**STUDIES ON THE CHEMICAL PROPERTIES OF
 α -LIPOAMIDE (1,2-DITHIOLANE-3-VALERAMIDE)
I. FORMATION OF 5-(2-THIACYCLOBUTYL) VALERAMIDE
WITH POTASSIUM CYANIDE AND THE POSSIBILITY
OF ITS ANALYTICAL APPLICATION**

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Concerning the cleavage of the S-S linkage of aliphatic disulfides with cyanide ion, there have been several reports (1). The formation of sulfide from unsymmetrical disulfide through the elimination of sulfur has been interpreted to proceed by the following mechanism (2).

Chart 1

where R' is more electron-withdrawing than R.

The present study was undertaken to investigate the reaction of α -lipoamide, one of the unsymmetrical aliphatic disulfides, with potassium cyanide.

EXPERIMENTAL

1. Reaction of α -Lipoamide with KCN

To a solution of 8 g of α -lipoamide (0.039 mole) in 70 ml of 50 % ethanol was added 8 g of KCN (0.123 mole) in 20 ml of water. The solution was refluxed over a flame for 3.5 hours and cooled. It turned orange in color. After acidification to pH 5 with 5 N HCl and addition of 3 g of NaCl, the solution was extracted several times with CHCl_3 . The combined CHCl_3 extract was dried with anhydrous K_2CO_3 and evaporated to dryness, leaving about 5 g of pale yellow crystals, which were recrystallized from 30 % ethanol to give white leaflets, mp 114.5—115.5. Elemental analyses: Calculated for $\text{C}_8\text{H}_{15}\text{ONS}$, C, 55.49, H, 8.67, N, 8.09, S, 18.50. Found: C, 55.26, H, 8.66, N, 8.25, S, 18.21. The mother liquor exhibited CNS^- reaction with FeCl_3 .

2. UV Spectrum of the Reaction Product

The reaction product exhibited the absorption spectrum with a peak at 265 m μ ,

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showing no maximum in the vicinity of $330\text{ m}\mu$ peculiar to the absorption of the cyclic trimethylene disulfide (3). The absorption at $265\text{ m}\mu$ was reported to be due to the presence of the thiacyclobutyl radical (4).

FIG. 1 UV Spectra of the Reaction Product (a) and α -Lipoamide (b) in 50 % Ethanol

3. IR Spectrum of the Reaction Product

Some differences were recognized in the finger print region of the IR spectra of the reaction product and α -lipoamide, though they were very similar.

FIG. 2 IR Spectra of the Reaction Product (—) and α -Lipoamide (---) (KBr)

4. Gaschromatographic Behavior of the Reaction Product

The reaction product was examined gaschromatographically together with α -lipoamide. Experimental conditions are: column temperature, 207°; carrier gas, nitrogen; column, Chromosorb W coated with 3% 1,4-butanediol succinate; hydrogen flame ionization detector; sample size, 2 μ l.

There appeared significant differences both in their retention times and sensitivities, as shown in Fig. 3.

FIG. 3 Gas Chromatograms of the Reaction Product (b) and α -Lipoamide (c)
a: solvent (ethanol)

Furthermore, the relationship between the concentration and the peak height of the reaction product was examined by the absolute method, giving a good linearity.

FIG. 4 Relationship between the Concentration and the Peak Height of the Reaction Product

DISCUSSION

The above findings, especially UV absorption maximum at 265 $m\mu$ and the results of elemental analyses, show that α -lipoamide was converted to 5-(2-thiacyclobutyl)

valeramide with loss of sulfur. As the sulfur atom nearer to the carbonyl radical in α -lipoamide molecule is considered to be more electronegative than the other sulfur atom, the reaction may be, through a labile intermediate as shown in brackets, as follows:

Chart 2

Good reproducibility as well as enhanced sensitivity and short retention time of 5-(2-thiacyclobutyl) valeramide in gaschromatography may make it possible to use this reaction for the determination of α -lipoamide. The details of the analytical application will be reported later.

SUMMARY

1. Reaction of α -lipoamide with potassium cyanide in dilute ethanol was investigated. It was thereby found that α -lipoamide was converted to 5-(2-thiacyclobutyl) valeramide almost quantitatively with loss of sulfur.

2. 5-(2-thiacyclobutyl) valeramide has many advantageous points in its gaschromatographic behavior, such as sensitivity, reproducibility and retention time, as compared with those of α -lipoamide.

The conversion of α -lipoamide to 5-(2-thiacyclobutyl) valeramide, therefore, will be a very useful means for the determination of α -lipoamide.

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