

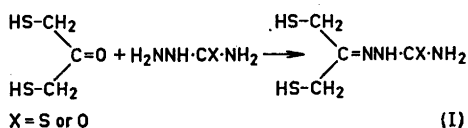
## The Semicarbazone and Thiosemicarbazone of 1,3-Dimercaptoacetone

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Although 1,3-dimercaptoacetone is a well known compound, its semicarbazone and thiosemicarbazone do not seem to have been reported. However, Schotte<sup>1</sup> has prepared the semicarbazone of 1,2-dithiolane-4-one. The cyclic ketone was synthesized by oxidation by iodine of dimercaptoacetone which was not isolated before the treatment with semicarbazide. The same method was applied by him in the preparation of the corresponding thiosemicarbazone (private information).

In our attempts to prepare these two derivatives of dimercaptoacetone we found that thiosemicarbazide yielded the expected thiosemicarbazone. Elemental analyses as well as the fact that oxidation with iodine gave the known 1,2-dithiolane-4-one thiosemicarbazone proved that the reaction proceeded according to scheme I (X = S).

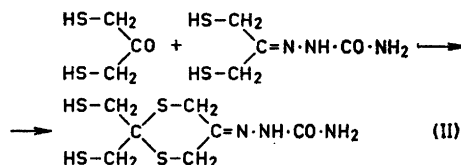


When the general procedure (acid solution) was applied in our attempts to prepare the semicarbazone from equivalent amounts of dimercaptoacetone and semicarbazide, a compound with quite another composition than that of the expected semicarbazone was obtained. However, the semicarbazone could be obtained when the reaction was carried out in only slightly acid solution (pH 6). The structure was proved by analytical data and oxidation by iodine to the known 1,2-dithiolane-4-one semicarbazone. In this case the reaction has followed mainly scheme I (X = O).

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In our attempts to elucidate the structure of the unexpected compound, we found that it could be obtained in good yield, when dimercaptoacetone semicarbazone was treated with an equivalent amount of dimercaptoacetone in acid solution, indicating that a formation of a thioketal according to scheme II had taken place.



Elemental analyses and iodometric titration supported the suggestion that the compound was 2,2-bis-(mercaptomethyl)-1,3-dithiacyclohexane-5-one semicarbazone. Iodometric titration gave 100–103% when compared with the equiv. weight for the formula proposed.

We were not able to obtain the corresponding cyclic thiosemicarbazone by applying the analogous procedure.

Dimercaptoacetone is known to undergo uncontrolled polymerization and condensation. The dimer containing a blocking semicarbazone group is interesting since it indicates a possibility of obtaining an oligo- or polyspiro compound of dithiane type. However, we have not investigated this possibility further.

*Experimental. Dimercaptoacetone semicarbazone.* 22.3 g (0.2 mole) of semicarbazide hydrochloride, dissolved in 100 ml of water, was added, while stirring, to a solution of 24.5 g (0.2 mole) of freshly prepared dimercaptoacetone in 750 ml of ethanol. The pH of the mixture was about 3. After stirring for about 1 min, the mixture was neutralized to about pH 6 by addition of a solution of 16.4 g (0.2 mole) of sodium bicarbonate in 150 ml of water. The mixture was cooled with an ice-salt mixture for about 45 min. At a temperature of about +15° a precipitate began to separate. It was collected and washed with ethanol. Yield 24.0 g (67%). M.p. 121–122° (decomp.). (Found: C 27.13; H 5.25; N 23.37; S 35.48. Calc. for C<sub>4</sub>H<sub>8</sub>N<sub>3</sub>OS<sub>2</sub> (179.25): C 26.80; H 5.06; N 23.44; S 35.77).

*1,2-Dithiolane-4-one semicarbazone.* 3.6 g (0.02 mole) of semicarbazone from the preceding step were dissolved in 300 ml of ethanol.

While stirring a solution of 5.1 g iodine (and some potassium iodide) in 100 ml of 50 % ethanol was added in portions until the colour persisted. Almost the theoretical amount of iodine was consumed. On cooling with a dry ice-alcohol bath, 2.4 g (70 %) of 1,2-dithiolane-4-one semicarbazone were obtained as a precipitate, m.p. 174–176° (decomp.).

*2,2-Bis-(mercaptomethyl)-1,3-dithiacyclohexane-5-one semicarbazone.* (a) Directly from dimercaptoacetone: To a solution of 18.4 g (0.15 mole) of dimercaptoacetone in 500 ml of ethanol, was added, while stirring, a solution of 8.4 g (0.075 mole) of semicarbazide hydrochloride in 150 ml of water. The mixture was kept, while stirring, at room temperature for about 1 h. The solution was neutralized to about pH 6 with a solution of sodium bicarbonate as described above. On cooling the semicarbazone precipitated. Yield 14.5 g (69 %), m.p. 161–164° (decomp.). Recrystallisation improved the m.p. to 167–169° (decomp.). (Found: C 29.67; H 4.61; N 14.48; S 44.65. Calc. for  $C_8H_{13}N_3OS_4$  (283.44): C 29.66; H 4.62; N 14.83; S 45.24).

(b) From dimercaptoacetone semicarbazone: 11.8 g (0.06 mole) of dimercaptoacetone semicarbazone were dissolved in 100 ml of ethanol. While stirring a solution of 7.4 g (0.06 mole) of dimercaptoacetone in 150 ml of ethanol was added rapidly. The temperature was kept at 60–70° for about 1 h. During this time some precipitate was formed. The mixture was diluted with 100 ml of water and was then cooled with an ice-salt mixture. The precipitate was collected and yielded 15.3 g (65 %), m.p. 171–172° (decomp.). The m.p. of a mixture with the compound prepared according to (a) showed no depression.

*Dimercaptoacetone thiosemicarbazone.* 5.0 g (0.042 mole) of freshly prepared dimercaptoacetone were dissolved in 200 ml of ethanol. To this solution was added a solution of 4.0 g (3.83 g = 0.042 mole) of thiosemicarbazide in 20 ml of 2 N hydrochloric acid. Water was added to a total volume of 250 ml and the solution was neutralized to pH 6 with a solution of potassium carbonate. After cooling in an ice bath, 7.1 g (86 %) were collected as white crystals, m.p. 127–130° (decomp.). Recrystallisations from acetone and ethanol raised the m.p. to 145–146° (decomp.). (Found: C 24.46; H 4.67; S 48.15. Calc. for  $C_4H_9N_3S_2$  (195.31): C 24.60; H 4.64; S 49.24). Iodometric titration showed a purity of about 97 %.

Oxidation with iodine in ethanol yielded a product with m.p. 167–169°. Mixed melting point with 1,2-dithiolane-4-one thiosemicarbazone showed no depression.

I. Schotte, L. *Arkiv Kemi* 5 (1953) 533.

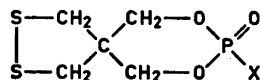
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## Some 8-Substituted Derivatives of 2,3-Dithia-7,9-dioxa-8-phosphaspiro [4,5] decane-8-oxide

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The compounds which have been prepared for pharmacological purposes have the general formula:



and are phosphoric acid derivatives of 4,4-bis-hydroxymethyl-1,2-dithiolane. By treating this last compound with phosphorus oxychloride, the 8-chloro derivative is easily obtained. This has been converted to the acid ( $X = OH$ ) and the morpholide ( $X = N \begin{array}{c} \diagup \\ \diagdown \end{array} O$ ). The compounds in which X is an ester group ( $X = OR$ ) or amide group ( $X = NR_1R_2$ ) may also be prepared directly from the bishydroxymethyldithiolane and esters of phosphorodichloridic acid,  $Cl_2PO(OR)$ , and N,N-disubstituted phosphoramidic dichloride,  $(R_1R_2N)POCl_2$ . The bis-( $\beta$ -chloroethyl)-amide ( $X = N(CH_2CH_2Cl)_2$ ) has been synthesized in this way from N,N-bis-( $\beta$ -chloroethyl)-phosphoramidic dichloride.

*2,3-Dithia-7,9-dioxa-8-chloro-8-phosphaspiro [4,5]decane-8-oxide.* 230 ml of freshly distilled phosphorus oxychloride were heated to about 40° in a flask equipped with a mechanical stirrer and an inlet fitted with a calcium

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