carbons of 4 or 5 carbon atoms were obtained, a fact which seems to leave but little hope that the cracking of petroleum ether will provide an easy means for the preparation of synthetic organic compounds.

CAMBRIDGE 39, MASSACHUSETTS

[CONTRIBUTION FROM THE ORGANIC LABORATORY OF THE MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

THE ACTION OF HYDROGEN PEROXIDE UPON CERTAIN PHENYL-SUBSTITUTED URIC ACIDS

FOURTH PAPER ON PURINES

BY F. J. MOORE AND ELIZABETH S. GATEWOOD

Received July 10, 1922

In previous papers[1] it had been shown that the action of hydrogen peroxide upon uric acid may lead to two distinct series of products, according to experimental conditions. In a solution whose alkalinity is less than normal and whose temperature is above 80°, the products are allantoin and carbonyl di-urea, though the latter in a solution more alkaline than 0.5 N is transformed to cyanuric acid. At room temperature and in alkali more concentrated than normal, the product of oxidation is allantoxanic acid which, if the solution be acidified without removing the hydrogen peroxide, is oxidized in the acid solution to cyanuric acid.

These studies, however, revealed no intermediate between uric acid and the products mentioned, and threw no light upon any relationship which may exist between the mechanism of this reaction and that of the permanganate oxidation, which has been studied so intensively by Emil Fischer, Behrend and Biltz. Accordingly, after the publication of the third paper, Miss Ruth Thomas, working in this Laboratory, studied the action of hydrogen peroxide upon numerous purine derivatives including theobromine, caffeine, xanthine, guanine, 3-methyl-uric acid, 7-methyl-uric acid, 7-oxymethylene-uric acid, 9-methyl-uric acid and 3, 7-dimethyl-4,5-uric acid glycol.[2]

In summary it may be said that in all these cases the results were negative in the sense that they did not invite immediate further study. Some compounds were unaffected, some were decomposed by the alkali; in still other cases the reaction led to jelly-like mixtures. At some future time it may seem advisable to return to these reactions, but the immediate purpose of the experiments was to find substances which, when treated with hydrogen peroxide, would give homogeneous products in reasonable yields. The first compound which fulfilled these conditions was 9-phenyl-uric acid. From this compound Miss Thomas was able to obtain am-

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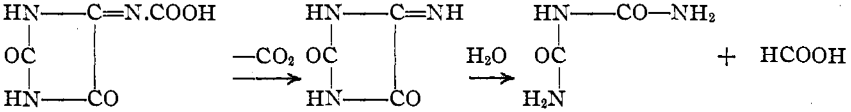
[1] Venable and Moore, THIS JOURNAL, 39, 1750 (1917). Venable, *ibid.*, 40, 1099 (1918). Moore and Thomas, *ibid.*, 40, 1120 (1918).

[2] Miss Thomas, unpublished notes.

monia, oxalic acid, phenyl-urea, *asym*-phenyl-biuret and a new compound melting at about 198° which was transformed into *asym*-phenyl-biuret when treated with ammonia. At this point, she was obliged to sever her connection with the investigation, and the present paper is devoted to a more thorough study of this reaction and to other experiments suggested by its results.

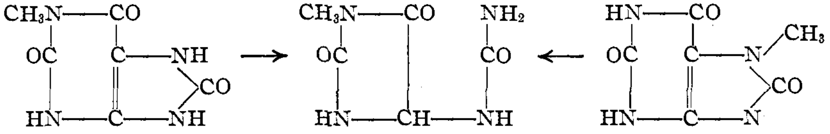
Interest at once centered in the new compound which yielded *asym*-phenyl-biuret with ammonia. It proved to be a new phenyl-biuret, entirely distinct from the two already known, and a full account of what we know concerning its properties and its relation to the other isomers will be found in the following paper. We are, for the present, concerned only with the transformation just mentioned, which can also be effected by alkali in the presence of hydrogen peroxide. This, in connection with the fact that the united yields of the two biurets is about constant, has convinced us that the *asym*-phenyl-biuret (and perhaps the phenyl-urea) owe their formation to secondary transformation of the new compound. Its constitution can best be discussed in connection with the products of two analogous oxidations a little further on. Meantime, the formation of a biuret derivative interested us from another point of view.

Behrend[3] once obtained a 28% yield of biuret by the action of warm alkaline permanganate solution upon uric acid, and while it has never been found among the products of direct oxidation by hydrogen peroxide, it is formed almost quantitatively by the hydrolysis of allantoxäidin whose close relationship to allantoxanic acid is well known.



Allantoxanic acid Allantoxäidin Biuret Formic acid

Meantime, Biltz and his pupils[4] have shown that allantoxanic acid, first recognized in this Laboratory as a product of oxidation by hydrogen peroxide, is really identical with the "oxonic acid" which has so long figured conspicuously in the literature of the permanganate oxidation. The most important clue to the mechanism of the latter reaction is the observation



1-Methyl-uric Acid 3-Methyl-allantoin 7-Methyl-uric Acid

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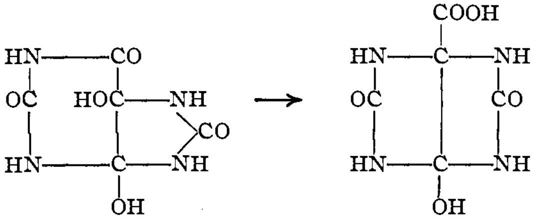
[3] Behrend, *Ann.*, **365**, 21 (1909).

[4] Biltz, *Ber.*, **53**, (a) 1950, (b) 1964, (c) 1967 (1920); *ibid.*, **54**, (d) 2441, (e) 2451 (1921).

made by Emil Fischer and Ach[5] that both 1-methyl- and 7-methyl-uric acids yield the same 3-methyl-allantoin, while both 3-methyl- and 9-methyl-uric acids yield 1-methyl-allantoin. The conclusion is unavoidable that a symmetrical intermediate must exist between uric acid and allantoin. Behrend[6] soon after made the important suggestion that the first step in the oxidation of uric acid by permanganate was the addition of hydroxyl radicals to the double bond, forming first a glycol and then hydroxy-glycoluril-carboxylic acid.


Uric-acid-glycol

Hydroxy-glycoluril-carboxylic Acid

When Behrend wrote, both compounds were hypothetical, but after Biltz[7] had prepared the glycol it was found to be very sensitive to alkali and yielded with permanganate none of the oxidation products of uric acid. For a time this discredited Behrend's suggestion, but Biltz[8] has recently observed that uric-acid-glycol dimethyl ether yields smoothly both uroxanic acid and allantoin. He, therefore, now supports the view that while uric-acid-glycol never really comes into existence in the oxidation, yet the double bond at 4–5 must be the point of attack, hydroxyl adding to 4 while the bond set free at 5 attracts the nitrogen at 1 to form hydroxy-glycoluril-carboxylic acid. The advantages in assuming the latter as an intermediate are obvious, for it not only explains the results of Fischer and Ach, but also accounts for the fact first noted by Behrend that by the action of permanganate upon uric acid a solution can be obtained from which allantoin, uroxanic acid and allantoxanic acid may be obtained at will. At the same time the close structural relationship to other allied compounds like *spiro*-dihydantoin and carbonyl-diurea is no less clear.

Although the action of hydrogen peroxide upon uric-acid-glycol and upon glycoluril had met with only negative results,[9] nevertheless the formation of a phenyl-biuret from 9-phenyl-uric acid suggested a means by which a parallel between the two types of oxidation might be traced. It seemed natural to suppose that a substituted biuret resulted from a corresponding allantoxanic acid or its hypothetical product of hydration,

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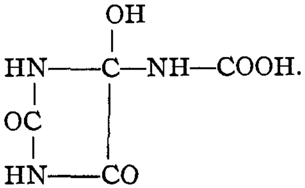
[5] E. Fischer and Ach, *Ber.*, **32**, 2723 (1899).

[6] Behrend, *Ann.*, **333**, 104 (1904).

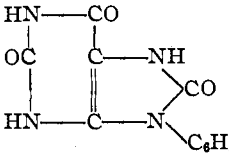
[7] Biltz, *Ber.*, **43**, 1511 (1910).

[8] Ref. 4b. Ref. 4e, p. 2465.

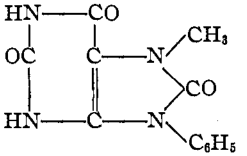
[9] Moore and Thomas, THIS JOURNAL, **40**, 1120 (1918).



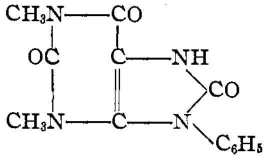
Hence, if it could be expected that any substituted phenyl-uric acid would yield a substituted biuret on oxidation, it would not be a difficult matter, by tracing the reaction backward, to reach a decision concerning the point in the uric acid molecule where the first break occurred, and also to decide whether the assumption of a symmetrical intermediate like hydroxy-glycoluril-carboxylic acid was here a logical necessity. 1,3-Dimethyl-9-phenyl-uric acid seemed particularly well suited for the purpose, because different biurets might be expected according to the nature of the earlier steps of the reaction, even if no more complex intermediates could be isolated. This compound and 7-methyl-9-phenyl-uric acid were, therefore, prepared (for the first time) and treated with hydrogen peroxide. In neither case, however, was any substituted biuret formed. In both cases the products of the reaction were ammonia, oxalic acid and α,β-methyl-phenyl-urea. These results raise some interesting questions of mechanism.



9-Phenyl-uric Acid



7-Methyl-9-phenyl-uric Acid

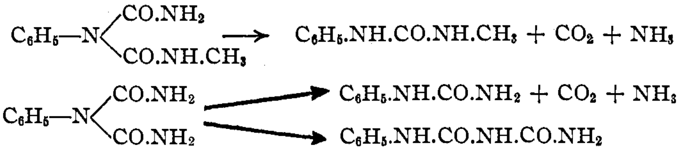


1,3-Dimethyl-9-phenyl-uric Acid .

for if we consider the three formulas, the formation of *asym*-phenyl-biuret from the first, and of α,β-methyl-phenyl-urea from the last two would seem to involve a different splitting in each of the three cases, and this is extremely unusual in the purine group, the substituted compounds following the mother substance with surprising regularity in almost all degradations. Furthermore, as was pointed out at the beginning of the discussion, *asym*-phenyl-biuret is probably formed only by the transformation of the new phenyl-biuret, so that the constitution of the latter becomes of interest. This will be discussed more fully in the following paper, but it would certainly better suit our present purpose to assume that it is symmetrical phenyl-biuret. It is true that another compound now bears this name in the literature,[10] but the evidence is unconvincing. At all events, this assumption permits the interpretation of the three oxidations from a single point of view. We can regard as the first step the breaking of the bonds between 2 and 3, 4 and 5, and 5 and 7, forming in the first case

[10] See Schiff, *Ann.*, 352, 72 (1907).

sym-phenyl-biuret, and in the last two the same methyl-phenyl-biuret. Now Schiff presents some evidence to show that biurets substituted upon the central nitrogen are sensitive to ammonia, yielding the corresponding ureas. Adding this assumption to the other we can say that the methyl-phenyl-biuret then splits to ammonia, carbon dioxide, and *sym*-methyl-phenyl-urea; while the symmetrical phenyl-biuret partly undergoes a similar decomposition forming phenyl-urea, and another portion is rearranged by the ammonia to form *asym*-phenyl-biuret.



$$C_6H_5{-}N\begin{cases}CO.NH_2\\CO.NH.CH_3\end{cases} \longrightarrow C_6H_5.NH.CO.NH.CH_3 + CO_2 + NH_3$$

$$C_6H_5{-}N\begin{cases}CO.NH_2\\CO.NH_2\end{cases} \begin{matrix}\longrightarrow C_6H_5.NH.CO.NH_2 + CO_2 + NH_3\\ \longrightarrow C_6H_5.NH.CO.NH.CO.NH_2\end{matrix}$$

It is no part of our purpose to claim too much for this interpretation. Its weakest point lies in the fact that no phenyl-urea has yet been found when the new phenyl-biuret was subjected to the same experimental conditions, so this product may come from another source. This, however, does not necessarily invalidate the other assumptions. These questions cannot be definitely settled until a thorough study of the aryl substituted biurets has been made, and such an investigation is now contemplated in this Laboratory.

It is obvious that in these oxidations, the intermediate formation of a substituted hydroxy-glycoluril-carboxylic acid might be assumed, but this is not necessary. On the other hand, no methyl-phenyl derivatives of the known oxidation products of uric acid can be considered as intermediates, because none of these account for the smooth formation of oxalic acid. Before this was so clearly realized, a few experiments were made upon the oxidation of uroxanic acid and *spiro*-dihydantoin by hydrogen peroxide. The former proved perfectly stable, while *spiro*-dihydantoin yielded allantoin and uroxanic acid, the latter by alkali alone. These substances, therefore, cannot be intermediates in the formation of allantoxanic acid or biuret.

1,3-Dimethyl-9-phenyl-uric acid also shows a smooth and interesting decomposition with alkali but the publication of the details must be postponed until the reaction has been further studied, and our ideas are more definite concerning the structure of the products. It is also hoped to study the action of alkalies upon other substituted uric acids. The experimental part of this paper gives an account of 9-allyl-uric acid which has been prepared for the first time. It has also been treated with hydrogen peroxide, but any discussion of the results would be premature until we know more about allyl ureas and biurets.

Experimental

9-Phenyl-uric Acid

Oxidation with Hydrogen Peroxide.—9-Phenyl-uric acid was prepared from alloxan[11] through the familiar steps of the Fischer[12] synthesis. Its optical properties were determined: habit, rectangular plates; extinction, parallel, γ parallel to elongation; indices, $\alpha = 1.525$, $\gamma = 1.717$.

Most of the oxidation experiments were carried out in potassium hydroxide solution (excess alkalinity 0.35 *N*). With sodium hydroxide, the same products were obtained but the yields were not so good. The following conditions are typical.

Two g. of 9-phenyl-uric acid was dissolved in a cold solution of 2.3 g. of potassium hydroxide in 24 cc. of water. Fifty-two cc. of 3% hydrogen peroxide was then added. The solution became yellow and an odor suggestive of carbylamine soon developed. Several times the potassium salt separated but it always went into solution on longer standing. After 1 or 2 days thin transparent crystals melting at 163–165° were formed. These usually appeared spontaneously, but sometimes it was necessary to add 10 cc. more of hydrogen peroxide and cool the solution thoroughly. This product proved to be *asym*-phenyl-biuret. When the filtrate was acidified with hydrochloric acid, there slowly separated small, reddish-brown particles melting at 194–195°.

This is the new phenyl-biuret which, when pure, is colorless and melts at 196–197.5° with decomposition. Its properties are more fully described in the following paper. The table below shows the relative yields of the two biurets from eight 2g. samples of 9-phenyl-uric acid.

asym-Phenyl-biuret G.	New phenyl-biuret G.	*asym*-Phenyl-biuret G.	New phenyl-biuret G.
0.00	0.40	0.13	0.27
0.00	0.46	0.17	0.17
0.09	0.42	0.20	0.16
0.10	0.43	0.28	0.31

The mother liquor from the phenyl-biurets when evaporated yielded crystals weighing on the average 0.13–0.20 g. They were purified and shown by a mixed melting point to be phenyl-urea melting at 147°. The final filtrates, when made alkaline with ammonia and treated with calcium chloride, yielded calcium oxalate. This was not always determined but in a sample experiment weighed 0.32 g. Oxidation in *N* alkali yielded no different products and had no advantages. Special experiments also showed that decomposition of the excess hydrogen peroxide with manganese dioxide, and acidification with acetic instead of hydrochloric acid had no influence upon the nature of the products.

7-Methyl-9-phenyl-uric Acid

7-Methyl-uramil, the starting point in the preparation of this acid has been prepared by several investigators. Attempts to follow Fischer's[13] method from alloxan through 7-methyl-thionuric acid resulted only in failure, confirming the results of Miss Thomas.[2] It was, however, suc-

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[11] Large quantities of alloxan were required throughout this investigation. It was prepared by the method of Biltz [*Ann.*, **413**, 60 (1907)] by the action of chlorine upon uric acid suspended in glacial acetic acid containing exactly the appropriate amount of water. The method is admirable, but sometimes fails when the uric acid employed is particularly old and dry. In such cases it should be dissolved and reprecipitated.

[12] Fischer, "Untersuchungen in der Puringruppe," Berlin, 1907, p. 543.

[13] Ref. 12, p. 256.

cessfully prepared by the seemingly longer method of Biltz[14] from uric acid through 5-chloro-pseudo-uric acid, 5-hydroxy-pseudo-uric acid, 5-methyl-amino-pseudo-uric acid and final reduction of the latter with stannous chloride.

Preparation of 7-Methyl-9-phenyl-pseudo-uric Acid.—Sixty cc. of *N* potassium hydroxide solution was cooled to 0°; then 5 g. of 7-methyl-uramil was added and the mixture was shaken until practically all of the solid had dissolved. To this solution, 5 g. of phenyl-isocyanate was added in small portions, and the solution was shaken after addition of each portion until the odor disappeared. The temperature was kept between 0° and 5°. The solution became purplish but little precipitate separated. The precipitate was collected and found to contain a little of an unidentified substance which did not melt, and some diphenyl-urea resulting from the hydrolysis of the isocyanate. The filtrate, when acidified with hydrochloric acid, gave a heavy precipitate (7 g.) of material which melted at 245–250° to a yellow liquid.

Of the pseudo-uric acids hitherto known, the 7-methyl compound is the only one which does not give a deep red material when it melts. This acid makes the second exception. It is also noteworthy that the potassium salt of this acid is more soluble than that of 9-phenyl-uric acid, just as the potassium salt of 7-methyl-pseudo-uric acid is more soluble than that of pseudo-uric acid.[15] The optical properties of 7-methyl-9-phenyl-pseudo-uric acid are: habit, needles; extinction, parallel, γ parallel to elongation; indices, $\alpha = 1.636$, $\gamma = 1.714+$.

Preparation of 7-Methyl-9-phenyl-uric Acid.—Three g. of 7-methyl-9-phenyl-pseudo-uric acid was boiled with 600 cc. of 35% hydrochloric acid. Much of it appeared not to dissolve. The mixture was concentrated by boiling to $^1/_3$ its volume, and filtered hot. The material on the filter weighed 1.55 g. and, when recrystallized from water, yielded a mat of glistening needles. These did not melt at 295°. The original filtrate on evaporation and cooling gave 0.7 g. more of the same material. The total yield was 76%. The product gave the murexide reaction with potassium chlorate and hydrochloric acid followed by ammonia.

Analyses. Calc. for $C_{12}H_{10}O_3N_4$: C, 55.81; H, 3.90; N, 21.70. Found: C, 56.22, 56.14; H, 4.35, 4.17; N, 22.00, 21.72.

Optical Properties. Habit, needles; extinction, parallel, γ parallel to elongation; indices, $\alpha = 1.557$, $\gamma = 1.674+$.

7-Methyl-9-phenyl-uric acid is quite stable toward 4 *N* alkali even when heated to boiling.

Oxidation with Hydrogen Peroxide.—To 0.5 g. of 7-methyl-9-phenyl-uric acid in 6 cc. water, 2.2 g. of potassium hydroxide was added. A white precipitate formed which was probably the potassium salt. On the addition of 40 cc. of hydrogen peroxide the precipitate did not entirely dissolve; so, after the mixture had stood for 15 or 20 minutes, it was warmed carefully until all of the solid passed into solution, the temperature rising to about 40°. The solution was kept in ice water for 2 hours and then left at room temperature. After 3 days a sample gave only a slight precipitate when acidified. The whole was then evaporated by a current of air until it yielded a precipitate, weighing 0.06 g. and melting at 145–150°. On recrystallization this yielded a product easy to

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[14] Biltz, *Ann.*, **413**, 23, 29, 46 (1907).

[15] Ref. 12, p. 253.

identify as α,β-methyl-phenyl-urea, by both mixed melting point and its optical properties: habit, square plates; extinction, parallel; indices, $\alpha = 1.513$, $\gamma = 1.636$.

The alkaline filtrate stood for a day longer and, as no further precipitate formed, it was acidified. This yielded some unoxidized acid and enough methyl-phenyl-urea to make the total yield 0.10 g. or 33%. The mother liquor was evaporated until potassium chloride began to crystallize, made ammoniacal and treated with calcium chloride. It yielded 0.07 g. of calcium oxalate. Calculation requires 0.25.

1,3-Dimethyl-9-phenyl-uric Acid

The first method employed for the preparation of this acid involved the use of 1,3-dimethyl-uramil. It was found that the best way to prepare it was to oxidize caffeine with chlorate, reduce the product to amalinic acid, oxidize this to dimethyl alloxan, and pass thence through dimethyl-thionuric acid to dimethyl-uramil. The way is long but the yields are good; several successive preparations, each employing 100 g. of caffein, yielded between 24 and 50 g. of 1,3-dimethyl-uramil.

Unfortunate experiences were encountered in attempting to follow Fischer's[16] directions for preparing amalinic acid.

It is better to work according to Biltz.[17] The method employs stannous chloride as reducing agent, and subsequent oxidation with fuming nitric acid instead of with chlorine. An attempt to shorten the route, by reducing amalinic acid to dimethyl-dialuric acid[18] and then transforming this to dimethyl-uramil by the action of ammonia, resulted in excessively poor yields.

Preparation of 1,3-Dimethyl-9-phenyl-pseudo-uric Acid.—FIRST METHOD.—1,3-Dimethyl-uramil is extremely sensitive to alkali; it is decomposed even by ammonium carbonate, so the first attempts to combine it with phenyl-isocyanate were made in neutral solution; the yields were extremely poor. It was soon found that, just as in the Schotten-Baumann reaction, alkali accelerates the reaction between phenyl-isocyanate and dimethyl-uramil more rapidly than it decomposes the latter, so that good yields can be obtained by observing certain precautions.

Thirty g. of dimethyl-uramil was finely powdered and added to 360 cc. of *N* potassium hydroxide solution. A deep red solution resulted; 30 g. of phenyl-isocyanate was added in small portions and the solution shaken vigorously after each addition till the odor disappeared. The temperature was kept below 4° and the addition required about an hour. The solution was light pink and thick with precipitate. This is the potassium salt of 1,3-dimethyl-9-phenyl-pseudo-uric acid. It was collected on a filter, dissolved in 500 cc. of hot water, then cooled slightly and acidified with dil. hydrochloric acid which must be added gradually and the solution must *not* be stirred. A heavy white precipitate of the free acid separated. This was allowed to stand overnight and then collected. A little more material could be obtained by acidifying the filtrate from the potassium salt. In 5 experiments carried out in this way the yields varied between 28 and 37 g. Vigorous shaking of the reaction mixture, low temperature and the gradual addition of the isocyanate favor good yields. For analysis the product was recrystallized twice from hot water from which it separates in colorless plates melting at 189–190°

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[16] Ref. 12, pp. 88, 128.

[17] Biltz, *Ber.*, **45**, 3674 (1912).

[18] Biltz, *ibid.*, **46**, 3671 (1913).

to the red melt common to most pseudo-uric acids. Habit, plates; extinction, 25–37°; interference figure, bi-axial, large optic angle; indices, $\alpha = 1.525$, $\gamma = 1.647$.

Analyses. Calc. for $C_{13}H_{13}O_4N_4$: C, 53.76; H, 4.86; N, 19.32. Found: C, 53.22, 53.39; H, 5.15, 4.97; N, 19.95, 20.02.

SECOND METHOD.—Biltz[19] has found that the pseudo-uric acids can be easily methylated by dimethyl sulfate, that homogeneous products are formed and that the methyl groups enter at Positions 1 and 3. Advantage was taken of this in developing the following procedure. Five g. of powdered 9-phenyl-pseudo-uric acid was dissolved in 40 cc. of 2 *N* sodium hydroxide and the solution cooled to 0°. Eleven g. of dimethyl sulfate was added, and the flask stoppered and vigorously shaken for an hour, the temperature being still maintained at 0°. The heavy crystalline precipitate was collected on a filter and dissolved in water in which it is quite soluble. It gave a residue when heated on platinum foil and turned pink at about 150°, but did not melt. On boiling it with water for a few minutes, a heavy precipitate appeared which weighed 1.15 g. and melted at 185–190°. When the substance was mixed with the product of the first method, the melting point was 190–192°. The original filtrate when acidified gave 3.9 g. of the same material—a total yield of 5 g.

Monohydrate of 1,3-Dimethyl-9-phenyl-pseudo-uric Acid.—On slow crystallization of the above product from water two kinds of crystals appear. One shows the properties described above, but the other differs quite markedly in optical properties: habit, needles; extinction, parallel, indices, $\alpha = 1.583$, parallel to elongation; $\gamma = 1.768+$, $1.800-$; birefringence, strong. These latter represent a monohydrate of the first, as was shown by heating at 100° to constant weight.

Analysis. Calc. for $C_{13}H_{13}O_4N_4$, H_2O: H_2O, 5.84. Found: 5.84.

When the hydrate is crystallized from alcohol the anhydrous form is obtained, while the latter is (partially) hydrated by crystallization from water. It is a curious circumstance, unusual in such cases, that both forms have the same melting point, and there is no lowering when they are mixed.

Preparation of 1,3-Dimethyl-9-phenyl-uric Acid.—Five g. of 1,3-dimethyl-9-phenyl-pseudo-uric acid was dissolved in 1 liter of hydrochloric acid (sp. gr. 1.19) and the solution was boiled over a free flame until crystallization began. The solution was then evaporated on the steam-bath to $^1/_3$ its volume, cooled and filtered. The yields varied from 1.3 to 1.6 g. but the product usually contained a little of the unchanged pseudo-uric acid, the presence of which was betrayed by the pink color which developed on heating the solid to about 200°. The pseudo acid can be removed by boiling the product with small portions of water, in which it is much more soluble. The pure substance does not melt, and remains perfectly white when heated to 300°. It is soluble with difficulty in water and in alcohol. It is decomposed readily by caustic alkali, but is stable toward sodium carbonate. It gives the murexide reaction. Habit: hexagonal or rectangular plates; extinction, symmetrical, α parallel to elongation; interference figure, biaxial, large optic angle, off the field; indices, $\alpha = 1.155+$, $\gamma = 1.684$.

Analyses. Calc. for $C_{13}H_{12}O_3N_4$: C, 57.32; H, 4.44; N, 20.60. Found: C, 57.63, 57.42; H, 4 83, 4.30; N, 20.24, 20.42.

Many fruitless attempts were made to improve the yield by using different concentrations of acid and by the use of both crystalline and anhydrous oxalic acid. Less concentrated acids gave poorer yields, while 40% acid, prepared by passing the gas into the cold conc. acid of commerce, caused a splitting of the pseudo-uric acid to phenylurea and the formation of a compound melting at 125–135°. Oxalic acid also produced

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[19] Biltz, *Ann.*, **423**, 186 (1921).

a substance of similar melting point, but the two were not identical. When mixed they melted at 85–100°.

Oxidation with Hydrogen Peroxide.—Experiments were carried out in concentrations varying from 0.3 N to N excess alkali, and at two different temperatures, 25° and 40–50°. The following is typical.

Two g. of 1,3-dimethyl-9-phenyl-uric acid was dissolved in 24 cc. of water, and 9 g. of potassium hydroxide and 140 cc. of hydrogen peroxide were added. After 10 days crystals began to separate, and, when collected on the following day, they weighed 0.085 g. The substance was α,β-methyl-phenyl-urea as shown by its optical properties and a mixed melting point. Ten cc. more of the hydrogen peroxide was then added to the filtrate and the mixture was evaporated by a current of air. In this way 0.145 g. was obtained. On acidifying the filtrate from this, 0.34 g. of less pure material separated; total yield, 0.57 g., or 54%. The mother liquors yielded 0.48 g. of calcium oxalate or 51%. In two experiments when the excess of alkali was greater than 0.5 N, small quantities of a substance melting at 177–180° appeared. It could not be identified.

9-Allyl-uric Acid

Preparation of 9-Allyl-pseudo-uric Acid.—Five g. of uramil was added to 100 cc. of N potassium hydroxide solution previously cooled to 0°. When the mixture was shaken part of the solid dissolved to give a purple-red solution. Three g. of allyl-isocyanate was then added in small portions, and the solution was shaken after each addition until the odor had disappeared. The operation required about an hour. The solution was filtered and acidified with hydrochloric acid, when it turned yellow and a heavy precipitate separated. This weighed 3 g. The filtrate on standing gave 0.5 g. more. The product is insoluble in alcohol and ether. It was crystallized twice from hot water from which it separated in colorless needles which turn pink at 170° and melt at 227–228° with decomposition. Habit, needles; extinction, parallel, α parallel to elongation; indices, $\alpha = 1.591$, $\gamma = 1.69$.

Analyses. Calc. for $C_8H_{10}O_4N_4 + H_2O$: C, 39.32; H, 4.96; N, 22.95. Found: C, 39.80, 39.61; H, 4.99, 5.04; N, 22.85, 23.02.

Preparation of 9-Allyl-uric Acid.—Three g. of 9-allyl-pseudo-uric acid was heated with 600 cc. of 20% hydrochloric acid until solution was complete and then the liquid was boiled for 15 minutes longer. The solution was evaporated rapidly to $^1/_3$ its volume, cooled and filtered. Two g. of 9-allyl-uric acid was obtained in glistening leaves. It was crystallized twice from hot water and dried at 110°. It did not melt at 300°. Habit, plates; extinction, symmetrical, γ parallel to elongation; interference figure, uni-axial; indices $\alpha = 1.75$, $\gamma = 1.775$, 1.80.

Analyses. Calc. for $C_8H_8O_3N_4$: C, 46.16; H, 3.87; N, 26.93. Found: C, 46.13, 46.34; H, 3.96, 3.62; N, 27.03, 26.80.

In the course of this investigation the optical properties of several familiar compounds were determined. The results are appended here since they do not seem to have been recorded elsewhere.

			Interference fig.	Indices		Birefringence
Substance	Habit	Extinction		α	γ	
Urea	prisms	parallel		1.4743	1.6005	
Phenyl-urea	plates	parallel, γ par. to elongation		1.602	1.627	weak
Diphenyl-urea	needles	parallel, α par. to elongation	biaxial 1 brush	1.583	1.74 (?)	

Substance	Habit	Extinction	Interference fig.	Indices		Birefringence
				α	γ	
sym-Diphenylbiuret	needles	parallel, α par. to elongation	biaxial, large opt. ang.	1.591	<1.656 >1.649	
Allantoin	hexagonal plates	parallel, α par. to elongation		1.579	1.66−	
Uroxanic acid	sm. tetrahedra not well formed			1.5316	1.6005	
Acid potass. uroxanate	long needles	parallel, γ par. to elongation		1.4676	1.620+	
spiro-Dihydantoin	hexagonal plates	25–26°, α par. to elongation	biaxial sm. opt. ang.	1.571−	1.602	weak
Amm. chloroplatinate	thick hex. plates	optical orientation, isotropic		1.8		
Methylammonium chloroplatinate	thin hex. plates	optical orientation, isotropic		1.74		

Summary

1. 7-Methyl-9-phenyl-uric acid, 1,3-dimethyl-9-phenyl-uric acid, 9-allyl-uric acid, and several other compounds closely related to these, have been prepared for the first time and characterized.

2. The action of hydrogen peroxide upon the first two of these, as well as upon 9-phenyl-uric acid, has been studied and some insight gained into its mechanism.

3. It has not yet proved possible to establish any necessary connection between the mechanism of the permanganate oxidation of uric acid and that by hydrogen peroxide.

CAMBRIDGE 39, MASSACHUSETTS