

differently with the imido esters the action of ammonia on the *positive ion* is the essential action and the use of a catalytic agent,<sup>1</sup> an acid is advisable, in fact, necessary; with ordinary esters the action on the ion becomes negligible because the ion simply cannot be produced in sufficient quantity under these conditions and the action of ammonia on the *non-ionized ester becomes the essential action*. The addition of acid as a catalytic agent is *practically ineffective* and therefore inadvisable. But these apparently disconnected results are now easily understood as being perfectly consistent and logical—the one case representing an almost but not quite pure type of one of the *two natural simultaneous reactions*—the enormously rapid action of the ammonia on the *imido ester ion*—and the other case representing the almost pure type of the other simultaneous action, the extremely slow action of ammonia on the non-ionized ester molecule. And the connecting link is found when the adjustment of the affinity and the velocity constants involved bring *both actions out prominently at the same time*. Of course one must then expect every possible class of reactions lying between these extremes. The results show plainly then, I believe, why a catalytic agent will work smoothly in a number of cases, and why it will fail utterly in accelerating actions apparently of exactly the same organic type, *differing only in the numerical value of the physico-chemical constants included in the final expression governing the action of a catalytic agent*. We have been using the imido esters *simply as a kind of magnifying glass to measure* all these constants and thus to enable us to recognize some of the general underlying principles which govern catalysis by such chemical agents, as acids, bases and salts.

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## ON THE BIOCHEMISTRY OF NUCLEIC ACIDS.<sup>2</sup>

BY P. A. LEVENE.

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Life is the most complex phenomenon in nature and its manifestations are innumerable. They all mysteriously arise in the living organism and are all harmoniously centered in it. This, even in its simplest form is the most perfect laboratory, the seat of an infinite number of chemical reactions, none of them interfering with the equilibrium of the others. The substances produced by the most primitive of the living organisms are as large in number as they are varied in their properties. The discoveries of new substances manufactured by the plant or animal cell are not yet exhausted and for ages the chemist dreamed of no better reward for his labors than the finding in tissue juices of a new body with properties hitherto unknown. The living organism was the only retort, vital force the only reaction in his possession that could furnish him with carbon-containing substances. In that sense every chemist in those days was a biological chemist.

In the year 1828 a startling discovery was announced. Wöhler wrote to Berzelius: "I must tell you that I can make urea without the aid of the kidney, or generally without the living organism whether of man or dog," and four years later the divorce of biological and organic

<sup>1</sup> *Loc. cit.*

<sup>2</sup> Presented at the Second Decennial Celebration of Clark University, Worcester, Mass., September 15, 1909.

chemistry was apparently accomplished when Wöhler and Liebig laid the foundation of the organic chemistry of to-day by their work on the radicle of benzoic acid. However, the divorce was only apparent, for the reason that only the knowledge of molecular constitution made it possible to establish the relationship between the organism and the chemical bodies manufactured by it, only the knowledge of the dynamics of the chemical reactions could coördinate the observations of the functions of the living organism, and of the accompanying changes in the composition of the living cells.

The attitude of the biological chemist was altered. He saw his new goal in disclosing the nature of chemical reactions occurring within the living cell and finding their bearing on the manifestations of life.

If time permitted I would present to you the progress of all the work done in that direction in recent years. Within the narrow limits of this report, however, this is impossible to accomplish with any degree of justice to the subject and I shall, therefore, limit the discussion to only one phase, namely, to the work bearing on the chemical interpretation of one of the most cardinal properties of living matter.

Living matter is distinguished from inanimate by the fact that it undergoes cleavage and oxidation at a very perceptible velocity, and that the restoration of the loss sustained in that manner takes place at approximately the same rate. Thus the function of automatic regeneration lends to living matter its principal peculiarity.

Great credit is due to the biologist for the discovery that in an organized cell this function is seated in a formation possessing definite chemical properties, named chromatin or nuclein. At a time when the process of regeneration is very active, namely, during the development of the fertilized egg, the rate of the new formation of nuclein rises to a very perceptible degree, and the observer is led to see a genetic relationship between these two processes.

Our distinguished biologist, Jacques Loeb,<sup>1</sup> was the first to express the function of reproduction in terms of chemical reactions. In his address to the International Congress of Zoologists held in Boston in September, 1907, he stated: "If the question be raised as to what is the most obvious chemical reaction which the spermatozoan causes in the egg, the answer must be an enormous synthesis of chromatin or nuclear material from constituents of the cytoplasm." Thus, it becomes evident that the knowledge of the mechanism of regeneration is dependent on the knowledge of the chemistry of nucleins.

I shall for a moment forestall the systematic discussion of the chemical nature of nucleins by mentioning that at the time of Loeb's address we were in possession of considerable information on the composition of these substances. It was known that phosphoric acid entered into the formation of the molecule. Therefore, it became evident to Loeb that a supply of phosphoric acid was required in order to make a synthesis of nucleins possible. In a developing egg the phosphoric acid was furnished by the cell itself, for the formation of nucleins proceeded also when the eggs were placed in a medium free of phosphoric acid. The other components of the cell that are known to contain phosphoric acid in their molecule are the lipoids. In these substances phosphoric acid

<sup>1</sup> University of California Publications in Physiology, 3, 61-81 (1907).

is present in an ester-form combination, and Professor Loeb proceeded to argue that the first phase in cell reproduction *à priori* ought to consist in the saponification of its lipoids. This assumption was brilliantly verified in his experiments on artificial parthogenesis. He brought to light the fact that dissolution of the lipoids is actually the process which precedes the nuclein synthesis and the segmentation of the nucleus. He further demonstrated that agencies facilitating this saponification were able under favorable conditions to start the development of an unfertilized egg without the aid of spermatozoa. Thus only an elementary knowledge of the chemical nature of two cell components furnished Professor Loeb with the power at will to start or to impede cell development by chemical means, and in a way to furnish evidence that the function of regeneration was a chemical process. But the process of nuclein synthesis in the active cells is not yet disclosed in its harmonious entirety, and no one can entertain any hope of arriving at this knowledge without the discovery of the chemical constitution of nucleins.

The considerations that attracted the attention of so many chemists to the work on the chemical nature of these substances, therefore, are becoming very obvious, and I shall attempt to present the results and the achievements of the numerous endeavors towards the solution of this very difficult problem.

The first important contribution to the chemistry of nucleins was made by Altman, a biologist.<sup>1</sup> Altman was in possession of the information that nucleins were endowed with the properties of fairly strong acids, and further that they were quite resistant to the action of pepsin hydrochloric acid. The latter property enabled him to prepare considerable quantities of nuclein by removing the protein part of the tissues by means of peptic digestion, and the fats by the usual extractives. The remaining nuclein he found to consist of a protein combined with a conjugated phosphoric acid. The acid he named "nucleic acid." By means of alkaline hydrolysis, Altman succeeded in removing all the protein from his nuclein so that the final product analyzed by him refused to disclose any trace of protein even by the aid of the most sensitive color test.

The further development of the chemistry of nucleic acid was accomplished through the investigations of Miescher, of Schmiedeberg and his pupils, of Kossel and his school, by Haiser, G. H. Hammarsten and his pupil Ivar Bang, and in this country by the work of T. B. Osborne, of Walter Jones, and of my co-workers and myself. I must, however, add that the purest nucleic acid was obtained by the man who was first in so many lines of chemical activity, Liebig, although on this occasion he failed to discover the real significance of his finding.

I shall make no attempt to present all the work on nucleic acid in its chronological order, but I shall refer to individual investigations in connection with the discussion of the development of the various phases in our knowledge of chemical structure of those complex acids.

The three principal phases in the endeavors to reveal the nature of nucleic acid consist: first, of work aiming to obtain the substance in a convenient manner, and in a possibly unaltered condition with a

<sup>1</sup> *Arch. Anat. und Physiol. Physiol. Abt.*, 1889, 524.

view to ascertain the elementary composition of the substance; second, in the work directed towards finding all the components of the various nucleic acids; and third, in determining the actual structure of the molecule; or in other words the manner of arrangement of the individual components within the molecule.

### Ultimate Analysis of Nucleic Acids.

I shall touch only briefly on the first phase of the work, for the reason that it is of interest principally to the men personally engaged in it. The achievements obtained through that work are not very significant. Only in connection with the study of inosinic acid, a nucleic acid of beef muscle, the elementary analysis was of unmistakable service in ascertaining the composition of the substance. It was the first and thus far the only instance that a salt of a nucleic acid was obtained in a crystalline form. The fact that no other nucleic acid has been prepared in an absolutely pure condition renders the conclusions drawn from their analysis only of secondary value. The workers who contributed to the improvement in the methods of preparation of the substance are: Altman, Miescher, Schmiedeberg, Kossel, Neumann, Hammarsten, Bang, Haiser and myself.<sup>1</sup>

The methods of preparation and of purification of the substance employed by individual workers differed greatly either in principle or detail. Under such circumstances marked divergence was noted in the analytical figures obtained by different investigators for nucleic acids even of the same origin. The following table illustrates some of these discrepancies.

TABLE SHOWING THE ELEMENTARY COMPOSITION OF VARIOUS NUCLEIC ACIDS.

	C.	H.	N.	P.	O.	Base.
I. Thymonucleic acids of animal origin:						
1 Fisch sperni:						
a Salmon (Miescher and Schmiedeberg).....	37.8	4.5	15.8	9.7	33.2	.....
b Gadus (Levene).....	34.8	5.2	16.8	9.1	...	.....
c Homo (Katsuji and Inouye).....	37.5	4.4	16.0	9.7	...	.....
d Maifisch (Levene and Mandel).....	36.3	5.0	15.9	8.1	...	.....
2 Pancreas:						
a Ivar Bang.....	34.2	4.4	18.2	7.7	35.6	.....
b v. Fürth, and Jerusalem...	29.2	4.3	11.6	6.9	...	Cu = 14.2
3 Spleen (Levene).....	37.8	4.8	16.5	8.99	...	.....
4 Mammary gland (Levene and Mandel).....	34.7	4.4	15.6	8.5	...	.....
5 Intestinal wall (Katsuji Inouye)	37.5	4.8	15.5	9.4	...	.....
6 Thymus gland:						
a (Ivar Bang).....	35.8	4.2	15.3	9.3	...	Na — 6.25

<sup>1</sup> Altman, "Über Nukleinsäuren," *Arch. f. Anat. u. Physiol. Physiol. Abt.*, 1889, 524. Miescher, *Verhand. der naturforschenden Ges. in Basel*, 1874, 6, 138; *Arch. exp. Path. Pharm.*, 37, — (1896). Schmiedeberg, *Arch. exp. Path. Pharm.*, 43, 57 (1900). Kossel u. Neumann, *Ber.*, 27, 2215, (1894), Neumann, *Arch. Anat. und Physiol. Physiol. Abt.*, 1899, 552. Bang, *Z. physiol. Chem.*, 26, 133 (1898-9). Haiser, *Monatsh. Chemie*, 16. Levene, *Z. physiol. Chem.*, 32, 541 (1901); 37, 402 (1902-3); 45, 370 (1905).

	C.	H.	N.	P.	O.	Base.
<i>b</i> (Kostytschew).....	31.4	4.6	12.8	7.6	...	Ba — 17.5
<i>c</i> (Herlant).....	37.53	4.93	16.48	9.63	...	.....
<i>d</i> (Schmiedeberg).....	35.82	4.14	14.68	9.17	...	.....
II. Guanylic acid (animal origin):						
<i>a</i> Ivar Bang.....	34.28	4.39	18.21	7.64	34.48	.....
<i>b</i> Levene and Mandel.....	36.35	4.95	18.65	6.15	33.90	.....
III. Plant nucleic acid:						
1 Yeast:						
<i>a</i> Herlant.....	33.7	4.1	14.8	8.69	...	Cu — 10
<i>b</i> Levene.....	34.97	4.41	15.21	8.6	...	.....
2 Wheat embryo (Osborne and Harris).....						
	33.1	4.2	14.9	8.1	...	.....

In adopting an empirical formula for the nucleic acids the individual investigators were guided not only by the analytical figures, but also by considerations of a speculative nature based to some extent on information obtained on partial or complete hydrolysis of the acids. The basis for the speculations of the different workers varied considerably. This led to a great divergence in the views on the empirical formula of nucleic acid. The following table contains some illustrations of it:

	C.	H.	N.	O.	P.
Schmiedeberg <sup>1</sup> (sperminucleic acid).....	40	56	14	26	4
Stuedel <sup>2</sup> (thymus nucleic acid).....	43	57	15	26	4
Levene <sup>3</sup> (spleen nucleic acid).....	{54	71	20	37	5
	{43	55	15	31	4
Osborne and Harris <sup>4</sup> (wheat embryo nucleic acid).....	42	62	16	31	4
Kossel <sup>5</sup> (yeast nucleic acid).....	{17	26	6	14	2
	{25	36	9	20	3
Boas <sup>6</sup> (yeast nucleic acid).....	36	52	14	24	4
Levene <sup>7</sup> (yeast nucleic acid).....	38	50	15	29	4

### The Components of Nucleic Acids.

It has been stated that the first knowledge of the chemical nature of nucleic acids was limited to the information that it was a conjugated phosphoric acid. The first work of Altmann was followed by that of Kossel. The efforts of this investigator were directed towards the analysis of the products of hydrolytic cleavage of nucleic acids. His first achievement was the discovery of purine bases in the molecule of nucleic acids. These bases can be obtained on cleavage of nucleic acids with very dilute solutions of mineral acids. Kossel further devised methods for the separation of the individual bases. He arrived at the conclusion that four purine bases, namely, adenine, guanine, hypoxanthine and xanthine, enter into the molecule of nucleic acids. This view, however, was later revised as it was established that only two purine bases, adenine and guanine, actually enter into the composition of nucleic acids. Hypoxanthine and

<sup>1</sup> *Arch. exp. Path. Pharm.*, 57, 309 (1907).

<sup>2</sup> *Z. physiol. Chem.*, 46, 332 (1905).

<sup>3</sup> *Biochem. Z.*, 17, 120 (1909).

<sup>4</sup> *Z. physiol. Chem.*, 36, 85 (1902).

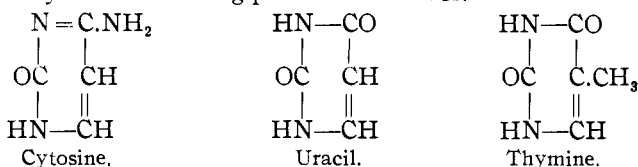
<sup>5</sup> *Arch. f. Anat. Physiol.*, p. 181 (1891).

<sup>6</sup> *Arch. exp. Path. Pharm.*, 55, 16 (1906).

<sup>7</sup> *Biochem. Z.*, 17, 120 (1909).

xanthine are now regarded as secondary products.<sup>1</sup> However, it was evident from the figures obtained on elementary analysis of nucleic acids, that their molecule contained substances other than purine bases. On the basis of the observation that on hydrolysis with dilute mineral acids only the purine bases are liberated and the other components remain intact, there was advanced a theory that in nucleic acids the phosphoric acid is combined with a complex radicle forming a conjugated phosphoric acid, and that this in its turn combined with the purine bases. The manner of this combination was the subject of considerable discussion and disagreement.

The efforts to elucidate the composition of the complex radicle resulted in the discovery of the following purine derivatives.<sup>2</sup>



However, in order to obtain these substances it was necessary to resort to the hydrolysis by means of mineral acids of considerable concentration. This procedure caused many investigators to express doubt as to the presence of the pyrimidine bases in the nucleic acid molecule. The doubt was particularly great regarding the origin of cytosine and uracil. R. Burian<sup>3</sup> with great persistence defended the view that these two bases took their origin in the partial cleavage of the purine ring. However, the majority of workers were inclined to consider cytosine also as a primary constituent of the molecule of nucleic acids, while uracil was considered a primary product in the acids of plant origin only.

Besides the purine and pyrimidine bases the molecule of nucleic acid was found to contain carbohydrates. The complex nucleic acids of animal origin contain a hexose, the exact nature of which is not yet established. The nucleic acid of plant origin and the simpler nucleic acid of the animal tissues contain a pentose. On the basis of the work of Neuberger<sup>4</sup> the pentose was considered *l*-xylose. However, very recently Jacobs and I have succeeded in isolating the substance in crystalline form. This made it possible to establish the true nature of the substance as *d*-ribose.<sup>5</sup>

As the methods of analysis had improved, and as approximately quantitative estimation of the components was made possible, it was found that in nearly all the acids the bases were present in approximately equimolecular proportions, that the number of molecules of phosphoric

<sup>1</sup> Levene, *Z. physiol. Chem.*, **45**, 370 (1905). W. Jones and Austrian, *J. Biol. Chem.*, **3**, 1 (1907).

<sup>2</sup> Kossel and Neumann, *Ber.*, **27**, 2215 (1894). Ascoli, *Z. physiol. Chem.*, **31**, 161 (1900-1). Kossel and Steudel, *Ibid.*, **37**, 177 (1902-3). Levene, *Ibid.*, **37**, 402, 527 (1902-3).

<sup>3</sup> R. Burian, *Ergebnisse der Physiol.* 3 Jahrg. 1 Abt., **98** (1904); *Z. physiol. Chem.*, **51**, 438 (1907). Steudel, *Z. physiol. Chem.*, **53**, 508 (1907). Osborne and Heyl, *Am. J. Physiol.*, **20**, 157 (1908). Levene and Mandel, *Biochem. Z.*, **9**, 233 (1908).

<sup>4</sup> Neuberger, *Ber.*, **32**, 3386 (1899).

<sup>5</sup> Levene and Jacobs, *Ibid.*, **42**, 2102, 3247 (1909).

acid corresponded to that of the bases, and the number of molecules of carbohydrate was equal to that of phosphoric acid.<sup>1</sup>

On the basis of these calculations, and on the basis of the numbers of the character of the bases entering into the molecule of the individual nucleic acids the following classification could be established:

1. Nucleic acids: Containing one purine base (no pyrimidine), a pentose and phosphoric acid. (Inosinic acid, guanylic acid.)
2. Nucleic acids: Containing two purine bases (guanine and adenine), two pyrimidine bases (cytosine and uracil) and phosphoric acid. (Phytoneucleic acids.)
3. Nucleic acids: Containing two purine bases (guanine and adenine), two pyrimidine bases (thymine and cytosine), and a hexose and phosphoric acid. (Nucleic acid of animal tissue—thymonucleic acids.)

### The Constitution of Nucleic Acids.

The early speculations regarding the constitution of nucleic acids were based on the results of partial hydrolysis by means of dilute acids or weak alkalis. Reference has been made already to the views expressed by Kossel.<sup>2</sup> By mere heating with water under increased pressure, this author thought he obtained a substance, which was free of purine bases, but contained all the other components of the original nucleic acid. The substance was named thymic acid. Nucleic acid was regarded therefore as a complex consisting of thymic acid and of purine bases. The author did not furnish any detailed information regarding the nature of thymic acid. Somewhat more definitely formulated was the view of Schmiedeberg. According to this author there existed a complex—nucleotin, this complex combined with phosphoric acid to form nucleotin phosphoric acid, and this acid in its turn combined with purine bases thus forming nucleic acid. Schmiedeberg ascribed to the nucleotin the formula  $C_{30}H_{42}N_4O_{13}$ . Alsberg,<sup>3</sup> working in Schmiedeberg's laboratory, actually succeeded in obtaining a substance which had the composition of the hypothetical nucleotin. However, these writers also failed to disclose the constitution of the complex radicle. In fact, they failed to furnish evidence that their substance was not a mixture composed of several cleavage products of nucleic acids.

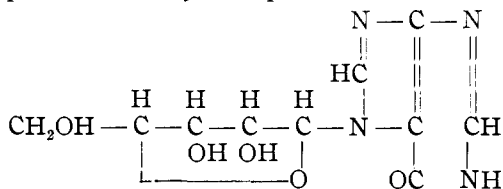
Results of actual significance for the interpretation of the structure of the nucleic acid were obtained only recently. The point of departure for the work was the study of inosinic acid by Levene and Jacobs. As has already been pointed out this acid is comparatively simple in its composition. It is composed of phosphoric acid, a pentose and hy-

<sup>1</sup> Schmiedeberg, *Arch. exp. Path. Pharm.*, 46, 57 (1900). Kossel u. Neumann, *Ber.*, 27, 2215 (1894). Kossel u. Steudel, *Z. physiol. Chem.*, 37, 119, 120, 121, 131, 177 (1902-3); 145, 377 (1903); 38, 49. Ascoli, *Ibid.*, 31, 161 (1900-1). Steudel, *Ibid.*, 42, 165 (1904); 43, 402 (1905); 44, 157 (1905); 46, 332 (1905); 48, 425 (1906). Osborne and Harris, *Ibid.*, 36, 85 (1902). Jones, W., and Austrian, *J. Biol. Chem.*, 3, 1 (1907). Levene, *Z. physiol. Chem.*, 37, 402, 527 (1902-3); 38, 80 (1903); 39, 4, 479 (1903); 43, 199 (1904); 45, 370 (1905). Levene and Stookey, *Ibid.*, 44, 404 (1904). Mandel u. Levene, *Ibid.*, 46, 155 (1905); 47, 140 (1906). v. Fürth u. Jerusalem, *Beiträge Chem. Physiol. u. Pathol.*, 10, 174 (1907).

<sup>2</sup> Kossel and Neumann, *Z. physiol. Chem.*, 22, 74 (1896-7).

<sup>3</sup> Schmiedeberg, *Arch. exp. Path. Pharm.*, 43, 57 (1900). Alsberg, *Ibid.*, 51, 239 (1904).

poxanthine. Through prolonged action of dilute acid at the temperature of 50° it was possible to break up the molecule into hypoxanthine and a pentose-phosphoric acid.<sup>1</sup> This substance was obtained by Jacobs and myself in the form of its crystalline barium salt. This acid had all the properties of a conjugated phosphoric acid, and on cleavage yielded the phosphoric acid. The acid reduced Fehling's solution on heating without previous hydrolysis. It was concluded from this that in the molecule the phosphoric acid and the carbohydrate are bound in ester-form, and that the aldehyde group of the pentose phosphoric acid was free and that therefore in the inosinic acid the base and pentose were coupled in a glycoside union. This assumption was strengthened by the fact that inosinic acid was found to be very resistant towards the action of alkalis even at fairly high temperatures, and even on prolonged boiling the acid underwent only partial hydrolysis with formation of phosphoric acid and of the complex: pentose-base. Furthermore, it was found that by hydrolysis at nearly neutral point the conditions for the reaction were more favorable and it was possible in this manner to isolate and to identify the pentoside-inosine (C<sub>10</sub>H<sub>12</sub>N<sub>4</sub>O<sub>5</sub>). On the basis of this we concluded that the order of combination of the components in the molecule of the inosinic acid was established. I could add here that only on hydrolysis of the pentoside was it possible to obtain the crystalline sugar which was identified as *d*-ribose. The structure of the complex pentose-hypoxanthine may be represented in the following manner:



The same substance had been found by Haiser and Wenzel in beet extract.<sup>2</sup>

Regarding the place of the purine base which entered into union with the sugar, there still remains only the evidence of Burian that place 7 is attached to the sugar and no information exists regarding the place of the hydroxyl in the pentose that is coupled with the phosphoric acid.

The following step in the progress of the work was the application of the experience obtained on inosinic acid to the other nucleic acids. Jacobs and I next directed our attention to the remaining acid of comparatively simple composition, namely guanylic acid. Employing the same methods of hydrolysis as applied to inosinic acid, we obtained guanosine (C<sub>10</sub>H<sub>13</sub>N<sub>5</sub>O<sub>6</sub>), a substance analogous to inosine; it possessed nearly the same crystalline form, differed in its physical constants, and on hydrolysis gave guanine and the same pentose as the inosine, namely *d*-ribose. This pentoside had the same properties as inosine in its behavior towards alkalis and acids.<sup>3</sup> For the sake of convenience we named the substances of this order "nucleosides" and the combination of the nucleoside and phosphoric acid we named "nucleotides." Thus according to that nomencla-

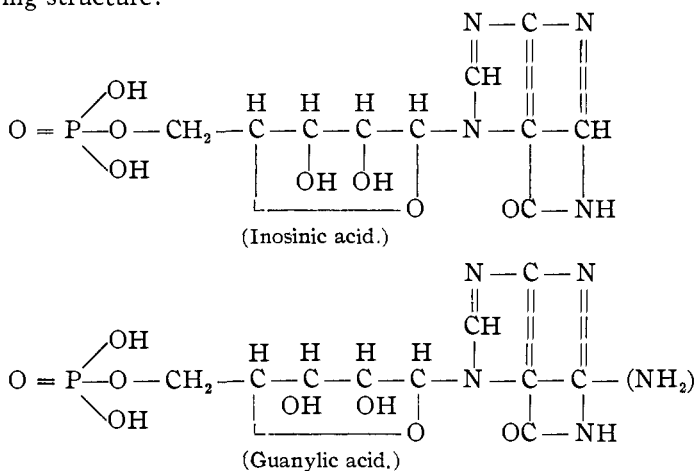
<sup>1</sup> *Ber.*, 44, 2703 (1908).

<sup>2</sup> Haiser and Wenzel, *Monatsh. Chem.*, 29, 157 (1908)

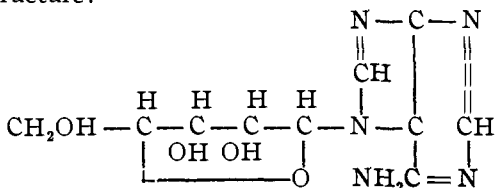
<sup>3</sup> *Ber.*, 42, 2474 (1909).



ture inosine and guanylic acid were to be regarded as mononucleotides of the following structure:



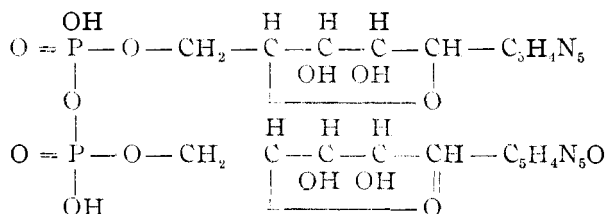
The further application of the same methods to a more complex nucleic acid, to that of the yeast, led to the conviction that this also was composed in the same manner. Thus the same nucleoside-guanosine, as obtained from guanylic acid, was also found on hydrolysis of the yeast nucleic acid. When the proper conditions are observed the nucleoside can be chilled out and a nearly quantitative separation accomplished. In the filtrate from this nucleoside other substances of the same nature were expected. On the basis of considerations expressed by me in an earlier article on the composition of the yeast nucleic acid the molecule of the acid is composed of four nucleotides and therefore four nucleosides should be found on cleavage of the substance. The work in that direction is of comparatively recent date, and a second nucleoside has already been obtained from the mother liquor of guanosine.<sup>1</sup> The second nucleoside has practically the same crystalline appearance as inosine or guanosine, and differs from these two only by its physical constants and by the fact that on hydrolysis it yields in place of guanine the base adenine, and is, therefore, named adenosine. Also on hydrolysis of this nucleoside the crystalline *d*-ribose is obtained. The substance therefore had the following structure:



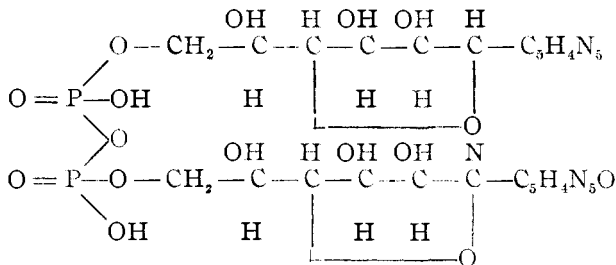
It possesses the melting point of 229° and the rotation:  $[\alpha]_D = -67.30^\circ$ . On the ground of this the structure of the yeast nucleic acid may be presented in the following manner:<sup>2</sup>

<sup>1</sup> Levene and Jacobs, *Ber.*, **42**, 2703 (1909).

<sup>2</sup> Bloch, *Zeitsch.*, **120**, 17 (1909).



All this work is of comparatively recent date so that as yet it could not have been extended to the analysis of thymonucleic acid. But evidence had been furnished that this substance also has a structure analogous to that of the yeast nucleic acid.<sup>1</sup> In fact considerations based on the work on thymus nucleic acid were the first that led to formulating the structure of the complex nucleic acid as a polynucleotide, of which the individual mononucleotides were composed of phosphoric acid, sugar and base. Levene and Mandel have on hydrolysis of the spleen nucleic acid with dilute sulphuric acid obtained a substance which had the elementary composition ( $\text{C}_{11}\text{H}_{17}\text{N}_2\text{PO}_{10}$ ) of a complex consisting of phosphoric acid, hexose and thymine. On cleavage with 25 per cent. sulphuric acid this body gave rise to phosphoric acid, levulinic acid and thymine. This assumption is in harmony with subsequent discoveries on the simple nucleic acid and on the yeast nucleic acid, and one feels justified in formulating the structure of thymonucleic acid in the following manner:



Thus the details in the structure of the molecule of nucleic acids are not yet known. But some general information is already obtained and the route is singled out, by which the solution of the problem will be reached. An indication is given for a point of departure for the work on the synthesis of these substances. Work in that direction is now in progress in our laboratory.

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### NEW BOOKS.

**General Inorganic Chemistry.** By CHARLES BASKERVILLE, Ph.D., Professor of Chemistry in the College of the City of New York. Boston, Mass.: D. C. Heath & Co. 1909. pp. vii + 357.

This book is of considerable interest as Professor Baskerville has departed from what has become the more or less standard method of pre-

<sup>1</sup> *Ber.*, 41, 1905 (1908).