and the fact that capillary condensation is negligible, it is shown that the film of water on graphite attains a minimum thickness of 10 Å. at a relative pressure very close to saturation. The extrapolation of the isotherm to unit relative pressure indicates a minimum thickness of 16 Å. These figures are obtained on the postulate that the density of the adsorbed material is that of the liquid at the same temperature. The physical relations indicate that the packing must be looser than in the liquid. Consequently, the figures quoted are to be considered minima and not a reliable estimate of the true thickness.

6. It is shown thermodynamically that the film can be polymolecular with a contact angle not equal to zero. It is also pointed out that this situation leads to a difficult problem in the construction of a model compatible with both conditions.

7. It is shown that $E_1 - E_L > 0$, $E_2 - E_L > 0$ and $E_3 - E_L < 0$.

8. The integral and differential heats of adsorption of water on graphite are determined from the heats of emersion.

9. The heats of emersion are used to determine the change in total surface energy caused by the adsorption of water. These values combined with the free surface energy changes as determined from the adsorption isotherm permit the calculation of the change in surface entropy.

CHICAGO, ILLINOIS RECEIVED AUGUST 11, 1947

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF MERCK AND CO., INC.]

Synthesis of DL-Methionine

BY EARL PIERSON, MARIO GIELLA[1] AND MAX TISHLER

Consideration of the various syntheses of methionine indicates that the first recorded synthesis, that of Barger and Coyne,[2] using β-methylmercaptopropionaldehyde, is the most direct in approach. The over-all yield of about six per cent. by the modified Strecker reaction and the difficulty in obtaining the required aldehyde discouraged the use and the further development of this synthesis.

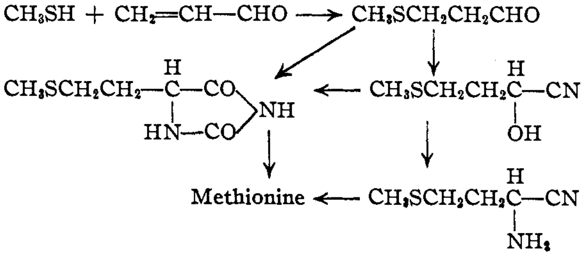
With the recent availability of commercial acrolein, and the reports that β-methylmercaptopropionaldehyde has been prepared from acrolein and methylmercaptan,[3] the development of a practical synthesis of methionine became of interest.

Catch and his collaborators[4] recently prepared methionine from acrolein and methyl mercaptan in 29% yield by a modified Strecker reaction employing liquid hydrogen cyanide. We have also prepared methionine in about the same over-all yield (25%) by the Strecker reaction without resorting to the use of liquid hydrogen cyanide. Further improvement was observed using the well-known Bücherer hydantoin synthesis, whereby an over-all yield of 50% was obtained.

It was found that methyl mercaptan adds smoothly to acrolein at atmospheric pressure when the reaction is catalyzed by a small amount of copper methyl mercaptide.[5]

The conversion of β-methylmercaptopropionaldehyde into 5-(β-methylmercaptoethyl)-hydantoin was accomplished by the usual Bücherer procedure and also by transformation into the cyanohydrin followed by treatment with ammonium carbonate.

The hydrolysis of the hydantoin to methionine was effected by concentrated hydrochloric acid at 135°, by ammonium sulfide solution at 135°, and by aqueous sodium hydroxide at 100°. The routes investigated are indicated.



Experimental

1. **β-Methylmercaptopropionaldehyde.**—Gaseous methyl mercaptan, 48 g., 1.0 mole, was bubbled during the course of thirty minutes under the surface of a cooled, stirred mixture of 56 g. (1.0 mole) of acrolein and 0.5 g. of cupric acetate, while the internal temperature was maintained at 35–40°. The mixture was agitated for an hour and distilled under reduced pressure giving β-methylmercaptopropionaldehyde, 87 g., 84%; boiling 52–54° (11 mm.), n^{20}_D 1.4850, d_{20} 1.036; MR_D (calcd.) 28.4, found 28.7. The undistilled aldehyde is sufficiently pure for use in the reactions described below.

The **2,4-dinitrophenylhydrazone** was prepared in the conventional manner, m. p. 116–119°.

Anal. Calcd. for $C_{10}H_{12}O_4N_4S$: C, 42.45; H, 4.26; N, 19.70. Found: C, 42.23; H, 4.20; N, 19.61.

2. **α-Hydroxy-β-methylmercaptobutyronitrile.**—β-Methylmercaptopropionaldehyde, 10.4 g., 0.10 mole, was shaken for ten minutes with a solution of 10.4 g., 0.10 mole, of sodium bisulfite in 35 ml. of water. A substantial amount of the adduct crystallized upon cooling to room temperature. A solution of 4.9 g., 0.10 mole, of sodium cyanide in 15 ml. of water was added in three portions, without permitting the temperature to exceed 35°. The oil that separated immediately was extracted

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[1] Present address: A. C. Lawrence Leather Company, Peabody, Mass.

[2] Barger and Coyne, *Biochem. J.*, **22**, 1417 (1928).

[3] Kaneko and Mii, *J. Chem. Soc. Japan*, **59**, 1382 (1938); Rothstein, *J. Chem. Soc.*, 1560 (1940).

[4] Catch, Cook, Graham and Heilbron, *Nature*, **159**, 578 (1947).

[5] The English investigators[4] used a tertiary amine as a catalyst.

three times with benzene; the combined benzene extracts were extracted with sodium bisulfite solution and then the solvent was removed under reduced pressure. The crude cyanohydrin was thus obtained as a colorless oil weighing 11.8 g. (90%). For analyses, a small sample of this product was distilled at 100° under a pressure of three microns.

Anal. Calcd. for C_5H_9NOS: C, 45.8; H, 6.87; N, 10.68. Found: C, 46.0; H, 6.88; N, 10.49.

3. **5(β-Methylmercaptoethyl)-hydantoin. A. From β-Methylmercaptopropionaldehyde.**—A mixture of 26 g. (0.25 mole) of β-methylmercaptopropionaldehyde, 113 g. (1.17 moles) of finely divided ammonium carbonate, 24.5 g. (0.5 mole) of sodium cyanide, 335 ml. of ethanol and 335 ml. of water was agitated and heated for four hours at 50–55°. The light yellow reaction mixture was filtered, and the filtrate was concentrated at 60° to a volume of 300 ml., acidified with 50 ml. of concentrated hydrochloric acid and heated for five minutes at 90° to cyclize the hydantoic acid, which was found to be present in small amounts. After crystallization, separation and drying, the hydantoin weighed 34 g. (79% yield) and melted at 103–105°. The melting point remained unchanged after recrystallization from ethanol.

Anal. Calcd. for $C_6H_{10}O_2N_2S$: C, 41.38; H, 5.74. Found: C, 41.36; H, 5.81.

B. From α-Hydroxy-γ-methylmercaptobutyronitrile.—The cyanohydrin was prepared by the method given previously from 2.0 moles of the aldehyde. Removal of the benzene solvent left 255 g. of crude cyanohydrin, which was converted into the hydantoin, 174 g. (50% yield based on β-methylmercaptopropionaldehyde), by reaction with 420 g. of ammonium carbonate in 1000 ml. of 50 volume per cent. methanol for two and one-half hours at 50–55°. The product was isolated by the procedure described above.

4. **DL-Methionine. A. From the Hydantoin.**—5-(β-Methylmercaptoethyl)-hydantoin, 17.4 g. (0.10 mole) was refluxed for six hours with a solution of 8.8 g. of sodium hydroxide in 75 ml. of water contained in a stainless steel flask; an additional 4.4 g. of sodium hydroxide was added, and refluxing was continued for a total of twenty-four hours. The reaction mixture was decolorized with Norit, neutralized to litmus with concentrated hydrochloric acid, and allowed to crystallize at 5°. The product weighed 10.8 g. (73.5%); m. p. 269° with decomposition. An additional 1.7 g. (11%) of material could be isolated by a procedure involving acidification (hydrochloric acid), concentration to dryness, extraction with ethanol, and neutralization of the filtered ethanol extract to Congo with pyridine. After recrystallization of the combined fractions from aqueous ethanol, 10.6 g. of analytically pure methionine was obtained.

By omitting the isolation of both the β-methylmercaptopropionaldehyde and 5-(β-methylmercapto)-hydantoin, pure methionine was obtained in 50% yield based on the charge of acrolein and methyl mercaptan.

B. From the Cyanohydrin.—Gaseous ammonia was passed into 123 g. (0.94 mole) of the stirred cyanohydrin, maintained at 60° for thirty minutes. The reaction mixture was dissolved in benzene, heated to expel excess ammonia, and extracted with dilute hydrochloric acid. The aqueous layer was made alkaline with ammonia water and extracted with benzene; evaporation of the solvent left 49 g. (40%) of crude methionine nitrile. Several futile attempts were made to purify this intermediate and to obtain a crystalline derivative. The crude aminonitrile (10 g.) was hydrolyzed by heating on the steam-bath for five and one-half hours with 20 ml. of concentrated hydrochloric acid. The reaction mixture was diluted with 50 ml. of water, decolorized with Darco, and the solution concentrated to dryness under vacuum. The resulting solid was extracted with hot ethanol, and the ethanolic solution was filtered and neutralized to Congo with pyridine. Methionine in 75% yield (8.5 g.) was obtained.

Summary

A three-step synthesis of methionine has been devised based on the catalyzed addition of methyl mercaptan to acrolein, followed by the Bücherer hydantoin reaction, and then by hydrolysis.

RAHWAY, NEW JERSEY RECEIVED NOVEMBER 7, 1947

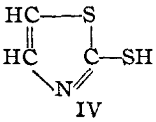
[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE B. F. GOODRICH CO.]

A Synthesis of 2-Thiazolethiol and its Disulfide

BY ROGER A. MATHES AND ADOLPH J. BEBER

2-Thiazolethiols, particularly 2-mercaptobenzothiazole, have been used extensively for many years as accelerators for the vulcanization of rubber. The preparation of 2-thiazolethiol (IV), the parent compound of this series, recently has been reported[1] in the patent literature. This synthesis which was effected by treating α-chloroacetaldehyde (I) with ammonium dithiocarbamate (II), has been investigated by us in some detail and under varied conditions. The intermediate, formylmethyl dithiocarbamate (III), was isolated and characterized. The yield of IV was 50% based on I. The synthesis of IV is attended by troublesome side reactions, giving rise to gummy by-products, which apparently result from intermolecular reactions of aldehydes I and III with amino groupings in II and III. Acetaldehyde is known to react with II,[2] and I likewise reacts as a typical aldehyde.[3] Substituted 2-thiazolethiols,[4] on the other hand, can be prepared, usually in high yields,[4c] by the conventional reaction of α-halogen ketones with II. 1,2-Dichloroethyl ether which is known to replace I in thiazole syntheses[5] reacts with II to give a liquid of uncertain composition.[6]

$$\underset{I}{ClCH_2CHO} + \underset{II}{NH_2CSSNH_4} \longrightarrow \underset{III}{NH_2CSSCH_2CHO} \longrightarrow$$



IV

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(1) Jones, U. S. Patent 2,426,397.

(2) Levi, *Gazz. chim. ital.*, **59**, 757 (1929).

(3) Natterer, *Monatsh.*, **3**, 442 (1882); Glinsky, *Z. Chemie*, N. F., **6**, 647 (1870).

(4) (a) Miolati, *Gazz. chim. ital.*, **23**, 575 (1893); (b) Levi, *ibid.*, **61**, 719 (1931); (c) Mathes, U. S. Patent 2,186,419.

(5) Traumann, *Ann.*, **249**, 36 (1888); Hantzsch, *ibid.*, **250**, 271 (1889).

(6) Mathes, U. S. Patent 2,411,219.