

the details of which will be given in a subsequent paper, are not strictly comparable with those of Table IV for the reason that phosphotungstic acid precipitates, in addition to proteoses and peptones, also diamino acids, ammonia, bases like choline, betaine, etc. Broadly speaking, however, the results obtained by the last method fully corroborate the outstanding fact presented in Table IV that the wheat varieties in question contain in their ungerminated kernel considerable proportions of peptide nitrogen. The presence of peptides in the wheat kernel may have considerable physiological significance, such as in protein synthesis and more generally in nitrogen metabolism, because of the fact that they form a necessary link between the amino acids on the one hand and the proteins on the other.

Summary

The results thus far obtained permit drawing the following conclusions.

1. The wheat varieties investigated contain peptides in their ungerminated kernels, the percentages of peptide nitrogen for Kanred, Fultz, Marquis, and Kubanka being, respectively, 26.86, 28.09, 32.20 and 37.76, on the basis of the water-soluble nitrogen, and 3.89, 4.67, 4.98 and 5.13, calculated to the total nitrogen.

2. The wheat varieties under consideration contain free amino acids in their ungerminated kernels, the proportions (in round figures) for Kubanka, Fultz, Marquis, and Kanred being, respectively, 10, 11, 11 and 16% of amino acid nitrogen, calculated to the water-soluble nitrogen, and 1.4, 1.8, 1.8 and 2.3%, calculated to the total nitrogen.

3. The proportions of acid amide nitrogen in the ungerminated kernel of the varieties Fultz, Marquis, Kubanka and Kanred are, respectively, 8.76, 12.33, 12.61 and 12.99%, calculated to the water-soluble nitrogen, and 1.46, 1.91, 1.72 and 1.88% calculated to the total nitrogen.

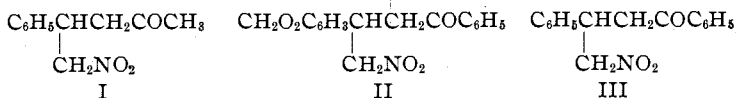
WASHINGTON, D. C.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]
**THE CATALYTIC REDUCTION OF NITRO COMPOUNDS. II.
GAMMA-NITRO KETONES**

BY E. P. KOHLER AND N. L. DRAKE

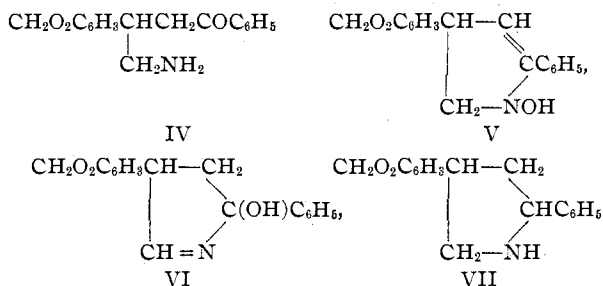
Received June 14, 1923

The first step in the reduction of nitro compounds, the transition from nitro to nitroso compounds or, in the case of primary aliphatic nitro compounds, to oximes is as yet a complete mystery. Since γ -nitro ketones on hydrogenation would form substances in which active hydrogen and a carbonyl group are in a relation that is favorable for intramolecular condensation, it seemed possible that they might serve better than simpler nitroparaffins for permitting an insight into this process. With this end in view we have reduced the following 3 nitro ketones.



The results are disappointing, for while the reduction products undergo internal condensation as expected, the condensation products are themselves so easily reduced that it is impossible either to confine the action to a single step or to deduce the successive steps from the products finally obtained. The final result, moreover, depends to such a degree upon factors that cannot be controlled, that both the nature of the products and their relative amounts vary in reductions which are carried out as nearly as possible under the same conditions.

Thus in an experiment with the nitro ketone II in which the operation was interrupted when approximately 2 molecular equivalents of hydrogen per equivalent of ketone had been absorbed, the solution contained unchanged nitro ketone, the amino ketone IV, an hydroxy pyrroline V or VI, and the pyrrolidine VII.



The 3 reduction products, the only ones obtained by reducing this nitro ketone under a variety of different conditions, are here formed side by side long before all of the nitro compounds have disappeared from the solution, and neither the nature of the products nor the rate at which hydrogen is consumed gives any clue as to the stage at which condensation takes place.

The amino ketone IV is the only open chained reduction product that we obtained from any of these nitro ketones. It is also the only γ -amino ketone that is known, all earlier attempts to prepare this type of compound having failed, owing to the ease with which such compounds undergo internal condensation.¹ While it readily undergoes this condensation, it is stable in neutral and weakly alkaline solutions. It is unlikely, therefore, that the pyrrolidine derivative VII is formed by way of the amino ketone.

The hydroxy pyrroline also represents a new type of compound. It was isolated with such difficulty and in such small quantities that its

¹ Hielscher, *Ber.*, 31, 278 (1898). Gabriel, *ibid.*, 42, 1242 (1909). Gabriel and Colman, *ibid.*, 42, 1248 (1909).

structure could not be established with certainty; the only facts available are its composition and its ability to form a benzoyl derivative. Its indifference to permanganate in acetone is hard to reconcile with either formula. Since it is always present in the solutions after all absorption of hydrogen has ceased, it cannot be the source for the pyrrolidine derivative. The 3 reduction products, amino ketone, pyrroline, and pyrrolidine, must therefore be reached by separate paths.

The relative amounts of the 3 reduction products vary greatly with the nature of the nitro ketone. The 2 phenyl ketones give but small quantities of pyrrolidine derivatives, but in the case of the methyl ketone this is the principal product. Since the reduction takes place very readily and it is easy to isolate the product without allowing it to come in contact with air, this is at present, doubtless, the best method for getting pyrrolidine derivatives with groups in the 2,5 positions. The yield from the nitro ketone I was 86.5%.

Experimental Part

The reductions were carried out by shaking suspensions or solutions of the nitro ketones in methyl alcohol with hydrogen in the presence of 0.5 g. of Loew's platinum black. As the nitro ketones are only moderately soluble, solutions were used only in attempts to get earlier stages of reduction. The rate at which hydrogen was absorbed was measured but it had little significance beyond indicating whether or not the reduction was proceeding normally. When suspensions were used, the rate of absorption usually remained constant until all of the solid had disappeared, then slowly fell off, and finally stopped when approximately 4 molecules of hydrogen had been absorbed for 1 of the ketones. In the few cases in which a sharper break in the absorption curve was observed, the corresponding quantities of hydrogen did not represent any definite stages of reduction.

During the reduction the catalyst changed into a more compact form, hence was easily removed by filtration. If the reduction to the pyrrolidine derivative was complete, the clear filtrate remained colorless both when allowed to remain in contact with air, and when treated with acid. But if the operation was interrupted before the reduction was completed, the colorless liquid soon became pink and the color gradually deepened to dark red or purple.

I. γ -Nitro- β -phenyl Pentanone

Preparation.—The nitro ketone was made by adding nitromethane to benzalacetone. The addition takes place readily, but the yield is not nearly so satisfactory as that obtained with benzalacetophenone, and even under the most favorable conditions half of the material goes into oily products. The best procedure was as follows.

A paste of sodium nitromethane was made by adding gradually and with constant stirring 15 g. of nitromethane to a well-cooled solution of 5 g. of sodium in 50 cc. of dry methyl alcohol. This was added rapidly to a solution of 25 g. of benzalacetone in 50 cc. of dry methyl alcohol that had previously been heated to near the boiling point. The mixture was kept at this temperature, and shaken vigorously to ensure as rapid addition as possible. As soon as all the solid had disappeared the clear, orange-colored solution was cooled in an ice-and-salt mixture and then acidified *very slowly* with 20 g. of glacial acetic acid. The nitro ketone slowly separated as a pasty solid. After standing for an hour the crystal mass was filtered, pressed on a suction funnel, washed first with a little alcohol and then very thoroughly with water, pressed as dry as possible, and dissolved in chloroform. The water layer was separated, the chloroform solution dried with calcium chloride, and freed from chloroform by distillation. The residue thus obtained was recrystallized from methyl alcohol from which it separated in lustrous needles. The substance is moderately soluble in cold ether and methyl alcohol; m. p., 99–100°; yield, 48%.

Analysis. Calc. for $C_{11}H_{18}O_2N$: C, 63.8; H, 6.3. Found: C, 63.7; H, 6.4.

REDUCTION.—A suspension of 40 g. of the nitro ketone in 200 cc. of methyl alcohol was shaken with hydrogen and 0.5 g. of platinum black until absorption ceased. The platinum was then removed from the solution by filtration, the methyl alcohol distilled, and the residue subjected to vacuum distillation. This gave, along with a small quantity of low-boiling product and a tarry residue, 27 g. of a colorless oil which on redistillation boiled at 112° (10 mm.). As this proved to be extremely hygroscopic it was distilled from sodium in preparation for analysis.

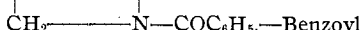
Analysis. Calc. for $C_{11}H_{16}N$: C, 82.0; H, 9.3. Found: C, 81.7; H, 9.4.

2-Methyl-4-phenyl-pyrrolidine, $C_6H_5CH-CH_2-CHCH_3$.—This is a colorless



liquid which can be kept unchanged in sealed tubes, but which gradually turns yellow when exposed to the air. It is most easily identified by its solid benzoyl derivative.

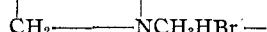
1-Benzoyl-2-methyl-4-phenyl-pyrrolidine, $C_6H_5CH-CH_2-CHCH_3$



chloride was gradually added in excess to an ethereal solution of the pyrrolidine derivative which was then shaken with 10% potassium hydroxide until the odor of the chloride had disappeared. The ethereal solution was dried over calcium chloride, the ether removed, and the residue distilled under diminished pressure. It distilled without decomposition at 260–270°, and the colorless distillate solidified in large, colorless tablets melting at 79–80°. When the substance was recrystallized from a mixture of ether and petroleum ether the melting point became constant at 82–83°. The substance crystallizes in large prisms. It is readily soluble in ether or alcohol, sparingly in ligroin.

Analysis. Calc. for $C_{19}H_{19}ON$: C, 81.5; H, 7.2. Found: C, 82.0; H, 7.2.

1,2-Dimethyl-4-phenyl-pyrrolidine Hydrobromide, $C_6H_5CH-CH_2-CHCH_3$



Methylphenyl-pyrrolidine reacts very energetically with methyl iodide, but it is difficult to isolate a pure product even when the reaction is moderated by diluting the reagents with dry ether. It is better, therefore, to methylate with dimethyl sulfate. For this purpose 8 g. of dimethyl sulfate was gradually added to 5 g. of the base suspended in 70 cc. of 10% potassium hydroxide solution which was cooled in ice and salt. The mixture was shaken until all of the sulfate was hydrolyzed, then extracted with ether. The ethereal solution was dried with solid potassium hydroxide and finally with metallic sodium. From the resulting solution dry hydrogen bromide precipitated the hydro-

bromide of the methylated compound in fine, colorless needles. After recrystallization from methyl alcohol ether these melted at 144–146°, probably with decomposition.

Analysis. Calc. for $C_{12}H_{17}NHBBr$: C, 56.3; H, 7.0. Found C, 56.6; H, 7.0.

II. β -(3,4-Methylene-dioxy-phenyl)- γ -nitro-butyrophenone

Preparation and Properties.—The method of preparation was the same as that used in the case of γ -nitro- β -phenyl pentanone, but the yield was much better; 68 g. of piperonal acetophenone condensed with 30 g. of nitro methane gave 61 g. of the nitro ketone.

The substance was purified by recrystallization from methyl alcohol. It separated in fine needles that melted at 95–96°.

Analysis. Calc. for $C_{17}H_{16}O_3N$: C, 65.2; H, 4.8. Found; C, 65.0; H, 5.1.

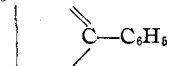
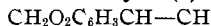
REDUCTION.—A solution of 31.3 g. of the nitro ketone in 200 cc. of methyl alcohol was reduced in the presence of 0.5 g. of platinum. The solution began to absorb hydrogen at a rate of about 2.3 cc. a minute. This rate was maintained with little change until somewhat more than the quantity of hydrogen had been absorbed which was calculated for reducing the nitro to the amino group. It then dropped sharply to nearly a third of this value and remained constant at the new level until absorption ceased.

A colorless solid separated from the solution during the reduction and remained mixed with the catalyst when the operation was stopped. This was filtered off, washed with ether, and dissolved in boiling dry methyl alcohol. It crystallized in colorless needles, but the melting point was less sharp than it had been before solution. It was, therefore, recrystallized from dry ether and ligroin before analysis.

Analysis. Calc. for $C_{17}H_{17}O_2N$: C, 72.1; H, 6.0. Found: C, 72.4; H, 6.0.

β -(3,4-Methylene-dioxy-phenyl)- γ -amino-butyrophenone, IV.—The amine is readily soluble in chloroform and acetone, moderately soluble in methyl alcohol and in ether, slightly soluble in ligroin. It crystallizes in colorless needles or plates and melts at 129–130°. When it is perfectly pure and dry it is stable; but in solution and when moist it changes more or less rapidly into gummy, discolored condensation products. It appeared to form a hydrochloride, but this was not adapted either for purification or identification.

2-Phenyl-4-(3,4-methylene-dioxy-phenyl)phenyl Sulfone,



—When the amine is treated with benzene sulfone chloride and alkali it undergoes both acylation and condensation. The product is a sparingly soluble sulfone which crystallizes well and serves to distinguish between the amine and all other substances except the corresponding pyrrolidine. The substance is very sparingly soluble in ether, somewhat more readily soluble in methyl alcohol, readily soluble in chloroform. It was purified by recrystallization from chloroform-petroleum ether. It crystallizes in minute plates, begins to turn brown at 220°, and melts with decomposition at 225–227°.

Analysis. Calc. for $C_{22}H_{19}O_4NS$: C, 68.1; H, 4.7. Found: C, 68.6; H, 4.9.

PARTIAL REDUCTION.—Since the preceding experiment showed a fairly sharp drop in the rate of reduction after 2 molecular equivalents of hydrogen had been absorbed, we repeated it as nearly as possible under the same conditions, but interrupted the operation when the solution which contained 31.3 g. of ketone had absorbed 4.97 l. of hydrogen. The liquid contained no solid other than platinum. This was removed and the

filtrate concentrated and set aside. It deposited 7.0 g. of unchanged nitro ketone which was identified by a mixed melting point. After further concentration it deposited 3.3 g. of a mixture of nitro ketone and amine, and later 4.5 g. of a new product that melted at 144–145°. Finally, when all the alcohol was removed, there remained a gummy residue that could not be induced to crystallize.

1-Hydroxy-2-phenyl-4-(3,4-methylene-dioxy-phenyl)-pyrroline, VI.—The solid that melted at 144–145° was purified by recrystallization from methyl alcohol or ether. It crystallizes in colorless needles, is moderately soluble in alcohol, ether or benzene, is not changed by contact with air, and does not reduce permanganate in acetone.

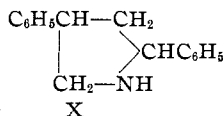
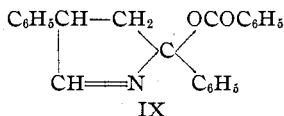
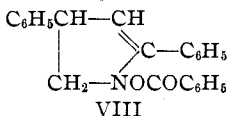
Analyses. Calc. for $C_{17}H_{15}O_2N$: C, 72.6; H, 5.3. Found: C, 72.5, 72.4; H, 5.6, 5.6.

2-Phenyl-4(3,4-methylene-dioxy-phenyl)pyrrolidine Hydrochloride, VII.—The gummy mass left after all of the alcohol had been removed turned dark red or purple on treatment with hydrochloric acid. On cautious dilution with a mixture of methyl alcoholic hydrogen chloride and ether it deposited a solid that crystallizes from alcohol and ether in beautiful, long, thin, white needles. The color of the solution was doubtless due to the presence of the amino ketone, because the solutions of the pyrrolidine hydrochloride in methyl alcohol and in ether are colorless, and remain so when left in contact with air. The salt melts with decomposition at about 208°.

Analysis. Calc. for $C_{17}H_{17}O_2NHCl$: C, 67.2; H, 5.9. Found: C, 67.2; H, 5.8.

III. β -Phenyl- γ -nitro-butyrophenone

The nitro ketone III gave only oily products that could not be distilled under diminished pressure. By indirect methods it was possible to prove that these oils contained an hydroxy pyrroline, which was isolated as benzoate VIII or IX, and the pyrrolidine X which was isolated as hydrochloride and oxalate.



2,4-Diphenyl-pyrrolyl Benzoate, VIII or IX.—A small quantity of the oil, left after distillation of the methyl alcohol in which the nitro ketone had been reduced, was mixed with 5 times its weight of benzoyl chloride and an excess of 10% potassium hydroxide. The mixture immediately turned to a deep purple. It was shaken until the odor of benzoyl chloride had disappeared, then diluted with water and separated. The oil was washed with water and dissolved in methyl alcohol. This solution deposited a solid which was recrystallized from methyl alcohol. It separated in colorless needles; m. p., 179–180°.

Analysis. Calc. for $C_{28}H_{19}O_2N$: C, 80.9; H, 5.6. Found: C, 80.5; H, 5.4.

2,4-Diphenyl-pyrrolidine Hydrochloride.—A methyl alcoholic solution of the oil obtained by reducing phenylnitro-butyrophenone was saturated with dry hydrogen chloride, then cautiously diluted with dry ether until a slight cloudiness appeared, and set aside. It deposited thin, colorless needles which were recrystallized from dry methyl alcohol and ether; m. p., 171–172°.

Analysis. Calc. for $C_{16}H_{17}NCl$: C, 74.0; H, 6.9. Found: C, 73.9; H, 6.9.

Di(2,4-diphenyl)pyrrolidine Oxalate.—A solution of 5.4 g. of the nitro ketone in 50 cc. of methyl alcohol was reduced in the presence of 0.9 g. of oxalic acid and 0.5 g. of platinum black. A colorless solid began to separate long before all of the nitro compound had disappeared from the solution. As it was impossible to dissolve the sparingly

soluble salt without decomposing it, the mixture of salt and platinum was thoroughly dried and analyzed, the amount of platinum in the sample being determined by weighing the boat after the analysis.

Analysis. Calc. for $C_{34}H_{28}O_4N_2$: C, 76.1; H, 6.7. Found: C, 75.7; H, 6.8.

Both the pure hydrochloride and the pure oxalate were decomposed with alkali in the hope of getting a solid pyrrolidine, but the product in each case was a colorless oil.

Summary

1. When γ -nitro ketones are reduced with hydrogen in the presence of Loew's platinum black there is a succession of reduction and condensation reactions that overlap to such a degree that the rate at which the hydrogen is absorbed is represented by a smooth curve.

2. The principal reduction products are the amino ketone, hydroxy-pyrroline and pyrrolidine, corresponding to the nitro ketone that is reduced.

3. These products do not represent successive stages in the reduction; they are formed, simultaneously, along different routes.

CAMBRIDGE 38, MASSACHUSETTS

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF APPLIED CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, AND THE LABORATORY OF PHYSIOLOGICAL CHEMISTRY, TULANE UNIVERSITY SCHOOL OF MEDICINE]

DETERMINATION OF FORMALDEHYDE IN PRESENCE OF SUBSTANCES FOUND IN FORMALIN

BY P. BORGSTROM

Received June 15, 1923

The object of this paper is to present the results of a study of certain methods for the determination of formaldehyde in the presence of some of the organic substances that may be present in a formalin solution. The substances whose effect will be noted are methyl alcohol, ethyl alcohol, sodium formate, acetone and methylal.

The methods chosen are (1) iodimetric, (2) "alkali-peroxide" and (3) neutral sulfite.¹ These methods have been studied in previous work,² and as the procedure used in this work is the same no detailed explanation of the procedure will be given.

The paraformaldehyde used is the same as in previous work, and gave by the Liebig combustion method 96.8% of formaldehyde and 3.2% of water. Sodium formate was

¹ The determination of formaldehyde, methyl alcohol, and sodium formate in the same solution was attempted by the oxidation with permanganate and the absorption of the carbon dioxide produced. The method used is that suggested by Messinger [*Ber.*, 21, 2910 (1888)]. By this method the purity of the methyl alcohol was determined to be 95.35% and the sodium formate 100%; 0.2466 g. of paraformaldehyde and 0.7510 g. of sodium formate produced 0.8284 g. of carbon dioxide; calc., 0.8352 g.; 0.1170 g. of paraformaldehyde, 0.2722 g. of sodium formate and 0.2270 g. of methyl alcohol produced 0.6448 g. of carbon dioxide; calc., 0.6397 g.

² Borgstrom and Horsch, *THIS JOURNAL*, 45, 1493 (1923).