-6-chloropyridine (X). A solution of 0.66 g (3.1 mmole) of β-bromopropiophenone (III) in ethanol was added at 0°C to a solution of 0.5 g (3.1 mmole) of pyridine IIa in 30 ml of ethanol containing 0.18 g (3.1 mmole) of KOH. After stirring at 20°C for 2 h, the precipitated substance was removed by filtration to give 0.2 g of X; another 0.1 g of X was isolated from the mother liquor.

2-(β-Benzoylethyl)thio-3-amino-6-chloropyridine (XI). A solution of 0.93 g (4.3 mmole) of β-bromopropiophenone was added in the course of 30 min to a suspension of 0.7 g (4.3 mmole) of IIa in 70 ml of acetone containing 0.3 g (2.2 mmole) of K_2CO_3, and the mixture was stirred for 3 h, after which the precipitate was removed by filtration and washed with acetone. The acetone mother liquor was evaporated *in vacuo* to dryness, and the residue was triturated with petroleum ether. The solid substance was removed by filtration to give 0.85 g of XI.

α-Methyl-β-(3-amino-6-chloro-2-pyridyl)thiobutenal (XII). A solution of 1.5 g (12 mmole) of β-chlorobutenal in 10 ml of ethanol was added at −10°C in the course of 15 min to a solution of 1 g (6.2 mmole) of IIa in 30 ml of ethanol containing 0.36 g (6.2 mmole) of KOH. After stirring for 1.5 h, the precipitate was removed by filtration and washed with alcohol and water to give 0.6 g of XII. The alcohol mother liquor was evaporated *in vacuo* at 20°C almost to dryness to give another 0.25 g of XII.

2-(β-Cyanoethyl)thio-3-amino-6-chloropyridine (XIII). A mixture of 0.75 g (4.7 mmole) of IIa and 0.5 g (10 mmole) of acrylonitrile in 25 ml of water containing 0.19 g (4.7 mmole) of NaOH was shaken vigorously in a sealed flask for 15 min, after which it was trans-

ferred to a flask equipped with a stirrer and stirred at 20°C for 2 h. The substance was removed by filtration to give 0.8 g of XIII. Acidification of the mother liquor after separation of XIII with CH_3COOH gave 0.1 g of unchanged IIa, from which an additional 0.1 g of XIII was obtained by treatment with acrylonitrile under the conditions indicated above.

Conversion of 2-(β-Benzoylethyl)thio-3-ureido-6-chloropyridine (VIII) to Bis(3-amino-6-chloro-2-pyridyl) Disulfide (XIV). A 0.25-g (0.7 mmole) sample of VIII and 0.04 g (0.7 mmole) of KOH were refluxed in 30 ml of ethanol for 1 h, after which the ethanol was removed by distillation *in vacuo*, the residual oily substance was triturated with water, and the liberated substance was removed by filtration to give 0.1 g of XIV. No melting-point depression was observed for a mixture with a genuine sample, and their IR spectra were identical.

Conversion of 2-(β-Benzoylethyl)thio-3-amino-6-chloropyridine (XI) to Disulfide XIV. A total of 0.18 g (90%) of XIV was obtained from 0.3 g (1 mmole) of XI and 0.056 g (1 mmole) of KOH under conditions similar to those in the conversion of VIII to disulfide XIV. No melting-point depression was observed for a mixture with a genuine sample, and their IR spectra were identical.

Conversion of α-Methyl-β-(3-amino-6-chloro-2-pyridyl)thiobutenal (XII) to Disulfide XIV. A total of 0.05 g of disulfide XIV was obtained from 0.1 g (0.4 mmole) of XII under the conditions described for the conversion of XI to disulfide XIV. No melting-point depression was noted for a mixture with a genuine sample, and their IR spectra were identical.

Conversion of 2-(β-Cyanoethyl)thio-3-amino-6-chloropyridine (XIII) to 2-Mercapto-3-amino-6-chloropyridine (IIa). A 0.06-g sample of pyridine IIa was obtained from 0.1 g (0.5 mmole) of XIII under the conditions described for the conversion of XII to disulfide XIV. No melting-point depression was observed for a mixture with a genuine sample, and their IR spectra were identical.

Hydrochloride of 2-Propylthio-3-amino-6-chloropyridine (XV). A solution of 0.76 g (6.2 mmole) of 1-bromopropane in 3 ml of acetone was added at 20°C to a solution of 1 g (6.2 mmole) of IIa in 30 ml of acetone containing 0.43 g (3.1 mmole) of K_2CO_3. After stirring for 2 h, the reaction mixture was filtered, the acetone mother liquor was evaporated to dryness, and the residue was treated with ether saturated with HCl. The precipitate was removed by filtration and washed with ether to give 1.5 g of XV.

2-(β-Bromopropionyl)thio-3-(β-bromopropionyl)amino-6-chloropyridine (XVI). A solution of 0.54 g (3 mmole) of β-bromopropionyl chloride was added at 20°C in the course of 15 min to a suspension of 0.5 g (3.1 mmole) of IIa in 80 ml of dry ether containing 0.43 g (3.1 mmole) of K_2CO_3. After stirring for 2 h at 20°C, the precipitate was removed by filtration and washed with ether and water to give 0.3 g of XVI. The ether mother liquor was evaporated *in vacuo* to dryness, the oily substance was triturated with water, and the solid substance was removed by filtration to give an additional 0.3 g of XVI. Acidification of the aqueous solution obtained after separation of XVI yielded 0.15 g of IIa.

2-(β-Cyanoethyl)thio-3-(β-bromopropionyl)amino-6-chloropyridine (XVII). A solution of 0.8 g (4.2 mmole) of β-bromopropionyl chloride in 10 ml of benzene was added at 20°C in the course of 30 min to a mixture of 0.9 g (4.2 mmole) of pyridine XIII and 0.29 g (2.1 mmole) of K_2CO_3 in 35 ml of benzene. After stirring at 20°C for 2.5 h, the precipitate was removed by filtration and washed with benzene and water to give 0.4 g of XVII. Evaporation of the benzene solution gave an additional 0.8 g of XVII.

2-(β-Cyanoethyl)thio-3-N-(1'-aza-2'-cyclobutanonyl)-6-chloropyridine (XVIII). A mixture of 0.5 g (1.4 mmole) of XVII and 2 ml of a 4% alcohol solution of KOH in 15 ml of ethanol was stirred at 20°C for 1.5 h, after which the precipitate was removed by filtration and washed with alcohol and water to give 0.25 g of XVIII. Evaporation of the alcoholic mother liquor and trituration of the residue with ether gave 0.08 g of XVIII.

2-Mercapto-3-N-(1'-aza-2'-cyclobutanonyl)-6-chloropyridine (XIX). A mixture of 0.5 g (1.9 mmole) of XVIII and 10 ml of a 4% alcohol solution of KOH in 50 ml of ethanol was refluxed for 2 h, after which the ethanol was removed by vacuum distillation, and the residue was triturated with water. The aqueous solution was acidified with CH_3COOH and extracted with ether. The ether solution was evaporated, and the residue was triturated with a mixture of ether and petroleum ether. The substance was removed by filtration to give 0.2 g of XIX.

2-(β-Carboxyethyl)thio-3-amino-6-chloropyridine (XX). A solution of 0.96 g (6.2 mmole) of β-bromopropionic acid was added at 0°C in the course of 15 min to a solution of 1 g (6.2 mmole) of IIa in 30 ml of ethanol containing 0.72 g (12 mmole) of KOH, and the mixture was stirred at 20°C for 6 h. It was then evaporated to dryness *in vacuo*, and the residue was triturated with water. The side product disulfide XIV was removed by filtration, and the aqueous mother liquor was acidified with CH_3COOH. The precipitate was removed by filtration to give 1.1 g of XX.

2-(β-Carboxyethyl)thio-3-amino-6-methoxypyridine (XXI). A solution of 0.68 g (4.5 mmole) of β-bromopropionic acid in 15 ml of ethanol was added at 0°C in the course of 15 min to a solution of 0.7 g (4.5 mmole) of IIb in 30 ml of ethanol containing 0.5 g (9 mmole) of KOH, and the mixture was stirred at 20°C for 3 h. The ethanol was removed by distillation *in vacuo*, and the residue was triturated with water; a 10% aqueous solution of NaOH was added to this mixture until the solid material dissolved. The alkaline solution was filtered and acidified with CH_3COOH, and the acidic solution was extracted with ether. The ether solution was separated and evaporated to dryness, and the residue was triturated with petroleum ether. The substance was removed by filtration to give 0.55 g of XXI.

2-Chloropyrido[2,3-b][1,5]thiazepin-6-one (XXII). A solution of 0.4 g (1.9 mmole) of dicyclohexylcarbodiimide in 10 ml of chloroform was added at 20°C in the course of 15 min to a solution of 0.45 g (1.9 mmole) of XX in 40 ml of dry chloroform, and the mixture was stirred for 3 h. The precipitated dicyclohexylurea was removed by filtration and washed with chloroform. The chloroform solution was evaporated *in vacuo* to half its original volume, the precipitated dicyclohexylurea was again removed by filtration, and the chloroform solution was evaporated to dryness. The residue was triturated with alcohol and removed by filtration to give 0.26 g of XXII. Evaporation of the alcohol solution gave an additional 0.1 g of XXII.

2-Methoxypyrido[2,3-b][1,5]thiazepin-6-one (XXIII). A 0.16-g sample of XXIII was obtained from 0.2 g (0.8 mmole) of XXI and 0.17 g (0.8 mmole) of dicyclohexylcarbodiimide under the conditions described for the preparation of thiazepinone XXII.

2-Chloro-5-N-methylpyrido[2,3-b][1,5]thiazepin-6-one (XXIV). A mixture of 0.7 g (3.3 mmole) of pyridothiazepinone XXII, 0.2 g (5 mmole) of NaOH, and 7 g (33 mmole) of methyl iodide in 30 ml of ethanol was refluxed for 3 h, after which the ethanol was removed by distillation *in vacuo*, and the residue was triturated with water. The substance was removed by filtration to give 0.6 g of XXIV.

LITERATURE CITED

1. L. G. Levkovskaya and T. S. Safonova, Khim. Geterotsikl. Soedin., No. 1, 68 (1971).
2. L. G. Levkovskaya and T. S. Safonova, Khim. Geterotsikl. Soedin., No. 6, 970 (1969).
3. C. Hurd and L. Gershbein, J. Am. Chem. Soc., 69, 2328 (1947).
4. N. I. Traven' and T. Safonova, USSR Inventor's Certificate No. 429062; Byul. Izobret., No. 19, 77 (1974).
5. N. I. Traven' and T. S. Safonova, Khim. Geterotsikl. Soedin., No. 6, 787 (1980).
6. L. G. Levkovskaya, Master's Dissertation, Moscow (1968).