was easily obtained by action of *p*-toluidine on ethyl isothiocyanacetate. It was purified by crystallization from ether and alcohol and separated in long needles which melted at 96°. The hydantoate is soluble in benzene, ether and alcohol and insoluble in water.

Calc. for $C_{12}H_{16}O_2N_2S$: N, 11.13%. Found: N, 11.01, 10.96.

Ethyl *o*-Tolylthiohydantoate, $CH_3C_6H_4NHCSNHCH_2COOC_2H_5$.—From *o*-toluidine and ethyl isothiocyanacetate. The compound is soluble in alcohol and ether and insoluble in water. It melts at 90°.

Calc. for $C_{12}H_{16}O_2N_2S$: N, 11.13%. Found: N, 11.00, 10.97.

Ethyl *m*-Tolylthiohydantoate, $CH_3C_6H_4NHCSNHCH_2COOC_2H_5$.—From *m*-toluidine and ethyl isothiocyanacetate. It crystallizes from alcohol or ether in the form of prismatic needles and melts at 97°.

Calc. for $C_{12}H_{16}O_2N_2S$: N, 11.13%. Found: N, 11.25, 11.21.

Ethyl *p*-Nitrophenylthiohydantoate, $NO_2.C_6H_4NHCSNHCH_2COOC_2H_5$. —This ester crystallizes from alcohol in the form of light yellow needles arranged in rosets. It melts at 191.5°.

Calc. for $C_{11}H_{13}O_4N_3S$: N, 14.87%. Found: N, 14.82, 15.00.

The Action of Thiophosgene on the Hydrochloride of Glycocoll.—Twenty grams of the hydrochloride of glycocoll were suspended in 60 cc. of toluene and 22 g.of thiophosgene added to the toluene. The mixture was then digested for two days at 110–115°. The unaltered hydrochloride was then separated by filtration and dried. Practically the whole amount taken was recovered unaltered.

NEW HAVEN, CONN.

[CONTRIBUTIONS FROM THE SHEFFIELD CHEMICAL LABORATORY OF YALE UNIVERSITY.]

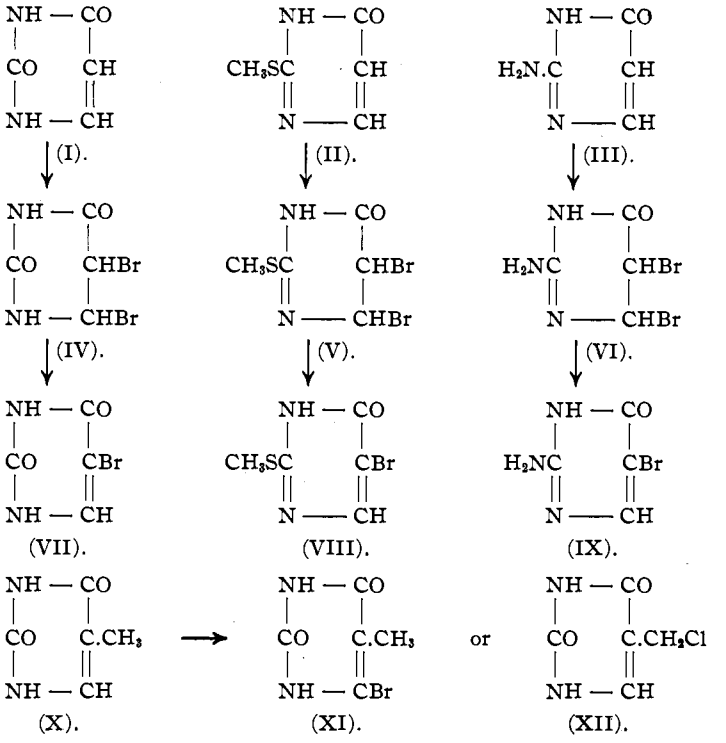
RESEARCHES ON PYRIMIDINES. LXXX. THE MECHANISM OF THE ACTION OF BROMINE ON 2-MERCAPTOPYRIMIDINES.

BY TREAT B. JOHNSON AND A. WILLARD JOYCE.

Received June 17, 1916.

It is known that 6-oxypyrimidines of the three types represented by uracil (I), 2-methylmercapto-6-oxypyrimidine (II), and isocytosine or 2-amino-6-oxypyrimidine (III), interact, respectively, with chlorine, bromine and iodine with substitution of one hydrogen atom of the pyrimidine ring by halogen. Wheeler and Bristol[1] showed that the 5-position of the pyrimidine ring is the point of attack in such reactions leading to the formation of the corresponding 5-halogenated pyrimidines (VII, VIII and IX). These transformations, when bromine is used, are represented by the following formulas:

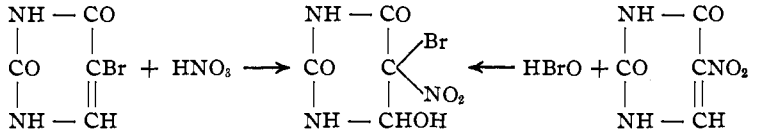
[1] *Am. Chem. J.*, **33**, 437 (1905); Johnson and Johns, *Ibid.*, **34**, 175 (1905); *J. Biol. Chem.*, **1**, 305 (1905).



When the 5-position of the ring in these series is occupied by an alkyl group (CH_3^-, $C_2H_5^-$, etc.) and the 4-position is unsubstituted as, for example, in the case of thymine (X), the pyrimidine shows no tendency to interact with halogens, under normal conditions, with formation of halogen derivatives substituted in the 4-position (XI), or even in the side chain (XII), as is observed to take place with the higher homologs of benzene. The behavior of thymine towards halogens at high temperatures has not been investigated.

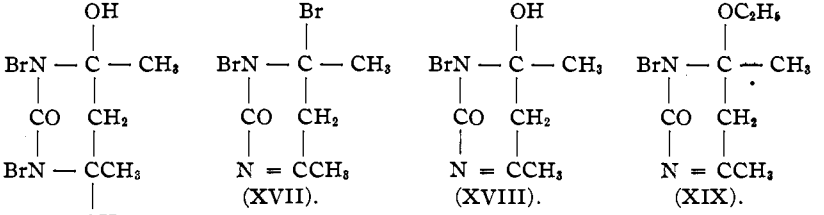
All these transformations very probably involve primarily an addition of bromine to the double bond of the pyrimidine ring giving unstable combinations (IV, V and VI), which then break down with formation of hydrobromic acid and 5-bromopyrimidines. In no case, however, has a halogen addition product of this type been isolated in these series. On the other hand, it has been shown that 2,6-dioxypyrimidines (thymine) readily combine with hypochlorous, hypobromous and even nitric acid giving stable addition products. For example, 5-bromouracil (XIII) and 5-nitrouracil (XV) interact with concentrated nitric acid and hypobromous acid, respectively, giving the same hexahydropyrimidine (XIV).

[1] Johnson, *Am. Chem. J.*, 40, 19 (1908).

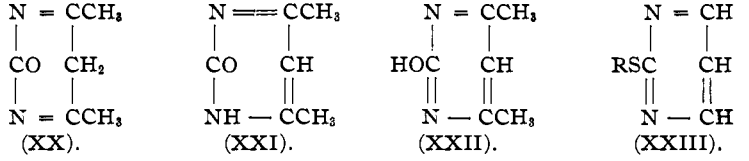


(XIII). (XIV). (XV).

Our knowledge of the action of halogens on 2-oxypyrimidines (XX), is very limited while the behavior of these elements towards the corresponding 2-mercaptopyrimidines (XXIII) has never been investigated. Evans[1] was the first to investigate the action of halogens on 2-oxypyrimidines and showed that 2-oxy-4,6-dimethylpyrimidine (XX) interacts with bromine water, giving a hexahydropyrimidine to which he assigned the constitution (XVI). This reaction was later reinvestigated by Stark[2] who made the interesting observation that this ketopyrimidine (XX) readily adds bromine in chloroform, forming an addition product which is unstable in the presence of water and alcohol. He assigned to this addition product the constitution XVII, and represented the products formed by treatment with water and alcohol according to Formulas XVIII and XIX. In other words, this pyrimidine, which is both acidic and basic in character and consequently can react in a tautomeric manner, adds bromine to the unsaturated group —N = C.CH_3 instead of the ethylene grouping in positions 4 and 5 of the ring, as represented in the two tautomers of 2-oxy-4,6-dimethylpyrimidine (XXI) and (XXII).



(XVI). (XVII). (XVIII). (XIX).



(XX). (XXI). (XXII). (XXIII).

In the light of these results it was of great interest to investigate the action of bromine towards 2-mercaptopyrimidines as represented by the general Formula XXIII. Compounds of this type are basic in character and cannot react in a tautomeric manner. In other words, they

[1] *J. prakt. Chem.*, **48**, 489 (1893).

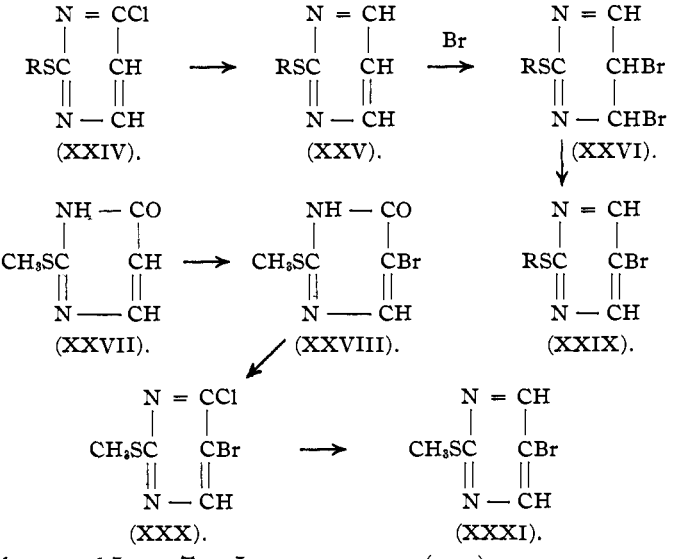
[2] *Ber.*, **42**, 708 (1909).

do not contain a mobile hydrogen atom and consequently can be assigned only one constitution. This corresponds with that represented by the tautomeric formula of 2-oxy-4,6-dimethylpyrimidine (XXII).

We have now investigated the action of bromine on 2-methylmercaptopyrimidine and 2-ethylmercaptopyrimidine[1] (XXV). These two mercapto bases were prepared by reduction of their corresponding 2-mercapto-6-chloropyrimidines (XXIV). We find that both these pyrimidines add bromine quantitatively in carbon tetrachloride solution, forming addition products (XXVI) insoluble in this solvent. The 2-methylmercapto compound is a solid while its higher homolog was always obtained as a dark colored oil. In other words, the transformation of 2-mercapto-6-oxyprimidines into 2-mercaptopyrimidines is productive of greater unsaturation within the molecule, and the valency-force of the unsaturated ethylene grouping between positions 4 and 5 is greatly increased.

These addition products are the first representatives of a new class of dihydropyrimidines and are characterized by very unique properties. They easily undergo dissociation when warmed with water or dilute alkali, with regeneration of the original mercaptopyrimidines. This same change is also brought about quantitatively by the action of acetone. Both of the dihydropyrimidines (XXVI) interacted with this ketone at ordinary temperature with formation of bromoacetone and the hydrobromic acid salt of the original mercaptopyrimidines.

(R = CH_3— and C_2H_5—.)



[1] Johnson and Joyce, THIS JOURNAL, 37, 2151 (1915).

These changes are perfectly analogous to those which have been observed to take place with similar combinations in the acyclic series. For example, Erlenmeyer and Muller[1] observed that α,β-dibromobutyric acid (XXXII) easily looses bromine when warmed in aqueous solution with potassium iodide with formation of crotonic acid (XXXIII) and iodine.

$$\underset{\text{(XXXII).}}{\overset{\text{Br Br}}{\overset{|\ \ |}{CH_3CH.CHCOOH}}} + 2KI = 2KBr + \underset{\text{(XXXIII).}}{CH_3CH = CHCOOH} + I_2.$$

Especially interesting in this connection are observations of Pfeiffer[2] on the behavior of the asymmetric isomers or dibromostilbene and related compounds towards pyridine. While the β-modifications of dibromostilbene (XXXV) and β-dinitrodibromostilbene (XXXVIII) interact with this reagent, on warming, to give the corresponding unsaturated monohalides represented by Formulas XXXVI and XXXIX, the α-modifications, on the other hand, behave in an entirely different manner. They undergo dissociation in presence of the same reagent with formation of stilbene (XXXIV) and dinitrostilbene (XXXVII), respectively. These changes may be represented as follows:

$$\underset{\text{(XXXIV).}}{C_6H_5CH:CHC_6H_5} \longleftarrow \underset{\text{(XXXV).}}{\overset{\text{Br Br}}{\overset{|\ \ |}{C_6H_5CH.CH\ C_6H_5}}} \longrightarrow \underset{\text{(XXXVI).}}{C_6H_5CBr = CHC_6H_5}$$

$$\underset{\text{(XXXVII).}}{(NO_2)_2C_6H_3CH:CHC_6H_5} \longleftarrow \underset{\text{(XXXVIII).}}{\overset{\text{Br Br}}{\overset{|\ \ |}{(NO_2)_2C_6H_3CH.CH.C_6H_5}}} \longrightarrow \underset{\text{(XXXIX).}}{(NO_2)_2C_6H_3CBr:CHC_6H_5}$$

So far as the writers are aware the behavior of such combinations towards acetone has never been investigated.

When the addition products (XXVI) are heated under pressure, hydrobromic acid is evolved and halogenated mercaptopyrimidine (XXIX) is obtained containing bromine in position 5 of the pyrimidine ring. The structure of the bromine derivative (XXXI), which was obtained by heating its corresponding methylmercapto addition product (XXVI), was established as follows: 2-methylmercapto-6-oxypyrimidine[3] (XXVII) was prepared and combined with bromine, when the bromopyrimidine (XXVIII) was easily formed. This was then converted into the pyrimidine (XXX) by interaction with phosphorus oxychloride. When this bromochloropyrimidine was reduced with zinc dust, the chlorine atom only was replaced by hydrogen and 2-methylmercapto-5-bromopyrimidine (XXXI) was obtained. This was identical with the bromopyrimidine

[1] *Ber.*, **15**, 49 (1882).

[2] *Ibid.*, **45**, 1810 (1912); **48**, 1048 (1915).

[3] Wheeler and Merriam, *Am. Chem. J.*, **29**, 478 (1903).

formed by heating the methylmercapto addition product (XXVI). Therefore *when 2-mercaptopyrimidines interact with bromine they form addition products, which break down on heating with substitution of the halogen in the 5-position of the pyrimidine ring.*

Experimental Part.

The Behavior of Bromine towards 2-Methylmercaptopyrimidine in Carbon Tetrachloride Solution: 2-Methylmercapto-4,5-dibromodihydropyrimidine (XXVI).—The 2-methylmercaptopyrimidine used in this preparation was obtained by the reduction of 2-methylmercapto-6-chloropyrimidine.[1] Two grams of the 2-mercaptopyrimidine were dissolved in 20 cc. of carbon tetrachloride and the solution cooled with ice-water. To this were then added 3.5 grams of bromine dissolved in 20 cc. of cold carbon tetrachloride. The bromine which was used here was previously dried by washing with concentrated sulfuric acid. On mixing the above reagents a turbidity was produced and after standing a short time clusters of red needles deposited on the sides of the flask. After standing about 15 minutes, when the reaction was apparently complete, these crystals of the addition product were filtered off quickly by suction, washed with carbon tetrachloride and finally dried over concentrated sulfuric acid in a vacuum desiccator. The crystals could not be exposed to the air for any prolonged time, the substance being decomposed by moisture. We obtained 3.75 g. of the addition product while a theoretical yield would be 4.15 g.

This pyrimidine is very unstable in the presence of moisture and even on warming in anhydrous solvents, so that we were not able to purify it by crystallization. It is insoluble in carbon tetrachloride, benzene and ether. It is decomposed by water, alkalies and acids, with formation of the original 2-mercaptopyrimidine. We were not able to assign a sharp melting point to the compound. It began to melt, when heated in a capillary tube, at 65°, giving finally a clear oil at 75°.

Calc. for $C_5H_6N_2SBr_2$: N, 9.79%. Found: N, 9.53, 9.58.

The Action of Acetone on the Addition Product.—The dihydropyrimidine interacts with acetone at ordinary temperature. When treated with this reagent the addition compound dissolves, giving a yellow solution which becomes colorless on stirring and finally deposits the original 2-methylmercaptopyrimidine in the form of its hydrobromic acid salt. At the same time bromoacetone is formed which is easily recognized by its odor and irritating action on the eyes. The hydrobromide of the pyrimidine base was purified by crystallization from absolute alcohol and melted at 188° with decomposition.

Calc. for $C_5H_6N_2S.HBr$: N, 13.52%. Found: N, 13.7.

[1] Johnson and Joyce, THIS JOURNAL, 38, 1385 (1916).

This salt was decomposed by treatment with an aqueous solution of alkali and the free pyrimidine extracted with ether. After removal of the ether the pyrimidine was converted into a double platinum chloride salt, which proved to be identical with the platinum salt of the base described in our previous paper.[1] It melted at 207–208° with decomposition.

Behavior of 2-Methylmercapto-4,5-dibromodihydropyrimidine on Heating: The Formation of 2-Methylmercapto-5-bromopyrimidine (XXXI). —Four grams of the 2-methylmercaptopyrimidine were dissolved in 20 cc. of carbon tetrachloride and the solution transferred to a pressure tube. Five grams of bromine, dissolved in 20 cc. of carbon tetrachloride, were then added and the tube sealed. The addition product separated almost at once in a crystalline condition. The tube was then heated at 100° for 10 hours. There was no pressure when it was opened, and underneath the colorless tetrachloride was a layer of a dark colored oil. The carbon tetrachloride was poured off and the solvent evaporated under diminished pressure, when we obtained a yellow liquid which solidified on cooling. This material weighed 1 g. This was triturated with ether, in which most of it dissolved, but leaving a small amount of solid material which was very soluble in water. The latter product was identified as the hydrobromic acid salt of 2-methylmercapto-5-bromopyrimidine. On evaporating the ether solution a crystalline substance was obtained which was easily purified by crystallization from dilute alcohol or a mixture of acetone and water and deposited in the form of transparent plates melting at 64–65°. It was identified as 2-methylmercapto-5-bromopyrimidine. This pyrimidine is insoluble in water, dilute alkali and dilute acids, but soluble in alcohol, ether and acetone.

Calc. for $C_6H_5N_2SBr$: N, 13.65%. Found: N, 13.49.

In another experiment the dibromo addition product was heated in a pressure tube at 125–135° for 4 hours. Under these conditions there was much more decomposition and a larger proportion of the hydrobromic acid salt of the bromopyrimidine was formed. In place of the dark-colored oil obtained in the previous case there was formed a black decomposition product which was not examined further. When the tube was opened there was some pressure due to the presence of hydrobromic acid and a crystalline substance was suspended in the carbon tetrachloride. This material was identified as the hydrobromide of 2-methylmercapto-5-bromopyrimidine and melted at 205–206°. It dissolved in water with dissociation into hydrobromic acid and the free 2-methylmercaptobromopyrimidine. The latter crystallized from dilute alcohol in the form of plates and melted at 65–6°.

[1] Johnson and Joyce, *Loc. cit.*

Experimental Proof of the Structure of the Mercaptobromopyrimidine: 2-Methylmercapto-5-bromo-6-oxypyrimidine (XXVIII).—This new pyrimidine was prepared in a similar manner as that employed by Wheeler and Johnson[1] for the preparation of the corresponding 2-ethylmercaptopyrimidine. Our procedure was as follows: Ten grams of 2-methylmercapto-6-oxypyrimidine were dissolved in 60 cc. of glacial acetic acid and 11.2 g. of bromine (in 20 cc. of glacial acetic acid) added slowly through a dropping funnel. The bromopyrimidine began to separate very quickly. After final addition of the bromine the mixture was allowed to stand for 2 hours and the bromopyrimidine then separated by filtration. It was purified by crystallization from alcohol and separated, on cooling, in the form of needles which melted at 239° with decomposition. The yield of purified pyrimidine was 10.6 g. or 70% of the theoretical.

Calc. for $C_5H_5ON_2SBr$: N, 12.67%. Found: N, 13.00.

2-Methylmercapto-5-bromo-6-chloropyrimidine (XXX).—This chloropyrimidine was obtained by the action of phosphorus oxychloride on the above mercaptopyrimidine. Nine grams of the mercaptopyrimidine were suspended in 25 cc. of the phosphorus halide and the mixture heated in an oil bath at 125° for 2 hours. Hydrochloric acid was evolved and the pyrimidine dissolved completely. The excess of phosphorus oxychloride was then removed by heating at 100° under diminished pressure, when we obtained the pyrimidine in the form of a thick oil. This was triturated with cold water to destroy any phosphorus halide present and the pyrimidine then extracted with ether and dried over anhydrous calcium chloride. After removing the ether, the bromochloropyrimidine was obtained as an oil which solidified on cooling. It crystallized from ether in the form of needles and melted at 44° to an oil.

Calc. for $C_5H_4N_2SClBr$: N, 11.69%. Found: N, 11.72.

Reduction of 2-Methylmercapto-5-bromo-6-chloropyrimidine with Zinc Dust. The Formation of 2-Methylmercapto-5-bromopyrimidine.—Three grams of the mercaptopyrimidine were dissolved in 25 cc. of alcohol (95 per cent.) and the solution diluted with 25 cc. of water. To the slightly turbid solution 5 g. of zinc dust were added. There was an indication immediately that there was partial reduction, because the zinc dust assumed a granular or flaky condition. The mixture was digested under reflux condenser for 15 minutes, cooled and finally filtered to remove the excess of zinc. The alcohol and water were then removed by evaporation under diminished pressure, when we obtained an oil which was insoluble in water. This was dissolved in ether and dried over anhydrous calcium chloride. When the ether was evaporated an oil was obtained which did not solidify after standing for several days in a vacuum over sulfuric

[1] *Am. Chem. J.*, 31, 603 (1904).

acid. In order to isolate the 5-bromopyrimidine this oil was treated with concentrated hydrobromic acid, when the hydrobromide of the pyrimidine separated at once in a crystalline condition. On dissolving this in alcohol it underwent dissociation, and after cooling the solution the 2-methylmercapto-5-bromopyrimidine separated in the form of needles. They melted at 65° to an oil. The yield of this pyrimidine was 1 g.

Calc. for $C_6H_6N_2SBr$: N, 13.65%. Found: N, 13.60.

The Addition of Bromine to 2-Ethylmercaptopyrimidine.—Bromine combines with this pyrimidine in carbon tetrachloride solution at ordinary temperature. Two and three-tenths grams of bromine dissolved in 20 cc. of the tetrachloride were added to a cold solution of 2 g. of the pyrimidine in 20 cc. of carbon tetrachloride. The resulting mixture was then cooled to 0° with ice-water and allowed to stand for several hours at this temperature. The addition product did not separate in a crystalline condition as in the case of the 2-methylmercaptopyrimidine but deposited as a dark colored oil which showed no sign of crystallizing on standing. The carbon tetrachloride was removed by evaporation under diminished pressure and the oil again allowed to stand for several days in a desiccator, but it still showed no evidence of solidifying and was used for the following experiments:

Action of Acetone and the Crude Addition Product. The Formation of 2-Ethylmercaptopyrimidine (XXV).—This addition product interacts immediately with acetone at ordinary temperature, giving monobromoacetone and the hydrobromic acid salt of this pyrimidine. On mixing the two reagents and allowing to stand this hydrobromide deposits in the form of prisms. It was purified by crystallization from alcohol and melted at 140–141°. A mixture of this salt with that originally prepared by Johnson and Joyce[1] melted at the same temperature.

Calc. for $C_6H_8N_2S.HBr$: N, 12.67. Found: N, 12.35, 12.40.

Conversion of the Addition Product into 2-Ethylmercapto-5-bromopyrimidine (XXIX).—This new pyrimidine is formed by heating 2-ethylmercaptopyrimidine (2 g.) with the required amount of bromine in carbon tetrachloride solution for 10 hours at 125–130°. When the bomb tube was opened there was pressure due to the presence of hydrobromic acid and a dark tarry product adhered to the sides of the tube. Suspended in the tetrachloride was a considerable amount of material crystallized in the form of needles, which melted at 180° with decomposition. This was the hydrobromic acid salt of 2-ethylmercapto-5-bromopyrimidine. It was very soluble in water and on warming the solution immediately underwent dissociation. When the salt was dissolved in hot, dilute alcohol and the solution cooled the free base separated in the form of

[1] *Loc. cit.*

needles melting at 43–5° to an oil. The substance contained sulfur and bromine and a nitrogen determination agreed with the calculated value for 2-ethylmercapto-5-bromopyrimidine.

Calc. for $C_6H_7N_2SBr$: N, 12.78. Found: N, 12.90.

When the carbon tetrachloride was evaporated more of this same base was obtained and melted at 43–45°.

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[CONTRIBUTION FROM THE CARBOHYDRATE LABORATORY, BUREAU OF CHEMISTRY, UNITED STATES DEPARTMENT OF AGRICULTURE.]

SOME NUMERICAL RELATIONS AMONG THE ROTATORY POWERS OF THE COMPOUND SUGARS.

BY C. S. HUDSON.

Received June 8, 1916.

The general group of polysaccharides includes many pure crystalline substances of definite chemical individuality, such as the di-, tri-, and tetrasaccharides, together with a series of amorphous products, such as starch, glycogen, inulin, cellulose, pentosans, mannans, galactans, etc. To distinguish the pure crystalline polysaccharides from their less definitely characterized relatives, it is suggested that they be classed under the group name of *compound sugars*, a designation which separates them very well also from the simple sugars, or monosaccharides, into which they may be decomposed by hydrolysis. In the present article, it is sought to extend to several of the compound sugars the numerical relationships that have been found to hold among the rotatory powers of the alpha and beta forms of the monosaccharides and their glucosidic derivatives.[1]

Sugars of the Sucrose Group.

Known Members of the Group.—The trisaccharide raffinose may be split by complete hydrolysis into its three component simple sugars, galactose, glucose and fructose; by partial hydrolysis, best through the agency of enzyme action, it may be split either into fructose and melibiose (= galactose<glucose<[2]) by the use of invertase or weak acids, or into galactose and sucrose (= *glucose*<>*fructose*) by the aid of emulsin. Raffinose may accordingly be regarded as *galactose*<*glucose*<>*fructose*, a derivative of sucrose, a combination between that sugar and galactose. Other sugars which are now regarded as derivatives of sucrose are[3] gentianose (= *glucose*<*glucose*<>*fructose*) and stachyose (= *galactose*<

[1] THIS JOURNAL, 31, 66 (1909).

[2] The symbol < denotes the carbonyl or lactonyl group. See THIS JOURNAL, 31, 661 (1909). The term lactonyl, which has been suggested by S. F. Acree (*Science*, 42, 101 (1915)) to indicate an aldehyde or ketone group that has formed a lactone-like ring, as in the sugars, seems very appropriate.

[3] Bourquelot and Bridel, *Compt. rend.*, 152, 1060 (1911).