The Formation of ^{35}S Labeled Dithiocarbamate by the Reaction of Thiurumdisulfide with Inorganic Sulfide- ^{35}S

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The decomposition reaction of thiurumdisulfide with ^{35}S labeled inorganic sulfide ion and the distribution of ^{35}S in the products were investigated.

No radioactivity was found in the dithiocarbamate in the reaction at 30°C . This result shows that the decomposition of thiurumdisulfide is caused by the nucleophilic attack of sulfide ion on a $-\text{S}-\text{S}-$ bond as is generally accepted. In the reaction at 80°C ^{35}S labeled dithiocarbamate was yielded, and its radioactivity was increased by additional heating of the reaction mixture. The incorporation of ^{35}S into the product was explained in terms of the isotope exchange reaction with $^{35}\text{SH}^-$.

The corresponding ^{35}S labeled dithiocarbamates were isolated from the reaction mixtures.

1. Introduction

It is known that tetramethylthiurumdisulfide (TMTD) is decomposed by nucleophilic attack on a sulfur-sulfur bond¹⁾. For example, it gives dimethyldithiocarbamate by the reaction with sodium sulfide according to the following mechanism:²⁾

If the sulfide ion is labeled with ^{35}S in this reaction, sulfur- ^{35}S and unlabeled dithiocarbamate would be formed. The sulfur atoms in the produced dithiocarbamate may be exchangeable with formed sulfur- ^{35}S or residual sulfide- ^{35}S ³⁾. Sulfur- ^{35}S may also exchange with sulfur atoms in TMTD molecule.⁴⁾ Such a possibility for the distribution of ^{35}S in the decomposition of thiurumdisulfide is of interest.

In this paper the decomposition reactions of two thiurumdisulfides, TMTD and dimethylthiurumdisulfide (DMTD), with sodium hydrosulfide- ^{35}S or sodium sulfide- ^{35}S were described in expectation of being produced ^{35}S labeled dithiocarbamate.

2. Experimental

2.1 Reagents

Commercially available TMTD was recrystallized from chloroform-ethanol solution, mp 146.5°C . DMTD was prepared by oxidation of sodium N-methyldithiocarbamate, which was obtained by the reaction between methylamine and carbon disulfide.⁵⁾ Yield was quantitative. The product was recrystallized from chloroform-ethanol solution, mp 107°C . Sodium hydrosulfide- ^{35}S and sodium sulfide- ^{35}S were prepared from sulfuric acid- ^{35}S by the method reported previously.³⁾

2.2 Reaction procedure

A mixture of about 0.5 mmol of a thiurumdisulfide and 2 ml of 1 M sodium sulfide- ^{35}S or 2.5 ml of 1 M sodium hydrosulfide- ^{35}S solution was enclosed in a glass ampule. The ampule was allowed to stand for 1.5 hours at room temperature (30°C) or warmed at 80°C for 30 minutes under occasional shaking. Then the ampule was heated under a given condition.

The ampule was opened after cooling, and the reactants in the ampule was assayed as described below.

2-3 Measurement of radioactivity and determination of the amount of sulfur containing in the overall reaction mixture

A portion of the reaction mixture was treated with alkaline hydrogen peroxide solution, and then acidified with hydrochloric acid. A known excess amount of 0.1 *M* barium chloride was added to it to precipitate barium sulfate. The excess Ba^{++} was titrated with 0.05 *M* EDTA solution. The total amount of sulfur in the sample was determined from the titer. Barium sulfate was collected on a small disk of filter paper. After subsequent washing with diluted hydrochloric acid, water and ethanol, it was dried and placed in a planchet for measurement of the radioactivity together with the filter paper. The radioactivity was measured under the end window GM tube. The appropriate amount of the sample solution was initially picked up so as to give the precipitate of barium sulfate with infinite thickness. The radioactivity was measured within the limit of $\pm 5\%$ error.

2-4 Measurement of radioactivity and determination of the amount of sulfur containing in dithiocarbamate

A portion of the reactant was placed in a flask (A) as is shown in Fig. 1. The flask was connected through a condenser with four absorption tubes. The first two tubes (B, C) which is containing 20 ml of 0.5 *M* zinc acetate solution were for absorption of hydrogen sulfide, and the others (D, E) which is containing 20 ml of 2 *M* potassium hydroxide methanol solution were for absorption of carbon disulfide. Ten ml of 80% phosphoric acid was added to the reactant through a dropping funnel and then the flask was heated under aeration at a rate of 100 ml/min. The reactant was completely decomposed after heating for 30 minutes. To adsorb entirely the evolved gas, additional aeration for 10 minutes was necessary. Hydrogen peroxide was added to the combined content of D and E. Subsequent measurement of the radioactivity and determination of amount of sulfur in the solution were

carried out in a similar manner as above.

Fig. 1 Apparatus for analysis of the reaction products.

2-5 Isolation of dithiocarbamates

The reaction mixture was evaporated to dryness on a water bath. Absolute ethanol was added to the residue, and the solution was filtered after stirring under warm. Ether was added to the filtrate to precipitate the crystals of dithiocarbamate. The crystals were collected on a filter paper, washed with ether, dried and then weighed. The paper chromatogram of the product gave only one spot with R_f of 0.55 of dimethyldithiocarbamate and 0.56 of *N*-methyldithiocarbamate, respectively. The corresponding thiurumdisulfide from each product obtained by oxidation with sodium nitrite showed no depression of melting point with the authentic samples.

2-6 Paper chromatography

In order to identify the reaction product the following paper chromatography was employed.

Paper: Toyo filter paper No. 51, 24×40cm
Solvent: Methanol 5, water 1 (by volume)

Detection agent: Ammoniacal 5% silver nitrate solution. R_f values of the materials related in this paper were as follows: TMT-D, 0.67; DMTD, 0.18; Dimethyldithiocarbamate, 0.55; *N*-methyldithiocarbamate, 0.56; Sodium sulfide or sodium hydrosulfide, 0.22.

3. Results and Discussions

By the reaction of thiurumdisulfides with

Table 1 The reaction of thiurumdisulfide with sodium sulfide-³⁵S

Reactant			Decomposition		Heating		Products			
Thiurumdisulfide		Sodium sulfide	Temp.	Time	Temp.	Time	Total sulfur		Dithiocarbamate	
Compd.	Amounts (mmol)	Amounts (mmol)					Amounts (mmol)	Apparent radio-activity (10 ³ cpm)	Amounts (mmol)	Apparent radio-activity (10 ³ cpm)
TMTD	0.50	1.66	30	1.5	—	—	3.64 ^{a)}	1.60	0.81	0.00
	0.50	1.66	80	0.5	—	—	3.60	1.60	0.81	0.02
	0.50	1.66	80	0.5	130	3	3.64	1.59	0.78	0.25
	0.50	1.66	80	0.5	130	5	3.60	1.59	0.73	0.53
DMTD	0.50	2.32	30	1.5	—	—	4.20 ^{b)}	1.82	0.95	0.00
	0.50	2.32	80	0.5	—	—	4.20	1.81	0.95	0.49
	0.50	2.32	80	0.5	100	3	4.15	1.88	0.73	1.82
	0.50	2.32	80	0.5	100	5	4.20	1.80	0.66	1.79

Calculated total sulfur in the reaction mixture is a) 3.66 mmol and b) 4.32 mmol.

Table 2 The reaction of thiurumdisulfide with sodium hydrosulfide-³⁵S

Reactant			Decomposition		Heating		Products			
Thiurumdisulfide		Sodium hydro sulfide	Temp.	Time	Temp.	Time	Total sulfur		Dithiocarbamate	
Compd.	Amounts (mmol)	Amounts (mmol)					Amounts (mmol)	Apparent radio-activity (10 ³ cpm)	Amounts (mmol)	Apparent radio-activity (10 ³ cpm)
TMTD	0.50	2.67	30	1.5	—	—	4.01 ^{a)}	1.72	0.85	0.00
	0.50	2.67	80	0.5	—	—	3.95	1.73	0.85	0.45
	0.50	2.67	80	0.5	130	1	3.74	1.71	0.92	1.66
DMTD	0.50	2.56	30	1.5	—	—	4.10 ^{b)}	4.46	0.96	0.00
	0.50	2.56	80	0.5	—	—	4.10	4.48	0.93	2.34
	0.50	2.56	80	0.5	100	1	3.84	4.50	0.90	2.81
	0.50	2.56	80	0.5	100	3	3.90	4.48	0.92	4.30

Calculated total sulfur in the reaction mixture is a) 4.67 mmol and b) 4.56 mmol.

sodium sulfide-³⁵S, the corresponding dithiocarbamates were obtained. Table 1 shows that the theoretical amounts of dithiocarbamates were obtained by the reactions at both 30°C and 80°C. No radioactivity was found in the dithiocarbamates that was formed by the decomposition reaction at 30°C. The reactions may be expressed as follows.

Since the isotope exchange reaction between N-methyldithiocarbamate and sodium sulfide-³⁵S was observed at 100°C,⁶⁾ a little incorporation of radioactivity into the dithiocarbamate at 80°C may be due to the exchange reaction.

The reaction mixture of DMTD and sodium sulfide-³⁵S was heated to 100°C after decomposition of the mixture at 80°C. The radioactivity of N-methyldithiocarbamate increased (see Table 1), and after 5 hours it

Table 3 The isolated ^{35}S labeled dithiocarbamates

Reaction	Thiurum-disulfide	Sulfide	Total sulfur	Heating		Dithiocarbamate				
	Amounts (mmol)	Amounts (mmol)	Apparent radio-activity (10^3cpm)	Temp. ($^{\circ}\text{C}$)	Time (h)	Yield (mmol)	Apparent radio-activity (10^3cpm)	Radio-chem. yield (%)	S analysis	
									Found (%)	Calcd. (%)
TMTD+ Na_2^{35}S	0.50	1.66	1.59	130	5	0.49	0.52	9	45.2	44.8
DMTD+ Na_2^{35}S	0.50	1.44	1.88	100	3	0.51	1.87	30	38.4	38.4
TMTD+ NaH^{35}S	0.51	2.39	4.63	130	3	0.43	4.47	19	44.9	44.8
DMTD+ NaH^{35}S	0.53	2.39	4.55	100	3	0.40	4.02	16	38.5	38.8

reached the same order as those of overall sulfur in the reactant. Labeled N-methyldithiocarbamate was actually isolated from such a reactant with the yield of 50%, and the radiochemical yield on the basis of sodium sulfide- ^{35}S was 30% (Table 3).

On the other hand dimethyldithiocarbamate in the reactant from TMTD showed little radioactivity even after heating at 130°C for 5 hours as is shown in Table 1. This result is reasonable since little exchange of sulfur has been observed between sodium dimethyldithiocarbamate and sodium sulfide- ^{35}S .³⁾ The labeled dithiocarbamate was isolated with the radiochemical yield of only 9% from the reaction mixture (Table 3).

The decomposition of thiurumdisulfide with sodium hydrosulfide- ^{35}S was undertaken by the similar procedures described before. The results are shown in Table 2. The formation of dithiocarbamate was confirmed by paper chromatography. In this case there is remarkable difference from the result given in the reaction with sodium sulfide- ^{35}S . The amount of total sulfur decreased strikingly (over 10%) after the decomposition. Since the evolution of a gas, which was identified as hydrogen sulfide by passing through the solution of zinc acetate, was observed, the decrease in amount of total sulfur may be caused by evolution of hydrogen sulfide. On the basis of these results the reaction should be expressed as follows:

The amount of dithiocarbamate determined in the decomposition at 30°C was close to the theoretical value, and no radioactivity was found in it.

It has been reported^{3), 6)} that the isotope exchange reaction of sodium hydrosulfide- ^{35}S occurred slightly with N-methyldithiocarbamate at 50°C (10% exchange after 25 hours) and did not at all with dimethyldithiocarbamate at the same temperature. On the basis of this result, it was assumed that ^{35}S does not incorporate into dithiocarbamate by the decomposition reaction of the thiurumdisulfides with sodium hydrosulfide- ^{35}S at 30°C for 30 minutes. Hence the reactions are expressed by

The large incorporation of ^{35}S into dithiocarbamate, which was observed in the course of the decomposition at 80°C for 30 minutes, may be brought by subsequent exchange reaction, because the isotope exchange reaction of dimethyldithiocarbamate as well as N-methyldithiocarbamate with sodium hydrosulfide- ^{35}S proceeded markedly after 1 hour at 100°C .^{3), 6)}

With aim to increase the radioactivity of dithiocarbamate produced by decomposition, the reaction mixtures of thiurumdisulfides

and sodium hydrosulfide- ^{35}S were heated at 130°C or 100°C . As was expected, the radioactivity of dimethyldithiocarbamate and N-methyldithiocarbamate increased, after heating for 1 and 3 hours, respectively, to nearly equal level to those of overall sulfur in the reaction mixture.

On the basis of the observed results, the incorporation of ^{35}S into dithiocarbamate was considered to be caused by exchange reaction with hydrosulfide- ^{35}S ion. In an aqueous solution elementary sulfur- ^{35}S may not play an important part on the reaction of ^{35}S incorporation.

From these reaction mixtures ^{35}S labeled dithiocarbamates were isolated. The radiochemical yield of sodium dimethyldithiocarbamate- ^{35}S and sodium N-methyldithiocarbamate- ^{35}S was 19% and 16%, respectively. Both were lower than those obtained by the direct exchange reaction of dithiocarbamate

as reported before.^{3,6)} Data for all isolated ^{35}S labeled compounds in this paper are summarized in Table 3.

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要 旨

チウラムジスルフィドと硫化物- ^{35}S との反応による ^{35}S 標識 ジチオカルバミン酸塩の生成

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チウラムジスルフィドの ^{35}S 標識硫化物イオンによる分解反応と、反応生成物中の ^{35}S 分布に関して検討した。

30°C における反応では、ジチオカルバミン酸塩中に放射能がみとめられない。この結果は、一般にみとめられているように、硫化物イオンの-S-S-結合に対する求核的攻撃によってチウラムジスルフィドの分解が起こることを示している。 80°C では ^{35}S 標識ジチオカルバミン酸塩の生成がみとめられ、かつその放射能は反応溶液を加熱することにより増加する。生成物への、この ^{35}S の取込みを $^{35}\text{SH}^-$ との同位体交換反応による機構で説明した。

反応溶液から、相当する ^{35}S 標識ジチオカルバミン酸塩を単離した。