Calc. for $C_{10}H_4O_4Br_2$: Br, 45.98; C, 34.48; H, 1.15. Found: Br, 46.15, 45.77; C, 34.69; H, 1.28.

Work is under way in this laboratory extending this field in a number of directions.

Summary.

1. The chlorination of juglone in cold glacial acetic acid gives a dichloride, an addition product, which loses a molecule of hydrochloric acid with alcohol, giving a monochlorojuglone and this is acetylated with acetic anhydride.

2. The chlorination of juglone in hot glacial acetic acid gives a substitution product, dichlorojuglone, which is a new dye, imparting a rich golden-bronze color to silk. It is acetylated by acetic anhydride.

3. The bromination of juglone in cold glacial acetic acid gives a dibromide which loses one molecule of hydrobromic acid with alcohol, forming a monobromojuglone which is acetylated by acetic anhydride.

4. The bromination of juglone in hot glacial acetic acid gives a substitution product, tribromojuglone, one more halogen atom entering than in the chlorination. Tribromojuglone is acetylated by acetic anhydride. One atom of bromine is replaced (1) by chlorine by the action of alcoholic hydrochloric acid, (2) by hydroxyl by the action of hot caustic alkali.

5. Tribromojuglone is a new type of dye in the naphthalene series. Its sodium salt is soluble and dyes silk a champagne, wool a tan, and cotton, mordanted with tannic acid, is dyed an ecru.

CHAPEL HILL, NORTH CAROLINA.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY, UNIVERSITY OF MICHIGAN.]

THE PREPARATION OF β-AMINOPROPIOPHENONE.

BY WILLIAM J. HALE AND EDGAR C. BRITTON.

Received March 8, 1919.

The action of potassium phthalimide upon organic halides to give a potassium halide and a phthalimide derivative of the organic radical, which by hydrolysis was resolved into phthalic acid and an amino derivative of that same radical, was first announced by Gabriel.[1] By this synthesis a large number of amino compounds were made possible of preparation and to Gabriel we owe the advancement made in this direction. It recently became necessary for us, in the course of an investigation soon to be reported, to prepare β-aminopropiophenone and to this purpose we were required to study the possible methods for its preparation. From among the syntheses applicable for amines, only a few can find use where a keto group is present in the radical.

In addition to the Gabriel method we have attempted to prepare this compound by the action of ammonia upon halides of the alkyls contain-

[1] *Ber.*, **20**, 2224 (1887).

ing the keto group. Our work here is not reported as it agrees with that of Gabriel in every particular. The impossibility of checking the further substitution of alkyl for hydrogen in the resulting primary amine leads to poor yields of the latter. A third method seemed possible in the formation of an amide of the keto compound and the subsequent reduction of the amido group to the amine by the Hofmann reaction. The work of Biedermann,[1] however, has demonstrated the great tendency for such compounds, as the ketobutyric acids, when keto and amido groups are present in the same chain, to undergo intramolecular condensation, and the difficulties we have encountered merely emphasize the impracticability of this method. Our work therefore has resolved itself into a full consideration of the details necessary for the Gabriel method,—that method which we consider as the only practical one. More particularly we have attempted to secure the best results in the preparation of β-aminopropiophenone.

The complete details of the Gabriel method were published in 1908;[2] but the earlier steps were described in previous papers.[3] Trimethylene bromide and potassium phthalimide were brought into reaction to give at once γ-bromopropyl phthalimide, with a yield of slightly over 60%. From this point the several steps are expressed below in equations which are self explanatory.

$$C_8H_4O_2:NK + Br.CH_2.CH_2.CH_2.Br \longrightarrow C_8H_4O_2:N.CH_2.CH_2.CH_2.Br. \quad (1)$$

$$C_8H_4O_2:N.(CH_2)_3.Br + KOH \longrightarrow C_8H_4O_2:N.(CH_2)_3.OH. \quad (2)$$

$$C_8H_4O_2:N.(CH_2)_3.OH + O_2 \longrightarrow C_8H_4O_2:N.(CH_2)_2.COOH. \quad (3)$$

$$C_8H_4O_2:N.(CH_2)_2.COOH + PCl_5 \longrightarrow C_8H_4O_2:N.(CH_2)_2.COCl. \quad (4)$$

$$C_8H_4O_2:N.(CH_2)_2.COCl + C_6H_6(Al_2Cl_6) \longrightarrow C_8H_4O_2:N.(CH_2)_2.CO.C_6H_5. \quad (5)$$

$$C_8H_4O_2:N.(CH_2)_2.CO.C_6H_5 + HCl.Aq \longrightarrow C_8H_4O_2(OH)_2 + C_6H_5.CO.(CH_2)_2.NH_2.HCl. \quad (6)$$

Our criticisms of the Gabriel method lay primarily in the poor yield obtained by the action of potassium phthalimide on trimethylene bromide, —the tendency here for production of a diphthalimide undoubtedly gives rise to poor yields. In order to obviate this particular difficulty it seemed advisable to attempt the preparation of the aminopropiophenone from a monohalide. For this purpose we chose a β-halogen propionic ester for direct action with the potassium phthalimide. Upon hydrolysis this ester yields γ-phthalyl propionic acid, the same compound reached in step (3) in the Gabriel method. From this point on Gabriel's work was followed. The ester employed in our work was the isoamyl ester. Both chloro- and iodo-

[1] *Ber.*, **24**, 4074 (1891).
[2] *Ibid.*, **41**, 244 (1908).
[3] *Ibid.*, **21**, 2671 (1888); **38**, 633 (1905).

propionic isoamylester react well with potassium phthalimide, a point in keeping with the results of Weizzmann.[1] Holm,[2] on the other hand, reported that β-iodopropionic ethyl ester would not react with potassium phthalimide. The hydrolysis of the isoamyl ester, however, is best carried out by hydrobromic acid (49%) at 40°. Sodium or potassium hydroxide is not suitable for this purpose owing to the formation of phthalamic acids; the yields from the hydrobromic acid hydrolysis were not above 40%. This departure from the Gabriel method lead therefore to no better result than that obtained by Gabriel.

By a final improvement in this method just described we were able to avoid the saponification of the ester, with its consequent poor yields, and pass direct from the halogen propionic acid through its acid chloride to the ketone proper. The introduction of the amino group then proceeded through the agency of potassium phthalimide upon the halogen group of the original β-halogen propionic acid. Starting with β-chloro or β-iodopropionic acid we first prepared the corresponding acid chloride by the action of phosphorus trichloride (1); this acid chloride with benzene in the presence of aluminium chloride yielded β-chloro or β-iodo-propiophenone (2), and this ketone when treated with potassium phthalimide gave at once the β-phthalyl-propiophenone (3), which latter by hydrolysis with conc. hydrochloric acid yielded β-aminopropiophenone hydrochloride (4). Steps (1) and (2), combined, proceeded in excellent manner to a yield of 90% of the theoretical. Step (3) reacted in 70% yield and the final reaction (4) is practically quantitative.

$$Cl.(CH_2)_2.COOH + PCl_3 \longrightarrow Cl.(CH_2)_2.CO.Cl. \quad (1)$$

$$Cl.(CH_2)_2.CO.Cl + C_6H_6(Al_2Cl_6) \longrightarrow Cl.(CH_2)_2.CO.C_6H_5. \quad (2)$$

$$C_8H_4O_2:N.K + Cl.(CH_2)_2.CO.C_6H_5 \longrightarrow C_8H_4O_2:N.(CH_2)_2.CO.C_6H_5. \quad (3)$$

$$C_8H_4O_2:N.(CH_2)_2.CO.C_6H_5 + HCl.Aq \longrightarrow C_8H_4O_2(OH)_2 + C_6H_5.CO.(CH_2)_2.NH_2.HCl. \quad (4)$$

We conclude, therefore, that this process, as just described, is by far the most efficient for our purpose and results practically in doubling the amount of β-aminopropiophenone that can be prepared by the Gabriel method. In addition, we conclude that the best results are obtained by using β-iodopropionic acid as the starting product, owing to the fact that it is much simpler of preparation than the corresponding chloro acid and gives equally good yields of final product.

Experimental Part.

Preparation of Potassium Phthalimide.—We mention here our procedure which has served to facilitate the general mode of operation. The

[1] *Proc. Chem. Soc.*, **28**, 103 (1912).

[2] *Arch. Pharm.*, **242**, 602 (1904).

phthalimide was prepared according to the method of Dunlap[1] from phthalic anhydride and urea. Twenty g. of phthalimide was dissolved in 400 cc. of hot absolute alcohol and to this hot solution 7.6 g. of potassium hydroxide, dissolved in 30 cc. of 75% alcohol, was added. The final solution was cooled at once and the potassium phthalimide which separates was filtered off. In this filtrate another portion of 20 g. of phthalimide was dissolved by warming, and immediately upon effecting this solution, 7.6 g. of potassium hydroxide 30 cc. of 75% alcohol was added as above. The potassium salt finally separating was filtered off and together with the portion previously obtained well washed with acetone to remove any unacted upon phthalimide. The weight of the potassium phthalimide thus obtained from 40 g. of phthalimide amounted to 45 g.

β-Chloropropionic-isoamyl Ester, $Cl.(CH_2)_2.COOC_5H_{11}$.—Ten g. of β-chloropropionic acid, prepared according to the method of Jacobs and Heidelberger,[2] was dissolved in 8.2 g. of isoamyl alcohol and into the boiling solution, under reflux, a current of dry hydrogen chloride was led for one hour. The reaction mixture was then shaken with water and the alcoholic layer removed and dried over calcium chloride. The yield amounted to 90% of the theoretical. β-Chloropropionic isoamyl ester is a colorless liquid with pleasant odor and with the exception of ligroin and water is miscible with most organic solvents. The boiling point of the pure product is 207–8° under 740 mm. pressure.

Calc. for $C_8H_{15}O_2Cl$: Cl, 19.85. Found: 19.54.

β-Iodopropionic-isoamyl Ester, $I(CH_2)_2.COOC_5H_{11}$.—A portion of 20 g. of β-iodopropionic acid, prepared from glyceric acid and freshly prepared phosphorus iodide according to the method of Victor Meyer[3] was converted into its isoamyl ester by exactly the same procedure as outlined above for the chloro derivative. The properties of this iodo ester are closely similar to those of the chloro ester. The pure product boils at 183° under 140 mm. with slight decomposition.

Calc. for $C_8H_{15}O_2I$: I, 46.99. Found: 46.50.

β-Phthalylpropionic-isoamyl Ester, $C_8H_4O_2:(CH_2)_2.COOC_5H_{11}$.—18 g. of β-chloropropionic-isoamyl ester, or an equivalent amount of the corresponding β-iodopropionic-isoamyl ester, and 19 g. of potassium phthalimide were heated together in a sealed tube at 130° for one hour. The final product was repeatedly extracted with dry ether and the β-phthalylpropionic-isoamyl ester obtained at once upon the evaporation of the ethereal solution. The yield was 70% of the theoretical. This product is readily soluble in acetone, benzene, ethyl acetate, acetic acid or ether;

[1] *Am. Chem. J.*, 18, 333 (1896).
[2] THIS JOURNAL, 39, 1465 (1917).
[3] *Ber.*, 21, 24 (1888).

fairly soluble in alcohol or chloroform; and insoluble in ligroin or water. The product as purified by crystallization from alcohol melts at 61°.

Calc. for $C_{18}H_{19}O_4N$: C, 66.41; H, 6.62; N, 4.84. Found: C, 66.89; H, 6.80; N, 4.86.

β-Phthalylpropionic Acid, $C_8H_4O_2:N.(CH_2)_2.COOH$.—Ten g. of β-phthalylpropionic-isoamyl ester and 125 cc. of hydrobromic acid (49%) were shaken together in a closed flask under gentle warming at 40°. After two hours, the reaction mixture was filtered and the aqueous filtrate diluted with water and sufficient sodium carbonate added to neutralize 90% of the hydrobromic acid present. Upon cooling the solution, colorless crystals of β-phthalylpropionic acid appeared. The yield amounted to 40% of the theoretical. The product is readily soluble in acetone, chloroform, ethyl acetate, acetic acid or ether; fairly soluble in alcohol, benzene, or water; and insoluble in ligroin. Crystallized from water the compounds melt at 150–1° exactly, as reported by Gabriel.[1]

Preparation of β-Chloropropiophenone.—Ten g. (3 mols) of β-chloropropionic acid and 9 g. (2 mols) of phosphorus trichloride were heated together for one hour on a steam bath. To the warm mixture 100 cc. of benzene was added and the benzene solution of the acid chloride was removed from the insoluble phosphorus oxide portion by filtration. In order to involve only that chlorine present as acid chloride in this β-chloropropionyl chloride,[2] the benzene filtrate of the latter compound was now poured upon 15 g. (1 mol) of anhydrous aluminium chloride and the mixture gently warmed on a water bath, under reflux, for an hour. The final reaction mixture was now poured upon ice and a little ether added to effect a distinct separation of the two layers. The ether-benzene layer was removed, washed with water and dried over calcium chloride. Upon spontaneous evaporation, the β-chloropropiophenone appears in colorless crystals which purified by crystallization from alcohol, melt at 57–8°. The yield is 90% of the theoretical value. This same general procedure was employed by Collet,[3] save for the necessary precautions,—as stated above, in carrying out the Friedel-Crafts reaction, and also in the method of purification. For the latter step Collet resorted to distillation *in vacuo*. and obtained thus so little of the pure compound that he was able only to report its isolation through the formation of an anilide. The difficulty here experienced by Collet was explained later by Kohler[4] who demonstrated the ease with which this compound underwent decomposition into hydrogen chloride and phenylvinyl ketone even *in vacuo*. The preparation of the pure compound by Kohler was accom-

[1] *Loc. cit.*

[2] A. Collet, *Bull. soc. chim.*, [3] **17**, 66 (1897); J. Boeseken, *Ibid.*, **19**, 349 (1898).

[3] *Bull. soc. chim.*, [3] **17**, 80 (1897).

[4] *Am. Chem. J.*, **42**, 375 (1909).

plished by the direct addition of hydrogen chloride to phenylvinyl ketone in dry ether solution. The properties reported by Kohler agree with ours in every respect and hence the constitution as assigned by Kohler may find its verification in this method originated by Collet and amplified above.

β-Iodopropiophenone, $I.(CH_2)_2.CO.C_6H_5$.—This compound may be prepared from β-iodopropionic acid and phosphorus trichloride and the subsequent treatment of the benzene solution with anhydrous aluminium chloride exactly in the manner as described for the preparation of β-chloropropiophenone above. β-Iodopropiophenone when crystallized from alcohol appears in colorless prisms which melt at 61°. It is readily soluble in most of the organic solvents save ligroin in which it is fairly soluble. It is insoluble in water.

Calc. for C_9H_9OI: C, 41.55; H, 3.49; I, 48.81. Found: C, 41.69; H, 3.44; I, 48.69.

The acid chloride produced here as an intermediate product is mentioned but once in the literature[1] with no word of its properties. We isolated a small quantity of it but could not determine its boiling point owing to the great ease with which decomposition set in. The acid chloride is exceedingly irritating to the eyes.

The Preparation of β-Phthalylpropiophenone.—17 g. of β-chloropropiophenone (or an equivalent amount of β-iodopropiophenone) and 19 g. of potassium phthalimide were intimately mixed and heated in a sealed tube during constant shaking for one hour at a temperature of 130–40°. The reaction mixture was then repeatedly extracted with benzene to remove the product. The clear benzene solution was subjected to distillation with steam to remove all of the benzene and traces of unacted upon chloropropiophenone (here dissociating into hydrogen chloride and phenylvinyl ketone). When the distillate comes over free of odor, the product in the flask may be considered free from impurities. The water in the flask is then decanted from the solid residue and the latter crystallized from alcohol. The β-phthalylpropiophenone thus obtained is a colorless, highly crystalline compound melting at 130°. The yield is 68% of the theoretical. The product is identical in all respects with that obtained by Gabriel save for the yellow color he reports as present. β-Phthalylpropiophenone is readily soluble in acetone, chloroform or benzene; fairly soluble in alcohol, ethyl acetate, ether or acetic acid; and insoluble in ligroin or water. As Gabriel reported only a nitrogen determination we checked the nitrogen and determined further the carbon and hydrogen.

Calc. for $C_{17}H_{13}O_3N$: C, 73.1; H, 4.69; N, 5.02. Found: C, 72.92; H, 4.67; N, 4.84.

The Preparation of β-Aminopropiophenone Hydrochloride.—A mixture

[1] Abderhalden and Gressel, *Z. physiol. Chem.*, **74**, 472–80.

of 3 g. of β-phthalylpropiophenone, 12 cc. of glacial acetic acid, and 10 cc. of conc. hydrochloric acid (previously saturated at 0° with dry hydrogen chloride) were placed in a sealed tube and the contents heated at 145–50° for one hour. The reaction mixture, removed from the tube, was evaporated to a small volume (but not to dryness) upon a steam bath. The syrup was now taken up in 25 cc. of water and filtered from the insoluble phthalic acid. The filtrate was then allowed to evaporate slowly to dryness in a current of air and at a temperature not exceeding 60°. For final purification the β-aminopropiophenone hydrochloride was crystallized from absolute alcohol. The melting point is 128° exactly as reported by Gabriel[1] and the yield is 95% of the theoretical. As no analysis is to be found in the literature we determined these values.

Calc. for $C_9H_{11}ON.HCl$: C, 58.43; H, 6.47; N, 7.55. Found: C, 58.18; H, 6.56; N, 7.35.

ANN ARBOR, MICH.

NEW BOOKS.

Chemistry of Food and Nutrition. Second edition, rewritten and enlarged. By HENRY C. SHERMAN, PH.D., Professor in Columbia University. MacMillan Co. New York: $2.00.

The rewritten and enlarged edition of Professor Sherman's work brings the chemistry of foods and nutrition up to 1918 in a form easily accessible.

In the preface the author states the present work is the outgrowth of several years of teaching the subject and is published principally to meet the needs in teaching college classes. It is a work of far greater application. Its style is such that it can be readily comprehended by one who is not a chemist. It is a book that will be of great value to the teacher of dietetic and economic science and especially to physicians. The lack of exact knowledge of the science of dietetics is perhaps nowhere more greatly to be regretted than in the case of the physician, who, not very well trained in dietetics in his college course, has failed to keep pace with advancing knowledge.

The word "food" might very well be dropped from the title for the book is essentially an up to date treatise on the chemistry and physiology of nutrition.

Chapters that are especially opportune are those on the classification and general properties of enzymes and the activities of these ferments in digestion. "The Fate of the Foodstuffs in Metabolism" is a story of absorbing interest and well told. The chapter on proteins and their digestion products exposes in a systematic method the modern theories of the reduction of proteins to amino-acids prior to their assimilation. The chapters on the fuel value of foods and the methods of determining it are instructive and to the point.

[1] *Loc. cit.*