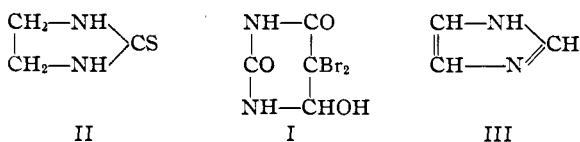


[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

The Action of 5,5-Dibromoxyhydrouracil on Ethylene-thiourea¹BY TREAT B. JOHNSON AND C. O. EDENS²

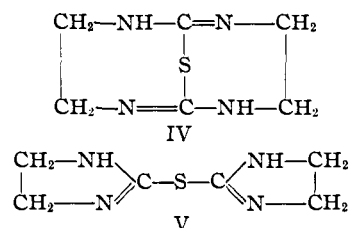
The study of the behavior of 5,5-dibromoxyhydrouracil³ I toward ethylene-thiourea II was undertaken for the purpose of determining whether this cyclic thiourea would undergo desulfurization and oxidation by interaction with this pyrimidine leading to the production of imidazole or glyoxaline III.



The authors find that ethylene-thiourea II and the pyrimidine I interact immediately when digested together in alcohol solution with profound alteration of the ethylene-thiourea molecule. The pyrimidine itself undergoes a normal dissociation in this interaction with formation of 5-bromouracil in practically theoretical yield, and generation of hypobromous acid. The latter acid interacts with the cyclic thiourea II with partial destruction of the heterocyclic ring leading to the production of (1) the hydrobromide or ethylenediamine, (2) free sulfur and (3) a crystalline basic compound containing sulfur and melting at 218–220°. This melting point approaches very closely to that of 2-mercaptoimidazole previously described by Marckwald⁴ and reported to melt at 222°. The results of a complete analysis, however, have now established the fact that it is to be assigned the empirical constitution $C_6H_{10}N_4S$, and not that of Marckwald's compound expressed by the formula $C_3H_4N_2S$. We now find that this new oxidation product is identical with the sulfur base prepared by Jaffe in 1894⁵ by the action of thiophosgene on ethylenediamine in chloroform solution and to which he assigned this same empirical formula.⁶ Both compounds showed the same chemical and

physical properties and there was no lowering of the melting point (218–220°) when samples of the pure base from the two sources were mixed and heated. The same sulfur base $C_6H_{10}N_4S$ is also formed by oxidation of ethylene-thiourea II with 5,5-dichloro-4-methoxyhydrouracil.⁷

Jaffe proposed two possible formulas, IV and V, to express the constitution of his sulfur base $C_6H_{10}N_4S$, and decided in favor of formula IV.

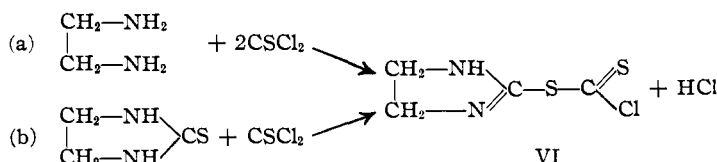


The fact, however, that the same sulfur compound is obtained by the authors by direct oxidation of ethylene-thiourea II leads to the conclusion that the reduced glyoxaline ring functions in this compound, and that formula IV is not a true expression of its constitution. The authors are now able to present new experimental evidence in support of this conclusion. They find that not only ethylenediamine, but also ethylene-thiourea II interact smoothly with thiophosgene to give Jaffe's base melting at 218–220°. Furthermore, they have succeeded in isolating ethylene-thiourea as a product of reaction by interaction of ethylenediamine with thiophosgene as first applied by Jaffe.

As regards the mechanism of reaction leading to the formation of the heterocyclic base V, by interaction of thiophosgene with ethylenediamine and ethylene-thiourea, respectively, the following formulations are proposed by the authors.

I. Ethylenediamine and ethylene-thiourea react with thiophosgene, respectively, to give the same intermediate VI as is expressed below

- (1) Researches on Pyrimidines, CLXIX.
 (2) Sterling Professorship of Chemistry Research Assistant, 1940–1941.
 (3) Wheeler and Johnson, *J. Biol. Chem.*, **3**, 183 (1907).
 (4) Marckwald, *Ber.*, **25**, 2359 (1892).
 (5) Max Jaffe, Inaugural Dissertation, Univ. Basel, Berlin, 1894; Jaffe and Kuhn, *ibid.*, **27**, 1664 (1894).
 (6) This sulfur base is recorded in Beilstein's "Handbuch" (Fourth Edition), Vol. IV, p. 250, as a product of unknown constitution prepared from ethylenediamine.



II. This common intermediate VI then could

- (7) Behrend, *Ann.*, **236**, 59 (1886).

analysis 27.7% of nitrogen, thereby establishing the identity of this reaction product as ethylene-thiourea. Jaffe did not detect this compound as a product of his reaction and its identification in our experiment indicates that it is very probably an intermediate product in Jaffe's original reaction for production of the base from ethylenediamine.

Preparation of Jaffe's Base $C_6H_{10}N_4S$ by the Action of Thiophosgene on Ethylene-Thiourea.—Five grams of ethylene-thiourea, 100 g. of chloroform and 5.6 g. of thiophosgene were refluxed for three hours, and the chloroform and excess of thiophosgene then expelled by evaporation. Carbon bisulfide was detected in this distillate by precipitation as copper xanthate. The dry residue remaining after evaporation was dissolved in 50 ml. of hot water and the solution made alkaline with ammonia and cooled when 3.0 g. of the base $C_6H_{10}N_4S$ separated, or 68.5% of the calculated on the conversion of ethylene-thiourea to the base. The unreacted thiourea is recovered by evaporation of the mother liquor and purified by crystallization from hot water.

The base $C_6H_{10}N_4S$ is best purified by dissolving in hot, dilute hydrochloric acid and cooling the solution when

the pure hydrochloride separates in the form of needles. This salt is converted quantitatively into Jaffe's base melting at 218° by treatment with ammonia.

Summary

1. Ethylene-thiourea is oxidized by 5,5-dibromoxyhydrouracil and 5,5-dichloro-4-methyl-oxyhydrouracil to *dihydroglyoxaline sulfide*, $C_6H_{10}N_4S$.

2. This sulfur base is identical with the compound obtained by Jaffe in 1894 by the action of thiophosgene on ethylenediamine.

3. The same base, $C_6H_{10}N_4S$, is formed in good yield by interaction of ethylene-thiourea with thiophosgene.

4. Ethylene-thiourea is an intermediate product formed in Jaffe's original reaction.

NEW HAVEN, CONNECTICUT

RECEIVED NOVEMBER 23, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF BOTANY, UNIVERSITY OF MINNESOTA]

The Geometric Isomerism of the Linolenic Acids. Elaidolinolenic Acid¹

By J. P. KASS, JOSEPH NICHOLS AND G. O. BURR

Linolenic acid having an essentially theoretical iodine value may be prepared only by the debromination of the ether-insoluble alpha-hexabromostearic acid, m. p. 178.3°, obtained by the bromination of the drying oil fatty acids. However, it is not certain whether the acid prepared in this manner is stereochemically identical with the natural form, since the regenerated $\Delta^9,12,15$ -octadecatrienoic acid yields on rebromination only 23–25% of the solid hexabromide, the remaining bromides being ether-soluble liquids. Erdmann and Bedford² therefore inferred that the debrominated acid is a 1:3 mixture of the stereoisomeric alpha and beta linolenic acids, the first being completely precipitable as the crystalline alpha hexabromide, the second forming the liquid beta bromides and having its origin in a geometric isomerization occurring during debromination. On the other hand, Rollett³ believed that the re-

generated linolenic acid is a homogeneous substance identical with the parent acid, and that the presence of three double bonds accounted for the production, on bromination, of four pairs of racemic hexabromides, only one of which happens to be an ether-insoluble solid.

In support of Rollett's theory, it has been shown^{3,4} that both the solid alpha- and liquid beta-bromides revert to the same unsaturated acid, which forms the same hexabromo- and hexahydroxystearic acids as the natural linolenic acid. However, Shinowara and Brown⁵ have found that the linolenic acid obtained in impure form from linseed and perilla oil acids by direct crystallization at -70° yielded the alpha hexabromostearic acid in 30–36% of theory, corresponding to an average calculated hexabromide value of 92, rather than the values of 70–75 they found for the debrominated acid. Moreover, Matthews, Brode and Brown⁶ were able to separate the latter substance into two or more components, one of which had a hexabromide value of 96, equal to that of the best available sample of the natural isomer. Granted the homogeneity of the starting mate-

(1) This work was aided by grants from the Hormel Foundation, the National Livestock and Meat Board and the Graduate School of the University. Presented before the Division of Agricultural and Food Chemistry, American Chemical Society Convention in Detroit, September 13, 1940.

Assistance in the preparation of these materials was furnished by the personnel of Work Projects Administration, Official Project No. 165-1-71-124, Sub-project 325.

(2) Erdmann and Bedford, *Z. physiol. Chem.*, **69**, 76 (1910).

(3) Rollett, *ibid.*, **70**, 404 (1910).

(4) McCutcheon, *Can. J. Research*, **18**, 231 (1940).

(5) Shinowara and Brown, *THIS JOURNAL*, **60**, 2734 (1938).

(6) Matthews, Brode and Brown, *ibid.*, **63**, 1064 (1941).