# NEW METHOD FOR THE SYNTHESIS OF cis-PERHYDROTHIENO[3,4-d]IMIDAZOL-2-ONE 5,5-DIOXIDES

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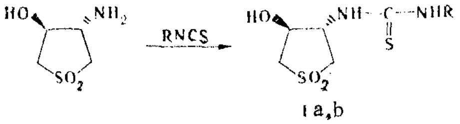
UDC 547.712.22'732'783.07:543.422

cis-Perhydrothieno[3,4-d]imidazol-2-one 5,5-dioxides were obtained in good yields by the reaction of N-(4-hydroxy-1,1-dioxothiolan-3-yl)-thioureas with methyl iodide and subsequent treatment of the mixture with aqueous triethylamine.

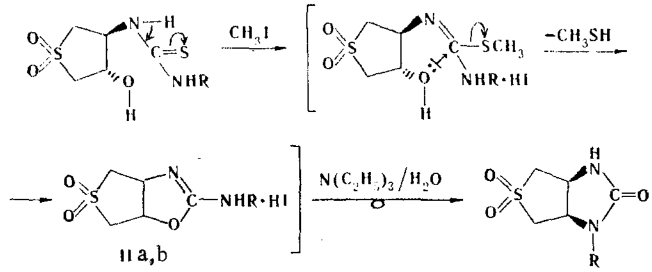
The synthesis of cis-perhydrothieno[3,4-d]imidazol-2-one 5,5-dioxides by cyclization of the difficult-to-obtain N-(1,1-dioxo-2-thiolen-4-yl)ureas has been described [1, 2]. In developing this research we investigated the possibility of the conversion of 2-aminotetrahydrothieno[3,4-d]oxazoline 5,5-dioxides to the corresponding cis-perhydrothieno[3,4-d]oxazoline 5,5-dioxides to the corresponding cis-perhydrothieno[3,4-d]imidzol-2-one 5,5-dioxides in analogy with the previously observed rearrangement of cis- and trans-perhydrothieno[3,4-d]oxazole-2-thione 5,5-dioxides to cis-perhydrothieno[3,4-d]thiazol-2-one 5,5-dioxides [3].

N-Aryl-N'-(4-hydroxy-1,1-dioxothiolan-3-yl)thioureas (I), which are readily obtained from the accessible 3-hydroxy-4-aminothiolane 1,1-dioxide and isothiocyanates, served as the starting compounds for the synthesis of the 2-aminotetrahydrothieno[3,4-d]oxazoline 5,5-dioxides:


I a,b

Ia $R=C_6H_5$; b $R-C_6H_4-OCH_3$-o

We obtained 2-aminotetrahydrothieno[3,4-d]oxazoline 5,5-dioxide hydrodides (II) by treatment of sulfones I with methyl iodide. The reaction proceeds via cyclodesulfuration with splitting out of methyl mercaptan.

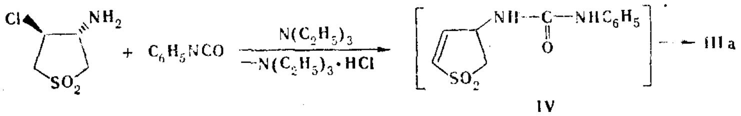

II a,b

II–III a $R=C_6H_5$; b $R=C_6H_4-OCH_3$-o

III a,b

Compounds II are unstable — they are oxidized in air during isolation — and we therefore treated the reaction mixture, after removal of the methyl mercaptan, with aqueous triethylamine in analogy with the method in [3].

As expected, we obtained the corresponding ureas III, the composition and structure of which were confirmed by the results of elementary analysis and data from the IR spectra. The cis fusion of the rings was proved by independent synthesis. We obtained IIIa from trans-3-chloro-4-aminothiolane 1,1-dioxide and phenyl isocyanate in the presence of triethylamine:


IV

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The reaction evidently proceeds thorugh the formation of N-(1,1-dioxo-2-thiolen-4-yl)-urea (IV). Evidence in favor of this is provided by the fact that N-(3-chloro-1,1-dioxothiolan-4-yl)-N'-phenylurea* does not undergo cyclization of IIIa when a tertiary amine is absent. cis Cyclization of analogs of IV has been proved by Ellis and Sammes [1].

No melting-point depressions were observed for mixtures of the compounds obtained by the two methods, and they were found to be identical with respect to the results of IR spectroscopy and thin-layer chromatography (TLC).

Thus we have shown that N-aryl-N'-(4-hydroxy-1,1-dioxothiolan-3-yl)thioureas can be converted to the corresponding two-ring ureas. The reaction gives the products in good yields and can serve as a preparative method for the production of cis-tetrahydrothieno[3,4-d]imidazol-2-one 5,5-dioxides, which are intermediates in the synthesis of biotin and its analogs.

## EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a UR-20 spectrometer. Thin-layer chromatography (TLC) was carried out on Silufol UV-254 plates in acetone; the chromatograms were developed in iodine vapors.

*N-Phenyl-N'-(4-hydroxy-1,1-dioxothiolan-3-yl)thiourea (Ia).* A solution of 2 g (0.013 mole) of 3-hydroxy-4-aminothiolane 1,1-dioxide and 1.8 g (0.013 mole) of phenyl isothiocyanate in 50 ml of alcohol was refluxed for 10 min, after which the mixture was cooled, and the resulting precipitate was crystallized from alcohol to give 3 g (81%) of thiourea Ia with mp 178-179°C. Found: N 9.7; S 22.3%. $C_{11}H_{14}N_2O_3S_2$. Calculated: N 9.8; S 22.4%. IR spectrum: 1280, 1105 ($SO_2$), 1520, 3210, 3370 (NH), 3430 $cm^{-1}$ (OH).

*N-(o-Methoxyphenyl)-N'-(4-hydroxy-1,1-dioxothiolan-3-yl)thiourea (Ib).* This compound with mp 114-115°C, was similarly obtained in 88% yield. The product was unstable: Its melting point was lowered and its IR spectrum changed upon storage.

*N-(o-Methoxyphenyl)perhydrothieno[3,4-d]imidazol-2-one 5,5-Dioxide (IIIb).* A 10-ml sample of CH I was added to a solution of 0.9 g (2.8 mmole) of freshly prepared Ib in 50 ml of alcohol, and the mixture was refluxed for 8 h. It was then evaporated to half its original volume, 30 ml of a 50% solution of triethylamine in water was added, and the mixture was refluxed for 1 h. It was then cooled, and the precipitate was crystallized from DMF-water (1:2) to give 0.45 g (57%) of IIIb with mp 287-288°C. Found: N 9.6; S 11.7%. $C_{12}H_{14}N_2O_4S$. Calculated: N 9.9; S 11.4%. IR spectrum: 1310, 1140 ($SO_2$), 1700 (C=O), 3280 $cm^{-1}$ (NH).

*N-Phenylperhydrothieno[3,4-d]imidazol-2-one 5,5-Dioxide (IIIa).* A) This compound, with mp 215°C, was obtained in 58% yield from thiourea Ia by a method similar to that used to prepare IIIb. Found: N 11.1; S 12.6%. $C_{11}H_{12}N_2O_3S$. Calculated: N 11.1; S 12.7%. IR spectrum: 1310, 1130 ($SO_2$), 1710 (C=O); 3300 $cm^{-1}$ (NH). The product has $R_f$ 0.45 (TLC).

B) A 1.68-g (16.6 mmole) sample of triethylamine was added to a mixture of 3.44 g (16.6 mmole) of 3-chloro-4-aminothiolane 1,1-dioxide hydrochloride and 1.98 g (16.6 mmole) of phenyl isocyanate in 150 ml of acetonitrile, and the mixture was refluxed for 3 h. It was then treated with 10 ml of triethylamine, and refluxing was continued for another 3 h. The solvent was evaporated in vacuo, and the precipitate was washed with cold water. The insoluble part was recrystallized from water to give 0.2 g (4.8%) of IIIa.

Compound IIIa was not isolated when 0.06 g of N-(3-chloro-1,1-dioxothiolan-4-yl)-N'-phenylurea was refluxed in 5 ml of acetonitrile for 6 h. Only the starting sulfone ($R_f$ 0.67) was present according to TLC.

## LITERATURE CITED

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2. P. I. Parkhomenko, T. A. Ovcharenko, S. M. Lukashev, and T. É. Bezmenov, Summaries of Papers Presented at the 13th Scientific Session on the Chemistry and Technology of Organic Sulfur Compounds and Sulfurous Petroleum Oils [in Russian], Zinatne, Riga (1974), p. 238.
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*This compound was obtained by P. I. Parkhomenko and M. V. Rybakova.