CONVERSIONS OF 2-THIOXO-1,3-DITHIOL-4,5-DICARBOXYLIC ACID DIMETHYL ESTER — THE PATH TO A NEW HETEROCYCLIC SYSTEM, (4H,6H)-1,3-DITHIOLO[4,5-d]PYRIMIDINE-2,5,7-TRIONE AND 5,6-DIMERCAPTOURACIL DERIVATIVES

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The conversions of 2-thioxo-1,3-dithiol-4,5-dicarboxylic acid methyl ester into anhydride, mono- and diamide, and monoamide methyl ester were demonstrated. The new heterocyclic system, (4H,6H)-1,3-dithiolo[4,5-d]pyrimidine-2,5,7-trione, was obtained by oxidative rearrangement-cyclization of 2-oxo-1,3-dithiol-4,5-dicarboxylic acid diamide with phenyliodosyl(hydroxy)tosylate and used to synthesize previously unknown 5,6-dimercaptouracil derivatives, including nickel dithiolene complex.

Derivatives of 1,3-dithiol-2-thione and 1,3-dithiol-2-one are the starting substances for synthesis of tetrathiafulvalene derivatives, which form conducting organic complexes [1-4].

We obtained amino-substituted 1,3-dithiol-2-thiones — the starting compounds for amino-substituted tetrathiafulvalenes, in whose complexes intermolecular hydrogen bonds can be formed. The method of oxidative rearrangement (Hoffmann splitting) of carboxylic acid amides was selected for obtaining amino-substituted dithiolthiones.

2-Thioxo-1,3-dithiol-4,5-dicarboxylic acid dimethyl ester (I) was selected as the starting compound since it is synthesized relatively easily [5, 6].

2-Thioxo-1,3-dithiol-4,5-dicarboxylic acid (II), which is decarboxylated into 2-thioxo-1,3-dithiol-4-carboxylic acid (III) when boiled longer, was obtained by hydrolysis of dimethyl ester I with hydrochloric acid. Compounds II and III were previously prepared by another method [5, 7].

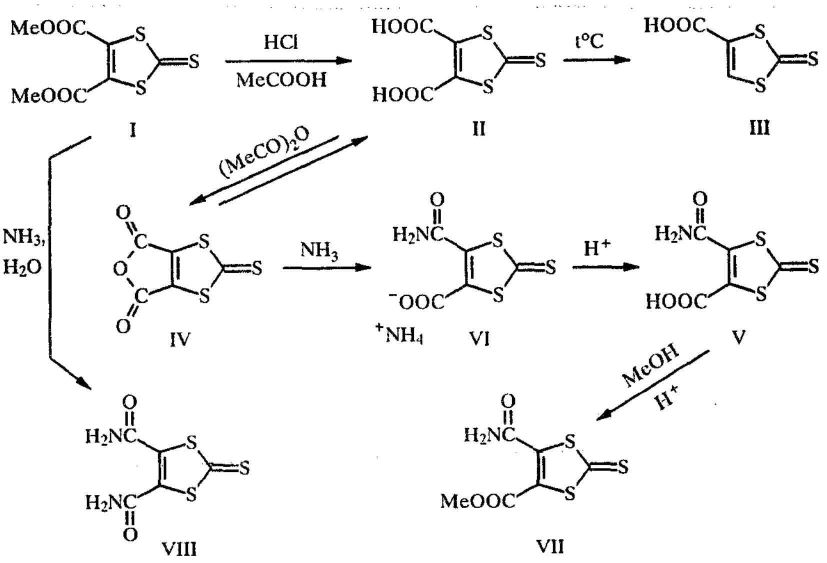

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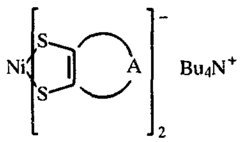
TABLE 1. Redox Potentials of Some Nickel(III) Dithiolene Complexes [17]



A	Redox potentials (V), NCE reference electrode, in CH_3CN solution	
	E_{ox}	E_{red}
SCH_2CH_2S [17]	0,06	-0,69
NHCONHCO (XV)	0,46*	-0,37
S(C=O)S [17]	0,025	-0,24
S(C=S)S [17]	0,22	-0,13

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*In DMF.

Acid II is easily converted into 2-thioxo-1,3-dithiol-4,5-dicarboxylic acid anhydride (IV) — a very reactive substance easily hydrolyzed by atmospheric moisture — with acetic or trifluoroacetic anhydrides. The formation of the anhydride is confirmed by the IR spectra (absorption at 1848 and 1778 cm^{-1}).

A yellow sediment of 2-thioxo-1,3-dithiol-4,5-dicarboxylic monoamide (VI) ammonium salt, readily soluble in water, rapidly separated when ammonia was bubbled through a solution of anhydride IV in benzene. When an aqueous solution of H_2SO_4 was acidified to pH 1, 2-thioxo-1,3-dithiol-4,5-dicarboxylic acid (V) crystallized from it. Compound V was easily converted into methyl ester VII by saturation with methanol solution of HCl.

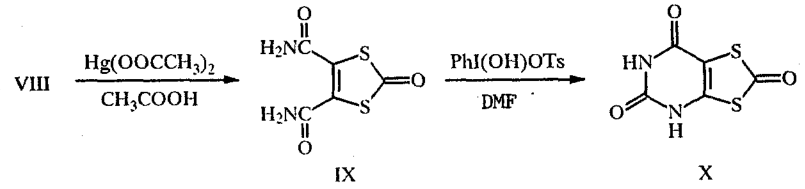
The reaction of the monoamido ester of VII with NaOCl in conditions of Hoffmann splitting did not produce the desired result — amino-substituted 1,3-dithiol-2-thione, but yielded unidentified red products.

2-Thioxo-1,3-dithiol-4,5-dicarboxylic acid (VIII) diamide — a light yellow substance — was easily obtained in the reaction of an aqueous solution of ammonia with the dimethyl ester of I in acetonitrile.

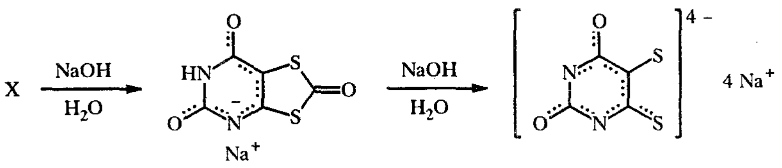
The diamides of some dicarboxylic acids are cyclized in the reaction with hypohalites as a result of oxidative Hoffmann rearrangement and are converted into pyrimidine derivatives; for example, phthalic acid diamide is cyclized into (1H,3H)quinazoline-2,4-dione [8], and maleic acid diamide is converted into uracil [9]. Organic derivatives of trivalent iodine — phenyliodosyl derivatives — were selected as oxidants for conducting oxidative rearrangement—cyclization of diamide VIII to prevent alkaline splitting of the 1,3-dithiol-2-thione ring. Phenyliodosyl diacetate [10], phenyliodosylbis(trifluoroacetate) [11], and phenyliodosyl(hydroxy)tosylate [12] easily react with monocarboxylic acid amides so that Hoffmann rearrangement takes place and an amine is obtained. The reaction of phenyliodosyl derivatives with diamides has not been described up to now.

Diamide VIII was reacted with phenyliodosyl(hydroxy)tosylate in dimethylformamide. Dark resinous products were formed — oxidative decomposition of the dithiolthione system probably took place.

The sulfur atom in the thione group was substituted by an oxygen atom with the method in [13] to increase the resistance of diamide VIII to oxidants and 2-oxo-1,3-dithiol-4,5-dicarboxylic acid (IX) diamide was obtained. Oxidative rearrangement—cyclization took place smoothly in the reaction of diamide IX with phenyliodosyl(hydroxy)tosylate and a new heterocyclic compound was obtained — (4H,6H)-1,3-dithiolo[4,5-*d*]pyrimidine-2,5,7-trione (X) — the first member of the heterocyclic system of 1,3-dithiolo[4,5-*d*]pyrimidine, with a yield of up to 85%. This reaction can also be conducted successfully with phenyliodosylbis(trifluoroacetate).



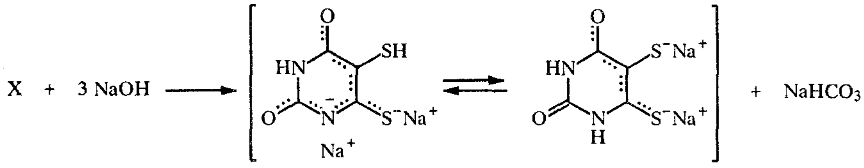
Compound X is a colorless, finely crystalline substance hardly soluble in water, alcohols, and acetonitrile, and insoluble in hydrocarbons, ethers, and halohydrocarbons. Compound X is a dibasic NH acid, pK_{a1} = 5.53 [14]. The dioxo structure of X is confirmed by the IR spectra. Monosodium salt (XI) — a colorless crystalline substance — is easily obtained from compound X.



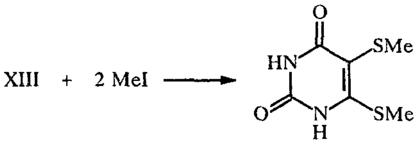
XI XII

Compound X is unstable in basic medium (pH > 11), and 5,6-dimercaptouracil (XII) tetrasodium salt, which is not separated from the solution, is probably the product of hydrolysis in an excess of NaOH solution.

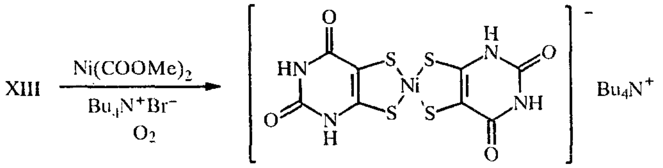
It is expedient to prepare the disodium salt XIII which is very sensitive to atmospheric oxygen and is not separated from solution for using 5,6-dimercaptouracil in subsequent sequences. Salt XIII in solution can preferably be a tautomeric mixture of two dianions. 5,6-Di(methylthio)uracil (XIV) is isolated in alkylation of a solution of salt XIII with methyl iodide.



XIII



XIV



XV

A new type of dithiol complex — tetrabutylammonium bis(5,6-dimercaptouracil)nickel-(III)ate (XV) — is precipitated as dark brown crystals in the reaction of salt XIII with nickel acetate and tetrabutylammonium bromide with admission of air. The electron absorption spectra confirm the nature of dithiolene complex XV as they have a broad absorption maximum in the near infrared region at 1050 nm. This is characteristic of nickel dithiolene complexes with a degree of oxidation of nickel of 3 [15]. The negative charge in the anion is delocalized in a system of four sulfur atoms and a nickel atom with some participation of the C=C—C=O uracil system. The IR spectra exhibit characteristic absorption of C—C and C—S bonds at 1264, 930, and 878 cm^{-1} [16].

Cyclic voltammetry showed that diothiolene complex XV is a two-stage reversible redox system. The redox potentials (with respect to NCE) of complex XV are reported in Table 1. The published data for other dithiolene complexes [16, 17] are reported for comparison. The substituents in Ni(III) dithiolene complexes strongly affect the redox potentials. The complex with A = SCH_2CH_2S is easily oxidized, for example, but at the same time it is difficultly reduced. The $E_{ox} - E_{red}$ difference for the ethylenedithio derivative is 0.75 V. This difference characterizes the stability of the Ni(III) complex. Compound XV, which is most difficultly oxidized, is especially isolated in this series of Ni(III) complexes [16, 17], and the $E_{ox} - E_{red}$ difference for this compound is 0.83 V.

Complex XV can be of interest as an electron-donor component for fabrication of conducting materials.

EXPERIMENTAL

The IR spectra were made on a Specord M-80 spectrometer, the UV spectra were made on a Specord UV-vis spectrophotometer in ethanol, and the PMR spectra were recorded on a Tesla BS 487-C (80 MHz) in DMSO, TMS internal standard cyclic voltammetry on a PI-50-1 potentiostat.

The data from elemental analysis of compounds IV, V, VII, VIII, IX, XI, and XIV for C, H, N, and S agreed with the calculated values.

2-Thioxo-1,3-dithiol-4,5-dicarboxylic acid (II, $C_5H_2O_4S_3$). Here 5 g (0.02 mole) of dimethyl ester I was dissolved in a mixture of 77 ml of hydrochloric and 77 ml of acetic acid. It was boiled for 3 h. Half of the solvent was distilled off and left to crystallize. The precipitated sediment was filtered off. IR spectrum: 1687, 1606, 1525, 1238, 1078 cm^{-1}. Mp = 170°C. Yield of 3.06 g (80%).

2-Thioxo-1,3-dithiol-4,5-dicarboxylic Acid Anhydride (IV, $C_5O_3S_3$). While heating, 1.72 g (7.7 mmole) of dicarboxylic acid II was dissolved in 20 ml of acetic acid and 1 ml (9.2 mmole) of acetic anhydride was added and boiled for 10 min. Half of the solvent was distilled off, and 5 ml of hexane was added and left to crystallize. It was recrystallized from benzene. IR spectrum, 1848, 1778, 1537, 1263, 1250, 1228, 1078, 1030, 912 cm^{-1}. Mp = 126-129°C (decomposition with evolution of gas). Yield of 1.2 g (70%).

2-Thioxo-1,3-dithiol-4,5-dicarboxylic Acid Monoamide (V, $C_5H_3NO_3S_3$). Here 3.89 g (0.02 mole) of anhydride IV was dissolved in 150 ml of dry benzene and bubbled through a solution of dry gaseous ammonia. A light yellow sediment precipitated from the solution for 5 min, and the solution was totally clarified. Yield of 4.4 g (97%). Ammonium salt VI obtained was dissolved in 750 ml of water and acidified to pH 1 with H_2SO_4. Orange sediment of V precipitated. IR spectrum: 3288, 3132, 2917, 2572, 1713, 1677, 1633, 1581, 1561, 1225, 1132, 1090 cm^{-1}. Mp = 220-222°C (decomposition with liberation of gas). Yield of 3.5 g (86%).

2-Thioxo-1,3-dithiol-4,5-dicarboxylic Acid Methyl Ester Amide (VII, $C_6H_5NO_3S_3$). Here 2.21 g (0.01 mole) of monoamide V was dissolved in 140 ml of methanol and dry, gaseous hydrogen chloride was passed through the solution. Light yellow, shiny crystals began to precipitate from the solution after 1 h. The reaction was conducted for 2 h. IR spectrum: 3249, 3117, 2807, 1708, 1672, 1624, 1580, 1529, 1259, 1241, 1075 cm^{-1}. Mp = 175-177°C (decomposition with liberation of gas). Yield of 2 g (85%).

2-Thioxo-1,3-dithiol-4,5-dicarboxylic Acid Diamide (VIII, $C_5H_4N_2O_2S_3$). At room temperature, 8 g (0.032 mole) of dimethyl ester I was dissolved in 140 ml of acetonitrile. While stirring in a magnetic stirrer, 4 portions of NH_4OH with 8 ml in each portion were added 10 min apart. After addition of the third portion, a bright yellow sediment began to separate. After addition of all of the NH_4OH, the mixture was stirred for another 30 min and the sediment was filtered off. It was recrystallized from 20% aqueous DMF. IR spectrum: 3270, 3150, 2792, 1660, 1536, 1112, 1064, 796, 720 cm^{-1}. Mp = 231-233°C (deocmposition with liberation of gas). Yield of 5.08 g (72%).

2-Oxo-1,3-dithiol-2,5-dicarboxylic Acid Diamide (IX, $C_5H_4N_2O_3S_2$). At 90°C, 4.1 g (0.0186 mole) of diamide VIII was dissolved in 460 ml of acetic acid. At 90°C, 9.5 g (0.0298 mole) of mercury diacetate was dissolved in 135 ml of acetic acid. While energetically stirring, the solutions were poured together. A white sediment immediately precipitated from the solution and rapidly turned black. It was boiled for 1.5 h. The boiling solution was filtered through thick filter paper and left to crystallize. It was recrystallized from 20% aqueous DMF. IR spectrum: 3412, 3240, 3075, 1784, 1700, 1680, 1642, 1616, 1540, 1140, 1072, 966, 832 cm^{-1}. Mp = 216-218°C (decomp.). Yield of 3 g (80%).

(4H,6H)-1,3-dithiolo[4,5-*d*]pyrimidine-2,5,7-trione (X, $C_5H_2N_2O_3S_2$). A. Here 670 mg (3.3 mmole) of diamide IX was dissolved in 6.5 ml of abs. DMF. While stirring, 1.94 g (5 mmole) of phenyliodosyl(hydroxy)tosylate was added. The solution turned from yellow-orange to yellow-green. Self-heating from 33 to 58°C was observed. The mixture was heated to 100°C and cooled to 20°C. Then 20 ml of 50% aqueous ethanol was added. A finely crystalline white sediment precipitated. IR spectrum: 3116, 2964, 2818, 1744, 1702, 1652, 1570, 1420, 1268, 1206, 1136, 944, 860, 832, 744, 730 cm^{-1}. Mp = 260-262°C (decomp.). Yield of 0.59 g (84%).

B. While heating to 60°C, 2.17 g (10.6 mmole) of diamide IX was dissolved in 20 ml of abs. DMF. The solution was filtered and cooled to 30°C. While stirring, 6.5 g (0.151 mole) of phenyliodosylbis(trifluoroacetate) was added. Self-heating from 30 to 74°C was observed. The mixture was heated to 100°C and cooled to 20°C. Then 50 ml of water was added. A finely crystalline white sediment precipitated. The characteristics of product X were identical to the compound obtained with method A. Yield of 1.511 g (75%).

Tetrabutylammonium bis(5,6-dimercaptouracil)nickel(III)ate (XV, $C_{24}H_{40}N_5O_4S_4Ni$). Here 0.5 g (2.5 mmole) of trione X was suspended in 25 ml of methanol in an atmosphere of argon. A solution of 0.23 g (0.01 g-atom) of sodium in methanol was added. Trione X dissolved after 20 min. Then 0.31 g (1.25 mmole) of nickel acetate was added. A brown-violet sediment precipitated from the solution. The sediment was dissolved in 140 ml of distilled water and a solution of 0.36 g (1.15 mmole) of tetrabutylammonium bromide in 20 ml of acetic acid was added. A brown sediment precipitated — nickel complex XV. It was recrystallized from 20% aqueous DMF. IR spectrum: 2960, 2872, 1684, 1630, 1264, 1168, 1032, 930, 878, 756, 722 cm^{-1}. ESR: 1050 nm. Mp = 238-240°C (decomp.). Yield of 80 mg (29%).

(4H,6H)-1,3-dithiolo[4,5-*d*]pyrimidine-2,5,7-trione sodium salt (XI, $C_4HN_2O_3S_2Na$). Here 0.4 g (2 mmole) of compound X was heated to boiling in 20 ml of methanol and 20 ml of 0.1 N aqueous solution of NaOH heated to 60°C was added. The substance dissolved. It was then heated to boiling and slowly filtered. Crystallization began. It was held for 24 h at 3-5°C. Small shiny flakes. IR spectrum: 3590, 3334, 3106, 2964, 2790, 1700, 1660, 1620, 1512, 1280, 1206, 1044, 960, 840, 772, 744, 722 cm^{-1}. Yield of 0.37 g (77%).

5,6-Di(methylthio)uracil (XIV, $C_6H_8N_2O_2S_2$). Here 0.37 g (1.8 mmole) of trione X was suspended in 19 ml of methanol in an atmosphere of argon. A solution of 0.17 g (7.25 mg-atom) of sodium in methanol (11 ml) was added. The substance was dissolved for 20 min. Then 0.25 ml (3.6 mmole) of methyl iodide was added to the solution. The solution immediately turned yellow. It was stirred for 10 min. The solution was diluted twice with water and HCl was added to pH 1. The solvent was distilled dry. The sediment was washed with acetone until the solution was more colored. IR spectrum: 3403, 3138, 3018, 2825, 1732, 1680, 1619, 1572, 1241 cm^{-1}. Mp = 257°C (decomp.). It gradually decomposed when heated above 257°C. Yield of 0.17 g (46%).

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