was separated and dried with anhydrous calcium sulfate, and the ether removed by distillation. The resulting material was distilled at reduced pressure to give 9.6 g. (80%) of a pale yellow viscous oil, b.p. 180–184° (0.014 mm.). This material solidified upon standing to a colorless sticky solid which was extremely difficult to crystallize to a sharp melting point. It was recrystallized finally from petroleum ether (b.p 60–70°) to give colorless needles, m.p. 75–78°.

Anal. Calcd. for $C_{20}H_{19}NSi$: Si, 9.33. Found: Si, 9.08, 9.16.

In another run employing 0.085 mole of *N*-ethyl-2,2′-dilithiodiphenylamine, there was obtained a 78% yield of 5-ethyl-10-phenyl-5,10-dihydrophenazasiline.

5-Ethyl-10-n-hexadecyl-5,10-dihydrophenazasiline. An ethereal solution containing 0.05 mole of *N*-ethyl-2,2′ dilithiodiphenylamine[2] was added over a period of 1.5 hr. to 14.0 g. (0.055 mole) of *n*-hexadecylsilane[12] in 100 ml. of ether, while cooling the reaction flask in an ice-bath. The reaction mixture was warmed to room temperature and refluxed for 2 hr. before Color Test I[9] was negative. After hydrolyzing by pouring upon crushed ice, ether was added, and the organic layer was separated and dried with anhydrous calcium sulfate. The ether was removed by distillation and the resulting oil was distilled at reduced pressure to give 16 g. of turbid liquid, b.p. 193–233° (0.008 mm.). This liquid was then redistilled to give 11.9 g. (53%) of liquid, b.p. 230–235° (0.003 mm.), which solidified upon standing. A portion of this material was recrystallized twice from a 10:1 mixture of methanol and benzene to give colorless crystals, m.p. 51–53°.

Anal. Calcd. for $C_{30}H_{47}NSi$: Si, 6.25. Found: Si, 6.41, 6.29.

Infrared absorption spectra. All of the infrared spectra of the 5,10-dihydrophenazasiline compounds showed a split band of weak to medium intensity in the 9.3 to 9.4 μ region. An absorption band at 13.1–13.2 μ (*o*-disubstitution) was present in all of the spectra, while those of the compounds containing substituents in the 2-position exhibited an additional band at 12.3–12.4 μ (1,2,4-trisubstitution). The two Si-H functional compounds had a strong band at 4.7 μ characteristic of the Si-H grouping.

Acknowedgment. This research was supported in part by the United States Air Force under Contract AF 33(616)-6127 monitored by the Materials Laboratory, Directorate of Laboratories, Wright Air Development Center, Wright-Patterson AFB, Ohio. Infrared analyses were obtained through the courtesy of the Institute for Atomic Research, Iowa State University, with special acknowledgment to Dr. V. A. Fassel, Mr. Richard Kniseley, and Miss Evelyn Conrad for the spectra.

AMES, IOWA

(12) M. B. Hughes, Ph.D. dissertation, Iowa State University (1958).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, FORDHAM UNIVERSITY]

Isomeric S-Methylthiamins[1,2]

EUGENE P. DIBELLA AND DOUGLAS J. HENNESSY

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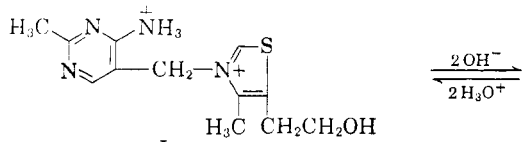
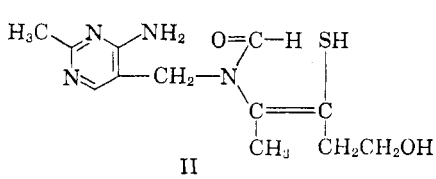
Two interconvertible isomeric forms of *S*-methylthiamin have been found to exist. The higher melting, more stable form is designated as 2-(4′-amino-2′-methyl-5′-pyrimidylmethylformamido)-2-methyl-3-methylmercaptotetrahydrofuran. The lower melting, less stable form is designated as 4-(4′-amino-2′-methyl-5′-pyrimidylmethylformamido)-3-methylmercapto-4-methyl-Δ^3-pentenol.

The hypothesis put forth in 1940 by Zima and Williams[3] suggests that thiamin (I) exercises some of its vital physiological functions in the so-called open form (II). The latter arises *in vitro* from I by the action of two equivalents of alkali.[4]

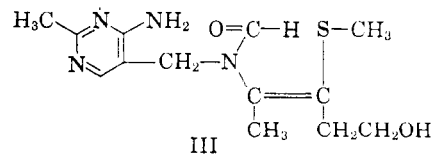


I



II

We planned the preparation of a structurally simple, locked open form of thiamin which might prove useful in testing this and other hypotheses on the functioning of thiamin. The preparation of *S*-methylthiamin (III) was attempted by reaction of I with three equivalents of aqueous alkali and one of dimethyl sulfate or methyl iodide. A product was obtained whose elementary analysis corresponded to the desired compound. It melted at 193°.



III

Shortly afterwards, however, Sykes and Todd[5] reported the preparation of an *S*-methylthiamin of melting point 133° by a procedure which utilized

(1) This work formed part of the Ph.D. thesis of Eugene P. DiBella, Fordham University, 1953, and was supported by a grant-in-aid from the Williams-Waterman Fund of the Research Corporation.

(2) Presented before the 122nd Meeting of the American Chemical Society at Atlantic City, September 1952.

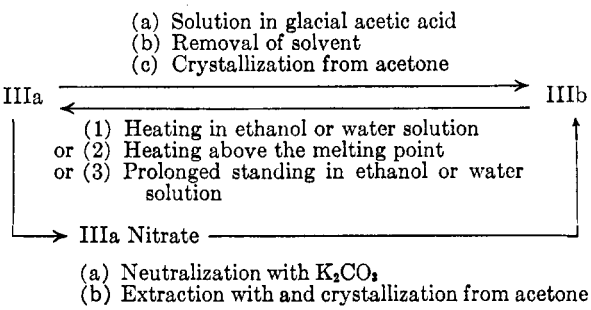
(3) O. Zima and R. R. Williams, *Ber.*, **73**, 941 (1940).

(4) R. R. Williams and A. E. Ruehle, *J. Am. Chem. Soc.*, **57**, 1856 (1935).

(5) P. Sykes and A. R. Todd, *J. Chem. Soc.*, 534 (1951).

liquid ammonia as a solvent. Although we were not able to reproduce all the details of this procedure, were nevertheless able to obtain a second form of *S*-methylthiamin which did melt at 133° and which possessed solubility properties different from the form melting at 193°. The lower-melting substance could also be obtained without the use of liquid ammonia as a solvent.

The following scheme illustrated the relationships that were found to exist between the two compounds which will be designated IIIa and IIIb for the *S*-methylthiamins melting at 193° and 133° respectively.



The lower melting compound (IIIb) seems to be the less stable, passing into IIIa by simple standing or heating in solution. This suggests that IIIb might be a less stable polymorphic modification of IIIa, which can be obtained from IIIa by the use of acetone as a crystallizing solvent. However, the following facts militate against this view:

(1) Although crystallization from acetone of a residue obtained by the evaporation of a glacial acetic acid solution of IIIa led to IIIb, similar crystallization from acetone of a residue obtained by the evaporation of a water solution of IIIa did not lead to IIIb but rather to unchanged IIIa.

(2) The two forms of *S*-methylthiamin yielded different picrates when these were prepared in alcoholic picric acid solution. The picrate of IIIa melted at 175° and was soluble in hot ethanol; the picrate of IIIb melted at 189° and was almost insoluble in hot ethanol. Neither of these picrates was affected by recrystallization from boiling water.

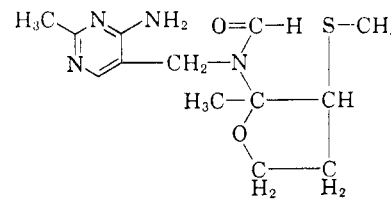
In trying to ascertain whether or not *cis-trans* isomerism around the double bond present in the *S*-methylthiamin structure (III) was responsible for the difference between IIIa and IIIb, hydrogenation of the two forms was undertaken.

No hydrogenation of either compound could be effected in water or ethanol solution even at high pressure and high temperature, or in glacial acetic acid at low pressure and room temperature. Using glacial acetic acid as a solvent at elevated pressure and room temperature, hydrogenation yielded a dihydro compound which could not be obtained in crystalline form, but which was isolated as a picrate. In as much as glacial acetic acid was the means used to effect transformation of IIIa to IIIb, and since hydrogenation did not occur in solvents in which IIIb was known to change to IIIa, it was concluded that IIIb was capable of hydrogenation and that IIIa was not.

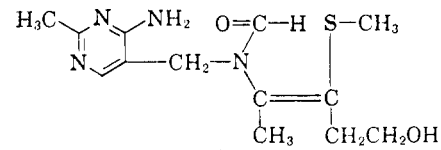
The insolubility of both compounds in suitable solvents precluded the determination of their respective infrared spectra in solution.[6]

The spectra were obtained from Nujol mulls of these substances. The spectrum of IIIb possessed an absorption band at 2.98 μ which was attributed to the hydroxyl group. The spectrum of IIIa possessed no such absorption band.

Thus it is proposed that IIIa is an intramolecular cyclization product—*i.e.*, a substituted tetrahydrofurane resulting from addition of the hydroxyl of the β-hydroxyethyl group across the double bond. IIIa would undergo hydrogenation after conversion in acid solution to IIIb.

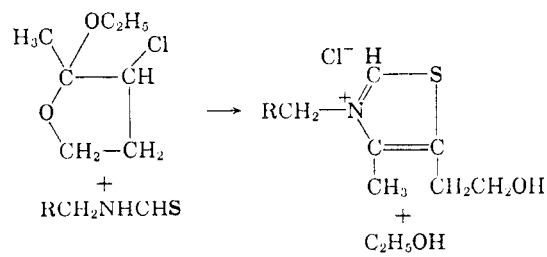


IIIa



IIIb

The reasonable nature of this explanation for the isomerism of IIIa and IIIb is further substantiated by the fact that one of the patented processes[7] for the manufacture of thiamin utilizes the condensation between 4-amino-2-methyl-5-thioformamidomethylpyrimidine (RCH_2NHCHS] and 3-chloro-2-ethoxy-2-methyltetrahydrofuran.



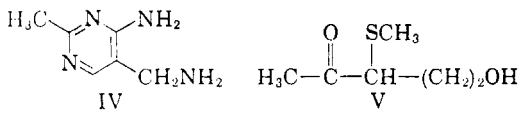
Here, the formation of the thiazolium ring with its stabilization due to the resonance energy of the aromatic system would provide the driving force for the opening of the tetrahydrofurane ring. In the case of *S*-methylthiamin, IIIb there is no thiazole aromaticity, but rather an isolated double bond which could participate reversibly in a ring-

(6) Such a determination would have been desirable in order definitely to exclude the possibility of polymorphism.

(7) Hoffman-LaRoche, Brit. Pat. 496,801.

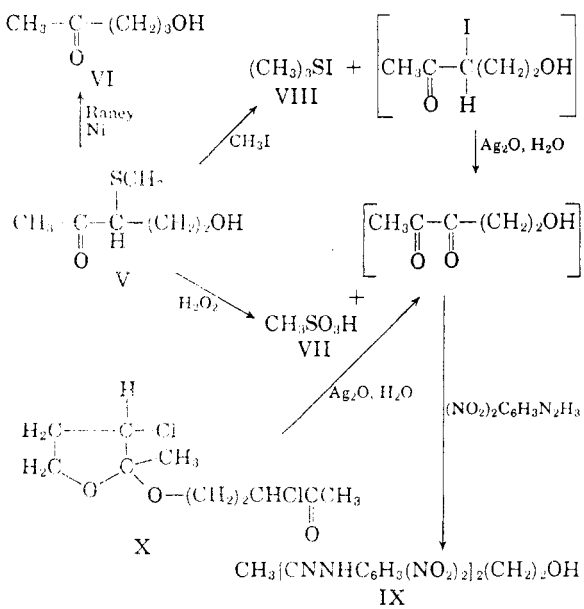
chain isomerism without involvement of aromatic resonance stabilization.

It seemed desirable to establish definitely that the methylation of thiamin occurred on the sulfur atom since there is the possibility of C-alkylation. Sykes and Todd[5] reported, without details, that *S*-methylthiamin, m.p. 133° underwent extensive decomposition when warmed with either acid or base. It appeared that hydrolysis could cleave the amide and eneamine linkages (as well as the postulated acetal-type linkage in *S*-methylthiamin, m.p. 193°) to yield 4-amino-5-aminomethyl-2-methylpyrimidine (IV) which had previously been obtained by Matsukawa and Iwatsu[8] from the hydrolysis of the *S*-2,4-dinitrophenyl ether of the open form of thiamin, and also by Zima and Williams[3] from the hydrolysis of thamin disulfide.



IV V

Alcoholic hydrochloric acid hydrolysis of *S*-methylthiamin, m.p. 193° did yield IV in addition to a sulfur-containing oil whose elementary analysis agreed with that calculated for the expected 5-hydroxy-3-methylmercapto-2-pentanone, (V). Although this substance gave positive iodoform and methylmercapto tests, no crystalline, sulfur-containing alcohol or ketone derivatives could be prepared from it. Nevertheless, the structure of this oil was established as that of V by means of its Raney nickel desulfurization to 5-hydroxy-2-pentanone (VI) as well as by its reactions both with hydrogen peroxide and with methyl iodide to yield, respectively, methane sulfonic acid (VII) and trimethylsulfonium iodide (VIII), in addition to



X IX

products which in each case could be transformed to the 2,4-dinitrophenylosazone of 3,5-dihydroxy-2-pentanone (IX).

The identity of the 2,4-dinitrophenylosazone (IX) was established by comparison with the product resulting from the successive treatment of the ketal (X)[9] with moist freshly prepared silver oxide and the 2,4-dinitrophenylhydrazine reagent.

IIIa is established as an *S*-methylthiamin by its acid hydrolysis to 4-amino-5-aminomethyl-2-methylpyrimidine (IV) and 5-hydroxy-3-methylmercapto-2-pentanone (V). The methods of obtention of IIIa and IIIb, the means used for their interconversion, the conditions required for hydrogenation and the difference in infrared spectra are each and all accounted for by ring-chain tautomerism. IIIa is designated as 2-(4′-amino-2′-methyl-5′-pyrimidylmethylformamido)-2-methyl-3-methylmercaptotetrahydrofuran and IIIb as 4-(4′-amino-2′-methyl-5′-pyrimidylmethylformamido)-3-methylmercapto-4`-methyl-Δ^3-pentenol.

EXPERIMENTAL

S-Methylthiamin, m.p. 193° (IIIa). To a solution of 33.7 g. (0.1 mole) of thiamin chloride in 100 ml. of water there was added a solution of 12.0 g. (0.3 mole) of sodium hydroxide in 50 ml. of water while maintaining the system at 5°. Then 12.6 g. (0.1 mole) of freshly distilled dimethyl sulfate[10] was introduced with stirring. After 10–13 min. a precipitate formed; this was filtered, washed three times with small portions of cold water and recrystallized from the minimum amount of boiling water as a white solid, m.p. 193°.[11] The yield was 21.8 g. (75%).

Anal.[12] Calcd. for $C_{13}H_{20}N_4O_2S$: C, 52.70; H, 6.76; N, 18.92; S, 10.81. Found: C, 52.80; H, 6.56; N, 18.87; S, 10.91.

When methyl iodide was used in place of dimethyl sulfate, the same product was obtained in 30% yield.

A potentiometric titration[13] on IIIa gave a pK_b of 8.60. The ultraviolet absorption spectrum[14] in ethanol showed a maximum at 236 mμ. A Rast molecular weight determination gave a value of 339 (calcd. 296).

A picrate of IIIa was prepared by dissolving a sample in a small amount of ethanol, and adding to this an excess of saturated alcoholic picric acid. The resulting precipitate was recrystallized from ethanol, m.p. 175°.

Anal. Calcd. for $C_{19}H_{23}N_7O_9S$: C, 43.43; H, 4.38; N, 18.67. Found: C, 43.70; H, 4.18; N, 18.90.

A picrolonate was similarly prepared, m.p. 192°.

Anal. Calcd. for $C_{23}H_{28}N_8O_7S$: C, 49.29; H, 5.00. Found: C, 49.72; H, 5.13.

(8) T. Matsukawa and T. Iwatsu, *J. Phar. Soc. Japan*, **69**, 550 (1949); *Chem. Abstr.*, **44**, 4475 (1950).

(9) J. R. Stevens and G. A. Stein, *J. Am. Chem. Soc*, **62**, 1045 (1940).

(10) The use of freshly distilled dimethyl sulfate is important. Technical dimethyl sulfate contains acid impurities which partially neutralize the alkali, thereby giving lower yields.

(11) All melting points were taken in capillary tubes; they are all uncorrected.

(12) Some of the reported analyses were performed by Mr. A. A. Sirotenko formerly of the Microanalytical Laboratory, Fordham University; others were performed by Dr. G. Weiler of the Microanalytical Laboratory, Oxford, England.

(13) Performed with a Macbeth continuous *p*H meter.

(14) Performed with a Beckman Model DU spectrophotometer.

A nitrate was prepared by slowly adding one equivalent of concentrated nitric acid to an alcoholic solution of Ia with cooling. The precipitate was recrystallized from ethanol, m.p. 143°C.

Anal. Calcd. for $C_{13}H_{21}N_5O_5S$: C, 43.45; H, 5.88. Found: C, 43.64; H, 5.81.

A dibromide was prepared by adding dropwise one equivalent of bromine to a sample of IIIa dissolved in glacial acetic acid, followed by removal of the solvent and recrystallization of the residue twice from alcohol-ether (charcoal) m.p. 219–220°. The water solubility of this derivative was indicative of a salt-like compound.

Anal. Calcd. for $C_{13}H_{20}N_4O_2SBr_2$: C, 34.21; H, 4.39. Found: C, 33.65; H, 4.29.

A qualitative test on IIIa for the methylmercapto group[15] was positive. A quantitative determination,[16] however, gave a value of 5.35%—S—CH_3 (calcd. 16.21%).

S-Methylthiamin, m.p. 133° (IIIb). The procedure of Sykes and Todd[5] for the preparation of this substance was followed to a point where the free base was in a water solution, a slight excess of silver nitrate having been removed by precipitation with hydrogen sulfide. After this, the directions were not explicit as to exactly how the substance of melting point 133° was isolated. We were, however, able to establish the following:

(1) Addition of excess silver nitrate solution to the water solution of any *S*-methylthiamin preparation, free from halide ions and adjusted to *p*H 8–9 with dilute ammonium hydroxide, led to the formation of an insoluble silver salt. This was separated, washed twice with water, suspended in water, and decomposed with hydrogen sulfide. The insoluble silver sulfide was filtered off and the filtrate was evaporated *in vacuo* to a sirup. This was crystallized (charcoal) and recrystallized from absolute ethanol, m.p. 143°. Mixed melting point determination showed this to be the hydronitrate of IIIa.

Anal. Calcd. for: $C_{13}H_{21}N_5O_5S$: C, 43.45; H, 5.88. Found: C, 43.48; H, 5.35.

(2) To a solution of 10.8 g. (0.03 mole) of the hydronitrate of IIIa in 15 ml. of water there was added 30 ml. of a saturated solution of potassium carbonate in water. An oily mass separated which was extracted with 50 ml. of acetone. The acetone solution was passed through a mat of Filtercel, evaporated *in vacuo* to a volume of 7 ml. and allowed to stand at −10° for 3 days. The resulting precipitate, recrystallized from acetone melted at 133°. The yield was 4.40 g. (51%).

Anal. Calcd. for $C_{13}H_{20}N_4O_2S$: C, 52.70; H, 6.76; N, 18.92; S, 10.81. Found: C, 52.32; H, 6.74; N, 18.80; S, 10.08.

(3) The compound IIIb could also be prepared more directly from IIIa by dissolving 2.96 g. (0.01 mole) of the latter in 10 ml. of glacial acid followed by removal of this solvent *in vacuo*. The resulting sirupy residue was taken up in 10 ml. of acetone which was then reduced in volume to 5 ml. and allowed to stand at −10° for 3 days. The resulting precipitate was *S*-methylthiamin, m.p. 133°. The yield was 1.75 g. (59%). When water replaced the acetic acid in this procedure, only *S*-methylthiamin, m.p. 193° (IIIa) was obtained. The compound IIIb was very soluble in cold water, cold ethanol, and acetone, while IIIa was soluble only in hot water and hot ethanol and quite insoluble in acetone.

Conversion of S-methylthiamin, m.p. 133°, (IIIb) *to S-methylthiamin, m.p. 193°* (IIIa). A sample of IIIb in water or ethanol solution was heated for 1 hr. on a steam bath. Evaporation to small volume resulted in the precipitation of IIIa in almost quantitative yield.

When IIIb was held a few degrees above its melting point of 133°, the liquid turned to a solid mass in 10–20 seconds. Melting did not occur again until the temperature had reached 190°.

The Picrates of IIIa *and* IIIb. The picrate of IIIa, prepared from alcoholic picric acid solution, melted at 175° after recrystallization from ethanol or from water. The picrate of IIIb was prepared by dissolving a sample of the compound in ethanol, and immediately adding an excess of saturated alcoholic picric acid solution. The resulting precipitate was virtually insoluble in ethanol, but could be obtained fairly pure by copious washings with ether. Its melting point of 189° remained unchanged after recrystallization from boiling water.

Anal. Calcd. for $C_{19}H_{23}N_7O_9S$: C, 43.43; H, 4.38; N, 18.67. Found: C, 43.15; H, 4.57; N, 18.90.

A mixed melting point determination with these two picrates gave an intermediate value.

When a sample of *S*-methylthiamin, m.p. 133°, was dissolved in ethanol or water, and the solution was allowed to stand for 24 hr. before the addition of an excess of saturated alcoholic (or aqueous) picric acid solution, only the picrate corresponding to *S*-methylthiamin, m.p. 193°, was obtained.

Dihydro-S-methylthiamin picrate. With ethanol or water as solvents, and with palladium on carbon or Raney nickel as catalysts, no hydrogenation could be effected on either IIIa or IIIb with any pressure up to 1400 lbs. at any temperature up to 110°. After each unsuccessful attempt, even those on IIIb, the higher melting IIIa was recovered from the mixture.

Successful reduction was achieved with both compounds by the following procedure: 2.96 g. (0.01 mole) of either form of *S*-methylthiamin was dissolved in 20 ml. of glacial acetic acid and submitted to hydrogenation at 1000 lbs. at room temperature for 4 hr. using 10% palladium on carbon as a catalyst. The catalyst was then filtered off and the acetic acid solution was evaporated *in vacuo* to a sirupy residue which could not be crystallized from ethanol, water, or acetone. A crystalline picrate was then formed from ethanol solution. Recrystallization from boiling water yielded a derivative which was not the picrate of either form of *S*-methylthiamin; it melted at 210° and the yield was 3.58 g. (68%).

Anal. Calcd. for $C_{19}H_{25}N_7O_9S$: C, 43.26; H, 4.74; N, 18.60. Found: C, 43.53; H, 4.76; N, 18.30.

Alcoholic acid hydrolysis of S-methylthiamin, m.p. 193°. (a) *The isolation of the pyrimidine* (VI). To a solution of 29.6 g. (0.1 mole) of *S*-methylthiamin, m.p. 193°, in 400 ml. of ethanol there was added 80 ml. of concd. hydrochloric acid. This mixture refluxed for 30 min., cooled, and poured into 1 l. of ether at −5° yielded a gummy precipitate. The mother-liquor was decanted and set aside. The precipitated product was taken up in 100 ml. of ethanol; upon standing a crystalline precipitate deposited. This product, recrystallized from water-ethanol, melted at 264–265°. The yield was 15.0 g. (65%).

Anal. Calcd. for $C_6H_{14}N_4OCl_2$[17]: C, 31.44; H, 6.25; N, 24.21. Found: C, 31.56, 31.91; H, 6.03, 6.25; N, 24.53.

A picrate was prepared from the dihydrochloride by dissolving a small sample in water and adding excess aqueous picric acid. The precipitated product recrystallized from water melted at 225°.

Anal. Calcd. for $C_{20}H_{16}N_{10}O_{14}$: C, 36.24; H, 2.69; N, 23.66. Found: C, 36.22, 36.68; H, 3.00, 2.76; N, 24.00.

The melting points given by Andersag and Westphal[18] for the dihydrochloride and dipicrate of 4-amino-5-aminomethyl-2-methylpyrimidine are 265° and 225°, respectively. The dihydrochloride was converted by the procedures of these

(15) Performed by Mr. J. Alicino, Metuchen, N. J.

(16) This low value for the methylmercapto group was not unexpected since F. Arndt *et al.*, *Ber.*, **70**, 2035 (1937) have shown that this grouping does not behave ideally in such determinations.

(17) The analytical results on this dihydrochloride agree with a monohydrate, although the results given in the literature for the compound of the same melting point agree with an anhydrous formulation. Possibly, dehydration took place upon the heating involved in the melting point determination.

(18) E. Andersag and K. Westphal, *Ber.* **70**, 2035 (1937).

authors to 4-amino-5-hydroxymethyl-2-methylpyrimidine, m.p. 194°, and to 4-amino-2-methyl-5-(*N*-formylaminomethyl)pyrimidine, m.p. 224°. A picrate of the latter prepared from water solution melted at 189°.

Anal. Calcd. for $C_{13}H_{13}N_7O_8$: C, 39.59; H, 3.30. Found: C, 39.13; H, 3.27.

(b) *The isolation of the sulfur-containing oil.* The mother liquor from the above hydrolysis was stirred with anhydrous potassium carbonate until the solution was no longer acid and until the addition of fresh portions of potassium carbonate did not seem to result in the further absorption of water. The supernatant liquid was then concentrated in volume by heating on the steam bath until most of the ether had distilled over. The alcohol was then removed *in vacuo*, leaving a pale yellow oil which was taken up in ether and dried over anhydrous sodium sulfate for 12 hr. The ether was then removed and the residual oil distilled. The yield was 8.53 g. (53%): n_D^{21} 1.4945; d^{25} 1.054. M_d 41.03. M_d Calcd. 39.45.

Anal. Calcd. for $C_6H_{12}O_2S$: C, 48.65; H, 8.11; S, 21.61. Found: C, 48.51; H, 7.88; S, 20.64.

An infrared absorption spectrum[19] on this substance showed hydroxyl absorption at 2.87 μ, and carbonyl absorption at 5.83 μ. An iodoform test was positive as was also the test for the methylmercapto group.[15] Attempts to prepare derivatives were unsuccessful. The use of all the commonly available alcohol and carbonyl reagents according to standard procedures[20] did not permit isolation of any crystalline sulfur-containing derivatives. In some cases, well defined products were obtained—*e.g.* with a dilute sulfuric acid solution of *p*-nitrophenylhydrazine, a sulfur-free solid resulted which when recrystallized from dioxane-water melted at 263–265°.

Anal. Found: C, 53.66; H, 5.46; N, 18.70.

The identity of this product was not ascertained.

Proof of structure of the sulfur-containing oil resulting from the hydrolysis of IIIa.

(a) *Desulfurization.* A mixture of 1.48 g. (0.01 mole) of the oil, 50 ml. of ethanol and 15 g. of Raney nickel was refluxed for 1 hr. The insoluble material was filtered off and the filtrate was concentrated to a volume of about 20 ml. This was then added to an excess of the 2,4-dinitrophenylhydrazine reagent. The resulting precipitate recrystallized from ethanol melted at 147°. The yield was 1.90 g. (67%).

Anal. Calcd. for $C_{11}H_{14}N_4O_5$: C, 46.81; H, 4.96; N, 19.86. Found: C, 47.29, 47.04; H, 4.83, 5.23; N, 20.45.

The 2,4-dinitrophenylhydrazone was prepared from an authentic sample of 5-hydroxy-2-pentanone.[21] Upon recrystallization from ethanol, this derivative also melted at 147°.

Anal. Calcd. for $C_{11}H_{14}N_4O_5$: C, 46.81; H, 4.96; N, 19.86. Found: C, 47.11; H, 4.78; N, 20.28.

A mixed melting point determination with the two samples showed no depression; also, their respective infrared spectra were identical.

(b) *Reaction with hydrogen peroxide.* To 1.48 g. (0.01 mole) of the oil there was added 20 ml. of 30% hydrogen peroxide. The mixture was placed in an ice bath and shaken a few times. Within a few minutes complete solution occurred with the evolution of heat. The mixture was then diluted with 100 ml. of water and evaporated *in vacuo*, to a small volume (3–5 ml.). This process of dilution and evaporation was repeated four times in order to remove the hydrogen peroxide. The final evaporation was carried out until only a viscous oil remained. This was extracted with three 10-ml. portions of ether. The combined extracts were reduced in volume to 5–10 ml. to which was added with stirring a few drops of phenylhydrazine. The small amount of precipitate was recrystallized from ethanol-ether, m.p. 195°. No yield was calculated since repeated extractions with ether on the oily residue still yielded the same precipitate upon treatment with phenylhydrazine.

Anal. Calcd. for $C_7H_{12}N_2O_3S$: C, 41.17; H, 5.75; N, 13.73. Found: C, 41.29: H, 5.75; N, 14.01.

A mixed melting point determination of this substance with an authentic sample of the phenylhydrazine salt of methane sulfonic acid[22,23] showed no depression.

The viscous material not soluble in ether was taken up in 15 ml. of ethanol and added to an excess of the 2,4-dinitrophenylhydrazine reagent. The resulting precipitate recrystallized from ethyl acetate, melted at 240°–242°. This product showed no depression upon mixed melting point determination with the 2,4-dinitrophenylosazone of 3,5-dihydroxy-2-pentanone. The yield was 1.59 g. (34%). This latter product was synthesized by refluxing a mixture of 2.55 g. (0.01 mole) of the ketal X,[24] 50 ml. of water, and 5 g. of silver oxide for 2 hr. After cooling, the insoluble material was filtered off and the filtrate was extracted with small portions of ether to remove any unchanged chloro compound. The water layer was evaporated *in vacuo* to a viscous oil which was dissolved in 15 ml. of ethanol and added to an excess of the 2,4-dinitrophenylhydrazine reagent. The precipitate recrystallized from ethyl acetate, melted at 240°–242°. The yield was 2.20 g. (46%).

Anal. Calcd. for $C_{17}H_{16}N_8O_9$: C, 42.86; H, 3.36; N, 23.53. Found: C, 42.65; H, 3.53; N, 23.23.

(c) *Reaction with methyl iodide.* To 1.48 g. (0.01 mole) of the oil there was added an excess of methyl iodide (10 g.). The solution became turbid within a few minutes. After 1 week the supernatant liquid was decanted and when the oily residue was treated with absolute ethanol, crystallization occurred. The resulting solid was separated and when recrystallized from ethanol-ether melted at 194°.[25] The yield was 0.51 g. (25%).

Anal. Calcd. for C_3H_9SI: C, 17.65; H, 4.41; S, 15.69. Found: C, 18.27; H, 4.32; S, 15.51.

This substance showed no depression upon mixed melting point determination with an authentic sample of trimethylsulfonium iodide.[25]

The supernatant liquid from the original reaction mixture was evaporated *in vacuo* at room temperature to a viscous oily mass. This was dissolved in a little ethanol and refluxed with 50 ml. of water and 5 g. of freshly prepared silver oxide for 2 hr. during which time a silver mirror appeared on the inside of the reaction flask. The 2,4-dinitrophenylosazone of 3,5-dihydroxy-2-pentanone isolated in the same manner as from the reaction of X with silver oxide melted at 240°–242°. The yield was 15%. The product showed no depression upon mixed melting point determination with the authentic sample of the 2,4-dinitrophenylosazone of 3,5-dihydroxy-2-pentanone.

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(19) Performed on a Perkin-Elmer double beam spectrometer.

(20) R. L. Shriner and R. C. Fuson, *The Systematic Identification of Organic Compounds*, 3rd ed., John Wiley & Sons, Inc., New York, N. Y., 1948, Chap. VIII.

(21) I. L. Knunyantz, G. V. Chelintzev, and E. D. Osetrova, *Compt. rend. acad. sci. (U.R.S.S.)* [N.S.], **1**, 312 (1934).

(22) P. H. Latimer and R. W. Bost, *J. Am. Chem. Soc.*, **59**, 2500 (1937).

(23) The melting point of this substance varied considerably with the rate of heating (194°–223°). The value given was obtained by heating at the rate of one degree per minute from 180°.

(24) Kindly furnished by Merck & Co., Rahway, N.J.

(25) W. Steinkopf and S. Muller, *Ber.*, **56**, 1926 (1923).