

The Decomposition of 4,4-Dialkylsubstituted Thiosemicarbazides

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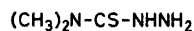
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In contrast to 4-alkylthiosemicarbazides, 4,4-dialkylthiosemicarbazides slowly decompose on standing.¹ The apparently general character of this phenomenon makes it desirable to study the underlying mechanism of the reaction. The present paper summarizes the preliminary work on the elucidation of the structure of the products formed.

The first sign of decomposition, a slight reddening of the otherwise colourless crystals, appears within a few weeks. The colour intensifies during the next weeks, but has almost disappeared in 6–8 weeks, when the light yellow, unpleasant-smelling product has partly liquefied. It should be noted that the reaction is catalyzed by basic substances. Highly purified 4,4-dialkylthiosemicarbazides can be kept unchanged for months, whereas a product containing traces of alkali begins to decompose in a few days.

4,4-Dimethylthiosemicarbazide (I) was chosen for closer investigation. Extraction of the liquefied product with ethanol followed by evaporation of the solvent *in vacuo* furnished a compound (III), m.p. 174–175°C after recrystallization from water. This was shown to be 2-dimethyl-amino-1,3,4-thiadiazoline-5-thione by elemental analysis, infrared spectroscopy, m.p. and mixture m.p. with an authentic sample prepared according to Kazakov and Postovskii.² Reference to the results obtained from pyrolysis of the higher dialkylthiosemicarbazides (see experimental part) supports the proposed mechanism involving an intermediate (II) formed by initial elimination of dimethylamine. Moreover, this intermediate has the merit of being able to explain the origin of the other products isolated from the decomposition of I.

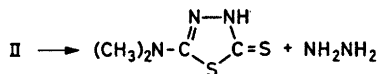
Separation of the compound responsible for the red colour from the reaction mixture was accomplished by extraction with ether. The ethereal solution showed strong



I



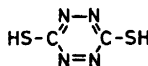
II



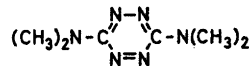
III

absorption at 519 $m\mu$, which would be compatible with the formation of a tetrazine.³ A virtually identical UV-spectrum was obtained from the red contamination in aged 4,4-diethylthiosemicarbazide. An unequivocal identification could not be accomplished because of the minute amounts formed. However, the following considerations seem appropriate.

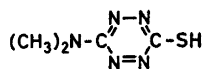
The tetrazine formed might conceivably have the structure IV, V, or VI.



IV



V

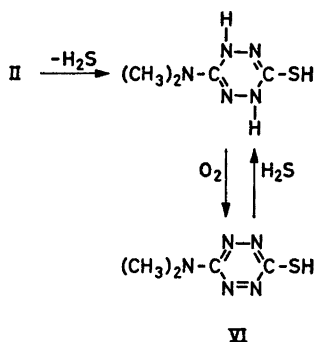


VI

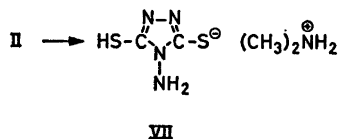
The formation of IV from II could be achieved by elimination of dimethylamine and subsequent dehydrogenation. This seems to be in disagreement with the isolation of sulfur from the decomposition mixture, which must originate from elimination of hydrogen sulfide from II or I. The ready oxidation to sulfur points to the presence of the redox system dihydro-tetrazine \rightleftharpoons tetrazine, in which the tetrazine is regenerated by the action of atmospheric oxygen. The formation of IV seems therefore to be precluded by the observation⁴ that its dihydroderivative (dithio-*p*-urazine) is stable to air. Com-

pound V might be formed by elimination of hydrogen sulfide from I, again followed by oxidation. To clarify this, V was prepared from I. The ultraviolet spectrum of V displayed a strong absorption at 492 $m\mu$, differing by *ca.* 30 $m\mu$ from the maximum of the red by-product. Furthermore, the absorption pattern from V is completely unchanged by the addition of hydrochloric acid or sodium hydroxide, whilst the tetrazine formed from decomposition of I showed a shift in the ultraviolet spectrum from 519 $m\mu$ to 426 $m\mu$ on the addition of hydrochloric acid. The assignment of the structure V to the red by-product is thus definitely ruled out by consideration of the ultraviolet spectrum.

This leaves VI as the only reasonable alternative, its formation being due to elimination of hydrogen sulfide from II and subsequent oxidation by air, *viz.*



Analogous products should be formed by pyrolysis of I. Heating for 5 min at 165°C resulted in the evolution of gases, identified gas chromatographically as dimethylamine and hydrogen sulfide. In addition to III, the residue was shown to contain a compound VII, m.p. 184–185°C. This proved to be the dimethylammonium salt of 4-amino-3,5-dimercapto-1,2,4-triazole, formed by cyclization of II and subsequent salt formation with the dimethylamine eliminated.



It was not possible to detect VI in the pyrolysis mixture. Parallel experiments with higher analogues did, however, give red products absorbing near 520 $m\mu$, thus supporting the plausibility of the above conclusions.

Experimental. Several 4,4-dialkylthiosemicarbazides were prepared and recrystallized according to the directions given by Jensen *et al.*⁵ (Repeated recrystallizations yielded more stable products without, however, changing the m.p.).

Decomposition of 4,4-dimethylthiosemicarbazide on standing. In the course of 8 weeks, 4,4-dimethylthiosemicarbazide (I) had changed to an unpleasant-smelling oil containing some crystals. These (0.4 g) were filtered and identified after recrystallization from water as unchanged starting material. The filtrate was extracted, first with ether and then with carbon disulfide, a residue remaining undissolved. The ethereal solution showed strong absorption at 519 $m\mu$; however, less than 1 mg of solid product was isolated on evaporation of the solvent. The carbon disulfide solution was evaporated to dryness. The residue proved to be elemental sulfur (0.4 g). The rest of the decomposition mixture was dissolved in hot ethanol. On cooling, colourless crystals (0.7 g) separated. After recrystallization from water the compound melted at 174–175°C and was identified as 2-dimethylamino-1,3,4-thiadiazoline-5-thione (III) (*vide supra*). (Found: C 29.85; H 4.18; N 26.22; S 39.95. Calc. for $\text{C}_4\text{H}_8\text{N}_3\text{S}_2$: C 29.79; H 4.38; N 26.06; S 39.76).

Pyrolysis of 4,4-dimethylthiosemicarbazide. 4,4-Dimethylthiosemicarbazide (I) (2 g) was placed in a small flask and immersed in an oil bath at 165°C. After 1 min the thiosemicarbazide had melted and an evolution of hydrogen sulfide and dimethylamine started. Five min later, the flask was removed and cooled in an ice bath. Ethanol (20 ml) was added and the suspension was heated and filtered hot. The residue was washed with cold ethanol. Recrystallization from 50% ethanol afforded 0.3 g of colourless crystals, (VII), m.p. 184–185°C. (Found: C 24.80; H 5.71; S 33.14. Calc. for $\text{C}_4\text{H}_{11}\text{N}_3\text{S}_2$: C 24.85; H 5.75; S 33.17). The 4-amino-3,5-dimercapto-1,2,4-triazole (identified by its m.p. and infrared and ultraviolet spectra⁶) was liberated on treatment with aqueous hydrochloric acid; m.p. 212–214°C.

The ethanolic filtrate from the above washings was evaporated to dryness and the residue recrystallized from water. The colourless crystals (0.46 g), m.p. 174–175°C, were 2-dimethylamino-1,3,4-thiadiazoline-5-thione

(III) as shown by infrared spectroscopy, m.p. and mixture m.p. with an authentic sample.² (Found: C 29.60; H 4.40; N 26.28. Calc. for $C_4H_7N_3S_2$: C 29.79; H 4.38; N 26.06).

Pyrolysis of 4,4-diethylthiosemicarbazide. A flask containing 3 g of 4,4-diethylthiosemicarbazide was heated at 0.2 mm Hg in an oil bath at 110°C. As soon as the compound had melted, an evolution of gas was observed. After heating for 5 min more the melt solidified. Heating was then interrupted and the flask cooled. Boiling ethanol was added and the insoluble crystals filtered off and washed with ethanol. Yield 0.8 g, m.p. 183–184°C. (Found: C 32.61; H 6.88; N 30.63; S 27.96. Calc. for $C_6H_{15}N_3S_2$: C 32.55; H 6.84; N 31.64; S 28.96). The infrared spectrum indicated this to be 1- (or 2-) diethylthiocarbonylthiocarbohydrazide. The last alternative would account for the resistance of this compound to undergoing further changes analogously to II.

Pyrolysis of 4,4-dipropylthiosemicarbazide. The same procedure as described for the above thiosemicarbazide yielded 0.4 g of colourless crystals, m.p. 166–167°C, from 2 g of starting material. (Found: C 38.60; H 7.65; N 27.56; S 25.23. Calc. for $C_9H_{19}N_3S_2$: C 38.52; H 7.69; N 28.08; S 25.70). The infrared spectrum similarly suggested this to be 2-dipropylthiocarbonylthiocarbohydrazide.

3,6-Bis(dimethylamino)-1,2,4,5-tetrazine. This tetrazine was prepared according to the procedure given by Lin, Lieber and Horwitz⁷ for the preparation of 3,6-diamino-1,2,4,5-tetrazine. 4,4-Dimethylthiosemicarbazide (I) (15 g) and methyl iodide (17 g) were dissolved in ethanol (150 ml). On addition of 60 ml of 2 N sodium hydroxide, the solution turned red and methanethiol was formed. After standing for one week at room temperature the smell of methanethiol had almost disappeared, and the solution was evaporated to dryness *in vacuo*. The residue was extracted with two 100-ml portions of hot benzene (dried over sodium), and the combined extracts were evaporated to dryness. The residue (a red oil) was purified by column chromatography on alumina. Yield 0.5 g of red crystals, m.p. 121–123°C. (Found: C 42.90; H 7.37. Calc. for $C_9H_{12}N_4$: C 42.84; H 7.19). The ultraviolet spectrum showed an absorption at 493 m μ , log ϵ_{\max} 3.044. An essentially identical preparation⁸ has been reported recently.

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A Note on the Computation of Rate Constants by Steepest Decent and Related Methods

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In kinetic investigations of chemical reactions, the following problem often arises. The differential equation system thought to represent the reaction in question, can be integrated to an analytical function, but this is too complex to allow direct graphical evaluation of the rate constants from experimental data.

One frequently occurring example is the function

$$\alpha_t = \alpha_0 + \alpha_1 e^{-k_1 t} + \alpha_2 e^{-k_2 t} + \delta_t \quad (1)$$

which arises from some first order reaction schemes.¹ Wiberg^{2,3} has published two computer programs for the evaluation of the parameters α_0 , α_1 , α_2 , k_1 , and k_2 from experimental data given as a series of (α_t, t) pairs. The first program (P1) varies one parameter at a time until no further decrease in $U = \sum |\delta_t|$ can be observed, and the second program (P2) is based on the method of steepest decent.

In connection with a kinetic investigation⁴ both these methods have been tested on data represented by eqn. 1, and found