acid. After the first crystallization this melted at 130–150°, indicating a mixture of the two isomeric hydantoins. Separation was finally effected by fractional crystallization from acetic acid. The *cis*-modification is more soluble in this solvent than the *trans*-form and in this case sufficient material was available to enable us to isolate the *cis*-modification. It crystallized from acetic acid in needles which melted at the same temperature as the hydantoin obtained by desulfurization of the corresponding 2-thiohydantoin. A mixture of the two substances melted at 150–2°.

Reduction of *cis*- and *trans*-1,3-Diphenyl-4-benzalhydantoin.

1,3-Diphenyl-4-benzylhydantoin (XI).—This hydantoin, which has been described in a previous paper by Johnson and Shepard,[1] is formed when the *cis*- and *trans*-modifications of 1,3-diphenyl-4-benzalhydantoin are reduced with hydriodic acid. This was accomplished by digesting the unsaturated hydantoins in glacial acetic acid with hydriodic acid and in presence of a little red phosphorus. After the reduction was complete the solution was then diluted with water when the hydantoin separated as a gum. In some experiments the excess of acetic acid was first removed by evaporation at 100°, but under both conditions the same gum was obtained. This was purified by dissolving in ether, washing with a little bisulfite solution to remove a trace of iodine and then drying the ether solution over anhydrous calcium chloride. On allowing the ether to evaporate the hydantoin was finally obtained in a crystalline condition melting at 58–62°. The compound is very hygroscopic. It is extremely soluble in cold alcohol, ether, benzene acetic acid, acetone, chloroform, ethylacetate and ligroin but practically insoluble in water. It does not dissolve in cold sodium hydroxide solution. The compound agreed in all its properties with Johnson and Shepard's *1,3-diphenyl-4-benzylhydantoin.*

NEW HAVEN, CONN.

[CONTRIBUTIONS FROM THE SHEFFIELD CHEMICAL LABORATORY OF YALE UNIVERSITY.]

RESEARCHES ON PYRIMIDINES. LXXIII. ALKYLATION OF 2-MERCAPTOPYRIMIDINES.

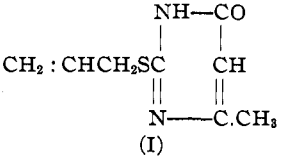
BY TREAT B. JOHNSON AND HOWARD W. HAGGARD.

Received November 23, 1914.

The papers so far published from this laboratory on the alkylation of *2-mercapto-6-oxypyrimidines* have been confined to a description of results obtained from the study of mercapto compounds in which the mercapto grouping contained a saturated alkyl radical, *viz.*, CH_3-, C_2H_5-, $C_6H_5CH_2$-, etc. In all of the cases examined, with one exception, mercapto groups of this type have favored substitution in the 1- and 3-positions of the pyrimidine ring. With these results at hand it then became

[1] *Loc. cit.*

of interest to determine what influence, if any, negative mercapto groupings would have on the formation of alkylation products. In other words, would such combinations be favorable to select for the preparation of 3-alkyl derivatives? In order to acquire further data on this interesting question[1] we selected for study a mercaptopyrimidine containing an unsaturated allyl group in the 2-position, *viz.*, *2-allylmercapto-4-methyl-6-oxypyrimidine* (I). The results of this investigation are now presented in this paper.



(I)

2-Allylmercapto-4-methyl-6-oxypyrimidine (I) was prepared by the action of allylbromide or iodide on the sodium salt of 2-thio-4-methyluracil (V). At the beginning of our work we first compared the behavior of this new mercaptopyrimidine (I) with that of 2-methylmercapto-4-methyl-6-oxypyrimidine (II)[2] towards methyliodide and allylbromide, respectively, in order to find out whether both reactions would lead to the formation of isomeric nitrogen-substitution products. To our surprise they underwent alkylation in an entirely different manner. The sodium salt of the allylmercaptopyrimidine (I) interacted with methyliodide giving smoothly 2-allylmercapto-1,4-dimethyl-6-oxypyrimidine represented by Formula VIII. We obtained no evidence of the formation of a 3-methylated derivative. On the other hand, the sodium salt of 2-methylmercapto-4 methyl-6-oxypyrimidine (II) interacted smoothly with allylbromide forming an oxygen derivative, or the imido ester combination, *viz.*, 2-methylmercapto-4-methyl-6-alloxypyrimidine corresponding to Formula III. This latter result is of especial interest and is not in accord with our previous observations. Alkylations with saturated primary halides have led to the formation of nitrogen substituted pyrimidines. The allyl group apparently has a greater affinity for the oxygen of the NH-CO grouping than for the nitrogen.

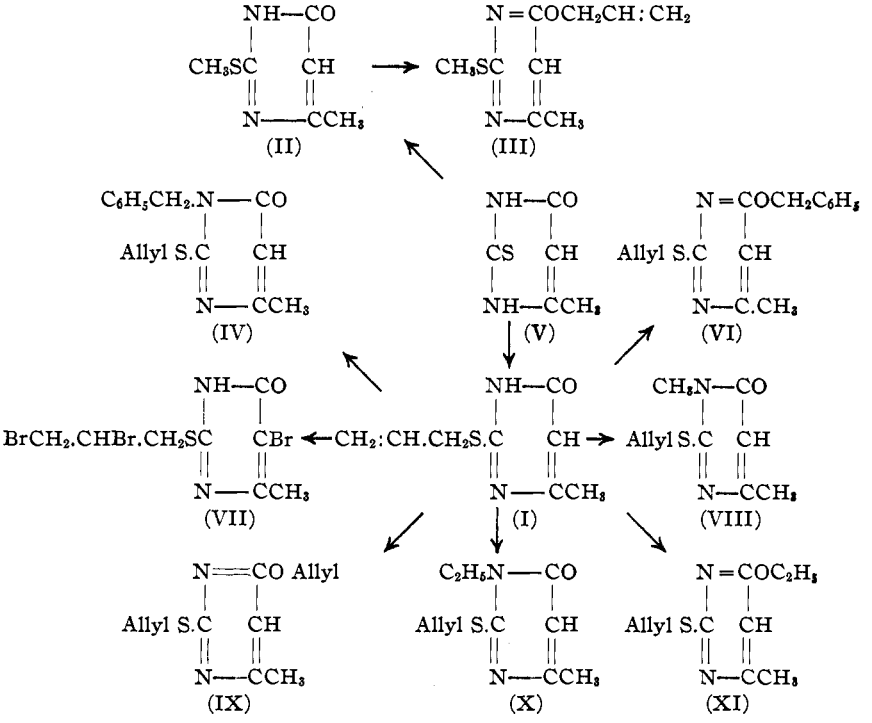
While methyliodide interacted with the sodium salt of 2-allylmercapto-4-methyl-6-oxypyrimidine (I), giving normally a 1-methyl derivative (VIII), on the other hand, when we applied a similar reaction with allylbromide, ethylbromide and benzylchloride abnormal results were obtained. *In no case did we observe the formation of 3-substitution products.* Allylbromide interacted with the sodium salt of the pyrimidine (I) giving exclusively an oxygen derivative corresponding to Formula IX. This

[1] This question is of special biochemical interest to us because of its connection with our synthetical work, now in progress, on pyrimidine nucleosides (T. B. Johnson).

[2] Wheeler and Merriam, *Am. Chem. J.*, **29**, 486 (1903).

result is perfectly analogous to that obtained by the action of the unsaturated halide (allylbromide) on the sodium salt of 2-methylmercapto-4-methyl-6-oxypyrimidine (II).

Benzylchloride and ethylbromide both reacted with the sodium salt of the allylpyrimidine (I) in an analogous manner giving mixtures of their corresponding oxygen derivatives (VI) and (XI) and 1-substituted pyrimidines represented by Formulas IV and X, respectively. The structures of these various mercaptopyrimidines were established by their behavior on acid hydrolysis. A description of the properties of these various compounds and their chemical behavior is given in the experimental part of this paper. When 2-allylmercapto-4-methyl-6-oxypyrimidine (I) was allowed to interact with bromine it was converted into the saturated pyrimidine (VII). The various changes discussed above are represented by the following formulas:



Experimental.

2-Allylmercapto-4-methyl-6-oxypyrimidine (I).—This mercaptopyrimidine was prepared by digesting the sodium salt of 2-thio-4-methyluracil[1] in alcohol, with the calculated amount of allylbromide. After the reaction was complete the solution was filtered from sodium bromide

[1] List, *Ann.*, **236**, 3 (1886).

and the alcohol then evaporated. The pyrimidine was obtained in a crystalline condition and was purified by recrystallization from hot water. It separated from this solvent, on cooling, in colorless needles which melted at 131° to a clear oil without decomposition. The pyrimidine is very soluble in alcohol. From 25 g. of 2-thio-4-methyl-6-oxypyrimidine we obtained 30 g. of the mercaptopyrimidine. Nitrogen determination (Kjeldahl):

Calc. for $C_8H_{10}ON_2S$: N = 15.4; found: 15.5 and 15.6.

1-Methyl-2-allylmercapto-4-methyl-6-oxypyrimidine (VIII).—One and five-tenths grams of sodium were dissolved in 75 cc. of absolute alcohol and 10 g. of the preceding 2-allylmercaptopyrimidine dissolved in the solution. An excess of methyliodide was then added and the mixture digested until neutral to turmeric and litmus. The alcohol was then removed by heating under diminished pressure, when we obtained the methylpyrimidine mixed with sodium iodide. This residue was then triturated with water to dissolve the iodide and the pyrimidine extracted with ether. Calcium chloride formed an insoluble addition-product with this pyrimidine and consequently we were obliged to dry its ether solution over anhydrous potassium carbonate. After complete drying, the ether was then allowed to evaporate in the air, when we obtained the pyrimidine in the form of hexagonal tables melting at 43° to an oil. It is very soluble in ligroin, ethyl acetate, chloroform and benzene. Nitrogen determination (Kjeldahl):

Calc. for $C_9H_{12}ON_2S$: N = 14.3; found: N = 14.4.

Hydrolysis with Hydrochloric Acid.—Four grams of the mercaptopyrimidine were dissolved in an excess of hydrochloric acid and the solution boiled for several hours to remove the mercapto group. On evaporating to dryness we obtained 1,4-dimethyluracil[1] which melted at 256° without further purification. This pyrimidine contained a small amount of impurity which was not removed by crystallization from alcohol or water. A mixture of this substance and some 1,4-dimethyluracil (m. 258°) melted at 256–7°. Nitrogen determination (Kjeldahl):

Calc. for $C_6H_8O_2N_2$: N = 20.00; found: N = 20.3.

2-Allylmercapto-4-methyl-6-alloxypyrimidine (IX).—This pyrimidine was formed by digesting the sodium salt of 2-allylmercapto-4-methyl-6-oxypyrimidine, in alcohol, with the calculated amount of allylbromide. After the reaction was complete the alcohol was then removed by heating under diminished pressure and the pyrimidine finally dissolved in ether and the solution dried over potassium carbonate. On evaporating the ether the pyrimidine was obtained as an oil, which showed no signs of crystallizing on long standing. No attempt was made to distil this oil but it was digested for several hours with concentrated hydrochloric acid.

[1] Behrend and Dietrich, *Ann.*, **309**, 268 (1899).

Allylmercaptan was formed and after evaporation of the acid, 4-methyluracil was the only pyrimidine identified. This was purified by crystallization from hot water and did not melt below 290°. Nitrogen determination (Kjeldahl):

Calc. for $C_5H_6O_2N_2$: N = 22.22; found: N = 21.95 and 22.1.

Action of Bromine on 2-Allylmercapto-4-methyl-6-oxypyrimidine: 2-Dibrompropylmercapto-4-methyl-5-bromo-6-oxypyrimidine (VII).—This pyrimidine is formed smoothly by dissolving 2-allylmercapto-4-methyl-6-oxypyrimidine in glacial acetic acid and then adding the required amount of bromine (2 molecular proportions). The bromine was introduced by passing air through the liquid bromine and then conducting the same into the acetic acid solution. The reaction was instantaneous. After allowing to stand for 2 or 3 days the tribromopyrimidine finally deposited. The yield was about 87% of the theoretical. It was purified by crystallization from boiling 95% alcohol and separated as rosets of needles, which melted at 160–165° with decomposition. Nitrogen determination (Kjeldahl):

Calc. for $C_8H_9N_2Br_3S$: N = 6.65; found: N = 6.9.

The Action of Ethylbromide on 2-Allylmercapto-4-methyl-6-oxypyrimidine.—By the action of ethylbromide on the sodium salt of this mercaptopyrimidine we obtained an inseparable mixture of 1-ethyl-2-allylmercapto-4-methyl-6-oxypyrimidine and 2-allylmercapto-4-methyl-6-ethoxypyrimidine. Two and two-tenths grams of sodium were dissolved in absolute alcohol and 15 g. of the allylmercaptopyrimidine dissolved in the solution. Ten and five-tenths grams of ethylbromide were then added and the solution warmed on the steambath until the reaction was complete. The sodium bromide was separated by filtration and the alcohol evaporated under diminished pressure, when we obtained an oil, which refused to solidify when cooled to 0°. It was dissolved in ether, dried over potassium carbonate and finally distilled under diminished pressure. We obtained 10 g. of the mixed pyrimidines boiling from 168–175° at 14–18 mm. This oil showed no signs of crystallizing, and a nitrogen determination (Kjeldahl) agreed with the calculated value for an ethyl derivative (13.2%). The oil was insoluble in sodium hydroxide solution. In order to determine the constitution of the ethylpyrimidines, the oil was suspended in an excess of strong hydrochloric acid, digested for 17–18 hrs. and the solution then evaporated to dryness. We obtained a mixture of 4-methyluracil and 1-ethyl-4-methyluracil. They were separated by trituration of the crude mixture with an excess of cold chloroform when the ethylpyrimidine dissolved. The insoluble material did not melt below 290°, was free from sulfur and agreed in all its properties with 4-methyluracil. The chloroform solution was evaporated to dryness and the residue of ethylmethyluracil purified by crystallization from hot water. It separated in color-

less prisms, which melted at 193–195°.[1] The weight of purified methyluracil was 3.2 g. and of ethylmethyluracil 3.0 g. Therefore, the original oil was a mixture of approximately equal parts of 1-ethyl-2-allylmercapto-4-methyl-6-oxypyrimidine (X) and 2-allylmercapto-4-methyl-6-ethoxypyrimidine (XI).

The Action of Benzylchloride on 2-Allylmercapto-4-methyl-6-oxypyrimidine.—Benzylchloride reacted with the sodium salt of this mercaptopyrimidine to form two pyrimidines, *viz.*, 1-benzyl-2-allylmercapto-4-methyl-6-oxypyrimidine and 2-allylmercapto-4-methyl-6-benzoxypyrimidine. The operation was conducted as described in the preceding experiment and the following proportions were used, *viz.*, 1.5 g. of sodium, 10 g. of the allylmercaptopyrimidine, 6 g. of benzylchloride and 75 cc. of absolute alcohol. After filtration from sodium chloride and removal of the alcohol under diminished pressure we obtained the mercaptopyrimidines in the form of a thick oil, which did not solidify on cooling. After drying in ether solution over potassium carbonate the oil was purified by distillation. It practically all boiled at 225–235° at 14–15 mm. and a nitrogen determination (Kjeldahl) agreed with the calculated value for a monobenzyl derivative.

Calc. for $C_{15}H_{16}ON_2S$: N = 10.3; found: N = 10.5.

In order to determine the composition of this mixture the oil was digested with concentrated hydrochloric acid until completely hydrolyzed and the acid solution then evaporated to dryness. A mixture of 4-methyluracil and 1-benzyl-4-methyluracil[2] was obtained. They were separated from each other by a fractional crystallization from water. The benzylpyrimidine was obtained in colorless prisms, which melted at 194–5°, and a mixture of this with some 1-benzyl-4-methyluracil prepared by Wheeler and McFarland[3] melted at exactly the same temperature. Methyluracil was isolated in a pure condition from the aqueous filtrates and did not melt below 300°. We obtained no evidence of the presence of 3-benzyl-4-methyluracil.[4] The weights of methyluracil and the benzylpyrimidine were about equal. Therefore, the product of the alkylation was a mixture of two pyrimidines, *viz.*, 2-allylmercapto-4-methyl-6-benzoxypyrimidine (VI) and 1-benzyl-2-allylmercapto-4-methyl-6-oxypyrimidine (IV).

Action of Allylbromide on the Sodium Salt of 2-methylmercapto-4-methyl-6-oxypyrimidine. 2-Methylmercapto-4-methyl-6-alloxypyrimidine (III).—The 2-methylmercapto-4-methyl-6-oxypyrimidine used in our work was prepared by alkylation of 2-thio-4-methyluracil with methyl iodide in alcoholic solution and in presence of the required amount of

[1] Hoffmann, *Ann.*, **253**, 68 (1889); Hagen, *Ibid.*, **244**, 8 (1888).

[2] Wheeler and McFarland, *Am. Chem. J.*, **42**, 101 (1909).

[3] *Loc. cit.*

[4] Wheeler and McFarland, *Loc. cit.*

sodium ethylate. For the alkylation, the following proportions were used, *viz.*, 15 g. of the 2-mercaptopyrimidine, 2.4 g. of sodium, 14 g. of allylbromide and 75–100 cc. of absolute alcohol. After the reaction was complete the sodium bromide was filtered off and the excess of alcohol removed in the usual manner, when we obtained the allyl derivative as a yellow oil. This was extracted with ether dried over potassium carbonate and then further purified by distillation under diminished pressure. It practically all boiled at 160–164° at 17 mm. A nitrogen determination (Kjeldahl) gave:

Calc. for $C_9H_{12}ON_2S$: N = 14.2; found: N = 14.3.

The constitution of this mercaptopyrimidine was established by its behavior on hydrolysis. It was converted smoothly into 4-methyluracil by digestion with hydrochloric acid. This was purified by crystallization from hot water and did not melt or decompose below 300°. Analysis (Kjeldahl):

Calc. for $C_5H_6O_2N_2$: N = 22.2; found: N = 22.2.

NEW HAVEN, CONN.

ON 1-PHENYL-4,5-DIHYDRO-5-OXY-3-TRIAZOLYLSULFINIC ACID AND 1-PHENYL-4,5-DIHYDRO-5-OXY-3-TRIAZOLYLMETHYLSULFONE.

[EIGHTEENTH[1] COMMUNICATION ON URAZOLES.]

BY E. W. ESSLINGER AND S. F. ACREE.

Received November 14, 1914.

In developing the study of tautomerism as illustrated in the urazoles, it has been found[2] that 1-phenyl-3-thiourazole (I) apparently gives only one mono-alkyl derivative (II) when treated with an alkyl halide, diazomethane or alcoholic hydrochloric acid, or when its salts are treated with an alkyl halide or sulfate. It will be recalled that the corresponding 3-oxyurazole always yields a mixture of the 2-N-ester (V) and 3-O-ester (VI) under these conditions, the yields varying widely with the different salts and alkyl halides used. A mathematical development of our theory[3] showed that the facts can be interpreted consistently on the idea that the salts of the 3,5-dioxyurazoles exist in two tautomeric[4] forms (III) and (IV),

[1] This work was presented in June, 1912, by E. W. Esslinger as a partial fulfillment of the requirements for the degree of Master of Arts in the Johns Hopkins University. For previous work see *Ber.*, 33, 1530 (1900); 35, 553 (1902); 36, 3139 (1903); 37, 184, 618 (1904); 41, 3199 (1908); *Science*, 30, 617 (1909); *Am. Chem. J.*, 27, 118 (1902); 31, 185 (1904); 32, 606 (1904); 37, 71, 361 (1907); 38, 1 (1907); 39, 124, 226 (1908); 43, 358 (1910); 44, 219 (1910); 49, 116 (1913). [We are indebted to the Carnegie Institution of Washington for aid in these researches.]

[2] *Ber.*, 36, 3152 (1903).

[3] *Ibid.*, 41, 3199 (1908); *Am. Chem. J.*, 43, 505 (1910).

[4] *Ibid.*, 37, 70 (1907); 38, 1 (1907); 43, 505 (1910); 44, 219 (1910); 49, 116 (1913).