As an example, the vapor pressures of water and benzene at 60° were determined by this method.

	P obs.	P found
Water	148.5	148.5
Benzene	390.0	392.5

Experiments lasting for two months were made with this manometer, and with pressures as high as 1.5 atmospheres. The membrane, since it is used near the position of rest, introduces only a small error due to elastic aftereffects. The manometer can be made of very different sensitivities but the more sensitive it is the more cautiously it must be used. One can be made very easily in which 1.5mm. rise of oil corresponds to a pressure of 1 mm.

I wish, here, to express my thanks to Mr. Karl Söllner for his assistance in performing the experiments.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

THE ACTION OF ALKALI ON SUBSTITUTED URIC ACIDS

II. 1,3,7-TRIMETHYL-9-PHENYL-URIC ACID

BY ELIZABETH STUART GATEWOOD[1]

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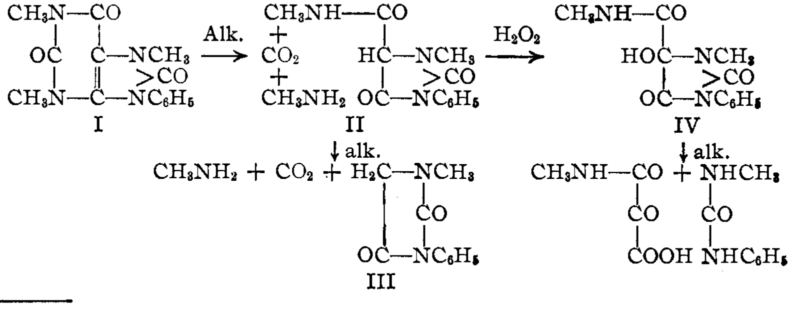
Only tetrasubstituted uric acids and trisubstituted uric acids whose substituents are in Positions 1,3 and 9 show marked instability toward alkali. In Part I of this investigation, the action of alkali on 1,3-dimethyl-9-phenyl-uric acid was described,[2] and in the following paper an account is given of the action of alkali on tetramethyl-uric acid and 1,3,9-trimethyl-uric acid.

1,3,7-Trimethyl-9-phenyl-uric acid (I) is decomposed by alkali in the following way.



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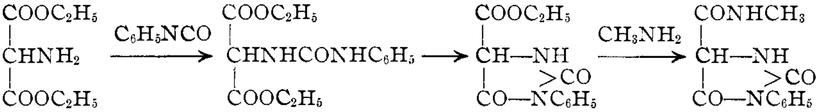
[1] National Research Fellow in Chemistry.

[2] Gatewood, THIS JOURNAL, 45, 3056 (1923).

At 100° the primary decomposition is completed within a few minutes. When the solution is acidified and partially evaporated, a substance of empirical formula $C_{12}H_{13}O_3N_3$ separates; m. p., 163°. It must be 1-methyl-3-phenylhydantoyl-methylamide (II), for with alkali it gives methylamine, carbon dioxide, and 1-methyl-3-phenylhydantoin (III), and with hydrogen peroxide, the corresponding hydroxyhydantoyl-methylamide (IV). The structure of the latter follows from the fact that on hydrolysis with alkali it gives α,β-methyl-phenyl-urea and the methylamide of mesoxalic acid.

The decomposition of trimethyl-phenyl-uric acid differs from that of dimethyl-phenyl-uric acid in that methyl-phenylhydantoyl-methylamide gives an hydantoin on further hydrolysis, while phenylhydantoyl-methylamide[2] gives phenylurea. Because of this latter fact it was suggested that the primary decomposition product of dimethyl-phenyl-uric acid might have an *iso*hydantoin structure, but it is now thought that this difference in decomposition is due to the unsubstituted nitrogen in Position 1.

An attempt was made to synthesize 3-phenylhydantoyl-methylamide by the following steps.



Phenyl-ureidomalonic ester was successfully prepared from amino-malonic ester and phenylisocyanate, but no way to bring about the next step could be found.

1,3-Dimethyl-9-allyl-uric acid, which has been prepared for the first time, is described in the experimental part of this paper.

Experimental Part

1,3,7-Trimethyl-9-phenyl-uric Acid

Preparation. 1. Methylation with Methyl Iodide.—Fischer[3] obtained trimethyl-phenyl-uric acid by methylating 9-phenyl-uric acid with methyl iodide. At first this method was used.

To a solution of 5 g. of phenyl-uric acid in 72 cc. of *N* potassium hydroxide solution in a pressure flask, was added 11.5 g. of methyl iodide. The flask was closed and shaken at 85–90° until crystallization began, which usually occurred after a half hour. The heating was continued for two hours longer, and the solution then cooled to below 5°, filtered, and washed first with very dilute, cold alkali and then with water; yield, 2.2 g. The substance was recrystallized from hot alcohol; m. p., 258–260°.

Optical Properties.—Habit, thin plates; extinction, symmetrical, α-parallel to elongation; interference figure, uniaxial; indices, $\alpha = 1.565$, $\gamma = 1.670$.

2. Methylation with Di-methyl Sulfate.—9-Phenyl-uric acid may be more readily methylated with dimethyl sulfate. The methylation can be carried out at a lower temperature and in much less time. The yield is

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[3] Fischer, *Ber.*, **33**, 1708 (1900).

about the same. As in the first method, all of the acid is not methylated to trimethyl-phenyl-uric acid, but as the latter is neutral it separates from the slightly alkaline solution unmixed with the di- and trisubstituted acids. The best conditions are as follows.

Ten g. of dimethyl sulfate is added to 5 g. of phenyl-uric acid dissolved in 55 cc. of 2 *N* aqueous sodium hydroxide. The solution is shaken vigorously and cooled by running water for a half hour. Trimethyl-phenyl-uric acid begins to separate after about ten minutes. The shaking is continued for another half hour, the precipitate then filtered off and washed with cold, very dilute alkali and finally with water; yield, 4–5 g. The melting point (260°) and the optical properties were the same as those of the substance prepared by Fischer's method.

3. Trimethyl-phenyl-uric acid may also be obtained by methylating 7-methyl-9-phenyl-uric acid, 1,7-dimethyl-9-phenyl-uric acid, or 1,3-dimethyl-9-phenyl-uric acid with dimethyl sulfate. 1,3-Dimethyl-9-phenyl-uric acid is completely methylated in a very few minutes and the product obtained is very white and pure. From 1 g. was obtained 0.6 g. of trimethyl-phenyl-uric acid which melted without recrystallizing at 260°.

The other two acids methylate more slowly and are never completely methylated. This is undoubtedly due to the fact that Position 3 is already methylated in the first acid but not in the other two. Biltz[4] has shown that when the various methyl-uric acids are methylated with dimethyl sulfate, only those hydrogen atoms that are least acidic—those in Positions 1 and 7—are replaced by methyl groups. 3,7-Dimethyl-uric acid gives only 1,3,7-trimethyl-uric acid, and 7,9-dimethyl-uric acid gives only 1,7,9-trimethyl-uric acid. Tetramethyl-uric acid is never obtained except when the strongly acidic hydrogens at Positions 3 and 9 are already substituted. The hydrogen in Position 3 of the 9-phenyl-uric acids can, however, be replaced by the methyl group, as shown. This is probably due to some effect of the phenyl group, but the replacement is decidedly slower than for the other positions and is not complete.

Action of Alkali.—Two g. of finely powdered trimethyl-phenyl-uric acid was boiled with 50 cc. of 2 *N* sodium hydroxide until the solution was clear. The cooled solution was made distinctly acid with dil. nitric acid and partially evaporated in a vacuum desiccator. Large clumps of the decomposition product, 1-methyl-3-phenylhydantoyl-methylamide, separated; yield, 0.9–1.3 g., or about 65%. It recrystallized from hot water in bunches of fine needles; m. p., 163–164°. It is easily soluble in alcohol, chloroform, ethyl acetate and acetone.

Anal. Subs., 0.1606, 0.1519: CO_2, 0.3422, 0.3272; H_2O, 0.0730, 0.0703. Subs., 0.1510, 0.1965: N, 23 cc. (25°, 765 mm.), 30.5 cc. (25°, 751.8 mm.). Calcd. for $C_{12}H_{13}O_3N_3$: C, 58.28; H, 5.28; N, 17.01. Found: C, 58.12, 58.28; H, 5.09, 5.18; N, 17.00, 17.04.

Optical Properties.—Habit, needles; extinction, parallel, γ-parallel to elongation; interference figure, biaxial; indices, $\alpha = 1.555$, $\beta = 1.585$, $\gamma = 1.627$.

When *N* or 4 *N* alkali was used, the product was the same; the yields, however,

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[4] Biltz, *Ber.*, **54**, 1679 (1921).

were not as good. Acidifying with dil. nitric acid rather than with sulfuric or hydrochloric acid gave better yields, too.

Action of Alkali on Methyl-phenylhydantoyl-methylamide.—The decomposition product (0.4 g.) dissolved readily in 4 *N* sodium hydroxide (2 cc.), and a strong odor of methylamine was evident almost at once. Carbon dioxide was evolved when the solution was acidified with acetic acid, and after about an hour clusters of needles began to form. The solution was filtered after several hours. The filtrate gave no test for oxalic acid. The crystalline product was recrystallized from hot water. It melted at 107–108°, and was identified by a mixed melting point and optical properties as 1-methyl-3-phenylhydantoin.[5]

1-Methyl-3-phenylhydantoin.—A solution of methyl-phenylhydantoic acid in 80 cc. of 20% hydrochloric acid was boiled to about one-fourth its volume. Fine needles in radiating clusters separated as the solution cooled; yield, 0.6 g.; m. p., 108–110°. The melting point was the same when the substance was mixed with a specimen obtained by heating sarcosine with phenylurea according to the directions in Beilstein.

Methyl-phenylhydantoin is much more stable toward alkali than 3-phenylhydantoin. Cold, dil. alkali readily dissolves phenylhydantoin and opens the ring almost at once, while not only is methyl-phenylhydantoin not affected under these conditions but it is also fairly stable toward warm alkali. It dissolves in alkali quite slowly and only after a day or two does it hydrolyze to methyl-phenylhydantoic acid. The latter is quite stable toward alkali, but when precipitated by dil. acid and allowed to stand in the acid solution it gradually dissolves and methyl-phenylhydantoin is obtained when the solution is evaporated.

Optical Properties.—Habit, needles: extinction, parallel, γ-parallel to elongation; indices, $\alpha = 1.515$, $\gamma = 1.665$.

Methyl-phenylhydantoic Acid.—This acid melts at 150° and not at 102°, as given by Paal and Gausen.[6] Their method of preparation, which consisted in shaking an alkaline solution of sarcosine with phenylisocyanate and then acidifying the solution with dil. sulfuric acid, was repeated. One g. of sarcosine gave 1.88 g. of a substance melting at 150°, with decomposition. It crystallized from water in shining flakes, and an analysis and its conversion into methyl-phenylhydantoin showed that it was methyl-phenylhydantoic acid. Their product was probably mixed with methyl-phenylhydantoin, formed when the acidified solution is allowed to stand. That could account for their low melting point.

Anal. Subs., 0.1609: CO_2, 0.3416; H_2O, 0.0837. Subs., 0.1688, 0.2123: N, 20.7 cc. (22°, 766.5 mm.), 26.0 cc. (23°, 762.5 mm.). Calcd. for $C_{10}H_{12}O_3N_2$: C, 57.69, H, 5.77; N, 13.46. Found: C, 57.90; H, 5.82; N, 13.79, 13.76.

Optical Properties.—Habit, plates; extinction, symmetrical, α-parallel to elongation; indices, $\alpha = 1.530$, $\gamma = 1.625$.

Oxidation of Methyl-phenylhydantoyl-methylamide.—To 1 g. of the decomposition product suspended in 13 cc. of water, 2.6 g. of potassium hydroxide and 65 cc. of cold, 3% hydrogen peroxide were added. The temperature was kept below 10°. After five minutes the solution was acidified with dil. hydrochloric acid, and the oxidation product soon separated. It was filtered off after several hours and recrystallized from aqueous alcohol; m. p., 195–196°; yield, 0.75 g. Methyl-phenylhydroxyhydantoyl-methylamide crystallizes with 1 molecule of water, which it loses when dried at 100°.

Anal. Subs. (dried in a vacuum), 0.1658, 0.2037: N, 22.0 cc. (20°, 763 mm.),

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[5] Beilstein, "Handbuch der organischen Chemie," Leopold Voss, Leipzig, **1896**, vol. 2, p. 383.

[6] Paal and Gausen, *Ber.*, **28**, 3233 (1895).

27.7 cc. (21°, 761.5 mm.). Subs., 0.4855, 0.5857: H_2O, 0.0306, 0.0379. Calcd. for $C_{12}H_{13}O_4N_3.1H_2O$: N, 15.16; H_2O, 6.406. Found: N, 15.17, 15.43; H_2O, 6.304, 6.471.

Subs. (dried at 100°), 0.1905, 0.1549: CO_2, 0.3811, 0.3116; H_2O, 0.0748, 0.0697. Subs., 0.1717: N, 24.5 cc. (22°, 770 mm.). Calcd. for $C_{12}H_{13}O_4N_3$: C, 54.74; H, 4.98; N, 15.97. Found: C, 54.55, 54.87; H, 5.18, 5.04; N, 16.30.

Optical Properties.—Habit, plates; extinction, parallel, γ-parallel to elongation; indices, $\alpha = 1.510$, $\gamma = 1.620$.

Action of Alkali on Methyl-phenylhydroxyhydantoyl-methylamide.—One cc. of 4 *N* sodium hydroxide was added to 0.1 g. of the oxidation product. A precipitate separated at once from the resulting solution, and a strong odor of methylamine developed. After several minutes, 0.05 g. of solid was filtered off. It melted at 150° and was identified as α,β-methyl-phenyl-urea by a mixed melting point and optical properties; yield, 88%.

The filtrate was carefully neutralized with dil. acetic acid and a solution of 0.04 g. of pure phenylhydrazine in 0.5 cc. of water and 3 drops of glacial acetic acid was added. A yellow precipitate gradually separated. The solution was warmed until clear, cooled, and acidified with dil. hydrochloric acid. A heavy, yellow precipitate separated at once. Part of it was dissolved in hot water and crystallized on cooling; m. p., 145–150°. A determination of the optical properties showed that it was a mixture of the phenylhydrazone of mesoxalic acid and of mesoxalic acid methylamide. The part insoluble in water dissolved readily in aqueous alcohol, and the solution deposited small plates that melted at 167°, either alone or mixed with a known specimen of the phenylhydrazone of mesoxalic acid methylamide. The optical properties were identical: habit, hexagonal plates; extinction, symmetrical, γ-parallel to elongation; interference figure, biaxial; indices, $\alpha = 1.600$, $\gamma = 1.715$.

An Attempt to Synthesize 3-Phenylhydantoyl-methylamide

Diethyl Phenyl-ureidomalonate.—Diethyl aminomalonate,[7] the starting point of the synthesis, was prepared from nitrosomalonic ester by reduction with hydrogen sulfide.[8] It was isolated as the hydrochloride.

A solution of 1.35 g. of sodium bicarbonate (1 molecular equivalent) in 15 cc. of water was added to 3 g. of diethyl aminomalonate hydrochloride. To the resulting solution 1.8 g. of phenylisocyanate was added in one lot and the flask vigorously shaken. After a short time a solid separated. The shaking was continued until there was no odor of phenylisocyanate, usually for about 15 minutes. The solid was filtered off and washed with water; yield, 3.5 g. It was recrystallized by dissolving in alcohol, in which it is very soluble, and adding water. It separated in fine needles and, after another recrystallization, melted at 112–114°.

Anal. Subs., 0.1698: CO_2, 0.3528; H_2O, 0.0864. Subs., 0.2347, 0.2452; N, 20.3 cc. (24°, 757 mm.), 21.45 cc. (25°, 763 mm.). Calcd. for $C_{14}H_{18}O_5N_2$: C, 57.12; H, 6.17; N, 9.545. Found: C, 56.65; H, 5.70; N, 9.614, 9.745.

Optical Properties.—Habit, needles; extinction, parallel, α-parallel to elongation; indices, $\alpha = 1.550$, $\gamma = 1.610$.

In spite of numerous attempts, ethyl 3-phenylhydantoin-carboxylate could not be obtained from the above-mentioned substance. Heating at its melting point for varying lengths of time, boiling with 20% hydrochloric acid, saturating a solution in absolute alcohol with hydrogen chlor-

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[7] Bouveault and Wall, *Compt. rend.*, **137**, 196 (1903).

[8] Johnson and Nicolet, THIS JOURNAL, **36**, 352 (1914).

ide gas at different temperatures, and treating with 5% alcoholic potassium hydroxide were all tried without success.

3-Phenylhydantoin separated from the 20% hydrochloric acid solution on cooling, which showed that a carboxyl group must have been split off leaving phenylhydantoic acid which, of course, closed to form the hydantoin in the presence of acid. It melted at 153–154°, alone or mixed with a known sample.

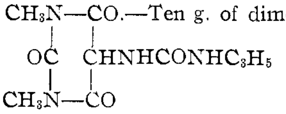
Methylamide of Phenyl-ureidomalonic Acid.—No product could be isolated from the alcoholic solution. On the addition of 33% methylamine until the solution was alkaline, a crystalline substance separated which, recrystallized from water, melted at 225°. Mixed with 3-phenylhydantoyl-methylamide (250°), it melted at 210°. The optical properties also differed. The same substance was obtained when methylamine was added to an alcoholic solution of diethyl-phenyl-ureidomalonate and the solution evaporated. A nitrogen analysis showed that it was the methylamide of phenyl-ureidomalonic acid, $(CH_3NHCO)_2CHNHCONHCONHC_6H_5$.

Anal. Subs., 0.1128: N, 21.2 cc. (27°, 759.1 mm.). Calcd. for $C_{12}H_{16}O_3N_4$: N, 20.92. Found: 20.62.

Optical Properties.—Habit, thin, hexagonal plates; extinction, symmetrical, β-parallel to elongation; interference figure, biaxial; index, β = 1.598.

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

1,3-Dimethyl-9-allyl-pseudo-uric Acid.



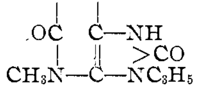
$$\begin{array}{ll} CH_3N— & CO \\ | & | \\ OC & CHNHCONHC_3H_5 \\ | & | \\ CH_3N— & CO \end{array}$$

—Ten g. of dimethyl-uramil[9] was added to 125 cc. of *N* potassium hydroxide solution which had been cooled to 0°. A deep red-purple solution resulted. Five g. of allylisocyanate was added in small portions, and the solution shaken after each addition until the odor was no longer evident. The temperature was kept below 5°. Then the solution was filtered and acidified with dil. hydrochloric acid. It became light red, and the pseudo-uric acid separated on scratching. After several hours, it was filtered off and washed with very dilute hydrochloric acid and water; yield, 3 g. It dissolved readily in hot water (about 50 cc.) and separated in glistening flakes as the solution cooled; m. p., 190° (softens at 180°) with decomposition. The melt is at first yellow and then turns the deep red characteristic of pseudo-uric acids.

Anal. Subs., 0.1733: CO_2, 0.3025; H_2O, 0.0827. Subs., 0.1632; N, 32.7 cc. (24°, 753.9 mm.). Calcd. for $C_{10}H_{14}O_4N_4$: C, 47.47; H, 5.18; N, 22.14. Found: C, 47.61; H, 5.34; N, 22.22.

Optical Properties.—Habit, octagonal plates; extinction, symmetrical, α-parallel to elongation; indices, α = 1.545+, γ = 1.605.

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



$$\begin{array}{lll} CH_3N— & CO & \\ | & | & \\ OC & C—NH & \\ | & \| & >CO \\ CH_3N— & C—NC_3H_5 & \end{array}$$

—One g. of the pseudo-uric acid was

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[9] Fischer, *Ber.*, **27**, 3088 (1894).

boiled over a free flame with 100 cc. of concd. hydrochloric acid until crystallization started. The mixture was then evaporated to a small volume, cooled and filtered; yield 0.32 g. It was recrystallized from hot water, in which it is moderately soluble, and did not melt below 280°. It was readily decomposed by hot, dil. alkali and was dried at 100–104° for analysis.

Anal. Subs., 0.1681: CO_2, 0.3143; H_2O, 0.0774. Subs., 0.1315: N, 27.6 cc. (21°, 769.6 mm.). Calcd. for $C_{10}H_{12}O_3N_4$: C, 50.83; H, 5.12; N, 23.72. Found: C, 50.98; H, 5.15; N, 24.07.

Optical Properties.—Habit, rectangular plates; extinction, parallel, α-parallel to elongation; interference figure, biaxial; indices, $\alpha = 1.665$, $\gamma = 1.730$.

Summary

1. The action of alkali on 1,3,7-trimethyl-9-phenyl-uric acid has been studied, and the course of the reaction and the nature of the decomposition products have been determined.

2. The primary decomposition product is 1-methyl-3-phenylhydantoyl-methylamide. This is further decomposed by alkali to methylamine, carbon dioxide and methyl-phenylhydantoin.

3. Methyl-phenylhydantoyl-methylamide is oxidized by hydrogen peroxide to 1-methyl-3-phenyl-5-hydroxyhydantoyl-methylamide, which is readily hydrolyzed by alkali to mesoxalic acid methylamide and α,β-methyl-phenyl-urea.

4. An attempt to synthesize 3-phenylhydantoyl-methylamide was not successful.

5. 1,3-Dimethyl-9-allyl-uric acid has been prepared for the first time and characterized.

NEW HAVEN, CONNECTICUT

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

THE ACTION OF ALKALI ON SUBSTITUTED URIC ACIDS. III. 1,3,7,9-TETRAMETHYL-URIC ACID AND 1,3,9-TRIMETHYL-URIC ACID

BY ELIZABETH STUART GATEWOOD[1]

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The stability of substituted uric acids toward alkali is dependent on their ability to form salts. As the acidity of the uric acid decreases, its salts become correspondingly less stable and the ease of decomposition is thereby increased. Thus, the neutral tetramethyl-uric acid is decomposed almost instantly by hot dil. alkali, while only 9% of the unsubstituted acid is attacked by alkali after boiling for 36 hours. Fischer[2]

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[1] National Research Fellow in Chemistry.

[2] Fischer, *Ber.*, **33**, 3266 (1899).