SYNTHESIS OF SUBSTITUTED THIENOTHIAZOLES

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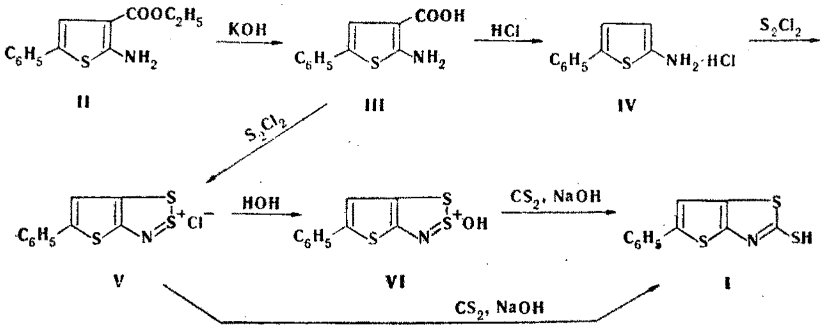
The action of sulfur monochloride on 2-amino-3-carboxy-5-phenylthiophene or 2-amino-5-phenylthiophene hydrochloride gave 5-phenylthieno[2,3-d]-2-thioniathiazole chloride, which is converted to the corresponding hydrate on treatment with water. Heating of the thionium salt or its hydrate with carbon disulfide in an aqueous alcohol solution of aklaki gave 2-mercapto-5-phenylthieno[2,3-d]thiazole, which under the influence of dialkyl sulfates or on oxidation with potassium permanganate in alkaline media is converted, respectively, to S-alkyl derivatives or a 5-phenylthieno[2,3-d]-thiazole-2-sulfonic acid salt. 2-Sulfo-3-alkylthieno[2,3-d]thiazolium betaines are obtained by heating the latter with alkylating agents. 2-Hydroxy-thieno[2,3-d]-thiazoles were synthesized by hydrolysis of thienothiazole-2-sulfonic acids.

It has been shown that polymethine dyes — 5-phenylthieno[2,3-d]thiazole derivatives [1] — are interesting spectral sensitizers of photographic materials [2]. In this connection, it seemed of interest to synthesize 2-mercapto-5-phenylthieno[2,3-d]thiazole (I), the use of which would make it possible to obtain a number of new symmetrical and unsymmetrical cyanine dyes with residues of this base and to investigate the behavior of I and the previously synthesized [3] 2-mercaptothienothiazoles in some chemical reactions as compared with 2-mercaptobenzothiazole (VII) [4].

Base I was synthesized from 2-amino-3-carbethoxy-5-phenylthiophene (II) via the scheme (see the experimental section)



Compound V was synthesized from thiophene derivatives III and IV in benzene rather than in acetic acid, which is ordinarily used (the respective yields are 65 and 72%), inasmuch as the use of benzene excludes a side reaction — chlorination of the thiophene ring. Base I was obtained by heating V or VI with carbon disulfide in an alkaline aqueous alcohol medium.

The characteristics of I as compared with mercapto-substituted thienothiazoles and benzothiazoles are presented in Table 1; the characteristics confirm the analogous character of the structure of these compounds. The IR spectrum of I does not contain the bands at 2550-2600 cm^{-1} that are characteristic for the stretching vibrations of the mercapto groups but does contain a band at 1540 cm^{-1} corresponding to a C=S group and indicating that I, like thienothiazoles VIII and IX and mercaptobenzothiazole VII, exists primarily in the thione form under ordinary conditions. The IR spectra of salts V and VI contain rather intense bands corresponding to C-H out-of-plane deformation vibrations of the phenyl group (at ∿740 cm^{-1}) and characteristic bands of an azole ring at ∿810 cm^{-1} (β ring) and ∿1485 cm^{-1} (ring stretching vibrations). A broad band at 3450-3600 cm^{-1} that indicates the presence in this

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TABLE 1. Characteristics of Mercapto-Substituted Heterocycles

Compound	mp, °C	Appearance	IR spectrum, cm^{-1}	Mass spectrum m/e
2-Mercaptobenzothiazole (VII)	177-179	Light-yellow needles	1495	167
2-Mercaptothieno[2,3-d]-thiazole (VIII)	170-171	Light-yellow prisms	1510	173
2-Mercaptothieno[3,2-d]-thiazole (IX)	194-195	Light-yellow prisms	1500	173
2-Mercapto-5-phenylthieno-[2,3-d]thiazole (I)	210-212	Light-yellow needles	1540	249

compound of an OH group is also characteristic for the spectrum of VI. As in the case of VII, the molecular ion peak is rather intense (15-20%) in the mass spectra of I and mercaptothienothiazoles.

The chemical properties of the mercaptothienothiazoles and I are similar to those of 2-mercaptobenzothiazole [5]. Under the influence of dialkyl sulfates in aqueous solutions of alkalies they are converted to the corresponding S-alkyl derivatives, heating of which with alkylating agents gives quaternary salts. Oxidation with potassium permanganate in alkaline media gives the salts of the corresponding thienothiazole-2-sulfonic acids, heating of which with dialkyl sulfates gives 2-sulfo-3-alkylthienothiazolium betaines. The free thienothiazole-2-sulfonic acids, the sulfo group in which is extremely labile and, as in the case of benzothiazole-2-sulfonic acids [6], is capable of undergoing replacement by a hydroxy group upon heating in an aqueous or acidic solution, can be isolated by acidification of cooled solutions of the salts.

When they are oxidized with hydrogen peroxide in acidic media, mercaptothienothiazoles are converted to the corresponding disulfides; when IX is oxidized in concentrated hydrochloric acid, a small amount (4%) of unsubstituted thieno[3,2-d]thiazole is formed along with the main product (78%) – bis-thieno[3,2-d]thiazol-2-yl) disulfide. It should be noted that benzo-substituted thieno-3,2-d]thiazol-2-yl disulfide is readily formed when a dioxane solution of 2-mercaptobenzothieno[3,2-d]thiazole is heated in the presence of catalytic amounts of peroxide.

EXPERIMENTAL

Compounds II and III were obtained by the method in [7], and IV was obtained by the method in [8].

5-Phenylthieno[2,3-d]-2-thioniathiazole Chloride (V). A) A 21.9-g (0.1 mole) sample of hydrochloride IV was added in small portions with stirring to 135 g (1 mole) of sulfur monochloride, and the mixture was stirred at room temperature for 5 h, after which it was refluxed with stirring with 50 ml of anhydrous benzene. It was then cooled, and the resulting precipitate was removed by filtration, washed with anhydrous benzene, and dried over phosphorus pentoxide to give 17.7 g (65%) of a brownish-red amorphous crystalline product (from anhydrous ethanol) with mp 254-255°C. Found: C 44.0; H 2.1; N 5.0%. $C_{10}H_6ClNS_2$. Calculated: C 44.2; H 2.2; N 5.2%.

B). An 11-g (0.052 mole) sample of aminothiophene III was added in small portions with stirring to 42 g (0.3 mole) of sulfur monochloride, and the mixture was stirred at room temperature for 4 h. It was then refluxed for 4 h with 45 ml of anhydrous benzene, after which it was washed with anhydrous benzene and dried. Workup gave 19.8 g (72%) of product. No melting-point depression was observed for a mixture of substances obtained by methods A and B, and the IR spectra of the two products were identical.

5-Phenylthieno[2,3-d]-2-thioniathiazole Hydrate (VI). A suspension of 13.6 g (0.05 mole) of salt V in 120 ml of water was stirred at room temperature for 12 h, after which the resulting precipitate was removed by filtration, washed with water, and dried to give 12.2 g (96.5%) of brown crystals (from anhydrous ethanol) with mp 156-158°C. Found: C 47.3; H 2.7%. $C_{10}H_7NOS_3$. Calculated: C 47.4; H 2.8%.

2-Mercapto-5-phenylthieno[2,3-d]thiazole (I). A 10-ml (0.17 mole) sample of carbon disulfide and 12.65 g (0.05 mole) of hydrate VI were added in a stream of nitrogen to a solution of 4.8 g (0.12 mole) of sodium hydroxide in a mixture of 125 ml of water and 65 ml of ethanol, and the mixture was heated at 60°C for 3 h, after which the precipitate was removed by filtration and treated with a dilute solution of sodium hydroxide. The alkaline solution was acidified with hydrochloric acid, and the resulting precipitate was removed by filtration, washed with water, and dried to give 1.5 g (15%) of I. Light-yellow needles with mp 210-212°C were obtained after reprecipitation from a dilute alkaline solution by the addition of hydrochloric acid and recrystallization from ethanol. IR spectrum (KBr): 1540 cm^{-1}. Found: C 53.1; H 2.7; N 5.4%; M 249. $C_{11}H_7NS_3$. Calculated: C 53.0; H 2.8; N 5.6%; M 249.

Potassium 5-Phenylthieno[2,3-d]thiazole-2-sulfonate (X). A solution of 0.45 g of potassium permanganate in 15 ml of water was added dropwise with stirring at 60-65°C to 0.35 g (1.4 mmole) of mercaptan I in a solution of 0.12 g of potassium hydroxide in 15 ml of water, and the mixture was stirred at 65-70°C for 2 h. It was then cooled and worked up to give 0.25 g (53.5%) of colorless plates (from 80% ethanol) with mp > 300°C. Found: C 39.5; H 1.7; N 4.0%. $C_{11}H_6KNO_3S_3$. Calculated: C 39.4; H 1.8; N 4.2%.

3-Ethyl-5-phenylthieno[2,3-d]thiazol-2-yl Sulfate. This compound was obtained by heating 0.2 g (1 mmole) of salt X with 0.35 g (2 mmole) of diethyl sulfate at 170-175°C for 20 min. Workup gave 0.08 g (41.2%) of colorless prisms (from acetonitrile) with mp > 250°C. Found: N 4.2; S 29.4% $C_{13}H_{11}NO_3S_3$. Calculated: N 4.3; S 29.6%.

2-Ethylmercapto-5-phenylthieno[2,3-d]thiazole. A 5-mmole sample of diethyl sulfate was added to a solution of 5 mmole of I and 5 mmole of sodium hydroxide in 12 ml of water, and the mixture was stirred at room temperature for 30 min, heated at 80°C for 1 h, cooled, and extracted with ether. The ether solution was dried with magnesium sulfate, and the ether was removed by distillation. The residue was vacuum distilled to give a light-yellow oil with bp 160-165°C (2-3 mm) in 76% yield. Found: C 56.1; H 3.9; N 4.0%. $C_{13}H_{11}NS_3$. Calculated: C 56.3; H 4.0; N 5.0%.

2-Ethylmercaptothieno[3,2-d]thiazole (XI). This compound was similarly obtained from 0.87 g (5 mmole) of thiazole IX and 0.76 g (5 mmole) of diethyl sulfate in a solution of 0.20 g of sodium hydroxide in 2 ml of water. Workup gave 0.82 g (82%) of a light-yellow oil with bp 163-165°C (8-10 mm); the oil began to crystallize on standing to give colorless needles (from ethanol) with mp 34-35°C. Found: C 42.0; H 3.6; N 6.85%. $C_7H_7NS_3$. Calculated: C 41.8; H 3.5; N 6.95%.

2-Ethylmercapto-3-ethylthieno[3,2-d]thiazolium 2-Toluenesulfonate. A mixture of 0.7 g (3.5 mmole) of thiazole XI and 0.8 g (4 mmole) of ethyl p-toluenesulfonate was heated at 150-155°C for 2 h, after which it was cooled and treated with 3 ml of anhydrous acetone. The resulting precipitate was removed by filtration and treated with 4 ml of boiling acetone to give 0.96 g (68.5%) of yellowish prisms (from acetone) with mp 146-147°C. Found: C 47.8; H 4.7; N 3.4%. $C_{16}H_{19}NO_3S_4$. Calculated: C 47.9; H 4.75; N 3.5%.

2-Ethylmercapto-3-ethyl-5-phenylthieno[2,3-d]thiazolium p-Toluenesulfonate. This compound was similarly obtained from 5 mmole of the 5-phenyl derivative and 6 mmole of diethyl sulfate. The yield of yellowish prisms (from anhydrous acetone) with mp 155-157°C was 61.5%. Found: C 55.2; H 4.7; N 3.0%. $C_{22}H_{23}NO_3S_4$. Calculated: C 55.3; H 4.85; N 2.9%.

Thieno[3,2-d]thiazole-2-sulfonic Acid (XII). A suspension of 0.26 g (1 mmole) of potassium thieno[3,2-d]thiazole-2-sulfonate (XIII) in 1 ml of water was acidified with concentrated hydrochloric acid at 0-2°C, and the resulting precipitate was removed by filtration, washed with ice water and ether, and dried to give 0.12 g (59%) of colorless needles (from ether) with mp 235-236°C. Found: S 43.4%. $C_5H_3NO_3S_3$. Calculated: S 43.5%.

5-Phenylthieno[2,3-d]thiazole-2-sulfonic Acid. This compound was obtained from 2 mmole of thiazole X by a method similar to that used to prepare XII. The yield of colorless needles (from ether) with mp 256-266°C was 61%. Found: S 32.2%. $C_{11}H_7NO_3S_3$. Calculated: S 32.3%.

2-Hydroxythieno[3,2-d]thiazole (XIV). A solution of 0.26 g (1 mmole) of sulfonic acid XIII in 5 ml of water was acidified with concentrated hydrochloric acid, and the mixture was refluxed for 30 min. It was then cooled, and the precipitate was removed by filtration, washed with water, and dried to give 0.05 g (32%) of colorless needles (from 50% ethanol) with mp 144-145°C. IR spectrum (mineral oil): 1650 (C=O) and 3220 cm^{-1} (NH). Found: C 38.1; H 1.8; N 8.8%. $C_5H_3NOS_2$. Calculated: C 38.2; H 1.9; N 8.9%.

2-Hydroxy-5-phenylthieno[2,3-d]thiazole. This compound was obtained from 2 mmole of salt X by a method similar to that used to prepare XIV. The yield of colorless needles (from

50% ethanol) with mp 166-167°C was 38%. IR spectrum (mineral oil): 1680 (C=O) and 3250 cm^{-1} (NH). Found: C 56.5; H 3.1; N 5.9%. $C_{11}H_7NOS_2$. Calculated: C 56.6; H 3.0; H 6.0%.

Bis(thieno[3,2-d]thiazol-2-yl) Disulfide (XV). A 2.46-g (0.22 mole) sample of 30% hydrogen peroxide was added dropwise at 70°C to a suspension of 1.56 g (0.09 mole) of IX in 4 ml of concentrated hydrochloric acid, and the mixture was heated at 70-75°C for 30 min, after which it was diluted with 15 ml of water. The resulting precipitate was removed by filtration, washed with water, treated with 5% sodium hydroxide solution, washed with water, and dried to give 1.2 g (78%) of XV as yellowish prisms (from benzene) with mp 175-176°C. Found: C 34.7; H 1.1; N 8.0%. $C_{10}H_4N_2S_6$. Calculated: C 34.8; H 1.2; N 8.1%.

The acidic filtrate after isolation of disulfide XV was made alkaline with a solution of sodium hydroxide and extracted with ether. The extract was washed with water and dried with potassium carbonate. The ether was removed by distillation, and the residue was vacuum distilled to give 0.5 g (4%) of thieno[3, 2-d]thiazole as a light-yellow oil with bp 110-115°C (25 mm). Found: C 42.4; H 2.0; N 10.0%. $C_5H_3NS_2$. Calculated: C 42.5; H 2.1; N 9.9%. The picrate had mp 164-165°C (from ethanol). Found: C 35.5; H 1.7; N 15.3%. $C_5H_3NS_2 \cdot C_6H_3N_3O_7$. Calculated: C 35.7; H 1.6; N 15.1%.

Bis(5-phenylthieno[2,3-d]thiazol-2-yl) Disulfide. This compound was obtained by a method similar to that used to prepare XV by oxidation of 0.1 mole of mercaptan I. Workup gave yellowish prisms (from benzene) with mp 194-195°C in 72% yield. Found: C 53.0; H 2.3; N 5.7%. $C_{22}H_{12}N_2S_6$. Calculated: C 53.2; H 2.4; N 5.6%.

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1,3-THIAZINEDIONES AND PYRIMIDINEDIONES.

4.* TAUTOMERISM OF 2-SUBSTITUTED 4,6-DIOXODIHYDRO-1,3-THIAZINES

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The character of the effect of substituents on the position of the keto—enol equilibrium in 2-substituted 4,6-dioxodihydro-1,3-thiazines and the structure of the enol form are examined. 2-Phenyl-4,6-dioxodihydro-^{15}N-1,3-thiazine was synthesized. It was shown by ^{13}C NMR spectroscopy that the 2-phenyl-4-hydroxy-1,3-thiazin-6-one structure corresponds to the enol form.

It has been shown [2] that 2-substituted 1,3-thiazinediones are potentially tautomeric compounds. The specificity of enolization in the unsymmetrical β-dicarbonyl fragment and the reasons for the different effects of substituents on the position of the keto—enol equilibrium have not been previously discussed. Enol forms A and B are presented in the literature without any stipulation [1-5].

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