dependent of temperature in the case of the four primary alcohols, but is dependent upon the temperature in the case of the secondary alcohols.

Over the temperature range of about 340° to 440° the percentage of dehydration as compared to that of the total activity is as follows: ethanol, 10%; *n*-propanol, 16%; *iso*propanol, 88 to 73%; *n*-butanol, 15%; *iso*butanol, 31.5%; *sec*-butanol, 89 to 71%.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

RESEARCHES ON HYDANTOINS. XLVI. NITROPYRUVIC UREIDE[1]

BY DAVID DAVIDSON

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In the course of the synthetic work in the hydantoin series now in progress in this Laboratory, one of the problems of immediate biochemical interest that has come up for solution is the development of a practical method of synthesizing the primary amine derivative of 5-methylhydantoin I. Nitropyruvic ureide II was suggested as a feasible starting point for the synthesis of this compound, but in order to determine the practicability of the method it was first necessary to acquire a better knowledge of the method of preparation, constitution, and properties of this nitro compound. This interesting substance was first prepared by Grimaux,[2] who has been the only investigator to study it, and who proposed for it the structure expressed by Formula III. The work of Fischer[3] and of Gabriel[4] on the bromopyruvic ureides has shown that these compounds are to be represented by Formulas IV and V and not by the tautomeric structures VI and VII. It is probable, therefore, that Formula II rather than Formula III represents the constitution of nitropyruvic ureide. Further evidence in support of this structure has been obtained by a study of its chemical behavior.

Nitropyruvic ureide II fails to give Victor Meyer's nitrolic acid test for primary nitro compounds.[5] This speaks against Grimaux's structure III which contains the primary nitro grouping —CH_2NO_2. When a solution of nitropyruvic ureide is boiled, the compound is rapidly hydrolyzed to nitromethane and parabanic acid VIII. This type of reaction is characteristic of the unsaturated grouping :$CHNO_2$, both in the aromatic and in

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[1] Constructed from part of a dissertation presented by Mr. David Davidson to the Faculty of the Graduate School of Yale University, June, 1924, in candidacy for the degree of Doctor of Philosophy. (T. B. Johnson.)

[2] Grimaux, *Bull. soc. chim.*, (II) **23,** 49 (1875); *Ann. chim. phys.*, (V) **11,** 367 (1877).

[3] Fischer, *Ann.*, **239,** 185 (1887).

[4] Gabriel, *Ann.*, **348,** 50 (1906).

[5] Meyer and Jacobson, "Lehrbuch der Organischen Chemie," Veit and Co., Berlin and Leipzig, **1922,** I, part 1, p. 406.

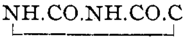
the aliphatic series, as has been shown, for example, in the cases of α-nitrostyrene[6] IX and nitro-*iso*butylene[7] X.

Bromine acts upon nitropyruvic ureide II, substituting in the side chain to form bromonitropyruvic ureide XI. As has been stated in a previous paper,[8] this is a general reaction for hydantoin compounds containing the grouping :CHR in the 5 position of the hydantoin ring. That the bromine has entered the side chain in this reaction is shown by the behavior of the product on hydrolysis. It is even more readily decomposed by water than the unbrominated substance II, yielding bromonitromethane and parabanic acid VIII.

Acetylation of nitropyruvic ureide II produces a diacetyl compound XII. This result indicates the presence in the molecule of two imido hydrogens in agreement with Formula II.

Behavior of Nitropyruvic Ureide When Reduced Catalytically

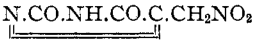
Due to the instability of nitropyruvic ureide II, no success was met in attempts to reduce this combination by ordinary chemical agents. By resorting to the catalytic method of reduction and operating at room temperature and at atmospheric pressure, it was found possible to obtain a fairly smooth reduction reaction. The absorption of hydrogen is very rapid, but stops abruptly when two molecular equivalents of hydrogen have been introduced, so that instead of the desired amino compound I, the oxime of hydantoin-5-aldehyde XIII is obtained. This behavior is in complete accord with the results obtained by Kohler and Drake[9] in their interesting work on the catalytic reduction of α,β-unsaturated nitro compounds. For example, they observed that nitrostyrene IX is reduced in the presence of platinum black to its corresponding oxime $C_6H_5CH_2$-$CH{:}\,NOH$. In all these combinations we are dealing with the unsaturated grouping $>C{:}\,\underset{|}{C}NO_2$. The study of this reduction reaction will be continued in this Laboratory.


$NH.CO.NH.CO.CH.CH_2NH_2$

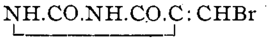
I


$NH.CO.NH.CO.C{:}\,CHNO_2$

II


$N.CO.NH.CO.C.CH_2NO_2$

III


$NH.CO.NH.CO.C{:}\,CHBr$

IV


$NH.CO.NH.CO.C{:}\,CBr_2$

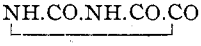
V


$N.CO.NH.CO.C.CH_2Br$

VI


$N.CO.NH.CO.C.CHBr_2$

VII


$NH.CO.NH.CO.CO$

VIII

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[6] Beilstein's "Handbuch," 3rd ed., **II,** p. 167.

[7] Haitinger, *Ann.,* **193,** 374 (1878).

[8] Davidson and Johnson, THIS JOURNAL, **47,** 561 (1925).

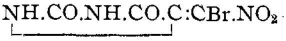
[9] Kohler and Drake, THIS JOURNAL, **45,** 1281 (1923).

$C_6H_5CH{:}CHNO_2$

IX

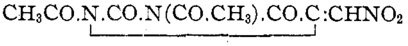
$(CH_3)_2.C{:}CHNO_2$

X



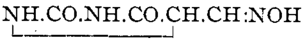
$NH.CO.NH.CO.C{:}CBr.NO_2$

XI



$CH_3CO.N.CO.N(CO.CH_3).CO.C{:}CHNO_2$

XII



$NH.CO.NH.CO.CH.CH{:}NOH$

XIII

Experimental Part

Preparation of Nitropyruvic Ureide II.—Dipyruvic triureide[10] is the most convenient source of nitropyruvic ureide.

Ten g. of the triureide is gradually added to 20 cc. of fuming nitric acid (d., 1.52) in an evaporating dish. The reaction proceeds vigorously with the evolution of heat. On cooling, the product separates in a mass of brilliant yellow leaflets, which are triturated with water, filtered off, and washed with water; yield, 8 g. Nitropyruvic ureide is best recrystallized from 25 parts of boiling glacial acetic acid from which it separates in stout, yellow, monoclinic prisms, often in fish-tail twins resembling gypsum crystals. It melts with decomposition at about 204°.

Anal. Calcd. for $C_4H_3N_3O_4$: N, 26.8. Found (Kjeldahl): 26.6.

Action of Water on Nitropyruvic Ureide.—Five g. of nitropyruvic ureide was dissolved in 125 cc. of boiling water and the solution boiled under a reflux condenser for 30 minutes. The originally bright yellow color faded gradually, while drops of oil appeared in the condenser. The solution was then distilled, three cc. of distillate being collected. The latter contained droplets of an oil of ethereal odor, which was identified as nitromethane by condensing it with benzaldehyde,[11] when it yielded yellow leaflets of α-nitrostyrene IX having a cinnamon-like odor and melting at 57°. A mixture with an authentic sample of α-nitrostyrene melted at 57–58°.

The residue from the distillation was concentrated on the steam-bath to a volume of about 25 cc. On cooling, 1.0 g. of unchanged nitropyruvic ureide was recovered. The filtrate was allowed to evaporate spontaneously and yielded 1.9 g. of pale yellow crystals which on recrystallization from a small amount of boiling water separated in brilliant, transparent, flat prisms characteristic of parabanic acid VIII. It melted at about 240° and gave a precipitate of calcium oxalate with ammoniacal calcium chloride only after being heated (Andreasch's test[12]).

Mol. wt. Calcd.: 114. Found (by titration): 114.

Anal. Calcd. for $C_3H_3O_3N_2$: N, 24.6. Found (Kjeldahl): 24.4.

Action of Bromine on Nitropyruvic Ureide.—To a suspension of 10 g. of pulverized nitropyruvic ureide in 25 cc. of glacial acetic acid heated under a reflux condenser on the steam-bath was gradually added 3.4 cc. of bromine, the flask being intermittently shaken. The heating was continued for 30 minutes, the solvent then distilled under diminished pressure and the residue crystallized from absolute alcohol. Bromonitropyruvic ureide XI separated in bright yellow, rhombic plates that decomposed at about 225°. With dil. alkali it forms an orange-colored salt that rapidly decomposes.

Anal. Calcd. for $C_4H_2BrN_3O_4$: N, 17.8. Found (Kjeldahl): 18.0.

Action of Water on Bromonitropyruvic Ureide. XI.—Bromonitropyruvic ureide was treated with water as in the case of nitropyruvic ureide. The distillate contained

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[10] Davidson, This Journal, 47, 255 (1925).

[11] Remfry, *J. Chem. Soc.*, 99, 285 (1911).

[12] Andreasch, *Monatsh.*, 2, 285 (1881).

a heavy oil of very irritating odor. After drying over calcium chloride it boiled at 148–149°, which is in agreement with the boiling point of bromonitro-methane XII given by Mulliken.[13] The parabanic acid obtained from the filtrate was identified by its melting point of 240°, the Andreasch test, and by its crystal habit.

Acetylation of Nitropyruvic Ureide.—Five g. of pulverized nitropyruvic ureide II was dissolved in 30 cc. of acetic anhydride by heating over a free flame. The solution was then heated for 45 minutes on the steam-bath, after which the solvent was distilled under diminished pressure and the residue recrystallized from absolute alcohol. Diacetyl nitropyruvic ureide XII separated in thin, pale yellow leaflets, melting at about 150° with decomposition.

Anal. Calcd. for $C_8H_7O_6N_3N$, 17.4. Found (Kjeldahl): 16.9.

Catalytic Reduction of Nitropyruvic Ureide.—Nine and three-tenths g. of pulverized nitropyruvic ureide II and 0.1 g. of platinum oxide catalyst[14] were suspended in 100 cc. of glacial acetic acid and shaken in an atmosphere of hydrogen.[15] Absorption began in two or three minutes when the brown (oxide) catalyst changed to black (platinum black). It proceeded very briskly, the yellow nitro compound gradually going into solution and being replaced by a precipitate of fine, white needles. In 45 minutes the absorption of two molecular equivalents of hydrogen was complete and no more was consumed when the shaking was continued for an hour [illegible] after revivifying the catalyst. After the hydrogen had been replaced by air and the mixture had been shaken for five minutes the liquid was filtered by suction. The mixture of product with platinum thus obtained was washed with glacial acetic acid and dried in a desiccator over soda lime. It was then subjected to extraction with methyl alcohol in the apparatus described by Clarke and Kirner.[16] The solid remaining on evaporation of the alcoholic extract was dissolved in ammonia and reprecipitated by the addition of acetic acid, when it separated in slightly discolored rhombic plates that did not melt below 300°. Its nitrogen content indicates its constitution to be that of the anticipated hydantoin-5-aldoxime XIII.

Anal. Calcd. for $C_4H_5O_3N_3$: N, 29.4. Found (Kjeldahl): 29.6.

Summary

1. Nitropyruvic ureide is prepared most conveniently by nitration of dipyruvic triureide.

2. Structurally the ureide is to be represented as an alkylidene derivative of hydantoin $\underline{NH.CO.NH.CO.C}: CHNO_2$.

3. Nitropyruvic ureide undergoes hydrolysis with the formation of nitromethane and parabanic acid.

4. Nitropyruvic ureide is attacked by bromine with the formation of the corresponding bromo derivative. The latter compound is converted by hydrolysis into bromonitromethane and parabanic acid.

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[13] Mulliken, "Identification of Pure Organic Compounds," John Wiley and Sons, Inc., New York, **1922,** vol. IV, p. 154.

[14] Adams and Shriner, This Journal, **45,** 2171 (1923).

[15] In an apparatus similar to that described by Maxted, "Catalytic Hydrogenation and Reduction," P. Blakiston's Son and Co., Philadelphia, **1919,** p. 22.

[16] Conant, "Organic Syntheses," John Wiley and Sons, New York, **1922,** vol. II, p. 49.

5. On reduction in the presence of platinum, nitropyruvic ureide is converted into the oxime of hydantoin-5-aldehyde.

NEW HAVEN, CONNECTICUT

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF BRISTOL]

GALLOTANNIN. XIV. THE ACTION OF YEAST ON GALLOTANNIN

BY M. NIERENSTEIN, C. W. SPIERS AND A. C. HADLEY

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Biddle and Kelley[1] have noticed that yeast (*Saccharomyces cerivisiae*) totally destroys the optical activity of gallotannin, without apparent formation of gallic acid. We have confirmed these observations, although Geake and Nierenstein[2] failed to do so, and we have prepared by this method a gallotannin which is optically inactive and gives no glucose on hydrolysis according to Fischer and Freudenberg[3] and Feist and Haun.[4] We also find (1) that no *m*-digallic acid is produced by the action of yeast on gallotannin and (2) that only little gallic acid is formed during this process.

These results are not in agreement with the penta-digalloylglucose formula (I) of Fischer and Freudenberg.[5] Their formula requires that the *complete* conversion of gallotannin into either *m*-digallic acid or gallic acid should *precede* the production of glucose, which is, however, obviously not the case. On the other hand the polydigalloyl-leucodigallic acid anhydride formula (II) of Nierenstein[6] which is also supported by the analytical observations of Mitchell[7] and which does not exclude the existence of a gallotannin-*glucoside*[8] seems to meet the case, if one assumes provisionally that the glucose in the gallotannin-glucoside is attached to the hydroxyl, marked α in Formula II, of the asymmetric carbon atom in the leucodigallic acid radical. Such an assumption, which is also in agreement with the fact that methylo-gallotannin yields tetramethyl glucose on hydrolysis,[9] would account for the production of an optically inactive gallotannin through yeast, probably due to racemization of the leuco-digallic acid radical and fermentation of the glucose.

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[1] Biddle and Kelley, THIS JOURNAL, **34,** 919 (1912).

[2] Geake and Nierenstein, *Ber.*, **47,** 895 (1914).

[3] Fischer and Freudenberg, *Ber.*, **45,** 923 (1912).

[4] Feist and Haun, *Arch. Pharm.*, **251,** 500 (1913).

[5] Fischer and Freudenberg, *Ber.*, **45,** 917 (1912).

[6] Nierenstein, *Ann.*, **388,** 226 (1912).

[7] Mitchell, *Analyst,* **48,** 7 (1923).

[8] Nierenstein, *Ber.*, **43,** 1268 (1910).

[9] Nierenstein, Spiers and Geake, *J. Chem. Soc.*, **119,** 278 (1921).