bluish white mass. The substance was analyzed with the following results:

0.3196 gave 0.7251 AgCl : Cl = 48.51. 0.2810 gave 0.1824 ZnO : Zn = 52.15. Calculated for Zn_3Cl_5; Zn = 52.43; Cl = 47.31.

The substance is extremely hydroscopic and rapidly undergoes hydrolysis when treated with water. The compound is evidently a subchloride of zinc and its constitutional formula could be conveniently represented by the formula $ZnCl.2ZnCl_2$.

We are at present engaged in studying this compound more fully and attempting to prepare, if possible, the true subchloride of zinc, *viz.*, ZnCl, as also similar other sub-salts.

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HYDANTOINS: THE HISTORY OF 2-THIOHYDANTOIN. XXII.

BY TREAT B. JOHNSON.

Received April 11, 1913.

2-Thiohydantoin (I) is not listed in the latest edition of Richter's Lexikon der Kohlenstoff Verbindungen, nor is it described in Beilstein's Handbuch. Therefore, one who depended upon these works for his literature references, would naturally conclude that such a compound has not been synthesized. This omission is an error. We find that this supposed, unknown compound was described several years ago (22), but apparently has been entirely overlooked by investigators in this field.[1]

2-Thiohydantoin (I), $\underline{\text{NH.CSNH.CH}_2\text{CO}}$ was apparently first synthesized by Peter Klason and is described in a paper entitled "Ueber Senfölessigsaüre und Thiohydantoin," which was published by this investigator in 1890.[2] Klason prepared the hydantoin by heating the hydrochloride of ethyl aminoacetate with potassium thiocyanate at 140–150°. Regarding the yield obtained by him, we have no knowledge because his paper is not accessible to us. The constitution of the hydantoin was established by its behavior on hydrolysis. Klason evidently obtained thiohydantoic acid (IV) by heating the hydantoin (1) with barium hydroxide. This acid crystallized from water in prismatic crystals and was

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[1] In connection with our hydantoin researches we are making a bibliography of papers on hydantoins and thiohydantoins. We intend to publish this later together with a bibliography of papers on the glyoxaline compounds. Since it is our desire to have these as complete as possible, the writer will consider it a favor if informed of any papers, which are not reviewed in *C. A.* or the *Chem. Zentr.*, and therefore likely to be overlooked.

[2] *Ofv. kongl. Vet.-Ak.*, 87 (1890); *Chem. Ztg.*, 14, Rep., 200; *Chem. Zentr.*, 2, 344 (1890).

desulfurized by interaction with mercury oxide forming hydantoic acid (V). Klason also prepared the ethylester of hydantoic acid (VI) by the action of potassium cyanate on the hydrochloride of ethyl aminoacetate. These various changes are represented as follows:

$$HCl.NH_2CH_2COOC_2H_5 + KSCN = KCl + \underset{\text{III.}}{NH_2CSNH.CH_2COOC_2H_5.} \longrightarrow$$

$$\underset{\text{I.}}{\underline{NH.CS.NH.CH_2.CO}} \xrightarrow{Ba(OH)_2} \underset{\text{IV.}}{NH_2CSNHCH_2COOH} \xrightarrow{HgO} \underset{\text{V.}}{NH_2CONHCH_2COOH.}$$

$$HCl.NH_2CH_2COOC_2H_5 + KCNO = KCl + \underset{\text{VI.}}{NH_2CONHCH_2COOC_2H_5.}$$

In the following year (1891) appeared Markwald, Neumark and Stelzner's paper[1] entitled: "Ueber Thiohydantoïne und von diesen derivirende Basen," in which they describe several substituted thiohydantoins. These were prepared by the action of aliphatic and aromatic mustard oils on α-aminoacids. They made no attempts apparently to prepare 2-thiohydantoin (I), and the following quotation from their paper is evidence that they were unaware of Klason's work. They wrote as follows: "Die den Hydantoïnen entsprechenden Derivate des Thioharnstoffs, welche sich von einem bisher nicht bekannten Thiohydantoïn $\underline{NH.CS.NH.CH_2.CO}$ ableiten, sind bisher noch fast völlig unbekannt gewesen" and "Wahre Thiohydantoïde konnten bisher nur in der aromatischen Reihe erhalten werden."[2]

2-Thiohydantoin (I) apparently received no further attention until 1900, when attempts to synthesize it were made by Harries and Weiss. In their first paper[3] entitled "Ueber eine Darstellungsweise des Hydantoïns," these investigators describe the preparation of hydantoin from ethyl hydantoate (VI), but give no experimental data regarding the corresponding sulfur compounds. They wrote, however, at the end of their paper, as follows: "Der Salzsäure-Glycinester setzt sich in analoger Weise wie mit Kaliumcyanat auch mit Rhodankalium beim Erwärmen um und man erhält den Thiohydantoïnsäureäthylester; es ist nun aber bisher nicht gelungen, aus diesem Product das normale Thiohydantoïn $\underline{NH.CS.NH.CH_2.CO}$, nach den angegebenen Methoden zu erhalten." A description of this ethyl thiohydantoate, and its method of preparation, is given in a later paper by Harries and Weiss,[4] which was published in 1903. Attempts, however, to convert the ester into 2-thiohydantoin by the application of heat or by digestion with hydrochloric acid were in vain.

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[1] *Ber.*, 24, 3278.

[2] Aschan, *Ber.*, 17, 420.

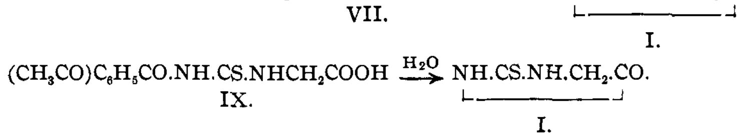
[3] *Ber.*, 33, 3418.

[4] *Ann. Chem.*, 327, 355.

Also attempts to introduce sulfur into hydantoin by heating with phosphorus trisulfide and ammonium sulfide were unsuccessful. There is no evidence, in either of these two papers, that Harries and Weiss were aware of Klason's work.

The next chemist to take up the investigation of 2-thiohydantoin was Komatsu, who described, in 1911, a practical method of synthesizing this compound.[1] He investigated the action of potassium thiocyanate on glycocoll, in acetic anhydride solution, and made the interesting observation that they combine giving a crystallin product. Komatsu concluded that this was thiohydantoic acid (VII) and found that it underwent a molecular condensation, when digested with hydrochloric acid, forming 2-thiohydantoin. During the same year Wheeler, Nicolet and Johnson also succeeded in synthesizing the same thiohydantoin by digesting benzoyl- and acetylthiohydantoic acids (IX) with hydrochloric acid.[2] These changes are represented by the following formulas:

$NH_2CH_2COOH + KSCN$ (acetic anhydride) =

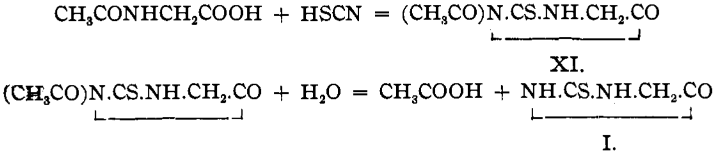


$$\underset{\text{VII.}}{NH_2\,CS.NH.CH_2.COOH} \xrightarrow{-H_2O} \underset{\text{I.}}{\underbrace{NH\text{-}CS.NH.CH_2.CO.}}$$

$$\underset{\text{IX.}}{(CH_3CO)C_6H_5CO.NH.CS.NHCH_2COOH} \xrightarrow{H_2O} \underset{\text{I.}}{\underbrace{NH.CS.NH.CH_2.CO.}}$$

Although Komatsu succeeded in obtaining, by his method, 2-thiohydantoin, it was later found that his interpretation of the mechanism of his reaction was wrong. Johnson and Nicolet[3] reinvestigated his reaction and found that thiohydantoic acid is not a product of the interaction of potassium thiocyanate and glycocoll in acetic anhydride solution. They observed, on the other hand, that these reagents interact in an unique manner forming acetylthiohydantoin (XI). The latter undergoes hydrolysis when heated with hydrochloric acid giving quantitatively 2-thiohydantoin (I). The reactions involved in this synthesis may therefore be regarded as taking place along the lines indicated by the following equations: This reaction has since been shown to be of very general

$$NH_2CH_2COOH + (CH_3CO)_2O = \underset{\text{X.}}{CH_3CO.NH.CH_2.COOH}$$



$$CH_3CONHCH_2COOH + HSCN = \underset{\text{XI.}}{\underbrace{(CH_3CO)N.CS.NH.CH_2.CO}}$$

$$\underbrace{(CH_3CO)N.CS.NH.CH_2.CO} + H_2O = CH_3COOH + \underset{\text{I.}}{\underbrace{NH.CS.NH.CH_2.CO}}$$

application and is still being investigated in this laboratory.

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[1] *Memoirs Coll. Sci. and Eng. Kyoto Univ. (Japan), B,* 1.

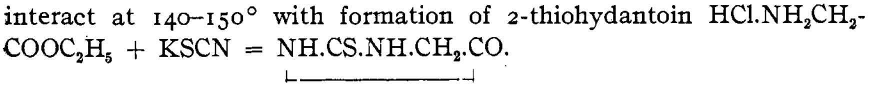
[2] *Am. Chem. J.*, 46, 456.

[3] THIS JOURNAL, 33, 1973.

A review of the literature, therefore, reveals the fact that Klason obtained 2-thiohydantoin by heating the hydrochloride of ethyl aminoacetate with potassium thiocyanate at 140–150°. This change involves the intermediate formation of ethyl thiohydantoate. Since Harries and Weiss[1] were unable to effect a transformation of this ester into 2-thiohydantoin it seemed very important, therefore, to repeat Klason's experiment and establish definitly whether thiohydantoin is actually formed. This has now been done and I have confirmed his original observation. Thiohydantoin is formed, but the method can not be recommended for its preparation. The yield is so small that the reaction is of no practical importance.

Summary.

Potassium thiocyanate and the hydrochloride of ethylaminoacetate interact at 140–150° with formation of 2-thiohydantoin



$$HCl.NH_2CH_2COOC_2H_5 + KSCN = \underbrace{NH.CS.NH.CH_2.CO}.$$

Experimental Part.

The Formation of 2-Thiohydantoin by the Action of Potassium Thiocyanate on the Hydrochloride of Ethyl Aminoacetate.—Five grams of the hydrochloride and 3.5 grams of dry, finely pulverized potassium thiocyanate were mixed and heated in an oil bath at 140–150°. There was no apparent reaction at first, but finally the mixture began to assume a dark color, gradually decomposed and alcohol was evolved. There was also a copious evolution of hydrogen sulfide. After heating exactly 2 hours, we obtained a black, amorphous product which was triturated with cold water. Part of the material was insoluble and consequently was separated by filtration. This insoluble substance was finally dissolved in boiling water, the solution acidified with hydrochloric acid and then decolorized by digestion with bone-coal. The solution was then concentrated and cooled when 2-thiohydantoin separated in prismatic crystals melting at 227–228° with decomposition. A mixture of this product with some pure thiohydantoin, prepared from hippuric acid,[2] melted at exactly the same temperature. The yield of purified thiohydantoin was only about 0.7 gram. Nitrogen determination (Kjeldahl):

Calculated for $C_3H_4ON_2S$: N, 24.12; found: N, 24.0.

In another experiment 5.0 grams of the hydrochloride of ethyl aminoacetate and 3.5 grams of dry potassium thiocyanate were dissolved in 50 cc. of absolute alcohol and the solution warmed on the steam bath for 4–5 hours. After cooling, the sodium chloride was then filtered off and the alcohol then expelled by evaporation on the steam bath. The crude ethyl thiohydantoate was then heated in an oil bath at 140–150° for 2

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[1] *Loc. cit.*

[2] Johnson and Nicolet, *Loc. cit.*

hours. It partially melted, turned dark colored and hydrogen sulfide was evolved copiously. In order to separate any thiohydantoin the reaction-product was triturated with water, as described in the previous experiment, and the insoluble thiohydantoin separated by filtration. This was then purified by digestion with bone-coal and crystallization from boiling water. It separated in prismatic crystals, melting at 225–227°. The yield was about 0.6–0.7 gram.

We obtained no evidence of the formation of 2-thiohydantoin when ethyl thiohydantoate was warmed with dilute hydrochloric acid. Hydrogen sulfide was evolved and the only crystallin substances identified were ammonium chloride and the hydrochloric acid salt of glycocoll.

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MANNITE ESTERS OF SULFURIC ACID.

BY W. R. BLOOR.

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In the course of the preparation of some esters of mannite with the higher fatty acids for a biochemical investigation,[1] it was found that the yield was unsatisfactory—less than 50% of the theoretical. The method of synthesis employed involved the heating of the two substances in solution in concentrated sulfuric acid to a temperature of 70° for four hours and it was suspected that the reason for the low yield was the destructive action of the strong acid on the mannite at this temperature. Accordingly, the synthesis was carried out at a lower temperature (38°–40°) with the result of a much improved yield. The esters obtained, however, were not the same as at the higher temperature. At 70° the main product was the iso-mannid ester, with small amounts of the mannitan ester, while at 40° only the mannitan ester was recovered. (The opinion was expressed at the time[2] that the reason for the different compound may have been the different method of separation. The mannid compound was extracted directly from the sulfuric acid with ether, while the mannitan compound was separated by pouring the sulfuric acid digestion mixture into excess of water and salting out. The opportunities for hydration were much greater in the second case and the mannitan ester was probably formed at the expense of the mannid ester.) In order to find an explanation for these phenomena the following study of the action of concentrated sulfuric acid on mannite was undertaken.

The literature on the subject[3] states merely that the action of con-

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[1] Bloor, *Biol. Chem.*, 2, 427 (1910); 11, 141, 421 (1912).

[2] *Loc. cit.*

[3] Favre, *Ann. chim. phys.*, 11, 77; Knop and Schnedermann, *Ann.*, 51, 132.