tose residues in larch gum and demonstrates the branched chain linkage thereof.

3. The galactose residues of arabo-galactan occurring as 2,4-dimethyl galactose in the hydrolysis products of arabo-galactan methyl ether are shown to be joined to one another in the original gum through the 1–6 position in some cases and through the 1–3 position in other instances.

MOSCOW, IDAHO RECEIVED OCTOBER 24, 1941

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

The Action of Ketene on 5,5-Dibromoxyhydrouracil[1]

BY MILTON FYTELSON[2] AND TREAT B. JOHNSON

It has been the experience of workers in this Laboratory that acetyl derivatives of cyclic ureides of the uracil type are difficult to prepare. In fact, very few acyl pyrimidine compounds in general have been described in the chemical literature. Some special citations, for example, from the literature of uracil derivatives are as follows. Ethyl 3-acetyluracil-4-carboxylate[3] is formed by the action of acetic anhydride on ethyl uracil-4-carboxylate. This compound is unstable and undergoes hydrolysis immediately when warmed with water. The corresponding 4-methyl- and 4-phenylpyrimidine carboxylates, uracil, 5-bromouracil, 4-methyluracil and thymine undergo no reaction when warmed with acetic anhydride. Hydrouracil, however, interacts to form 3-acetylhydrouracil, thereby illustrating the influence of saturation of the 4,5-position of the pyrimidine cycle on the reactivity of the uracil molecule.[4] On the other hand, in order to acetylate 1-phenylhydrouracil it is necessary to heat this pyrimidine with acetyl chloride under pressure. Acetic anhydride effects no change.[5] Like difficulties also arise when attempts are made to acetylate uric acid and its derivatives by the action of acetic anhydride.

So far as the authors are aware, the action of *ketene* on any pyrimidine structure has not been investigated. Our interest in the fundamental reactions of ureides of the uracil type called, therefore, for an examination of the reactivity of this reagent. The experimental evidence thus far obtained indicates no greater reactivity of this substance as an acetylating reagent than that exhibited by acetic anhydride, and we have had little success in adding the unsaturated *ketene* molecule to any ureide of the uracil type. Hydrouracil also failed to interact with ketene.

The most interesting experimental result to be reported by the author to date is the unexpected reactivity of *ketene* toward 5,5-dibromoxyhydrouracil (II).[6] It might be predicted that this hexahydropyrimidine (II) would interact with *ketene* to form the acetate expressed structurally by formula (V). Only one representative of this class has been described in the literature, namely: the acetate of 5,5-dichloroxyhydrouracil (VII). This was synthesized by Johnson and Sprague[7] (1) by the chlorination of uracil (I) in acetic anhydride solution and (2) by the direct action of acetic anhydride on 5,5-dichloroxyhydrouracil (IV). Acetic anhydride also reacts with 5,5-dibromoxyhydrouracil (II) to form the corresponding acetate (V) (see experimental part).

The authors now find that acetylation of the pyrimidine (II) with ketene is not accomplished without the use of a catalyst. Interaction with ketene alone leads only to the degradation of the hydrouracil molecule (II), giving 5-bromouracil (III). Interaction of ketene in the presence of silica gel, however, leads to only partial degradation of the hydrouracil (II), but is productive of a good yield of 3-acetyl-5-bromouracil (VIII). This new pyrimidine is easily converted into 5-bromouracil (III) by hydrolysis with formation of acetic acid.

As the pyrimidine (VIII) is not formed by the direct treatment of 5-bromouracil (III) with ketene, it is the conclusion of the authors that ketene first adds, in the presence of the catalyst, at position-3 of the pyrimidine (II) giving the acetyl

(1) Researches on Pyrimidines CLXXVI.

(2) (a) This paper was constructed from a dissertation presented by Milton Fytelson in June, 1941 to the Graduate Faculty of Yale University in partial fulfillment of the requirements for the degree of Doctor of Philosophy. (b) Present address: Department of Chemistry, Columbia University, New York, N. Y.

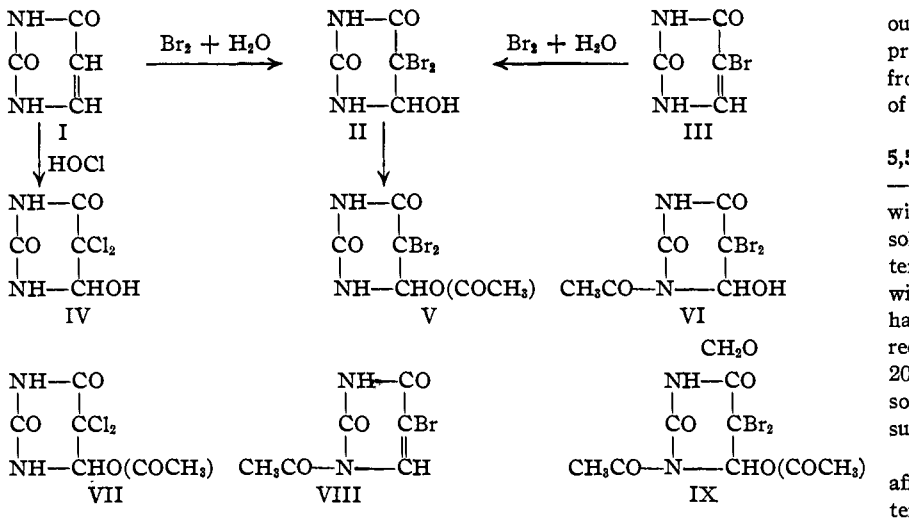
(3) Müller, *J. prakt. Chem.*, **56**, 492 (1897).

(4) Weidel and Roithner, *Monatsh.*, **17**, 176 (1896).

(5) Hoogewerf and Van Dorp, *Rec. trav. chim.*, **9**, 59 (1890).

(6) Wheeler and Johnson, *J. Biol. Chem.*, **3**, 187 (1907).

(7) Johnson and Sprague, THIS JOURNAL, **59**, 2437 (1937).



derivative (VI), which then undergoes degradation with formation of (VIII). Thus far we have not succeeded in isolating or identifying the pyrimidine (VI). It is also probable that the diacylpyrimidine (IX) may be the intermediate product in this ketene reaction, but, thus far, we have obtained no evidence of its formation.

Experimental

5,5-Dibromoxyhydrouracil (II).—All of this pyrimidine used in the present research was prepared according to the method described by Wheeler and Johnson.[6] The yield obtained by bromination of uracil (I) is practically 90%.

Acetate of 5,5-Dibromoxyhydrouracil (V).—This compound is formed by the direct action of acetic anhydride on 5,5-dibromoxyhydrouracil at ordinary temperature. It separates in the form of prismatic crystals melting at 146–148° with slight effervescence to an oil. It responds to the Wheeler and Johnson color test by treatment with barium hydroxide.

Anal. Calcd. for $C_6H_6O_4N_2Br_2 \cdot H_2O$: N, 8.04. Found: N, 8.08.

Preparation of Ketene, CH_2CO.—The ketene used in our experiments was prepared in quantity by the pyrolysis of pure acetone. The pyrolysis chamber consisted of a 30 in. fused quartz tube of 1.9 cm. diameter adapted to an electrically heated furnace.[8] The temperature was controlled by a 50-ohm variable resistance, and measured by a special chromel-alumel thermocouple connected to a standard millivolt calibrated directly in degrees. The inlet and outlet connections of the quartz tube were plugged with neoprene stoppers which proved very resistant to the action of ketene and acetone. Under our regular operating conditions about 30% of the acetone vaporized through the pyrolysis tube was decomposed between 600–700°. The measured yields of ketene based on the amount of recovered acetone and the absorption of generated ketene in aniline to form acetanilide averaged about 25–35%. The pyrolysis gases were passed directly into the reactors without preliminary purification to prevent complications arising from the rapid polymerization of ketene to diketene.

Interaction of Ketene with 5,5-Dibromoxyhydrouracil (II).—(1) Ketene failed to react with this pyrimidine in aqueous solution at normal laboratory temperature. After treatment with the gas for one and one-half hours the pyrimidine was recovered unaltered (m. p. 200–202°) after removing the solvent under diminished pressure.

(2) The pyrimidine was unaffected by treatment with ketene in boiling acetone solution. In a second experiment a solution of the pyrimidine in dry acetone was saturated with ketene at −5° and the solution then heated at 100° for twenty-four hours. Removal of the acetone yielded a solid product mixed with some oil. The solid was identified as 5-bromouracil (III).

Anal. Calcd. for $C_4H_3O_2N_2Br$: N, 14.66. Found: N, 14.54, 14.44.

(3) Ketene was vaporized through a layer of 4 g. of the dry pyrimidine in a long tube heated at 90–95° for three hours. There was immediate reaction with formation of a mixture of brown solid and oil. The solid proved to be 5-bromouracil (III) (N, 14.66%). Washing with ether removed a small quantity of oil which partially solidified and melted at about 50°. This was apparently impure bromoacetic acid.

Action of Ketene on 5,5-Dibromoxyhydrouracil (II) in the Presence of Silica Gel.—Equal proportions of this pyrimidine and silica gel (10 g.) were carefully mixed together, and ketene gas from the pyrolysis unit conducted through the mixture for three and one-half hours at 90°. The ketenized mass of 20 g. was then transferred to a Soxhlet extractor and extracted with dry ether for four and one-half hours.

After distilling off the excess ether from this extraction we obtained a crystalline product admixed with some red oil. The oil dissolved in cold ether leaving behind the solid material. This was easily purified by crystallization from 95% ethanol in the form of rosets. The purified product melted at 175.5–177° and the yield was 2.5 g. This compound contained bromine and was assigned the structure of **3-acetyl-5-bromouracil (VIII).**

Anal. Calcd. for $C_6H_5O_3N_2Br$: C, 30.90; H, 2.14; N, 12.01. Found: C, 30.71; H, 2.06; N, 11.96, 12.14.

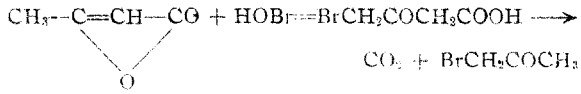
This new pyrimidine was not stable in the presence of hydrochloric acid and underwent a quantitative hydrolysis on boiling the acid solution, giving **5-bromouracil (III).**

Anal. Calcd. for $C_4H_3O_2N_2Br$: N, 14.66. Found: N, 14.60, 14.62.

The oil fraction soluble in cold ether was mixed with 25 ml. of absolute ethanol, acidified with sulfuric acid and the mixture refluxed for one and one-half hours. The solid material which separated on digestion was identified as 5-

(8) This was a special unit constructed by the technician in the Sterling Chemistry Laboratory.

bromouracil (III). The alcohol solution was characterized by its intense and potent lachrymatory odor which was apparently due to the presence of bromoacetone. The latter is probably formed as follows. Dissociation of the 5,5-dibromohydrouracil (II) in the presence of silica gel would give 5-bromouracil (III) and hypobromous acid. The latter acid would be expected to combine immediately with any diketene which might have been formed giving bromoacetoacetic acid which would decompose immediately into bromoacetone as expressed below



In a second experiment treatment of 5,5-dibromoxyhydrouracil (10 g.) with ketene in the presence of silica gel (10 g.) was applied at 60° for four and one-half hours. Extraction of this mixture with ether in a Soxhlet unit was then applied as previously. During this operation crystalline material continued to deposit from the ether extract. This was filtered off and crystallized from water in the form of prisms melting at 200°. It was identified as unaltered dibromoxyhydrouracil (II) and responded immediately to the Wheeler and Johnson[6] color test for uracil when tested with barium hydroxide.

The ether extract above gave, after removal of the ether, a crystalline product mixed with a small quantity of oil. The solid was easily purified by crystallization from 95% ethanol and 2.6 g. was obtained melting at 175°. It was identified as 3-acetyl-5-bromouracil (VIII). The red oil admixed with this pyrimidine was acidic and possessed a disagreeably lachrymatory odor. It was apparently a mixture of bromoacetic acid mixed with some bromoacetone.

Anal. Calcd. for $C_6H_5O_3N_2Br$: N, 12.01. Found: N, 11.96, 11.84.

Action of Ketene on 5,5-Dibromo-4-methyloxyhydrouracil.[9]—Ketene addition in the presence of dry silica gel was applied for three hours at 100°, and in a second experiment three and a quarter hours at 80°. In both cases the only definite pyrimidine identified was 4-methyl-5-bromouracil.[10] It melted after crystallization from water between 226–230° with decomposition.

Anal. Calcd. for $C_5H_5O_2N_2Br$: N, 13.66. Found: N, 13.57, 13.68.

Summary

1. All the ketene used in this research was prepared by pyrolysis of acetone.

2. Ketene reacts with 5,5-dibromoxyhydrouracil in the presence of silica gel to form 5-bromouracil and 3-acetyl-5-bromouracil. The latter derivative easily undergoes hydrolysis with formation of 5-bromouracil.

3. Ketene failed to interact with uracil, 4-methyluracil, thymine or hydrouracil.

4. 5,5-Dibromo-4-methyloxyhydrouracil simply underwent degradation when heated in an atmosphere of ketene giving 4-methyl-5-bromouracil.

5. 5,5-Dibromoxyhydrouracil reacts to form an acetate by treatment with acetic anhydride at ordinary temperature.

(9) Behrend, *Ann.*, **229**, 18 (1885); List, *ibid.*, **236**, 19 (1886).
(10) Behrend, *ibid.*, **229**, 17 (1885); **231**, 249 (1885).

NEW HAVEN, CONNECTICUT RECEIVED OCTOBER 21, 1941

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

Osage Orange Pigments. IX.[1] Improved Separation; Establishment of the Isopropylidene Group

BY M. L. WOLFROM AND JOHN MAHAN

In a previous communication from the Laboratory,[2] the separation of the two pigments of the fruit of the osage orange (*Maclura pomifera* Raf.) was accomplished by a very laborious, fractional crystallization procedure. We now find that the pigment pomiferin, which has the catechol configuration in its molecule, forms an insoluble lead complex while the other pigment, osajin, does not form such a complex. A very simple separation based upon this difference has been devised and is reported herein. One kilogram of the dried fruit yielded 32.5 g. of crude pigment (m. p. 175–178°) which on separation gave 14.5 g. of pomiferin of maximum purity (m. p. 200.5°) and 9.4 g. of osajin of maximum purity (m. p. 189°), together with lesser amounts of material of lower purity.

We report also that both pomiferin and osajin yield 0.7 mole of acetone on ozonization. This establishes the isopropylidene group as a constituent of both pigments and clarifies the nature of one of the two double bonds present in each of these substances.

Pomiferin trimethyl ether now has been subjected to fusion at high temperature with potassium hydroxide. From these fusions we have

(1) Previous publication in this series: M. L. Wolfrom and A. S. Gregory, THIS JOURNAL, **63**, 3356 (1941).
(2) M. L. Wolfrom and A. S. Gregory, *ibid.*, **62**, 651 (1940).