The Reaction of S-Acylthiamine and 2-Mercaptoethanol

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During the course of investigation on the inhibitory effect2) of S-acetylthiamine derivatives on some enzyme activities, it was found that O-acetylglucosyl-S-furoylthiamine (AFT) reacted with 2-mercaptopropanol (ME) used as a stabilizing agent for an enzyme to produce a precipitate in alkaline medium. We wish to report the structure of this product.

Since it has been known that acyl group of S-acetylthiamine is transferred to thiol of cysteine or glutathione,9) the reaction product of AFT with ME would be considered as S-furoylmercaptoethanol. However, the nuclear magnetic resonance (NMR) spectrum suggested the presence of six protons at 2–4 τ except two triplets for CH₃ at 5.49 and 6.58 τ. Neither NMR nor infrared (IR) spectrum shows any signal for hydroxyl group. Thus, hydroxyl group of ME should also be substituted by acyl group producing O,S-difuroylmercaptoethanol. This product was also identified with the sample synthesized from furanyl chloride and ME.

In the case of S-benzoylethiamine (SBT), O,S-dibenzoylethanol was also obtained in almost same condition. This dibenzoate was prepared by the reaction of ME and benzoyl chloride.4)

Acyl group of S-acetylthiamine derivatives is removed by some SH compounds such as thioglycolic acid or thiophenol but not by ethylenglycol and the migration of S-acetylmercaptoethanol to O-acetylmercaptoethanol has also been reported.4) Thus, acyl group of AFT or SBT might react with thiol of ME at first then be rearranged to hydroxyl, and another acyl group might attack thiol recovered as shown in the following scheme.

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\begin{align*}
\text{B₄-S-C-R} & + \text{HS-CH₂-CH₂} \rightarrow \text{R-C-S-CH₂-CH₂} \rightarrow \text{R-C-S-CH₂-CH₂} \\
\text{OH} & \quad \text{OH} \\
\text{H⁺} & \quad \text{R-C-O-CH₂-CH₂-SH} \rightarrow \text{R-C-S-B₄} \rightarrow \text{R-C-O-CH₂-CH₂-S-C-R}
\end{align*}
\]

The significance of this reaction in vivo and the application to the determination of S-acetylthiamine are under investigation.

Experimental

Reaction of AET and ME—MeOH solution of AFT was added to sodium glycerophosphate solution and pH was adjusted to 7.5 or higher. ME was added making final concentration of AFT, ME, and gly-
cerophosphate, 0.02 M, 0.01 M, and 0.05 M, respectively. After 1 hr keeping at 30°, crystals were collected by centrifugation and recrystallized from aq. MeOH producing needles of mp 88°.

**Synthesis of O,S-Difuroylmercaptoethanol** — To a mixture of 20 ml of pyridine and 7.8 g of furoyl chloride under cooling and stirring, 1.56 g of ME was added slowly. After 30 min, reaction mixture was poured into ice-water and crystals were filtered, washed with NaHCO₃ solution and recrystallized from EtOH giving needles of mp 88—89°. Both NMR and IR spectra (Fig. 1 and 2) were identical with those of the product mentioned above. *Anal. Calcd.* for C₁₀H₁₆O₂S: C, 54.14; H, 3.79. *Found:* C, 54.34; H, 3.98.

**O,S-Dibenzoylmercaptoethanol** — SBT was dissolved into 10 vol. of 40% MeOH and ME was added in alkaline medium. After standing, oil separated was dissolved into CHCl₃, washed with water and dried over Na₂SO₄, and the solvent was distilled off. Both NMR and IR spectra of this oil were identical with those of O,S-dibenzoylmercaptoethanol synthesized from benzoyl chloride and ME in pyridine.

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![Fig. 1. NMR Spectrum of O,S-Difuroylmercaptoethanol](image1)

![Fig. 2. IR Spectrum of O,S-Difuroylmercaptoethanol](image2)

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**Studies on the Synthesis of Munjistin. IV.** Synthesis of Munjistin through 1,4-Dihydroxy-2-methylanthaquinone

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In the previous communication the synthesis of munjistin (I), namely 1,3-dihydroxy-2-anthaquinonecarboxylic acid, had been reported. The purpose of the communication was concerned with the identification of synthetic I with the one derived from dammacanthal (II) (3-hydroxy-1-methoxy-2-anthaquinonecarbaldehyde), a natural pigment of *Dammacanthus* spp.

The present paper is to report the details of the synthesis of I. The discrepancy between the observed value and the theoretical value of the analyses of the synthetic specimens of I and 1,2,4-trihydroxy-3-anthaquinonecarboxylic acid (III) has now been discriminated.

2) Location: 5-1 Ōe-bōn-machi, Kumamoto.
6) D.R.P., 272301 (Friedländer, 11, 592 (1915)).
7) D.R.P., 260765 (Friedländer, 11, 592 (1915)).