CLARK UNIVERSITY

Celebration Lectures In Chemistry

1909


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CHEMICAL ADDRESSES

Delivered at the Second Decennial Celebration of

CLARK UNIVERSITY,

in September, 1909,

BY

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With a Preface by

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PREFACE.

Clark University was founded in 1889 as a *research university*, an institution in which the best part of the teaching and studying should be carried on through original investigation. On the one hand, and primarily, the University was to devote its activities to the advancement of scientific knowledge. On the other hand, it was believed that genuine knowledge and habits of independent thought can in no way be acquired by the mature university student as surely as through the labor of finding new truth.

While the new university has not perhaps attracted such attention from the public at large as it would have received had it been attended by large numbers of students, it soon gained a high reputation among men of science both at home and abroad. It has been stated by good authorities that the example of Clark University has had a profound influence on the ideals and organization of the American graduate schools established since 1889.*

At the time of its foundation Clark University was almost unique in this country in its ideals and methods. Even at present it can boast the distinction of having none but research professorships: chairs unhampered by the burdens of elementary teaching and routine administrative work. If any member of the University, professor or student, fails to contribute his share to the advancement of his science and thus himself gain greater and greater mastery over it, the fault is not that of the University's organization.

It seemed appropriate that the anniversary celebration of Clark University should consist in a series of research conferences, and the present volume reproduces most of the chemical addresses of the Celebration. In organizing the conferences, an effort was made to have all the more important chapters of American chemical research represented, and the effort was in large measure successful, owing to the generosity with which a majority of our chemical investigators responded to the Department's invitation.

The technical addresses have been gradually published in the *Journal of the American Chemical Society*, the educational addresses in *Science*.

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*For example, Professor Stieglitz, reviewing the progress of American chemical research, says: "The greatest recent impetus to all branches of research, including chemistry, came, in my opinion, from the founding of Clark University, with research as its chief and almost exclusive field. . . ." (See *Science*, Vol. XXVI, p. 700, for the year 1907.)

The Chemical Department of the University wishes to again express its deep appreciation of the honor bestowed upon it by the brilliant lecturers, and its confidence that their joint effort here will not have been without fruit.

The Department, which has recently been placed under the directorship of the present writer, also wishes to assure the chemists of the country that it is making a veritable effort to grow to the ideal of Clark University, which is the ideal of all sincerely scientific men.

M. A. Rosanoff.

November, 1911.

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RECENT INVESTIGATIONS IN THERMOCHEMISTRY.[1]

BY THEODORE W. RICHARDS.

Received September 17, 1909.

Within a brief space of time, the world has lost two masters of thermochemistry, Marcellin Berthelot and Julius Thomsen. To these great men chemical science owes much; their places in its history are forever secure. Each, by his indefatigable labors, added both new methods and new data to the sum of human knowledge; and upon the broad foundation which they laid, all the subsequent development of thermochemistry must be built. All honor to their memories! It is no discredit to their faithful work that as science progresses many of their methods must be subjected to revision and refinement, for mankind approaches precision only little by little, and those workers who come later have the benefit of all that has gone before, with fresh energy and new years with which to improve upon it. In the same way, a few decades hence, others will perhaps remodel the not yet perfect work of the present generation, may possibly marvel at inaccuracies which have escaped our detection, and will have opportunities for the exercise of charity similar to those which fall to our own lot.

It is not necessary to emphasize the importance of thermochemistry, or to trace in detail its history. You know that the first law of energy was applied in this science by Lavoisier and Laplace, and by Hess, before it was generalized by Mayer, Joule and Helmholtz. You are familiar with the fact that Berthelot and Thomsen and Stohmann and others utilized this principle to determine the heats of formation of most common substances with some degree of approximation; and that these data constitute the sum and substance of our knowledge of the heat evolved during chemical reaction.

Before we consider the revision of these multifarious data which is now in progress, it is worth while to pause for a moment and think of their significance.

Thermochemistry is concerned with the total energy-change of a chemical reaction, and not with the change of the free energy, hence it cannot serve as an infallible guide to the tendency of a reaction, for preponderance of free energy, not of total energy, determines the path which a change will take. Nevertheless, in spite of this limitation, thermochemistry includes some of the most important facts of the universe within its scope, both for the theorist and the practical man.

The total heat given out during any chemical change is one of the fundamental thermodynamic data concerning that change. Its exact evaluation is necessary to the complete understanding of the thermodynamics of any reaction, and without an understanding of the thermodynamics of a reaction, the phenomena are only half interpreted. Although free energy change is that which determines the tendency of the reaction, bound energy is also significant, and the interpretation of bound energy is being realized more and more generally as one of the coming problems in thermodynamics. But bound energy is the difference between total

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[1] Presented at the Second Decennial Celebration of Clark University, Worcester, Mass., on Sept. 16, 1909.

energy-change and the free energy-change, so that all these three quantities are as closely connected together as is possible. In short, the accurate determination of thermochemical data is essential to the precise application of thermodynamics to chemistry.

To the practical man, perhaps, the matter takes on a different aspect—although ultimately he, too, will profit more than he can now appreciate from the growth of pure thermodynamics. He is more immediately concerned with the every-day applications of thermochemistry, especially the developments of heat by combustion. Our text-books of chemistry discuss the union of carbon and oxygen with chief emphasis upon the formation of carbon dioxide, but that is the least important practical aspect of the matter. The really essential thing is the liberation of energy, a fact which falls within the province of the thermochemist. Numerous other reactions less striking but no less important, including the maintenance of our own bodily heat, are concerned with the same principles and methods. Hence it is not too much to say that thermochemistry is intimately related with every breath we draw. The accurate evaluation of its fundamental quantities is, therefore, one of the most important fields of scientific advance, because accurate data are needed to provide an adequate basis for precise thinking in an inductive science.

Let us consider systematically the dimensions concerned, in order that we may more clearly appreciate the advances which have been made possible in thermochemical work during the years which have elapsed since Berthelot and Thomsen carried out most of their work. The energy of heat is, of course, calculated as the product of two factors, temperature and heat capacity, and the accuracy of its determination is directly proportional to the accuracy of measurement of each of these dimensions.

The advances in the accurate measurement of temperature during the last thirty years have been very great. In the first place the standard of reference, namely the hydrogen scale, has been fixed with much greater accuracy than at that early time. There is very little evidence as to what the centigrade degree, as used by Thomsen or Berthelot, really meant. In the next place, the vagaries of the glass-mercury thermometer have been studied by Crafts and others with much greater completeness and understanding than in those earlier days. We know now how uncertain its indications may be when it is not properly handled; and we know, also, how to obtain very accurate results from this instrument when it is properly made and carefully used. Again, thermometry has gained through the introduction of new fixed points between the old classic ones of the early history of thermometry; I mean the transition temperatures of bi-component systems. These give a firm basis for a thermometric scale in their neighborhood and thereby contribute to its certainty and definiteness. All these things must be considered in the thermochemistry of to-day and all contribute to an accuracy exceeding that of olden times.

A further gain has to be found in the introduction of the new methods of measuring temperature electrically, which, when properly manipulated, may exceed in accuracy the readings of the mercury thermometer. One must not forget, however, that these methods are subject to their own peculiar and somewhat elusive sources of inaccuracy, and that their use does not yield the unqualified gain which is sometimes attributed to them.[1]

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[1] Emil Fischer and F. Wrede have made some excellent determinations in this way.

Turning now to heat capacity, we find that to some extent the same considerations apply. Heat capacity is, of course, determined by comparison with a standard substance, and the comparison is made by means of some kind of thermometer. The sources of error are partly eliminated here, however, because the determination is a purely relative one and does not hark back to the absolute standard, as in the case of temperature change. Specific heats are reckoned by finding the rise of temperature in two approximately equivalent masses of substance, one the standard substance and the other the substance to be determined. If the same thermometer is used in each and the quantities of substance are so adjusted that the temperature changes produced by a known quantity of heat energy are nearly the same, the inaccuracies of the thermometer are largely eliminated when the same thermometer is used as a standard in each set of determinations. Errors of reading the thermometer still appear, and indeed the range of inaccuracy here is doubled, because a specific heat determination depends upon four thermometer readings whereas temperature change depends upon only two. Obviously, however, an error in the standard interval makes no difference. The degree might really be two degrees and its inaccuracy would cancel. Hence, although the thermometer is used for determining heat capacity, the uncertainties of the determination arise in part from a different source and are chiefly to be traced to the errors of calorimetry, which deserve and will receive detailed consideration in a few minutes.

Before discussing the errors of calorimetry let us for a moment discuss the means of calculating the heat capacity of a given system which have been used in the determinations now accepted by the chemical world. We find upon studying the literature of the subject, that there has been considerable variety of usage, but that the usage has rarely, if ever, been precise. Marignac determined a number of specific heats by means of a kind of calorifer, and Thomsen also determined many by means of his combustion calorimeter, but these were seldom in either case within two-tenths of one per cent. Therefore the values calculated from them could not be expected to be closer than this, if as close, to the truth. Work of others has not yet actually been used. Berthelot relied largely on Marignac's determinations or more commonly adopted very rough approximations by assuming that the heat capacity of the solution is equal to that of a like volume of water—in other words, that the specific heat of a solution is inversely proportional to its specific gravity. This method of calculating may easily yield results several per cent. aside from the truth with concentrated solutions.

Moreover, we find a general haziness concerning the question as to whether the heat capacity of the factors or of the product of reaction is to be used in the calculation. Should one multiply the temperature rise by the heat capacity of the factors in order to obtain the heat evolved, or is it the products which must be considered as having been raised through the range of temperature in question? Only very recently has this question been answered scientifically, and its answer is simply this: either the one or the other may be used, provided that it is used intelligently. When the heat capacity of the factors is used in calculating the result, this result corresponds to the heat evolved by the reaction occurring isothermally at the final temperature attained when the adiabatic change is completed, whatever that may be. On the other hand, when the heat capacity of the products is used, the result corresponds to the heat of isothermal reaction at the initial temperature. When there is no change of heat capacity during the reaction, the results of the two methods will, of course, be identical. In other words, in this last case the heat evolved will be independent of the temperature at which the reaction takes place, according to the well-known thermodynamic rule of Kirchhoff.[1]

Further uncertainty concerning heat capacity arises from the fact that the specific heat of the standard substance, water, changes with the temperature and that therefore no expression for heat capacity is definitely fixed without a qualifying phrase. In order to overcome this disadvantage a proposition of Ostwald's to use the absolute C. G. S. scale has been revived and a convenient standard of heat capacity, namely the capacity raised one centigrade degree by one joule of energy, has been chosen. This unit fixes the dimension of heat capacity much more definitely than the old uncertain and changing one. Out of respect to the memory of one of the founders of the first law of energy, the name "mayer" has been suggested for this unit and its introduction seems to afford help in teaching as well as to add precision to scientific statement.[2]

In the coming revision of thermochemical data all the early incompletenesses in these respects will be eradicated, and the matter will be put upon the best basis possible to-day.

What now are the chief errors of calorimetry, which affect both the determination of specific heat and of reaction heat?

Any one with any calorimetric experience whatsoever will recognize that the greatest cause of uncertainty in results of this kind is the cooling effect of the surroundings of the calorimeter. The errors of thermometric reading, of the lag of the thermometer behind the temperature of the surrounding medium, and all other uncertainties are trifling compared with this. Therefore precise calorimetry is largely a question of properly correcting for this cause of uncertainty, or else avoiding it altogether. The well-known methods of Rumford and of Regnault as amplified by Pfaundler, serve to a certain extent to correct for the effect of the exchange of heat with the environment. But the former, although it has been much used in thermochemical work, is greatly at fault; and the latter, although far better, is still imperfect. Rumford started his determination as much below the temperature of the air around as he finished above this temperature, supposing that the intake of heat during the first part of the operation would balance the outgo during the latter part. We have been able to show that this is by no means the case—at any rate in a vessel containing a solution and enclosed in a jacket of definite temperature. Hence Rumford's method is not a very close approximation. The Regnault-Pfaundler method depends upon Newton's law of cooling, which under certain circumstances has been shown to be fairly accurate. We must remember, however, that the cooling of the vessel is due to convection and conduction as well as to radiation, so that the exact fulfilment of Newton's law is hardly to be expected. Moreover the evaluation of the rate of cooling depends upon the taking of a number of thermometric readings which are "caught on the wing," as it were, while the thermometer is moving. Hence, although the Regnault-

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[1] Richards, This Journal, 25, 209 (1903).

[2] *Proc. Amer. Acad.*, 36, 327 (1901).

Pfaundler method may serve with sufficient approximation for quick reactions, it still leaves much uncertainty in reactions which extend over many minutes; and even in quick reactions the lag of the cooling correction may introduce some error. Further, many fundamental processes are slow; and among them must be catalogued the determination of specific heat, or heat capacity, because considerable time is needed as a rule to communicate the heat to the substance to be studied.

It was with a view to eliminating these disadvantages that there has recently been put into practice at Harvard a method of calorimetry which wholly eliminates the correction for cooling by causing the temperature of the environment around the calorimeter to change at the same rate as the calorimeter itself. It is surprising that this obvious and easily carried out device had not been applied before. It had, indeed, been suggested by S. W. Holman[1] in 1895, although this paper was unknown to me at the time of the first Harvard work. The somewhat similar device used in the respiration calorimeter of Atwater and Benedict, suggested perhaps even before this, is not exactly comparable. In the respiration calorimeter the environment is not essentially changed in temperature. It is merely kept constant, as is also that of the calorimeter, by a suitable quantitative cooling device. Hence, so far as I am aware, the Harvard device was the first one in which the surroundings of the calorimeter were changed in temperature by any considerable amount during the progress of the experiment.

If the surrounding jacket about a calorimeter is thus changed in temperature at exactly the same rate as the temperature of the calorimeter itself, it is obvious that the calorimeter will neither gain nor lose heat from its equally hot surroundings, excepting for the negligible quantity of heat required to warm the small quantity of air immediately in contact with it inside the jacket. Thus a calorimetric reaction may be made really adiabatic.

Obviously there are several ways in which the outside water jacket in a calorimeter might be heated in order to accomplish this purpose. The simple device of pouring in hot water might be employed, or the water might be warmed by an electrically heated resistance coil, or the jacket itself might be made the scene of a chemical reaction of the same speed and thermal intensity as that within the calorimeter itself.

Of these and other methods which suggested themselves the last named seemed the most convenient and suitable for a chemical laboratory. It has the special advantages that before the beginning of operations all the apparatus and material employed may be at the temperature of the room; that the maximum temperature attained may be easily calculated with great nicety; that no point in the system can ever exceed this maximum temperature, if the reaction is suitably chosen; and that the speed of the reaction may be simply regulated by a stop cock admitting one of the reacting substances. A reaction easily regulated and well suited to this purpose, namely, the neutralization of an alkali with an acid, was chosen for this purpose.

The form of apparatus originally devised consisted of a lower jacket containing alkali and a separate movable lid. More recently we have found it convenient to enclose the calorimeter wholly in a water-tight vessel—a sort of submarine, provided with suitable conning towers or

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[1] *Proc. Am. Acad.*, **31**, 252 (1895).

periscopes.[1] This water-tight compartment is wholly immersed in the alkali to which is added, little by little, sulphuric acid in order to keep the bath precisely at the same temperature as the interior, however much this may be changed. Violent agitation of the warming alkali is necessary in order that the heat may be quickly distributed throughout the whole mass, and the interior of the calorimeter must be agitated also more energetically than has usually been the custom, if great precision is needed. In passing, I may state that we have evidence showing that in the past no one has stirred his calorimeter violently enough. The burettes delivering the sulphuric acid into the alkaline environment are graduated in tenths of degrees, instead of in cubic centimeters, so that a small deficiency in temperature may be instantly corrected with a minimum of mental arithmetic.

This form of chemical calorimeter serves not only to determine with great accuracy specific heats, but also to estimate the thermal output of all forms of chemical reactions. With it series of determinations of many kinds are in progress.

In the first place let me describe somewhat more closely the determination of specific heat with this apparatus, because upon this determination the calculation of all other thermochemical results must depend. Within the platinum calorimeter, enclosed in its submarine, is immersed a small platinum bottle; and inside of this bottle a carefully measured chemical reaction is allowed to take place which communicates its heat to the calorimeter. By placing in the calorimeter, in the first place water, and in the next place the unknown liquid whose specific heat is to be determined, and each time allowing the measured reaction to occur within the innermost platinum bottle, a direct comparison of the specific heats of the standard and the unknown liquid is obtained. As the results agree within one-twentieth of one per cent., the average of many experiments must be much nearer than this, and it is not unreasonable to believe that the results thus obtained are at least five times as accurate as those of Thomson or Marignac.

Having used this device and method for determining the specific heats of liquids, it is now possible to proceed with the more accurate evaluation of reactions in which liquids take part. In two recent investigations the heats of neutralization of the acids and alkalis on the one hand and the heats of solution of metals in acids on the other hand have been studied. Time does not permit the detailed statement of the various precautions necessary in these determinations. The former problem is of special interest because of its relation to the theory of electrolytic dissociation, and our revision of this work was prompted by the desire to discover the extent of the deviation of the several results for strong acids from the constant value, 137 calories or 57 kilojoules. Several unexpected points were brought out in the investigation, the most important being the irregularities in the results produced by the unequal distribution in heat during mixing and also the grave errors caused in previous results by the presence of carbonate in the alkali. The investigation is not yet finished, but has already shown that many of the accepted results are much in error even for this simple process of neutralizing an acid by an alkali.

The heats of solution of metals in acids are among the most essential

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[1] A device of this kind was employed by Richards and Forbes, *Publications of the Carnegie Inst.*, 56, 52 (1906).

and fundamental of thermochemical data. The heats of formation of all the metallic compounds depend upon them, because through them the heat values are referred back to the element. Hence it is highly important for exactness in thermochemistry that these values be determined with great precision.

As a matter of fact, in the past certain difficulties have interfered with the perfection of the measurements. First and foremost among these is the fact that the heat of solution of a metal requires much time, and therefore the always somewhat uncertain correction for cooling in the usual method becomes a serious fraction of the whole rise of temperature. In the second place, the method generally used—namely, the plunging of a weighed sheet of metal into acid, and then withdrawing it, checking the reaction as soon as possible, and determining the amount dissolved by loss in weight—is open to serious criticism. It is impossible that the withdrawal should be so quick as to introduce no error in the result.

The new method of adiabatic calorimetry, recently used at Harvard, seems to be especially suitable for such cases as this. With it cadmium, zinc, magnesium, aluminium and iron have already been investigated, and very concordant and satisfactory results have been obtained. Here again much greater purity of material than has been usual in work of this sort was sought, and the results justify the trouble thus taken. There can be no doubt that in these cases also the older work was defective.

The heats of combustion of organic substances form another very important field for thermochemical research. These reactions carried out in the calorimetric bomb of Berthelot seemed especially suitable for the application of the new method of calorimetry, and formed indeed one of the first series of experiments to which it was applied. The combustion of solid substances such as sugar presents no difficulty and imagination can easily picture the way in which this process might be carried out in an adiabatic calorimeter. Several long series of experiments with typical substances of this sort have been made in order to test the method, with satisfactory results.[1] The combustion of liquids is a more difficult problem. As you well know, Thomsen endeavored to burn liquids by first vaporizing them with the help of electrically generated heat in his so-called "universal burner." We now know that some of the superfluous heat from the electric coil must have found its way into the calorimeter, so that these results are usually too high. Berthelot and Stohmann on the other hand, determined the heat of combustion of organic liquids by saturating cellulose with the liquid, which was then ignited in the bomb. This latter method of procedure is evidently open to the error caused by a varying loss of the organic liquid by evaporation. Not all the vapor of the organic liquid spread throughout the bomb is capable of being burnt, hence Berthelot's results for volatile liquids are probably all too low. The truth would be expected to lie somewhere between them Thomsen's results for the more volatile liquids being probably the more accurate because there the accidental heating from his apparatus was unimportant, and Berthelot's results for the less volatile liquids being better because there the loss through evaporation would cause less error.

We sought to overcome these difficulties by enclosing the organic liquid in a small, very thin glass bulb, flattened on the sides and completely

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[1] *Proc. Amer. Acad.*, 42, 573 (1907).

full of liquid. No difficulty is found in making such bulbs, and they will stand several hundred atmospheres of pressure without bursting, if completely full of liquid, because the glass of the flattened sides is sufficiently flexible to permit of considerable compression. These closed glass bulbs were put inside the bomb in a very small platinum crucible, and upon a thin glass shelf above them was placed a small weighed quantity of powdered sugar. The sugar was ignited first in the usual way. This exploded the bulb and instantly lighted the vapor of the liquid at all points so that none escaped combustion. In this way we have been able to show that the heat of combustion of volatile organic liquids is as a rule distinctly higher than Stohmann and Berthelot supposed it to be. We have unquestionable evidence that complete combustion of their vapor has at last been attained. These methods open the way to an unlimited amount of further experimentation, and promise to afford results upon which interesting theoretical considerations may be founded.

It is a pleasure to acknowledge my thanks to my several assistants, Professor A. B. Lamb, and Drs. L. J. Henderson, G. S. Forbes, H. L. Frevert, A. W. Rowe, R. H. Jesse, Jr., and L. L. Burgess for their expert assistance in these protracted and often tiresome researches, as well as to express my obligations to the Cyrus M. Warren Fund of Harvard University, the Rumford Fund of the American Academy of Arts and Science and especially to the Carnegie Institution of Washington, for generous pecuniary help in the prosecution of the work.

Before closing let me review briefly the recent advances in thermochemistry which I have attempted to enumerate. In the first place, the thermometric scale has been far more definitely fixed than it was thirty years ago. In the next place, the determination of specific heat and therefore of heat capacity has been put upon a scientific basis and its precise treatment in the calculation of thermochemical results has been pointed out. In the next place the most serious correction for all thermochemical results in the past, namely the cooling correction has been entirely obviated by the use of the method preventing loss of any heat from the calorimeter by enclosing the latter in a jacket of similarly changing temperature. Again the necessity for more active agitation of the contents of the calorimeter has been demonstrated, and the necessity of the use of very pure materials has been put beyond question. In every case the effort has been made to insure the completeness of the reaction and to correct for any side reactions which may take place at the same time, so that the final results may represent truly the data sought. In short the effort has been made to apply to these fundamental figures concerning chemical energetics the same kind of precision which has recently been attempted in the revision of atomic weights; and although on account of the greater complexity of the problem the percentage accuracy thus far reached has probably not equaled that in the case of atomic weights, one cannot help thinking that the proportional gain over the previous investigations is perhaps as great in this case as in the other.

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MOLECULAR REARRANGEMENTS.[1]

By William A. Noyes.

Received September 16, 1909.

"The end of chemistry *is its theory.* The guide in chemical research *is a theory*" (*Phil. Mag.* [4], **16,** 104 (1858)). With these words A. S. Couper began one of the most remarkable papers in the history of chemistry. At the time when he wrote the system of types advocated by Gerhardt had come into very general favor. Chemists were busy arranging the compounds of carbon and of other elements as well, in classes according to a few simple types, especially in accordance with the type of water and its multiples. The advantages of the system in comparison with what had gone before were very evident and organic chemistry was making rapid progress with its aid. It answered very well for the classification of many of the compounds then known and as a guide in the discovery of a great many new ones. And most of the chemists of that day, as always, were satisfied in working away at the discovery of a vast array of new facts and marshaling these in accordance with a highly mechanical theory with very little thought about its philosophical basis.

Under these conditions two master spirits, Couper and Kekulé, succeeded, entirely independently, in grasping those simple principles which lie at the foundation of our knowledge of the structure of compounds of carbon. Only as the result of an unfortunate accident was Kekulé's paper published before that of Couper.

It is interesting, and I think profitable, for us to recall that it was chiefly a consideration of the philosophical basis for Gerhardt's system which led Couper to reject it and propose something better. In criticizing the system he says of Gerhardt "He is led, not to explain bodies according to their composition and inherent properties, but to think it necessary to restrict chemical science to the arrangement of bodies according to their decomposition, and to deny the possibility of our comprehending their molecular constitution. Can such a view tend to the advancement of science? Would it not be only rational, in accepting this veto to renounce chemical research altogether?"

I have dwelt thus on Couper's point of view because it carries with it, as it seems to me, a lesson which we chemists of to-day may well take to heart. Very few are gifted with the insight of a Dalton, a Faraday, a Couper or a Rutherford but when a glimpse of the real things which lie beneath the phenomena which we observe comes to such an one it may guide the development of science for a decade, for a century, or even, if sufficiently true, for all time. And it seems possible that if we directed our thoughts more toward fundamental problems instead of towards the accumulation of compounds and of facts which are little more than permutations of compounds and facts already known, more real progress could be made.

The new principles proposed by Couper were very simple: First, that atoms show "degrees of affinity" or as we should call it, valence, and second, that carbon atoms can combine with each other. But these two simple principles have been the foundation on which chemists have built a knowledge of the structure of one hundred thousand compounds of

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[1] An address delivered at Worcester, Mass., September 14, 1909, at the celebration of the twentieth anniversary of Clark University.

carbon. These principles involve a knowledge of the actual arrangement of atoms within the molecule in the sense of the order of their successive attachments to each other. Thus far, at least, they are accepted by all active workers in organic chemistry and there is, among these, a practically universal belief that atoms and molecules actually exist and that there is something in the structure of the molecules which actually corresponds to our formulas. The two principles just stated have been further extended, especially by the study of optically active and of cyclic compounds to include still more definite ideas with regard to the actual arrangement of atoms in space and this development of stereochemistry has also received very general, though not quite universal, acceptance.

For a clearer understanding of molecular rearrangements we are in need of more definite knowledge with regard to the nature of those interatomic forces or attractions which hold atoms together in molecules and which also cause atoms of different molecules to react with each other. Many theories with regard to these forces have been proposed but none has, as yet, received any very general acceptance and the majority of chemists feel that any satisfactory knowledge of this sort is beyond our reach. But in 1858 nearly all chemists believed that any definite knowledge of the arrangement of atoms in chemical compounds was impossible, yet all of the facts for the acquirement of such knowledge were already in their hands and it only needed a clear statement of the simple principles proposed by Couper and by Kekulé and the application of those principles in the explanation of facts already known to make clear the structure of a large number of substances. Is it not possible that the answer to other, equally fundamental questions lies at our hands to-day?

It is in the hope that this may be so that I shall venture to state some of these fundamental questions as they present themselves to me.

The first of these is as to the nature of the attractive forces between atoms. The question is, perhaps, bound up with that of the nature of attraction between material bodies in general and may be equally far from a solution. Newton seems to have assumed an attractive force as an inherent property of matter and most of the discussion of atomic forces starts with a similar tacit assumption. But, as soon as the question is raised the mind revolts against the assumption of a force exerted through space without a medium. Physics has abandoned any idea of inherent attractive or repulsive forces in sound, light, heat or electricity and has accepted a kinetic explanation instead. Is it not probable that we must ultimately do the same for atomic forces? The discoveries in connection with radium have made us familiar with the notion that the atoms are very complex in their structure and that their parts may possess an almost inconceivable amount of kinetic energy. The spectroscope long ago demonstrated to us that such an atom as that of iron can send out impulses through the ether similar in complexity to those impulses of sound which come from a whole orchestra. It seems altogether probable that these impulses come from motions *within* the atom and not from vibrations of the atom as a whole. If we think of such intraatomic motions as general and that such motions within the atoms may produce effects which are transmitted through the ether, a kinetic explanation of atomic and molecular attraction seems possible.

The second question with regard to the atomic forces is whether these forces are purely attractive, resembling gravitation, or polar, partly attractive and partly repulsive, resembling or identical with electrical forces. You are all familiar with the fluctuation of opinion on this point. During the first half of the nineteenth century chemists came gradually to a pretty general agreement that the atomic forces are electrical in their nature. Then came the discovery of the substitution of chlorine for hydrogen in organic compounds and the overthrow of the old dualistic, electrochemical theory. Then for several decades the question of any connection between electrical and atomic forces was generally ignored and the attractions of the atoms were considered as direct and positive, though, of course, specific in character. During the last twenty years, as the theory of Arrhenius with regard to electrolytic dissociation or ionization has come into quite general favor, many different writers have proposed theories which identify atomic attractions with electrical forces. Faraday's law and the whole group of phenomena which find their most satisfactory explanation in the theory of ionization point very strongly toward an intimate relation between the two in the case of electrolytes. But if we assume that the forces which hold atoms together in electrolytes are electrical it is difficult to escape from the conclusion that the forces are electrical in the molecules of non-electrolytes also, for the two classes pass over into each other so gradually that it is very hard to believe that after the line is passed we are dealing with a radically different kind of atomic force. Further than this, an electrolyte may be formed in many cases by two different processes, by double decomposition in solution and by the direct union of the elements. Hydrochloric acid, acetylene and probably methane (from zinc methyl and by direct union of carbon and hydrogen) may be cited as illustrations. The nature of the compounds does not seem to depend at all on whether they are formed by the one process or by the other.

The idea that organic reactions are all ionic in character enables us, also to understand many reactions not so easily understood otherwise. Thus ethyl alcohol gives with phosphorus pentachloride, chlorethane, while phenol gives with the same reagent partly chlorobenzene, partly phenyl phosphate. If we assume, as seems natural, that ethyl alcohol ionizes to ethyl and hydroxyl while phenol ionizes partly in the same way but chiefly to hydrogen and phenoxy ions these reactions become clear:

$$4C_2H_5^+ + 3OH^- + O^{--} + H^+ + P^{+++++} + 5Cl^- = 4C_2H_5Cl + H_3PO_4 + HCl$$

or

$$4C_2H_5^+ + 4OH^- + PCl^{++++} + 4Cl^- = 4C_2H_5Cl + PCl(OH)_4$$

$$PCl(OH)_4 = H_3PO_4 + HCl$$

$$3C_6H_5O^- + 3H^+ + C_6H_5^+ + O^{--} + H^+ + P^{+++++} + 5Cl^- = C_6H_5Cl + (C_6H_5)_3PO_4 + 4HCl.$$

If we accept the reasons given and identify atomic and electrical forces we have still the question as to the real nature of these forces, for after we have called them electrical and even after we have identified them, perhaps, as residing in electrons (Faraday's law and many other things point that way) we still have the inherent difficulty of conceiving an attraction existing between bodies at a distance without a medium and I can not help a strong belief that we must ultimately have a theory for the attractions as an effect produced by the motions of the electrons.

Such a belief need not interfere with our use of the idea of positive and negative charges as a convenient present hypothesis. It may, perhaps, help us to a theory with regard to a reversal of the charge which it seems necessary to assume in certain cases and which has led to Abegg's theory of normal and contravalences. The hypothesis proposed by J. J. Thompson[1] that combination is caused by the transfer of negative corpuscles from one atom to another has much in its favor but it assumes inherent attractions between negative corpuscles and positive atoms or parts of atoms. Although the distances are small such attractions are in as much need of further explanation as is the force of gravity. We assume that the attractions and repulsions between conductors conveying currents or between magnets are due to motions in the ether between them. Is it not possible that the attractions and repulsions between corpuscles and atoms amy be explained in a similar manner?

The third and last question which I wish to raise is as to the nature of the forces which atoms already combined with other atoms exert in the attraction or repulsion of still other atoms. Are these residual forces merely the same forces which hold the atoms in combination still acting past those atoms which are nearest and upon others further away or are they different forces—as seems to be implied rather indefinitely in the "partial valences" of Thiele? The former idea seems simpler and more logical. This question is intimately associated with the mechanism of chemical reactions, the causes for the stability or instability of compounds and especially with questions of molecular rearrangements. As illustrations of facts requiring an explanation by a more intimate knowledge of forces of this sort we may cite the stability of the union of carbon with carbon in ethane as compared with oxalic acid, in propionic and butyric as compared with malonic and acetoacetic acids and in the esters of these acids as compared with the free acids, in benzoic acid as compared with 2,6-dimethyl-4-aminobenzoic acid (*Am. Chem. J.*, **20**, 813 (1898)) in hydrocinnamic as compared with phenyl propiolic acid and in acetic as compared with trichloracetic acid. The instability of compounds similar to those mentioned has long been accepted as an empirical fact and it is easy to predict many cases where such instability will occur but the reason for the instability has scarcely been discussed. With one exception the separation always occurs between two carbon atoms, one, at least, of which is united to a group or atom commonly designated as negative; and the exception may be only apparent, for the decomposition of 2,6-dimethyl-4-aminobenzoic acid takes place in an acid solution in which the amino group is combined with hydrochloric acid and may be considered negative.

It is very noticeable that acetoacetic acid, $CH_3COCH_2CO_2H$, is much less stable than pyrotartaric acid, CH_3COCO_2H. This is some slight indication that the separation of the carbon atoms is ionic in character, taking place more readily when there is a greater contrast between the atoms united together. It may be that, in this connection, we have

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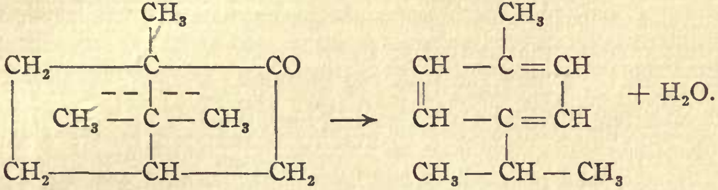
[1] "The Corpuscular Theory of Matter," p. 126. See also the recent discussion by Falk, *School of Mines Quarterly*, **30**, 179 (1909). My own discussion of the reaction between chlorine and ammonia, THIS JOURNAL, **23**, 460 (1901), also has an important bearing on Thompson's hypothesis of the transfer of electrons in the union of atoms of the same element, *Loc. cit.*, p. 127.

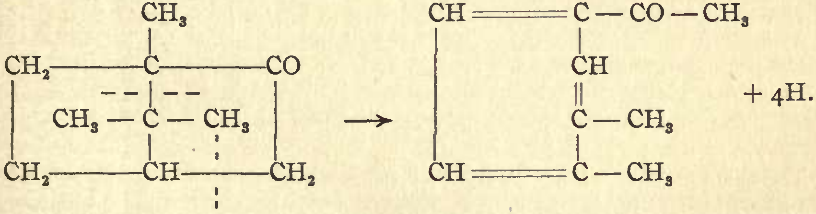
not sufficiently considered the difference between stability and reactivity. Thus sodium chloride and sodium nitrate are both instantaneously reactive in solutions, separating between the sodium and the chlorine or the sodium and the nitrate group but when heated the former compound is extremely stable while the latter decomposes between the nitrogen and oxygen rather than between the sodium and the nitrate group.

This leads me to the consideration of some of those molecular rearrangements in which I have been especially interested. When camphor is heated with phosphorus pentoxide it gives cymene.



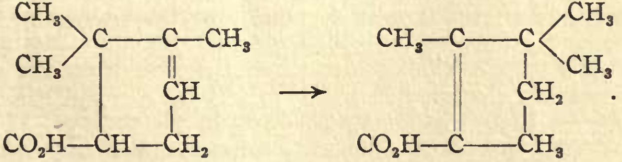
The two carbon atoms which separate from each other in this rearrangement bear the same relation to the carbonyl group as do the two carbon atoms which separate in either the acid or ketonic decomposition of acetoacetic ester. This primary separation of carbon from carbon is followed by the wandering of four hydrogen atoms, two of these leaving the molecule entirely with the oxygen.

When camphor is heated with sulphuric acid it undergoes a different rearrangement, giving *p*-acetyl-*o*-xylene (Armstrong and Kipping, *J. Chem. Soc.*, 63, 81).



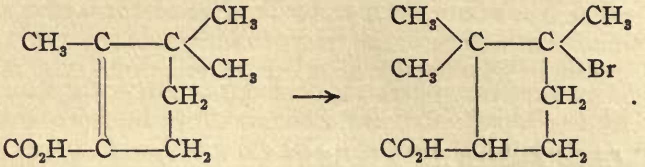
Here the rearrangement is much more complex and we must assume two primary separations of carbon atoms, both of which are again in the same relation as before to the carbonyl group. We have then a different carbon atom uniting with one of those which has separated, forming a six-ring and a transfer of a methyl group from one carbon atom to another, a transfer that has been noticed so many times in other compounds that it can no longer be considered abnormal. Four hydrogen atoms are lost but it is not necessary to consider that more than one hydrogen atom has wandered within the molecule.

When either dihydrohydroxycampholytic acid or α-campholytic acid is allowed to stand for a short time with dilute sulphuric acid (1 : 1) it is transformed into β-campholytic acid.



α-Campholytic acid. β-Campholytic acid.

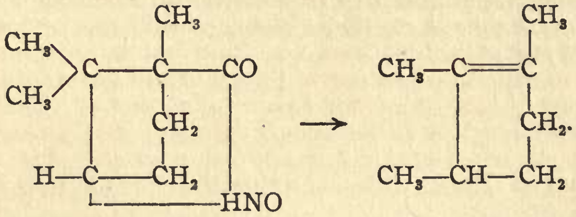
If β-campholytic acid is allowed to stand with concentrated hydrobromic acid it passes back to the hydrobromide of *dl*-α-campholytic acid:



β-Campholytic acid. *dl*-Hydrobromide of α-campholytic acid.

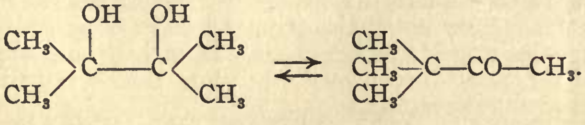
The latter compound may lose hydrobromic acid and give *dl*-α-campholytic acid, or it may exchange its bromine for hydroxyl giving *dl*-α-hydroxydihydrocampholytic acid (Walker and Cormack, *J. Chem. Soc.*, **77**, 380; Noyes and Blanchard, *Am. Chem. J.*, **36**, 285; Noyes and Patterson, *Ibid.*, **27**, 426).

In both of these transformations the methyl group separates from a carbon atom adjacent to a carbon atom which is doubly united to a third, just as in the acetoacetic ester the separation is from a carbon atom adjacent to one which is doubly united to oxygen. A similar relation, but with some variation is found in the transformation of the nitroso derivative of the anhydroaminolauronic acid to laurolene (Noyes and Derick, *J. Am. Soc.*, **31**, 669 (1909)).



Here the carbonyl group leaves (as carbon dioxide) a carbon atom attached to another which is united only to carbon. Doubtless the vibrations set up in the molecule at the moment of decomposition are an important factor in this rearrangement.

The pinacone-pinacolin rearrangement is, perhaps, the first of this type which was studied.



Tiffeneau and his collaborators have recently studied very many rearrangements similar to these, phenyl and other groups as well as methyl being transferred in many cases.

These shiftings of groups seem to take away from under us one of the most important principles on which we rely for the determination of structure, the principle that groups of atoms pass from one compound to another without changing their mutual relations. But when we think of the matter a little further we see that in all chemical reactions we expect the atoms to separate from each other at some point, and the only thing which surprises us is that a separation has taken place at a point where we did not expect it. We can already see some empirical relations between the compounds in which these separations and rearrangements take place and can predict to a certain extent where they are liable to occur. But we are still wholly in the dark as to the real forces which lie behind and are the cause of the transformations.

J. J. Thomson, Rutherford and others have shown that in the phenomena of conductivity of gases and of radioactivity we have new and most powerful means of studying the properties of matter and energy which have thrown a flood of light upon the nature of atoms. Ostwald at the other extreme has wished to discard atoms altogether and to explain structural organic chemistry on the basis of thermodynamics. Richards, from a somewhat intermediate point of view but with distinctly more sympathy with Ostwald than with Thomson, has given us a conception of compressible atoms which is surprisingly like the latter's corpuscular theory of chemical combination as developed in his latest book. Michael wishes to explain phenomena of this sort by the law of entropy. Thiele, imbued with the ideas of structure, explains them in part by partial valences. Still others have attempted to study such problems from the properties of crystals, the absorption of light, and a great variety of other phenomena. The great number of properties which must finally be coördinated in any true explanation of atomic and molecular forces is discouraging and gives some basis for that agnostic point of view which considers the number of possibilities infinite and that we can never hope for a knowledge of the truth even as to the existence of atoms. Let us rather take the more hopeful view that some one, in a not too distant future, will give us a simple and comprehensive theory of the nature of atoms and of the forces which bind them together in compounds. The one who is to do this must not look at science as cut up into water-tight compartments but must be able to coördinate the evidence which comes from workers in many diverse fields of chemistry, of physics and of other sciences.

URBANA, ILL.

ORGANIZATION OF INDUSTRIAL RESEARCH.[1]

BY WILLIS R. WHITNEY.

Received November 6, 1909.

The intimate connection between the purely scientific research of a people and its advance in the art of good living cannot be too frequently discussed. The organization of industrial research involves arranging and maintaining a body of involute parts as an operative whole of highest efficiency. It is never perfectly accomplished, and the fact that improvement can always be made is an incentive for its discussion.

A recent copy of *Life* has this to say, which, without straining, bears direct upon industrial research:

"This is the most interesting country in the world. The game here is the biggest that is being anywhere played. The problems of humanity that are being worked out here are the greatest problems under consideration, and the prospect of solving them is better than it is anywhere else."

Lord Bacon said: "The real and legitimate goal of the sciences is the endowment of human life with new invention and riches." He, in turn, cited King Solomon, who said, "it is the glory of God to conceal a thing, but the glory of a king to search it out."

Bacon distinguishes three degrees of ambition:

First, that of men anxious to enlarge *their own* power *in* their own country. This is "vulgar and degenerate."

Second, that of men who strive to enlarge the power and empire of their *country* over mankind. This is "more dignified, but not less covetous."

Third, that of those who strive to enlarge the power and empire of *mankind* in general over the *universe*. Evidently this is the best, and is the real ambition, whether recognized or not by himself, of any good experimenter.

For purposes of systematic analysis, the subject, "Organization of Industrial Research," may be divided into two parts:

Part one, the personal or mental organization, with its requirements, etc.

Part two, the objective or material organization.

For brevity, these may be called the mind and the matter organizations.

The former, or personal, I will subdivide into such parts as:

Its training and characteristics.

Division of its labors.

Its records, etc.

The objective or matter organization, I divide into:

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[1] An address delivered at the Twentieth Anniversary of Clark University, Worcester, Mass., Sept. 17, 1909.

The fields for material research.

The laboratory equipment and systems of its material co-operation.

Naturally, the personal comes first, relatively and chronologically, and the mental precedes the material. The personal factor is *everything* in industrial research. Strangely enough, it is everywhere and always dominant, while every other factor is sometimes recessive. In an organization "A" cannot work well with "B" because one is too slow, too fast, to egotistical, too jealous, too narrow, etc. Nowhere else do the personal traits protrude so much as in concerted research. And so I hold that above all, as an industrial experimenter, I should like as broad a *human* training as possible, before any other specific one. This probably means little more than acquirement of a *demonstrated* desire to play fair, and it may be no more applicable to this field than to others.

To one always in close touch with research, it seems as though there is an immutable law of nature which may be stated as follows: (It is an application of the principle of reversible reactions so as to include the reactions of the mind.)

The equilibrium between mental and material conception is so sensitive that anything which, to the fair mind, seems possible, is to the trained persistence permissible. If this should be proven not strictly true, it would still be a good working hypothesis for a research organization.

This theory requires, then, a certain characteristic in the generally successful research operator. This is recognized in *optimistic activity* and, to my mind, should be placed first among the requisites. It is placed above *knowledge*, because, without it, little that is new will ever be done except by accident. With active optimism, even in absence of more than average knowledge, useful discoveries are almost sure to be made.

Speaking from personal analysis and from the observation of others, I would say that general-chemical and physical knowledge may sometimes be as much a detriment as a help to one imbued *only* with a *need* of solving new problems. A possible explanation is this: We always reason deductively. We apply general laws in attempting to answer specific questions. To any specific problem of research there are usually general laws which may seem to forbid the solution. These laws are known and revered. Naturally, the unknown, specific ways by which it may be solved are more or less hidden. An illustration may not be out of place here:

Cotton may be dissolved in a solution of zinc chloride. The solution may be squirted through a die into alcohol in such a way that a smooth, coagulated cellulose thread is thereby obtained. This may be heated so as to give a solid, compact and pure carbon filament. Many are thus made. But as a new problem, it would certainly appear quite impracticable to one who might have a fairly extensive knowledge of the chemistry of the materials. Generally speaking, zinc chloride solution does *not* dissolve cellulose. Only a strong solution, kept at a high temperature for a long time, will give the desired solution. In general, too, it could *not* be squirted and coagulated into a smooth thread. Very specific conditions are necessary. Finally, the treatment with gradually rising temperature, which alone succeeds in giving the compact carbon filament, is a matter of specific detail. The places in this process where general reasoning points to failure are numberless. Years of multiplied effort are necessary to perfect such a process. Once established, it is easily analyzed along the lines of understood reason and theories of reactions may be based upon the facts. But such processes are not laid out greatly in advance of their accomplishment. The successful steps are found among the many which are actually attempted, and something more than general knowledge is necessary. This something is hopeful pertinacity, optimistic activity. To a chemist imbued with fair knowledge, it was recently apparently useless to attempt such an experiment as the continual removal of traces of hydrogen from oxygen by passing the gas through a red-hot iron pipe. He had seen iron wire burned rapidly in oxygen, he tried wrought iron and the iron was oxidized, and his knowledge was vindicated, but he also tried cast iron and found that it did not burn and that it would operate perfectly. A scramble for an explanation evolved the theory that the silicon burning to silica protected the iron. *Ex. postfacto* theories are permissible.

As the mental world is constituted, optimists are greatly in the minority, when one counts those only who are also imbued with knowledge. Therefore, in practice, the optimist must be used to crystallize the efforts of others less optimistic. Thus, any large industrial research laboratory is soon *perforce*, systematized into organized clusters of people, working along distinct and different lines. This permits, in our case, of the combined use, to maximum efficiency, of the delicate hands of young women, the strength and skill of trained mechanics, the mind of the useful dreamer, the precision and knowledge of the skilful chemist, and the data of the accurate electrical engineer.

Simple mathematical axioms make clear the fact that a group of operators working together on a subject, are related to the same group operating separately, as a power is related to a simple sum. This principle holds as well among a group of groups and to related subjects. It is evident, for example, that knowledge gained along the line of insulation would be of use in a study of conduction, and that the man who had studied the reduction of tungstic oxide by carbon *in vacuo* could help the one who is working with a pressure furnace, upon the equilibrium between carbon monoxide and carbon dioxide. Therefore, the strength of a research department, properly operated, should rise exponentially with its numbers.

To this audience, the importance of highest advance in specific chemical and physical training will probably be apparent, but an expression of it may be of use. The supply of highly trained men is below the demand. There is a healthy supply of moderately trained men. This applies to all general, scientific training. Let me give more concrete ideas. There are a hundred chemists who can fill satisfactorily an analyst's position, to one who knows what J. J. Thomson has done or who reads Drude's *Annalen*. Reading the *Annalen* is not a "sine qua non," but it is an indicator of no little merit. If a chemist or a physicist is not sufficiently interested to keep informed, he is probably not going to work at high efficiency as an investigator. This does not preclude the possibility of splendid research work being done by some one who is confined to a very limited field of vision, but such cases are the exception and cannot be used as bases for common application. In general, the man with the best tools and with the best knowledge and experience in their use, will advance most rapidly in industrial research. In my own experience, we frequently have a line of work which demands the addition to the force of well trained men. The difficulty which stands out most markedly when considering this problem is usually the scarcity of men who are highly enough trained along the line of pure research. While in many fields of *industrial* research new and brilliant discoveries will continue to be made suddenly and, as it were, out of new cloth, still many more are being made by the most careful application of highly refined methods and knowledge, to processes which already seem at first pretty well worked out. This *intensive farming* is most promising and demands the highest skill. It is to-day most difficult to find American trained men who can do this work. It is a German attribute which we would do well to make our own.

If the chemist is only a chemist or the physicist confined to pure physics, he is liable to overestimation of the laws he learns. He should be something of a "mental mixer," one who has enough history, enough psychology, and enough faith to read possibility of acquirement for the future out of knowledge of attainments in the past.

As we have said, one of the most practical detriments to successful industrial research is that automatic action of the mind which recognizes the possible grounds for a failure quicker than it sees the probable ways to success. Research needs more aviators. Those of us who feel the work-horse brand on our work have a call to cultivate a *flying* spirit, and are to be condemned only if we stand still.

In this connection, I am in favor of anything which helps train the American student in the path of sanguine research. It can be done by research men themselves, but probably not by others. It is not the *knowledge* which the student preparing for research needs, so much as the spirit of the investigator. His thoughts should not be fettered by laws, but helped by them to fly. This can be done best by those who are optimistic almost to the extinction of reason.

A search in the research laboratories of the world to-day would disclose large numbers of J. J. Thomson men, Ostwald men, Nernst men, van't Hoff men. The teacher probably made the school. The investigator probably endowed the students, not with facts alone, but with spirits. We are not of that hopeless class who assume that the sparks of genius are only Heaven-sent, but we are inclined to adopt as an axiom that man is flexible, auto-corrigible and mentally elastic beyond limit. Therefore the rare genius in research, as elsewhere, is the one most given to hopeful effort.

To dwell for a moment upon points in a system for co-operation of a research force, I will describe our own scheme.

The present corps comprises about eighty people, about thirty of whom are college men, mostly chemists. Every man or woman on the research staff is expected to give undivided effort to the work. Whatever invention results from his work becomes the property of the company. I believe that no other way is practicable. An attempt to reward systematically such labors by a scheme of royalty payment is more impracticable than the operation of a manufacturing plant upon a graded scheme of profit sharing. In this case an immediate and fairly equitable division of profits is sometimes possible. In research, the problem itself is an asset of the organization. Both the equipment and the risks belong to the organization. The accumulated experience of the force as a whole is its property. Finally, the privilege of directting the work of operators along lines where no direct financial benefit (or an immeasurable one) to the company could ever be determined, must belong to it. Every operator is expected to keep good notes and his books become a part of the laboratory files. In most cases weekly typewritten reports are made by each worker, and copies of these also become part of accessible library files. For purposes of establishment of dates, etc., witnesses who read and understand the notes also endorse them. Photographs of apparatus, curves, etc., are frequently added wherever useful, and each room of the laboratory is photographed regularly and the dated photographs are bound in books, to record standing conditions. Wherever practicable, single sheets, of standard reporr size, are printed to cover oft-repeating data, so that the experimenter regularly fills in certain blanks, as, for example, in experiments on carbon motor brushes: the composition of the particular lot, temperature and time of drying and firing, hardness, resistivity, tensile strength, and all other tests of the product. The use of plotted curves on standard millimeter paper, for use where one property of material is studied as a function of some other variable, is very common in our reports. This occurs, for example, in practically all cases where electric furnace work is described, and where the changes undergone by incandescent lamps during their life are recorded.

These conditions are the result of eight years of development. The system has been subjected to many changes and may still be greatly improved. It is possible to have such a complex system of record that efficiency is sacrificed. We have reached the present stage because of frequent indications of previous weakness in the simpler methods. Very few good investigators can keep good notes. The more interested the investigator becomes, the more difficult it seems for him to carefully record his passing work. His eyes and mind are always upon the exciting and more interesting advance. It seems not so tempting to actually make history by the writing as to metaphorically make it by the conception or experiment.

We now come to the material side of the subject.

In the early days, the same hands which mined the iron ore and operated the bellows, also forged the sword and plowshare and touched the goods which were the equivalent in exchange. The records of the development through which the distribution of the steps of such processes has gone is what we call the history of man. It is not always easy to recognize the extent to which this development is progressing in our own time. Statistics ought to show us, but these often fail to impress us. It may be that if used to a limited extent to armor an argument, a few data will be of interest in connection with industrial research.

The known chemical compounds of the earth are myriads. The still unknown, but knowable, are certainly many myriads more, but any consideration of either great mass is too huge a task. We may, however, consider for a moment a part of the alphabet from which that language is made. We will consider research as applied to the *metallic elements* alone.

There are about 75 elements. About two-thirds are metals. Of these, only a very few can be said to have been the subject of much industrial research. It is impossible to accurately measure the extent to which an element has been studied with a view to its possible use by the race, but we have no difficulty in recognizing that iron and copper have been much studied, while calcium and silicon have not. In these illustrations we have *not* selected *rare* elements. The calcium and silicon, which have been least used by man thus far, are more common than copper or iron. A natural explanation of the lack of development of such elements is a lack of need, but this is possibly incorrect. Copper, iron, etc., were certainly first obtained by accident as distinct from design. The uses to which they could be put were later developed by trial. The finding of some uses established the further supply, which insured the subsequent discovery of new uses. This mirrors the history now being made by new elements such as silicon. Only in the past year the commercial production of this element has been begun, and about 500 tons were sold for a deoxidizer in steel-making. Thus a substance absolutely out of reach of almost every chemist a few years ago, can now be obtained as cheaply as zinc.

Similarly, future needs, which only calcium, for example, can meet, are certain to be developed. More calcium will then be made. The cost of production will be reduced and the field of its usefulness will again and ever afterward continue to broaden. Never in the history of the world has the rate of iron production been so great as at present (nearly two million tons a month by the U. S. Steel Company alone). Copper is being mined more rapidly than ever before. We have ourselves seen the industrial birth and growth of a new metal which points to the great possibilities in case of the other unused elements. I refer to aluminium. Only two to three tons were made as late as 1884 while furnaces now exist which are capable of yielding three to four times this quantity every hour of the day and night. Its *present* uses could only have been, and were, very imperfectly predicted, before actual industrial research made tentative use of it. So it must be with other elements. One is not too bold who assumes that all the elements which are found in abundance will be industrially utilized when they have been economically isolated and thoroughly investigated.

I am considering the metallic elements only in order to point out in a concrete manner the need of high-quality research, physical, chemical, electrical, etc., in the *simplest* field. Evidently this field, among compounds of the elements, is again bounded only by the infinite. I am impressed with the idea that the commonest elements in nature have not been *studied* with anything like the care which has been given to those for which the demands are already developed.

In our age, a single investigator will probably not isolate, in large quantities, the metal tellurium, for example, and also put it to use to fill one of his individual needs, as did the warrior who first fashioned an iron blade or axe. The men who develop the myriad uses to which the common element titanium will be put, will have to rely upon the previous work of many investigators. It is in this respect that the conditions are continually changing, and always in one direction. I call it the direction of specific complexity. Our wants are very complex. We are learning to demand very specific properties. It is this fact which makes necessary the research work of the specialist, the specific or narrow investigation of the pure scientist, the pioneer work of the trail-blazer, the crude and hurried trials by the inventor, the long and exacting developments of the practical application in the factory, etc. Demands for new materials do not really precede the discovery of the product, any more than the demand for high-speed tool steel preceded the discovery of the properties of the chrome-tungsten-iron alloys. With the material discovered, its properties known, the world apparently could then hardly get along without it. This means that necessity is not the mother of invention. Knowledge and experiment are its parents. It sometimes happens that a successful search is made for unknown material to fill well recognized and predetermined requirements. It *more* often happens that the acquirement of knowledge of the previously unknown properties of a material suggests its trial for some new use. These facts strongly indicate the value of knowledge of properties of materials and indicate a way for research.

Among the recently developed uses for modern metals which were certainly not surmised until the metal itself had been made easily available, are the use of aluminium and silicon as deoxidizers in steel-making, where all the silicon and a large part of the aluminium are now used. This discovery of utility by experiment, rather than the discovery of material by *force of necessity*, is again illustrated by the metals titanium and vanadium. The former is used in arc lamps because it was found, by experiment, to give a good light. (Your Worcester streets are lighted by it.) The latter has been surprisingly useful in steel-making, where a fraction of 1 per cent. has been found to impart additional strength to the steel. In this way, about a thousand tons of vanadium are now used annually in America.

When the first step is taken from the study of the supply, production and utilities of our metallic elements, the next step is apparently along the lines of alloys and we readily see how quickly the field widens. The recent great advances in scientific foundation for much study are to be attributed to the physical chemists, to such men as Tamman and his school. In their work we begin to see the magnitude of the alloy field. There are probably over a *thousand pairs* of metals whose properties as alloys are still absolutely unstudied, and for alloys of three or more metals the number is legion.

It seems as though our advance could be quickened by a greater intimacy with the newly cheapened elements. When sodium, chlorine, bromine, silicon, magnesium, chromium, cobalt, manganese, tungsten, etc., etc., are many times as available or cheap as they were only ten years ago, it is probable that the possible uses are not up-to-date.

The field of material research really divides into two parts: the search for more economical production and the search for wider application. These two go hand in hand. If the one advances, the other is led along. In this way, in our laboratory, the knowledge of such elements as carbon, as in its forms of graphite in lamp filaments, in motor brushes, in electrodes, etc., has been widely and continually advanced. The result is not a conclusion that we know all about carbon, but rather that it still presents a wonderful field for useful research.

From the materials worked *upon*, to the tools is a step. Our experience here is concrete and clear, and we want to record our impressions. Good tools, new tools, rare tools, are most valuable. No good tool lives long for a single use alone. Many times we have questioned the advisability of installing some new apparatus—a vacuum furnace, a pair of metal rolls, some special galvanometer, some microscope, an hydraulic press, a power hammer, a steam digester, etc., etc. Never, after it became a part of the equipment, has it seemed possible to proceed without it. In the single case of the electric vacuum furnace, for example, our laboratory has made almost continual use of from three to eight for the past five years. The laboratory, piped several years ago with high vacuum and with electrolytic hydrogen, besides steam, air, water and gas, will probably never operate without them.

Similarly, this applies to a library. In general, the most useful and fertile of our investigators use the library the most. This is as it should be. The recorded research work in a library of a few thousand volumes frequently represents the work of millions of work-hours, and there is little excuse for not availing oneself of the published experience of others. A library containing ten of the leading research journals of the world may be said to have in each volume about 100,000 available brain-power-hours. So a library corresponds to a charged storage battery of great capacity.

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THE ACIDS OF THE PHENYLPROPIOLIC SERIES AND THEIR CONDENSATION TO NAPHTHALENE DERIVATIVES.[1]

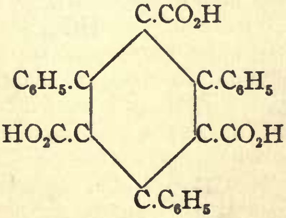
BY JOHN E. BUCHER.

Received December 9, 1909.

In an investigation of the action of acetic anhydride on acids of the acetylene series in 1895, Michael and Bucher[2] obtained the anhydride of a new acid from phenylpropiolic acid. Three years later,[3] after a thorough study of the compound, they proved it to be the anhydride of 1-phenyl-2,3-naphthalenedicarboxylic acid. It was found to have the composition corresponding to the formula $C_{18}H_{10}O_3$ and a molecular weight of 274.

This corresponds to the composition of a phenylpropiolic anhydride $(C_6H_5.C \equiv C.CO)_2O$, but the acid obtained from it was found to be saturated and entirely different from phenylpropiolic acid. This structural formula evidently does not represent its constitution.

It seemed probable that three molecules of the acid might have polymerized to triphenyltrimesic acid in a manner analogous to the for-



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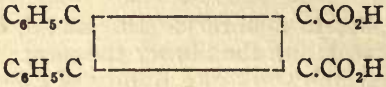
[1] Presented at the Second Decennial Celebration of Clark University, Worcester, Mass., September 14, 1909.

[2] *Ber.*, 28, 2511 (1895).

[3] *Am. Chem. J.*, 20, 89 (1898).

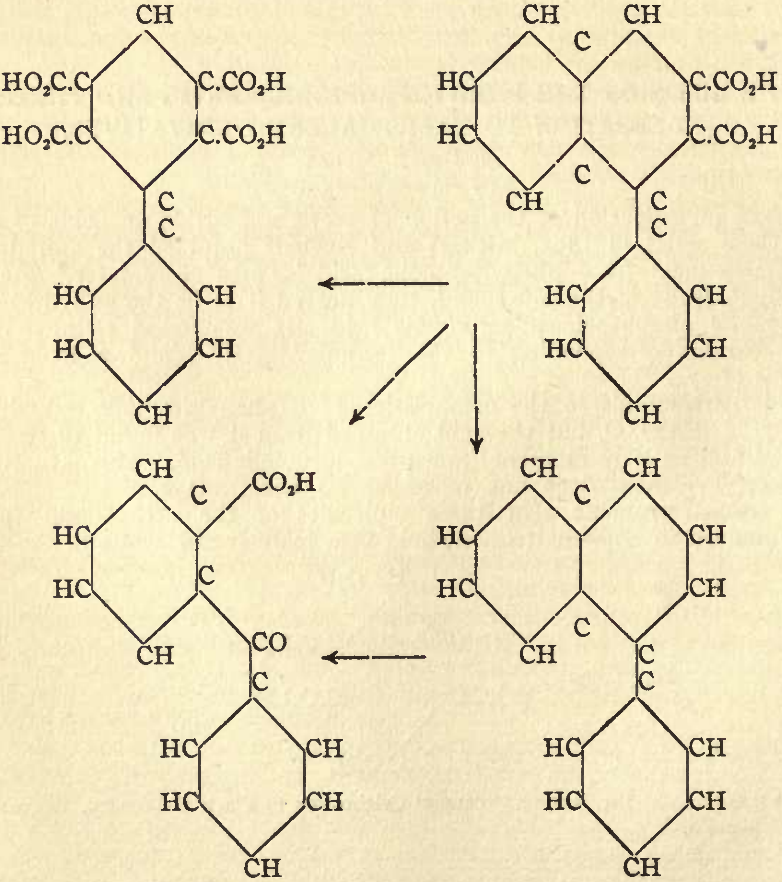
mation of benzene from acetylene. The resulting acid was found to be dibasic and to have only two-thirds of the required molecular weight. These facts showed conclusively that the compound is not the anhydride of triphenyltrimesic acid.

It was then thought possible that the compound might be the anhydride of diphenyltetrenedicarboxylic acid.



This acid would contain two carboxyl groups in the ortho position and it would be dibasic. One might expect benzil among the oxidation products of such an acid but many experiments failed to show the slightest trace of this substance. It was not possible to find any evidence in favor of the tetrene formula.

As none of these three formulas corresponded to the compound, it was evident that the polymerization of the phenylpropiolic acid must have proceeded in a very unusual manner.



They finally succeeded in isolating diphenyltetracarboxylic- and orthobenzoylbenzoic acids from its oxidation products and in preparing its hydrocarbon. The hydrocarbon was also oxidized to orthobenzoylbenzoic acid. The preceding formulas show these transformations.

These facts can only be explained by the above constitutional formula and the compound is therefore the anhydride of 1-phenyl-2,3-naphthalenedicarboxylic acid.

Later, several investigators who evidently had overlooked the above work obtained this compound. Basing their reasoning on insufficient experimental evidence, they described the substance first as the anhydride of triphenyltrimesic acid and afterwards as that of diphenyltetrenedicarboxylic acid, representing structural formulas which had already been shown to be untenable by Michael and Bucher. For example, Lanser[1] obtained the compound by heating phenylpropiolic acid with phosphorus oxychloride, and assigned the formula $C_{54}H_{30}O_9$ for triphenyltrimesic anhydride without making molecular weight determinations.

A little later Manthey[2] determined the molecular weight thus showing the formula to be $C_{18}H_{10}O_3$ and that the constitution must be different from that assigned by Lanser. This evidence together with the fact that the acid contains the two carboxyl groups in the ortho-position, led him to assign the tetrene formula.

In a later paper, Lanser and Halvorsen[3] acknowledge the correctness of Manthey's experimental work and they also accept the tetrene formula. The reactions which they study would, however, apply equally well to other ortho-dibasic acids.

Ruhemann and Meriman[4] also obtained the anhydride in studying the action of phenylpropiolyl chloride on acetone in pyridine solution. They proved the identity of their compound with that of Lanser and regarded it as a terene compound as they did not investigate its constitution.

Michael[5] next showed that the compound described by these investigators is 1-phenyl-2,3-naphthalenedicarboxylic anhydride. He proved this by preparing a specimen by Lanser's method and finding it identical in every respect with a specimen prepared by the method of Michael and Bucher.

Recently, Stobbe[6] obtained this anhydride by the action of light on dibenzalsuccinic anhydride. Failing to get diphenyltetracarboxylic acid by direct oxidation but obtaining ortho-benzoylbenzoic acid, he claimed to have shown the truth of the naphthalene formula of Michael and Bucher for the first time.

These investigators[7] showed that his failure to get the diphenyltetracarboxylic acid was due to incomplete oxidation[8] and that they had

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[1] *Ber.*, 32, 2478 (1899).

[2] *Ibid.*, 33, 3083 (1900).

[3] *Ibid.*, 35, 1407 (1902).

[4] *J. Chem. Soc.*, 87, 1389 (1905).

[5] *Ber.*, 39, 1908 (1906).

[6] *Ibid.*, 40, 3372 (1907).

[7] *Ibid.*, 41, 70 (1908).

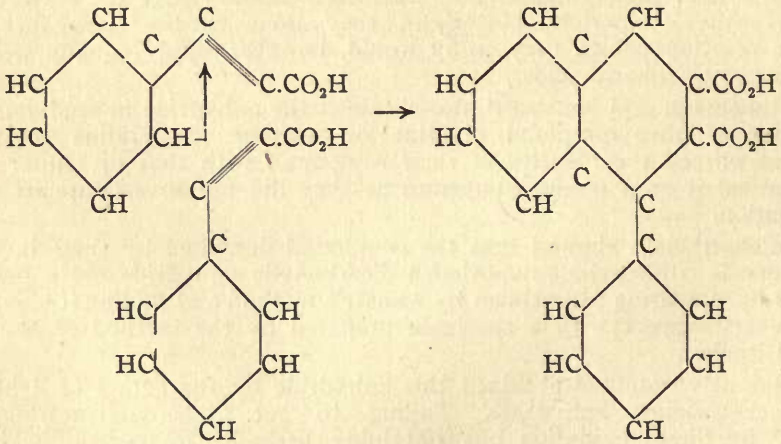
[8] THIS JOURNAL, 30, 1246 (1908).

noticed the formation of ortho-benzoylbenzoic acid by the *direct* oxidation[1] of the anhydride as well as from the hydrocarbon.

Pfeiffer and Möller[2] have polymerized phenylpropiolic ester to the ester of 1-phenyl-2,3-naphthalenedicarboxylic acid by simply heating to 200°. They point out that aromatic acetylene derivatives may thus be polymerized to naphthalene derivatives without the use of condensing agents. The earlier work of Lanser also shows this since Michael has shown that the so-called triphenyltrimesic acid is really a naphthalene derivative. Lanser obtained the anhydride of this acid by heating phenylpropiolic acid to a temperature above 200°. Pfeiffer and Möller's work, however, illustrates the additional fact that anhydride formation is not essential for this naphthalene condensation.

I have confirmed Lanser's experiment and have been able to get a much better yield of the ester of the naphthalene acid than Pfeiffer and Möller got. In my experiment, however, the phenylpropiolic ester was polymerized by heating it with acetic anhydride instead of heating it alone.

These investigations show that phenyl propiolic acid and its ester or chloride can be polymerized in a number of different ways to naphthalene derivatives but that the original method of Michael and Bucher which gives a quantitative yield is still the best. The following formulas indicate how this change takes place:



This work has been continued in this laboratory for a number of years in order to determine whether this transformation is general or not. Besides phenylpropiolic acid, eleven of its substitution products have been examined thus far and in every case they polymerized, on heating with acetic anhydride, to derivatives of 1-phenyl-2,3-naphthalenedicarboxylic anhydride. The facts thus far obtained justify the statement[3] that *phenylpropiolic acid and its substitution products show a strong tendency to polymerize, with the wandering of an ortho hydrogen atom, to phenylnaphthalene derivatives.*

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[1] *Am. Chem. J.*, 20, 112 (1898).

[2] *Ber.*, 40, 3839 (1907).

[3] THIS JOURNAL, 30, 1262 (1908).

In fact, this kind of polymerization is the only form which has been thus far obtained from aromatic propiolic acids.

In this work much time was spent in preparing the aromatic propiolic acids as it was usually necessary to either prepare new compounds or else to improve the methods of preparation of acids which were already known. In most cases methods were found by which these interesting acids could be prepared readily from comparatively inexpensive materials —providing that suitable precautions were observed.

Phenylpropiolic acid was prepared in the usual way from cinnamic acid by making cinnamic ester dibromide. It is well known that alcoholic potash converts this into a mixture of the salts of allo-bromocinnamic acid and bromocinnamic acid and that the latter is easily converted into phenylpropiolic acid by the loss of hydrobromic acid. The former acid is so stable, however, that it is not practicable to convert it into phenylpropiolic acid directly by further heating with alcoholic potash. It can, however, be converted into the isomeric acid by simply heating it. This acid can then be converted, in turn, into phenylpropiolic acid. This change of the labile bromo acids into the corresponding isomeric acids was found to be quantitative in several cases. In the case of the allobromocinnamic acid it was noticed that when it was heated with acetic anhydride to 100° its own anhydride was produced but at a higher temperature this was transformed into the bromocinnamic anhydride. The latter could then be transformed into phenylpropiolic acid. From this, it is evident that it is not necessary to use pure phenylpropiolic acid in this work. It generally seemed desirable, however, to separate the acids first. A very good way of doing this is to crystallize them from carbon disulphide or from carbon tetrachloride. In this way it is possible to separate much of the phenylpropiolic acid from the more soluble allobromocinnamic acid.

In some other cases, the potassium salts of the propiolic acids were found to be very sparingly soluble in the alcoholic potash, thus yielding the pure acids at once. In all cases the potassium salts of the labile bromocinnamic acids were found quite soluble while the ammonium salts of the isomeric acids were very sparingly soluble. These properties were found very useful in separating the resulting phenylpropiolic acids from these labile substituted bromocinnamic acids which were formed.

The meta- and para-nitrophenylpropiolic acids can be prepared from the corresponding nitrobenzoic aldehydes by Perkin's synthesis. In some other cases Claissen's synthesis was found preferable to that of Perkin.

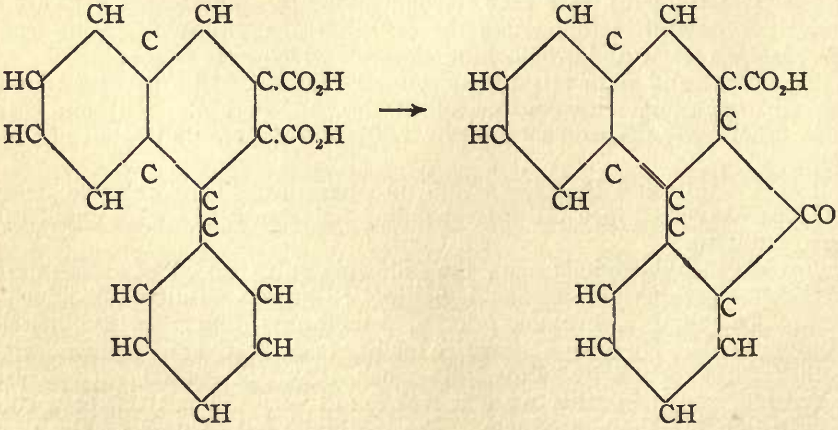
It was also found that the ortho- and para-nitrophenylpropiolic acids could be converted into the corresponding halogen acids by means of the diazo reaction.

Besides phenylpropiolic acid, the following substitution products were prepared: Piperonylpropiolic acid, *o*-chloro-, *o*-bromo-, *m*-nitro-, *m*-chloro-, *p*-nitro-, *p*-chloro-, *p*-bromo-, *p*-iodo-, *p*-methoxy-, and *p*-methylphenylpropiolic acids. These all polymerize readily to derivatives of 1-phenyl-2,3-naphthalenedicarboxylic anhydride when they are heated with acetic anhydride. In the earlier work it was found very difficult to prove this constitution for these products. The method used in case of the first compound has already been described. The meta- and para-nitro compounds were oxidized and then converted into diphenyltetracarboxylic acid thus showing them to be naphthalene derivatives. By means of the diazo reaction, they were then converted into the halogen derivatives identical with those obtained by direct polymerization. This showed the latter to have the same constitution. The constitution of the product from the para-methylphenylpropiolic acid was established by oxidizing it to a diphenylpentacarboxylic acid. In more recent work the very efficient method of oxidizing to benzenepentacarboxylic acid described below was used. By means of this method, which depends on the catalytic action of manganese nitrate in fuming nitric acid, eleven of these acids were oxidized to benzenepentacarboxylic acids, thus confirming the naphthalene constitution which had previously been assigned for some of the substances.

The following description gives an idea of some of the transformations which these substances undergo: They are all ortho-dibasic acids from which water splits out easily on heating. In fact, the first acid obtained is partially converted into its anhydride even on crystallizing it from only moderately heated glacial acetic acid. In this way, I obtained eight grams of the anhydride from twenty grams of the acid. This loss of water in crystallizing the acid from hot solvents led to the statement, made in the first description, that the acid passed into the anhydride spontaneously. This statement was corrected in a later paper by Michael. All of these acids have this general property and some of them, as well as their oxidation products, may show properties similar to those noticed by Orndorff in the case of tetrachlorophthalic acid.

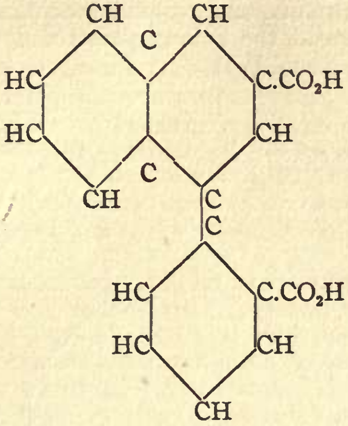
The acids all necessarily contain a carboxyl group with both ortho positions substituted. According to V. Meyer's observations one might expect difficulty in esterifying these acids. This was found to be the case, little or no neutral ester being found, on heating the substances with alcohol and sulphuric acid under the usual conditions. If more sulphuric acid is used and the heating continued for a longer time from 40 to 60 per cent. of neutral ester may be obtained.

Sulphuric acid converts the 1-phenyl-2,3-naphthalenedicarboxylic acid into red allo-chrysoketonecarboxylic acid.



I. II.

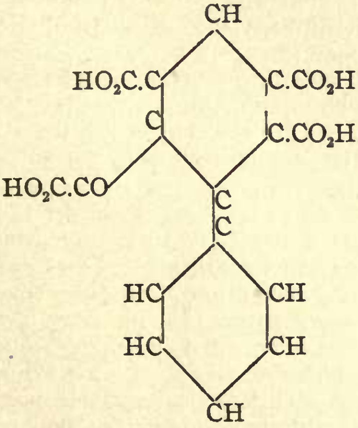
When this red acid is heated to 218° with potassium hydroxide, it is changed practically quantitatively into a new 1-phenylnaphthalenedicarboxylic acid.



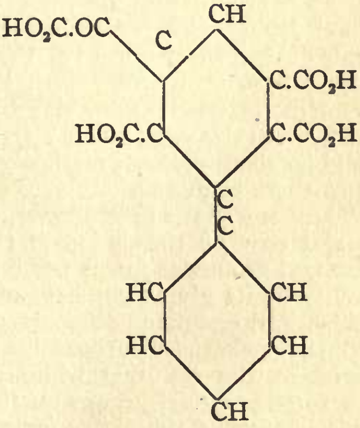
III.

Formulas I, II and III show a method of transferring a carboxyl group from the ortho position on one ring to the corresponding position on the other ring. When the new acid (III) is heated with sulphuric acid, a new red acid different from the allochrysoketonecarboxylic acid (II) is obtained.

The oxidation of these naphthalene acids in alkaline potassium permanganate solution has already been described. The yield of diphenyltetracarboxylic acid is usually small, since the intermediate ketonic acids are very stable towards alkaline potassium permanganate.



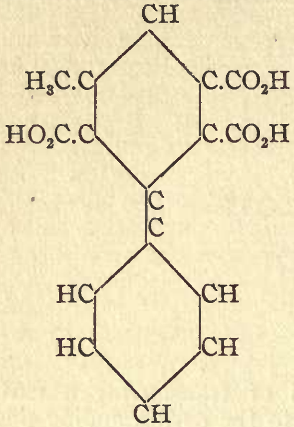
IV.



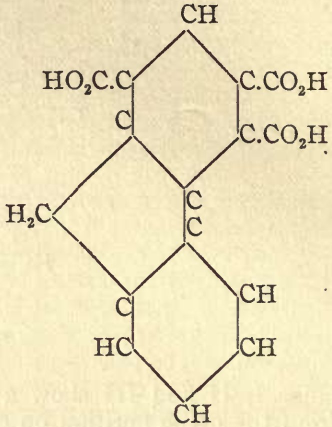
V.

These ketonic acids are very easily oxidized to diphenyltetracarboxylic acids when the solution is acidified. Formulae I, IV, V and VIII indicate these reactions. These acids are obtained in the form of siruplike solutions and they resemble phthalonic acid closely. Heated with caustic alkalies, they yield diphenyltricarboxylic acids and oxalic acid.

On reduction with hydriodic acid, the *meta*-glyoxylic acid (V) first yields methyldiphenyltricarboxylic acid (VI) which then reduces at a higher temperature to a methylfluorenecarboxylic acid. The isomeric *ortho*-glyoxylic acid (IV), even at the boiling point of hydriodic acid, reduces to a fluorenetricarboxylic acid (VII).



VI.



VII.

This shows the ease with which diphenylcarboxylic acids close the ring to form fluorene derivatives. The same tendency is shown by the action of sulphuric acid on diphenyltetracarboxylic acid (VIII) in forming the yellow diphenyleneketonetricarboxylic acid (IX), which can be reduced to the acid represented by formula VII. I have found this closing of the ring on heating to 100° with sulphuric acid, to take place when all the carboxyl groups were on the same ring but generally not when the carboxyl groups were on different rings. In diphenyleneketonecarboxylic acids of the general form IX, the ring is broken in such a way, on heating with potassium hydroxide, that the carboxyl group is transferred from the ortho position on one ring to the corresponding ortho position on the other.[1] In this case, about 299 parts out of 300 are changed in this way—making the process practically quantitative. The following formulas show these changes.

The very sharp breaking of the ring at *a* in formula IX and in the similar case of the red acid (II) indicates a tendency to remove the carboxyl groups as far as possible from each other and suggests the possibility of its giving a means of testing the constitution of the resulting acid. For example Bamberger and Hooker,[2] after heating a yellow diphenyleneketonedicarboxylic acid from retene with caustic alkali, represent the resulting white diphenylenetricarboxylic acid as having the three carboxyl groups on the same ring. This seemed scarcely possible in view of the above facts and an examination showed the acid to have a different structure.

The yellow diphenyleneketonetricarboxylic acid (IX) also furnishes a means of oxidizing these 1-phenyl-2,3-naphthalenedicarboxylic acids or diphenylpolycarboxylic acids (like I and VIII) to benzenepentacar-

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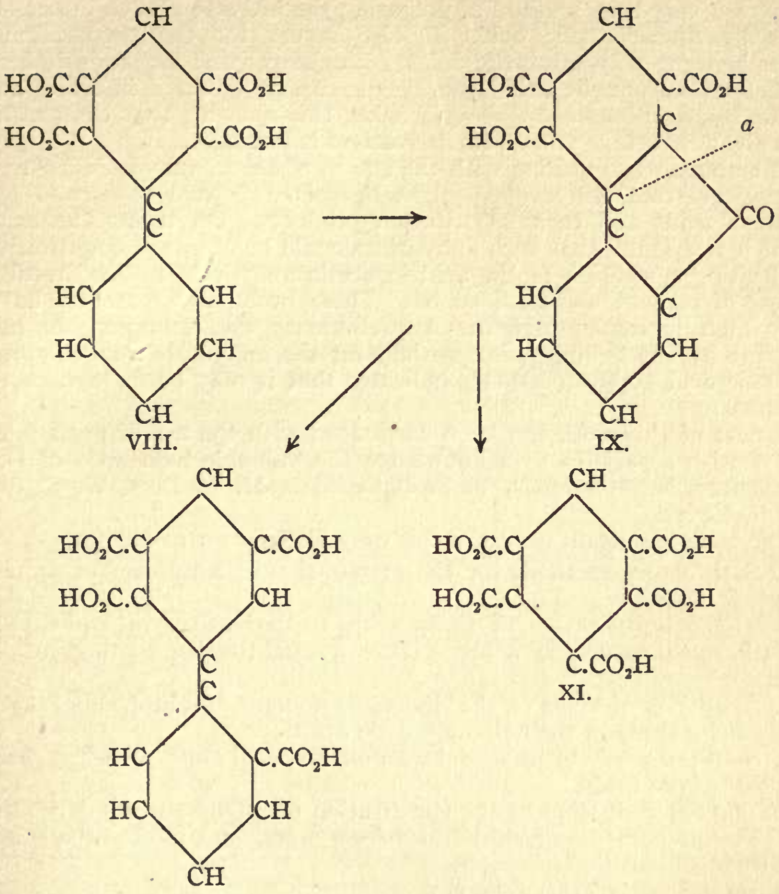
[1] THIS JOURNAL, 30, 1261 (1908).

[2] *Ann.*, 229, 159 (1885).



VIII. IX. X. XI.

boxylic acids. The latter acid (VIII) is very stable towards alkaline potassium permanganate as on heating for six weeks I recovered 28 per cent. of unchanged acid and could not isolate any benzenepentacarboxylic acid. The yellow acid (IX), however, decolorized the theoretical quantity of permanganate in less than two hours. The very soluble acid product was not completely oxidized but it yielded benzene for the hydrocarbon. Many experiments were made in attempting to complete the reaction but without success. Even heating on the water bath with fuming nitric acid did not aid very much. A small quantity of manganese nitrate was then added to the hot nitric acid. *Brisk effervescence began at once and in a few moments pure benzenepentacarboxylic acid separated from the liquid.* The yield in this experiment was about 90 per cent. of the theory. The manganese nitrate is evidently a very efficient catalytic agent in this case. This method was also applied to the acids without first converting them into ketone derivatives, and, in eleven cases out of the twelve tested, benzenepentacarboxylic acid was found. Not only does this give a very powerful method for determining constitution but it gives a very easy method of preparing the hitherto almost inaccessible benzenepentacarboxylic acid. It also serves for the preparation of other benzene polycarboxylic acids. Bamberger and Hooker's diphenyleneketonedicarboxylic acid from retene can be oxidized in a few hours to two isomeric *benzenetricarboxylic* acids, thus showing that the constitution given for retene and all its derivatives is incorrect.

The above work dealing with the action of acetic anhydride led to the supposition that anhydrides[1] might be prepared from *meta-* and *para*-phthalic acids and their substitution products. On trying the experiment it was found that such anhydrides could be obtained quantitatively by heating a solution of the acid in acetic anhydride to 200° until the excess of reagent was distilled off. These products apparently have a very high molecular weight. A preliminary determination, in nitrobenzene by the boiling point method, for the anhydride from chloroterephthalic acid, $[C_6H_3Cl(CO)_2O]_x$, indicates that it may be as high as 1500 or 2000.

A part of this work has been carried on with the aid of my students and I wish especially to acknowledge the valuable assistance of G. F. Parmenter, N. A. Dubois, V. S. Babasinian, M. L. Dolt, W. C. Slade and F. Keyes.

The more important results of this work thus far are as follows:

1. Satisfactory methods for the preparation of a number of aromatic propiolic acids.
2. The polymerization of these acids to derivatives of 1-phenyl-2,3-naphthalenedicarboxylic acids—giving a quantitative method of synthesis.
3. Syntheses of acids of the diphenyl, fluorene and diphenyleneketone series and a study of their characteristic reactions.
4. Syntheses of benzenepentacarboxylic acid and other benzene-polycarboxylic acids.
5. The determination of the constitution of retene and its derivatives.
6. The preparation of anhydrides from meta- and para-phthalic acids and their substitution products.

Brown University, Providence, R. I.

CATALYSIS ON THE BASIS OF WORK WITH IMIDO ESTERS.[2]

By Julius Stieglitz.

Received December 2, 1909.

I shall not attempt to discuss to-day the general subject of catalysis but shall use the short time rather to present briefly some results[3] in certain lines of our work which seem to shed some light on three fundamental points of interest in catalysis, namely, on the questions how in

[1] This Journal, 30, 1263 (1908) and 31, 1319 (1909).

[2] Presented at the Second Decennial Celebration of Clark University, Worcester, Mass., September 15, 1909.

[3] Certain parts of the work are still being carried out—as indicated below—and for such parts this report is preliminary to a final one. Complete discussion of the several parts lay outside the limits of this paper and will be brought in in later special reports.

certain cases a catalytic agent does its work, why it does it, and what limitations there are to its action.

It may be recalled that an imido ester, such as methyl imido benzoate, is very slowly decomposed by pure water. One of the decompositions it undergoes under these conditions is into ammonia and methyl benzoate[1] as expressed in the equation

$$C_6H_5C(: NH)OCH_3 + H_2O \longrightarrow C_6H_5CO_2CH_3 + NH_3. \qquad (1)$$

The addition of an acid, say hydrochloric acid, enormously accelerates this otherwise extremely slow action and we were able to show that the acceleration is due to the fact that the reacting component in this decomposition is the positive ion of the ester,[2] as expressed in the equation.

$$C_6H_5(: NH_2^+)OCH_3 + H_2O \longrightarrow C_6H_5CO_2CH_3 + NH_4^+. \qquad (2)$$

In arriving at this conclusion, account had to be taken of the so-called "salt-effect" or "salt-acceleration" produced by the presence of electrolytes, entirely analogous to the "salt-effect" in other decompositions in which water is a reacting component, as in the catalysis of esters by acids. This salt-effect being allowed for, the velocity of decomposition of an imido ester by water in the presence of acids is given in the equation[3]

$$dx/dt = K_{v(ion)} \times C_{pos.\ est.\ ion} \times [C_H \times C_{OH}]. \qquad (3)$$

I have not time more than to mention the fact that it was shown that the same fundamental equation may be applied to the saponification of ordinary esters under the influence of acids, the main difference being that for such exceedingly weak oxonium bases as esters are the concentration of the positive ester ion is practically proportional to the concentrations of the ester and the hydrogen ion present at any moment, so that we may transform (3) into[4]

$$dx/dt = K_v \times C_{ester} \times C_H \times [C_H \times C_{OH}] \qquad (4)$$

which is also the equation based on experience.

The work on which the above conclusions were based was carried out wholly with the hydrochlorides of the imido esters. More recently we have also carried out measurements with the hydrobromides and nitrates, and begun work also with sulphates; if the positive *ion* is the reacting component, then, determining rigorously the degree of ionization and making rigorous allowance for the salt-effect, we should find that the velocity constant for the decomposition of the positive ion in the chloride solution should also satisfy the observed rates of decomposition of these other salts. For the rigorous treatment, the "salt-effect" produced by the chlorides, bromides, nitrates, etc., has to be determined experimentally and this has been carried out[5] with the chlorides and bromides,[6] mixtures with varying amounts of the potassium and sodium salts being examined, the degrees of ionization of each salt in the mixture being

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[1] Stieglitz, *Report International Congress of Arts and Science*, St. Louis, 4, 276 (1904), and *Am. Chem. J.*, 39, 29 (1908).

[2] Stieglitz with Derby, McCracken, Schlesinger, *Am. Chem. J.*, 39, 29, 166, 402, 437, 586, 719.

[3] $C_{pos.\ est.\ ion}$ is a function of x.

[4] C_{ester} is a function of x.

[5] W. W. Hickman, Dissertation, 1909.

[6] Mr. Weatherby is completing the work begun by Mr. Hickman on the nitrates and sulphates.

determined with the aid of the principle of isohydric solutions, which was proved to apply to such mixtures.[1] The salt-effect is, except for minute quantities of salt, proportional to its concentration or rather, more probably, only to the concentration of the ionized part of the salt.. The salt-effect is an acceleration and if we call $K_{v(ion)o}$ the velocity of decomposition of the imido ester ion in the absence of any salt at all, this velocity will be increased proportionally to some specific acceleration factor A, and to the concentration $m\alpha$ of the ionized part of A salt. So we have

$$K_{v(ion)obs.} = K_{v(ion)o} (1 + A\,m\,\alpha). \qquad (5)$$

$K_{v(ion)obs.}$ is the constant calculated according to equation (3) from the observations without any allowance for a salt-effect.

$K_{v(ion)o}$, the velocity constant when the salt effect is eliminated, is easily found by extrapolation from the observations when imido ester salts are present without added salts, A from the results obtained when salts have been added. We arrived thus empirically at the rather unexpected result that the accelerating factor A is approximately the same for sodium, potassium and lithium chlorides and for the bromides as well as for the chlorides, *viz.*, about 185 per cent. per gram molecule of fully ionized salt. Table I illustrates this fact for potassium chloride and potassium bromide. K_v is the velocity coefficient calculated without regard to the degree of ionization of the imido ester salt, α is the degree of ionization of the salt calculated with the aid of the principle of isohydric solutions. In the columns headed "found" are given the values obtained for $K_{v/\alpha}$ by experiment; in the columns headed "calculated" are the values obtained according to equation (5), in which the velocity coefficient $K_{v(ion)o}$ in the absence of any salts at all is taken as 164 and the salt acceleration factor A is taken as 185 per cent. for both series.

TABLE I.[2]

K Hal.	KCl. 43430 $K_{v/\alpha}$.		KBr. 43430$K_{v/\alpha}$.	
m.	Found.	Calculated.	Found.	Calculated.
0	176	176	176	177
0.1	191	190	191	190
0.2	213	214	209	215
0.25	227	226	230	227
0.333	247	245	(268)	247

I wish to emphasize this result because the work of others, notably of Arrhenius and Euler, with cane-sugar and esters, shows varying specific accelerating factors for these salts. I believe our work has the advantage of our knowing from conductivity measurements the degrees of ionization of the imido ester salts as well as of the added electrolyte so that there seems to be no unknown factor left in our estimations. But we are simply presenting these results for the time being as an empirical contribution to the whole question of catalysis and we do not consider the very complex question of "salt catalysis" as at all settled.[3]

[1] Edith E. Barnard, Dissertation, 1907.

[2] Taken from W. W. Hickman's dissertation.

[3] Work on "salt catalysis" is being continued by L. S. Weatherby, preliminary results by Mr. Hickman on the effect of sulphates indicated an abnormally high effect.

With the aid of the determination of the salt factor for chlorides and bromides we have been able to show that the positive ester ion shows indeed the same rate of decomposition irrespective of its origin from either of these salts and very probably also for the nitrate[1] (see the values for $K_{v/\alpha}$ for the three salts in equi-molar concentrations as given in Table II). This is exactly what our theory would require, namely, that the simple reason why the addition of an acid accelerates this decomposition is that it forms a salt whose positive ion is the reacting component and that the concentration of the ion is enormously increased when the catalyzing acid is added to the free ester, which is a very weak and therefore little ionized base.

Table II.[2]—Ethyl Imido Benzoate.

Hydrochloride.				Hydrobromide.			Nitrate.		
$m.$	$\alpha.$[3]	$Kv.$[4]	$Kv/\alpha.$	$\alpha.$[2]	$Kv.$[2]	$Kv/\alpha.$	$\alpha.$[2]	$Kv.$[2]	$Kv/\alpha.$
0.05	77.8	136	175	75.9	133	176	75.1	133	177
0.1	71.8	132	185	69.4	128	184	68.3	127	186
0.2	64.5	121	188	61.7	119	193	60.4	118	195
0.33	57.7	114	198	54.7	108	198	52.7	107	201

It was suggested by Arrhenius and emphasized by Euler that the salt acceleration is probably largely due to the increased ionization of water in the presence of electrolytes, but quantitative evidence in support of such a conclusion has not been brought, as far as I am aware. In view of the increase observed by Arrhenius and others[5] in the strength of other acids in the presence of added foreign salts, *e. g.*, of acetic, formic and carbonic acids in the presence of sodium chloride, it seems a sufficiently rational assumption that water should show a similar increased ionization.[6] The imido esters, enabling us to measure the actual concentration of the reacting imido ester ion, gave us an opportunity to bring experimental evidence strongly supporting this view. From equation (3) it is obvious that if the salt acceleration is due to the increased ionization of water, *viz.*, an increase in the value of the third factor, $(C_H \times C_{OH})$ then, $C_{pos.\ est.\ ion}$ being known by experiment, the velocity constant $K_{v(ion)}$ calculated *without* taking any increased value of $[C_H \times C_{OH}]$ into account, should increase in the same proportion for all the imido esters for the same concentration of added salt ions, irrespective of the fact that, according to the ester used, the decomposition may be a comparatively slow or a very fast one. We have found this to be true[7]—all the esters used show the same acceleration per gram molecule ionized salt—*i. e.*, close to 185 per cent. per gram molecule ionized potassium chloride, etc.[8]

Having found that the reacting component in these and a number of other actions under the influence of acids is the positive ion of a salt formed with the acid, we were naturally most interested in the question

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[1] The salt effect for nitrates is now being determined.

[2] Taken from W. W. Hickman's dissertation.

[3] Taken from Edith E. Barnard's dissertation.

[4] Taken from Schlesinger's results, *Loc. cit.*

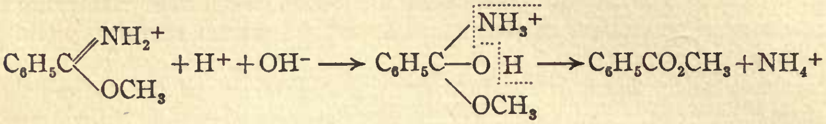
[5] E. J. Szyszkowski, *Z. physik. Chem.*, 58, 419.

[6] See a discussion of the other side of this question by Acree, *Am. Chem. J.*, 41, 474.

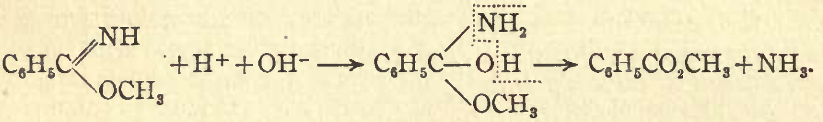
[7] Dissertation of Edith E. Barnard and W. W. Hickman.

[8] The investigation of the ionization of water in salt solutions is being continued with other substances and by other methods.

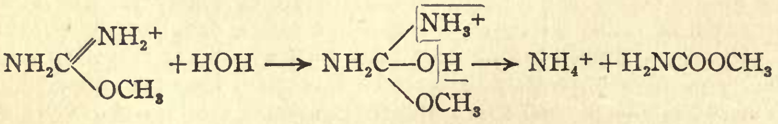
why the *ion* should be so reactive, why it should be so important a component. We can hardly consider the decompositions to be *purely* ionic reactions,[1] comparable with the hydrolysis of salts in aqueous solutions, as was mistakenly assumed, for instance, by Euler and by Kastle. Such assumptions run counter to the law of mass action applied rigorously in the analysis of the conditions.[1] The law is, however, in agreement with the assumption[2] based on experience gained in organic chemistry that the following are the stages for the action:


(6)

Now, we may well ask why this should be an enormously faster action than the entirely analogous possible action of water on the non-ionized free ester, which, it is clear, could proceed in a very similar series of stages as expressed in the equations:


(6′)

For me, one of the most interesting and important features of our work is found in the unmistakable way in which the fact is brought out more and more clearly that the accelerating or catalytic effect of the acid is most intimately associated with the transformation, in acid solution, of the positive ion of a weaker base into that of a stronger one—the results no doubt of the principle of the loss of a maximum amount of free energy.[3] This is shown most strikingly in the following illustration: whereas the above imido esters are very rapidly decomposed by water in the presence of acid, this is not the case for the closely related compounds, the urea ester salts, which, *structurally considered*, could react quite as easily with water but are as a matter of fact quite stable in acid solution. The transformation


(7)

only takes place to a very slight extent at 100°, and at ordinary temperatures, where imido ester salts are completely decomposed in one to ten hours, the urea ester salts have not been observed to decompose at all.[4] In this case we have the notable fact that such a transformation would involve the change of a salt of a stronger base into that of a much weaker one—an ammonium salt—and this does not take place. To test the legitimacy of our reasoning we recently examined the behavior of benzoyl urea ester salts: the benzoyl urea esters form very much weaker

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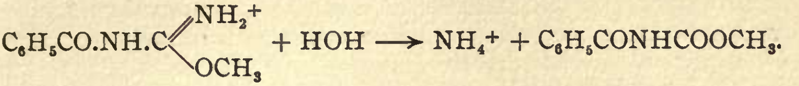
[1] See a more complete discussion by Stieglitz, *Am. Chem. J.*, 39, 402.

[2] Stieglitz, *Loc. cit.*

[3] *Ibid.*

[4] The degree of stability is being examined *quantitatively*.

bases than ammonia and our reasoning would lead us to expect that they, in turn, ought to be decomposed quite as smoothly in acid solution as the imido esters. Such is, in fact, the case;[1] urethanes and ammonium salts readily result according to the equation



$$C_6H_5CO.NH.C\begin{matrix}\diagup NH_2^+\\ \diagdown OCH_3\end{matrix} + HOH \longrightarrow NH_4^+ + C_6H_5CONHCOOCH_3. \quad (8)$$

We find then that perfect analogy in structure is of far less importance in determining the result of the action of water than a definite physico-chemical relation subject to quantitative measurement.

This is again brought out beautifully by the behavior of the urea esters towards ammonia. The imido esters give with ammonia amidines and again the action is accelerated by the addition of an acid or an ammonium salt and, as we shall see presently, this is due to the fact that again it is the positive ester ion that reacts with ammonia, an amidine resulting according to the equation

$$C_6H_5C(:NH_2^+)OCH_3 + NH_3 \longrightarrow C_6H_5C(:NH_2^+)NH_2 + HOCH_3 \quad (9).$$

Now, urea esters which, as explained above, would not react with *water* in acid solution because the salt of a stronger base would be converted into the salt of a weaker one if they did react, would give with *ammonia* guanidines which are still stronger bases than they are themselves. They should, therefore, according to this theory, react with ammonia in the presence of an acid; as a matter of fact they do, producing guanidines very readily, and we were able to prove again that the velocity of the formation is proportional to the concentration of the positive ester ion;[2] in fact, until our theory led us to recognize the importance of having a salt-forming acid present, all our efforts to prepare guanidines from urea esters—by using ammonia alone—had proved futile; so that this theory seems to agree equally well with the reactions of a given compound which *do occur* as with those which do not take place.

We have found too that in series of structurally closely related esters where what might be called the structural and stereochemical resistances to the action are perhaps approximately the same, the transformation of the positive ion of a weaker base in the presence of acids into that of a given stronger base, say into the ammonium ion, *proceeds with the greater velocity at a given temperature the weaker the original base is.*[3] This brings, as far as I am aware, the first complete experimental proof of a theory which others, notably van't Hoff and Euler suspected to be true,[4] although there appeared so many marked contradictions to the assumption that the theory appeared at best a very uncertain one. For instance, Hemptinne[5] and Lowenherz,[6] working on this problem at van't Hoff's suggestion, obtained the following results for the saponification of esters by acids:

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[1] J. C. Moore's dissertation, 1909.

[2] R. A. Hall's dissertation (1907).

[3] Cf. Stieglitz, *Loc. cit.*, and McCracken, *Loc. cit.*

[4] See the discussion by Euler, *Z. physik. Chem.*, 36, 410.

[5] *Ibid.*, 13, 561.

[6] *Ibid.*, 15, 395.

TABLE III.[1]

Ester.	Velocity constant.	Ioniz. const. of the acid.
$HCOOC_2H_5$	0.11	21×10^{-5}
$CH_3COOC_2H_5$	0.0057	1.8×10^{-5}
$ClCH_2COOC_2H_5$	0.0033	155×10^{-5}
$Cl_2CHCOOC_2H_5$	0.0053	5100×10^{-5}
$CH_3CH_2COOC_2H_5$	0.0061	1.3×10^{-5}

Assuming, as Euler did, that the strongest acids produce the weakest bases in their esters, one might expect the positive ions of the chloroacetic acid esters to be saponified most rapidly to give the positive ion of a *given* stronger base, the oxonium base of ethyl alcohol. As a matter of fact the velocity constants in the above table do not tell us anything at all as to whether that is so or not and that is why the theory, heretofore, has appeared as an unproved one; obviously it does not follow from the data in Table III, where the *weakest* bases, dichloroacetic ester and chloroacetic ester, have the *smallest*, not the largest, velocity constants of decomposition. But the fact that, for instance, the velocity coefficient for the saponification of dichloroacetic ester is even smaller than that for ethyl acetate *does not mean anything at all* in regard to the real *relative rates of transformation of their positive ions*: there is a second factor involved, namely, the concentrations of the positive ions of the esters are dependent on the strength of the esters as oxonium bases, as expressed in our fundamental equations for the catalysis of an ester by an acid.[2] In our fundamental equation

$$dx/dt = K_{v(ion)} \times C_{pos.\ est.\ ion} \times [C_H \times C_{OH}] \qquad (10)^{3}$$

we may substitute for $C_{pos.\ est.\ ion}$ the relation expressed in:

$$C_{pos.\ est.\ ion} = k_{aff.}/k' \times C_{ester} \times C_H \qquad (11)^{4}$$

and have

$$dx/dt = K_{v(ion)} \times k_{aff.}/k' \times C_{ester} \times C_H \times [C_H \times C_{OH}] \qquad (12)$$

$$= K_v \times C_{ester} \times C_H \times C_H \times C_{OH} \qquad (13)$$

which is the ordinary equation representing the velocity of decomposition of esters by acids. What we determine with esters, for instance in Hemptinne's and Lowenherz's work as expressed in Table III is K_v and not the *more fundamental constant* $K_{v(ion)}$. Now

$$K_v = K_{v(ion)} \times k_{aff.}/k' \qquad (14)$$

and it is obvious that if the basic strength of the ester as expressed in $k_{aff.}$ grows very much smaller, as it undoubtedly does when we go from ethyl acetate to ethyl chloroacetate, $K_{v(ion)}$ *could easily grow very much larger* and *yet* K_v *need not change appreciably or it might even grow smaller*, without the result being in any disagreement whatever with the theory expressed. This means, of course, that determinations simply of the velocity constants K_v of decomposition of such esters do not prove any-

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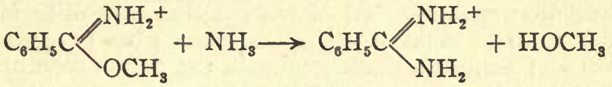
[1] The table is taken from Euler, *Loc. cit.*, p. 412.

[2] Stieglitz, *International Congress of Arts and Science*, St. Louis, 1904, 4, 276 of the report, and *Am. Chem. J.*, 39, 47 (1908).

[3] $C_{pos.\ est.\ ion}$ is a function of x.

[4] k' is the stability constant of the oxonium hydroxide. $k_{aff.}/k'$ may be considered the stability constant of the complex ester ion. Cf. Bredig, *Z. Elektrochem.*, 9, 118 (foot-note).

thing as to the principle at issue. A somewhat stronger base might well give a higher rate of change than a weaker one by virtue of the fact that a larger proportion of the base is present in its active form, the ion, and the real rate of decomposition of the ion may be much smaller than that of an ester giving a smaller velocity constant K_v. The imido esters have the advantage that their affinity constants are easily ascertained and we do not deal with any such unknown quantity at all, and thus we were able to bring what I believe is the first experimental proof of the soundness of the theory. An apt illustration of the correctness of our argument concerning the lack of data for a correct analysis of results like those given in Table III is found in the following facts: the formation of amidines from imido esters, as was stated, is greatly accelerated by the addition of acids or of an ammonium salt and we were able to show that the amidine formation may be considered essentially a function of the concentration of the positive ester ion, proceeding according to



$$C_6H_5C\Big\langle\begin{matrix}NH_2^+\\OCH_3\end{matrix} + NH_3 \longrightarrow C_6H_5C\Big\langle\begin{matrix}NH_2^+\\NH_2\end{matrix} + HOCH_3 \qquad (9)$$

and

$$dx/dt = K_v \times C_{pos.\ est.\ ion} \times C_{NH_3} \qquad (15)^1$$

Now, if we develop the expression for the concentration of the positive ion of a very weak base like an imido ester in the presence of a much stronger one like ammonium hydroxide we find that:

$$C_{pos.\ est.\ ion} = \frac{C_{ester} \times C_{NH_4^+}}{C_{NH_3}} \times \frac{k_{aff.\ est.}}{k_{aff.\ amm.}} \qquad (16)$$

and by substitution we get:

$$dx/dt = K_{v(ion)} \times \frac{k_{aff.\ est.}}{k_{aff.\ amm.}} \times \frac{C_{ester} \times C_{NH_4^+}}{C_{NH_3}} \times C_{NH_3} \qquad (17)$$

$$= K_{v(ion)} \times \frac{k_{aff.\ est.}}{k_{aff.\ amm.}} \times C_{ester} \times C_{NH_4^+}. \qquad (18)^2$$

Now, imido *ethyl* benzoate forms benzamidine considerably faster than does the *methyl* ester: in both cases the change is from the salt of the positive ion of a weaker base to that of a much stronger one, the amidine, but the *ethyl* ester is the stronger base and yet it reacts the faster and apparently contradicts our theory. A knowledge of the affinity constants shows, however, that it reacts the faster only because by virtue of its being a stronger base it takes a larger proportion of the catalytic agent, the acid, from the ammonium chloride, and forms a proportionally larger concentration of the active component, the ester ion, than does the methyl ester under the same conditions. Calculating with the aid

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[1] $C_{pos.\ est.\ ion}$ is a function of x.

[2] In passing, it may be remarked that this last form shows that the action may be considered one of the ion ammonium acting on the ester, but we believe our original assumption to be the right one for reasons found in the behavior of organic compounds which cannot be elaborated here; it may be said, for instance, that we have found NH_3 and not NH_4^+ to react with ordinary esters to form amides and are carrying out other more crucial experiments on this point. *Vide* Acree, *Am. Chem. J.*, 38, 308. Fitzgerald and Lapworth, *J. Chem. Soc.*, 93, 2163.

of the affinity constants the true *velocities of transformation of the positive ions*, we find the true relation: $K_{v(ion)}$ for the methyl ester is 140/0.434 and for the ethyl ester only 69/0.434.[1] So the true relations resulting from an exact knowledge of all the quantitative constants involved agree perfectly with the fundamental principle given.

This reaction shows other points of great interest: for instance, the fact that the concentration of ammonia cancels out of the mathematical equation leads to the conclusion that the velocity of decomposition is independent of the concentration of ammonia, one of the reacting components.

This peculiar conclusion has been fully verified by experience; the velocity constant is as a matter of experiment almost, although not absolutely, independent of the concentration of ammonia; in the case of the above methyl ester, the constant grows only about 10 per cent. with an increase of 400 per cent. in the concentration of the ammonia. This apparent contradiction with the law of mass action is readily understood if we remember that the concentration of ammonia has two effects which oppose each other; ammonia does accelerate the action in proportion to its mass as required by the law, but it also to the same degree retards the action by depriving the weaker base of the ionizing and therefore catalyzing acid. Within a year Lapworth[2] has made the extremely important discovery that water stands in exactly the same relation to the esters in the catalysis by acids—only then the two bases competing for the acid are two oxonium bases, the ester and water.

And now in conclusion I wish to call attention to one more result with these imido esters which has impressed us very much and which seems to me to throw a very clear light on the whole question of catalysis or acceleration by showing certain limitations to catalytic effects. It was mentioned a moment ago that the velocity of formation of benzamidine from methyl imido benzoate may be expressed as a function of the positive imido ester ion and that it is almost independent of the concentration of the ammonia; but it is not absolutely independent, there is a slight but steady rise in the value of the constants with increasing concentrations of ammonia. All other secondary reactions having been excluded (*e. g.*, for fourfold increase of NH_3, the constants rise gradually from 139/0.434 to 154/0.434) as the cause of this increase by a knowledge of their velocity constants, we suspected that besides the main action of ammonia on the positive ester ion, there is a much slower action of ammonia also on the non-ionized free ester, namely, that we have two simultaneous actions:

$$C_6H_5C(:NH_2^+)OCH_3 + NH_3 \longrightarrow C_6H_5C(:NH_2^+)NH_2 + HOCH_3 \quad (18)$$

and

$$C_6H_5C(:NH)OCH_3 + NH_3 \longrightarrow C_6H_5C(:NH)NH_2 + HOCH_3 \quad (19)$$

We had the more reason to suspect this as we had already found that water, besides decomposing the positive ion of an imido ester at a very high speed, also undoubtedly decomposes the non-ionized ester at a very slow rate.[3] It was found that the experimental results agree very well with this conception of two simultaneous actions in the formation of

[1] Miss Katharine Blunt's dissertation (1907).

[2] *Loc. cit.*

[3] In this case the products are different. *Vide* Stieglitz, Derby and Schlesinger, *Loc. cit.*

benzamidine and that the velocity constant for the action of ammonia on the positive ester methyl ion at 25° is 325, while that on the ester molecule is only 0.0069.[1] That is, the positive ion is almost 50,000 times as reactive as the non-ionized molecule. It may appear somewhat surprising that such a small constant could still be detected side by side with such an enormous one, the whole action being completed in one to two hours. But we must remember that for the ion action with the enormously high rate of change we have at any moment only minute quantities of the reacting component, *e. g.*, 0.000,005 gram ion at the beginning of a velocity measurement, which is used up at an enormous speed but always formed again instantly by the purely ionic action of imido ester on the ammonium chloride. On the other hand the transformation of the non-ionized molecule has the advantage of relatively high concentrations of each of the reacting components, say 0.05 both for the ammonia and for the free ester at the beginning of an action. With a concentration many thousand times in its favor it is then not surprising to find this very slow action becoming perceptible in careful quantitative work. Now, if we should use a much weaker base still, we might easily find the action with the non-ionized ester taking a *more and more prominent part* in the total change, even if the actual rate of change of the positive ester ion should still be very much the greater. We have recently found such to be the case for the action of ammonia and ammonium chloride on benzoyl urea ester:[2] the velocity constants are so nicely balanced against the affinity constants that the observed changes did not agree even approximately with either conception used alone, *viz.*, that the guanidine formation was due to the action of ammonia on the positive ester ion alone, or on the non-ionized ester alone. But they did agree well with the view that both actions occur simultaneously, the velocity coefficient for the action on the ion being 34.5 and the coefficient for the action on the non-ionized ester being 0.0015, a ratio of 23000 to 1 again. We were exceedingly pleased to find this case because it forms the connecting link with what we have found to be true for the formation of ordinary acid amides from acid esters in the presence of ammonia and ammonium salts:

$$CH_3COOCH_3 + NH_3 \longrightarrow CH_3CONH_2 + HOCH_3 \qquad (20).$$

This action seems to be essentially a function of the ester and ammonia and it is an extremely slow reaction.[3] We can easily understand this case now; the esters as extremely weak oxonium bases must be able to take only the faintest traces of acid from the ammonium chloride in the presence of ammonia and therefore the slow molecular transformation comes to the front as enormously favored by the concentrations of the reacting components. In the case of the actions of acids on esters and water, the esters compete only with an oxonium base of the same order of strength as they are themselves and rather weaker,[4] the oxonium base of water and here the reaction with the ion is again predominant.

These studies then show us a whole range of organic compounds, obviously of the *same type* and *family* but giving reactions which proceed quite

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[1] Mr. Norton is collecting more data on these relations.

[2] J. C. Moore's dissertation (1909).

[3] Unpublished work by J. Stieglitz and Dr. Barnard.

[4] Lapworth, *Loc. cit.*

differently with the imido esters the action of ammonia on the *positive ion* is the essential action and the use of a catalytic agent,[1] 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.

ON THE BIOCHEMISTRY OF NUCLEIC ACIDS.[2]

By P. A. Levene.

Received December 2, 1909.

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

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[1] *Loc cit.*

[2] 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,[1] 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

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[1] 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.[1] 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

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[1] *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.[1]

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 sperm:						
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

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[1] Altmann, "Über Nukleinsauren," *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.
b (Kostytschew)	31.4	4.6	12.8	7.6	...	Ba — 17.5
c (Herlant)	37.53	4.93	16.48	9.63	...	....
d (Schmiedeberg)	35.82	4.14	14.68	9.17	...	....
II. Guanylic acid (animal origin):						
a Ivar Bang	34.28	4.39	18.21	7.64	34.48	....
b Levene and Mandel	36.35	4.95	18.65	6.15	33.90	....
III. Plant nucleic acid:						
1 Yeast:						
a Herlant	33 7	4.1	14.8	8.69	...	Cu — 10
b 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[1] (spermnucleic acid)	40	56	14	26	4
Steudel[2] (thymus nucleic acid)	43	57	15	26	4
Levene[3] (spleen nucleic acid)	54	71	20	37	5
	43	55	15	31	4
Osborne and Harris[4] (wheat embryo nucleic acid)	42	62	16	31	4
Kossel[5] (yeast nucleic acid)	17	26	6	14	2
	25	36	9	20	3
Boas[6] (yeast nucleic acid)	36	52	14	24	4
Levene[7] (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

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[1] *Arch. exp. Path. Pharm.*, 57, 309 (1907).

[2] *Z. physiol. Chem.*, 46, 332 (1905).

[3] *Biochem. Z.*, 17, 120 (1909).

[4] *Z. physiol. Chem.*, 36, 85 (1902).

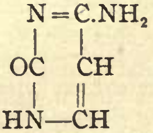
[5] *Arch. f. Anat. Physiol.*, p. 181 (1891).

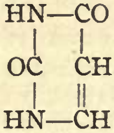
[6] *Arch exp. Path. Pharm.*, 55, 16 (1906).

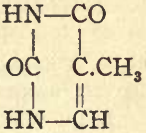
[7] *Biochem. Z.*, 17, 120 (1909).

xanthine are now regarded as secondary products.[1] 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.[2]


Cytosine.


Uracil.


Thymine.

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 orgin of cytosine and uracil. R. Burian[3] 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 Neuberg[4] 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.[5]

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

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[1] Levene, *Z. physiol. Chem.*, 45, 370 (1905). W. Jones and Austrian, *J. Biol. Chem.*, 3, 1 (1907).

[2] 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).

[3] 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).

[4] Neuberg, *Ber.*, 32, 3386 (1899).

[5] 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.[1]

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. (Phytonucleic 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 alkalies. Reference has been made already to the views expressed by Kossel.[2] 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,[3] working in Schmiedeberg's laboratory, actually succeeded in obtaining a substance which had the composition of the hypothetic 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-

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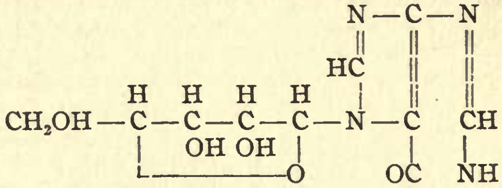
[1] Schmiedeberg, *Arch. exp. Path. Pharm.*, 46, 57 (1900). Kossel u. Neumann, *Ber.*, 27, 2215 (1894). Kossel u. Steudel, *Z. physiol. Chem.*, 37, 119, 120, 121, 131, 177 (1902–3); 145, 377 (1903); 38, 49. Ascoli, *Ibid.*, 31, 161 (1900–1). Steudel, *Ibid.*, 42, 165 (1904); 43, 402 (1905); 44, 157 (1905); 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).

[2] Kossel and Neumann, *Z. physiol. Chem.*, 22, 74 (1896–7).

[3] Schmiedeberg, *Ach. 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.[1] 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 alkalies 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 ($C_{10}H_{12}N_4O_5$). 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.[2]

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 ($C_{10}H_{13}N_5O_5$), 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 alkalies and acids.[3] 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-

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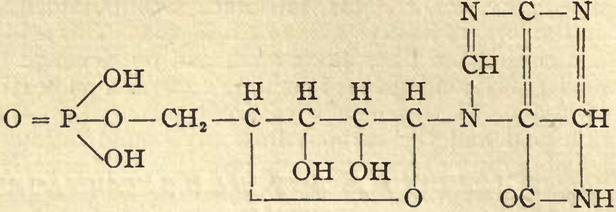
[1] *Ber.*, 44, 2703 (1908).

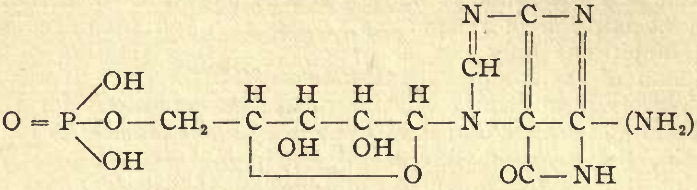
[2] Haiser and Wenzel, *Monatsh. Chem.*, 29, 157 (1908)

[3] *Ber.*, 42, 2474 (1909).

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

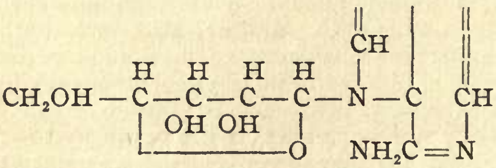


(Inosinic acid.)



(Guanylic acid.)

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.[1] 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: $[\alpha]_D = -67.30°$.

On the ground of this the structure of the yeast nucleic acid may be presented in the following manner:[2]

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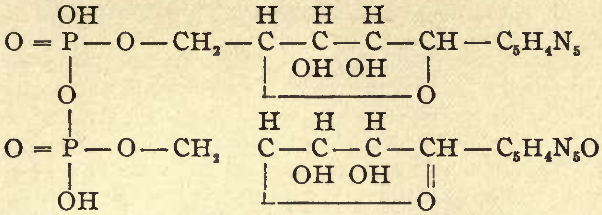
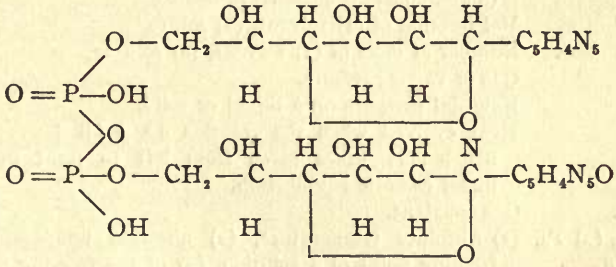
[1] Levene and Jacobs, *Ber.*, 42, 2703 (1909).

[2] 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.[1] 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 ($C_{11}H_{17}N_2PO_{10}$) 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 nulceic 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.

THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH,
NEW YORK CITY.

THE FUNDAMENTAL LAW FOR A GENERAL THEORY OF SOLUTIONS.[1]

By Edward W. Washburn.

Received March 3, 1910.

Nomenclature.

C	Volume concentration.
(1) C_P, (2) c_p	Molecular heat capacity of (1) a liquid, (2) a gas.
ΔC_P	Decrease in molecular heat capacity attending a change in state of aggregation.
(1) K_C, (2) K_N	Equilibrium constant in terms of (1) volume concentrations, (2) mol fractions. (Products of the reaction in the denominator.)
K_S	Solubility product in terms of mol fractions.
(1) L_S (2) L_v (3) L_F	Molecular heat of (1) sublimation, (2) vaporization, (3) fusion (under constant external pressure).
(1) N, (2) N'	Mol fraction of (1) solvent, (2) solute.
(1) n, (2) n'	Number of mols of (1) solvent, (2) solute.
p	Gas or vapor pressure.
P	External pressure on a liquid or solid.
Q_π	Heat evolved when the reaction $a\mathrm{A} + b\mathrm{B} + \ldots. = m\mathrm{M} + n\mathrm{N} + \ldots.$ takes place from left to right in a solution under osmotic equilibrium.
R	Gas constant.
(1) T, (2) T_F, (3) T_O, (4) T_B, (5) T_{Bo}	(1) Absolute temperature, (2) absolute temperature of the freezing point of a solution, (3) of the freezing point of the pure solvent, (4) of the boiling point of a solution, (5) of the boiling point of the pure solvent.
U	Total energy decrease produced when the reaction $a\mathrm{A} + b\mathrm{B} + \ldots. = m\mathrm{M} + n\mathrm{N} + \ldots$ takes place from left to right.
(1) v, (2) V	Molecular volume of (1) a gas, (2) a liquid.
π	Osmotic pressure.
μ	Thermodynamic potential.
ϕ	Fugacity.
ξ	Activity.

I. The Development of the Modern Theory of Solutions.

Upon the foundations laid by the labors of van't Hoff and Arrhenius has arisen the structure which we know to-day as the Modern Theory of Solutions. Before van't Hoff's epoch-making discovery of the ther-

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[1] Presented at the Second Decennial Celebration of Clark University, Worcester, Mass., September 16, 1909.

modynamic relations which bind together the colligative properties[2] of dilute solutions, our knowledge concerning these important quantities was confined to a set of apparently unconnected empirical laws. Van't Hoff's generalization of these laws, followed almost immediately by the Ionic Theory of Arrhenius, stimulated greatly the study of solutions and made possible the rapid development and perfection of our present theory. Investigation has, however, been confined chiefly to the domain of dilute solutions and the Modern Theory of Solutions has remained almost entirely a theory of dilute solutions. The reason for this is, I believe, due largely to one of those historical "accidents" which occur now and then in the development of science. The history of this "accident" and the manner in which it came about forms a chapter in physical chemistry of interest alike to the chemist and to the philosopher.

Perhaps the best way to form a clear idea of the process of evolution of our present theory of solutions is to consider first the colligative properties of solutions and the relations which connect them. These quantities—the osmotic pressure, vapor pressure, freezing point, boiling point, etc.—have played such an important and vital part in the development of our solution theory that a clear idea of their relations to one another is absolutely essential to a proper understanding of the theory and of its development. The nature of these relations is expressed by the following statement: *The colligative properties of a solution are connected by a set of rigorous differential equations which involve no assumptions except the two laws of thermodynamics.* The equations are as follows:

(1) Osmotic Pressure and Freezing Point,

$$d\pi = \left(\frac{-L_F}{V}\right) \frac{dT_F}{T_F}. \tag{82}$$

(2) Vapor Pressure and Freezing Point,

$$dp = \left(\frac{L_S}{v}\right) \frac{dT_F}{T_F}. \tag{92}$$

(3) Osmotic Pressure and Vapor Pressure,

$$d\pi = \left(\frac{-v}{V}\right) dp. \tag{77}$$

(4) Osmotic Pressure and Boiling Point,

$$d\pi = \left(\frac{L_v}{V}\right) \frac{dT_B}{T_B}. \tag{90}$$

To these should be added a number of others, such as the relation between the electromotive force of a concentration cell and either vapor pressure (74) or osmotic pressure (70), and (16 and 14) the mutual relations among the osmotic pressures or vapor pressures of the constituents of a physical mixture or (30 and 30*a*) the substances concerned in a

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[2] Following Ostwald, the term "colligative properties" is used to embrace such properties as osmotic pressure, boiling point raising, freezing point lowering, vapor pressure lowering, etc.

chemical equilibrium, etc.[3] While the following discussion applies with equal force to all of these relations, it will perhaps be conducive to clearness, if we confine our attention chiefly to the four relations given above.

From the method of derivation of these relations, it is clear that they do not involve any assumptions regarding the concentration of the solution, nor do they depend in any way upon the nature of the dissolved solute or its degree of association, dissociation, or solvation. In fact, if one knows, for example, the vapor pressure, freezing point lowering or boiling point raising for a solution of any nonvolatile solute, he has the means of calculating the osmotic pressure for the same temperature without knowing either the concentration of the solution or the nature of the solute. There may be one or several solutes present and they may associate, dissociate, or unite with each other or with the solvent in any manner and to any extent. These questions are in no way involved in the calculation. Since relations such as those existing among the colligative properties of a solution involve only the two laws of thermodynamics, it will be convenient to refer to them as "*purely thermodynamic relations*," to distinguish them from an important group of relations which involve the composition of the solution and the nature of its components, and which we will now proceed to consider.

Let us consider a solution of any solute A in any solvent B, and let our problem be to express each of the colligative properties of the solution as a function of its composition or its "concentration." This problem can in general be solved only by direct experiment for the particular solvent and solute under consideration. From what has preceded, however, it is evident that as soon as we know the relation between *any one* of the colligative properties and the composition of the solution, the other relations become thereby determined. If, for example, we determined the freezing point of the solution for a series of concentrations, we could calculate thermodynamically the osmotic pressure, the vapor pressure, etc., for the same concentrations and thus derive an equation connecting each of these quantities with the concentration. The colligative property which should be chosen for experimental study in a given case would depend upon the relative ease and accuracy with which the several quantities could be determined and the temperature range which it was desired to cover; also in some cases upon whether the requisite "caloric quantities"[4] were known with sufficient accuracy or could be determined readily.

The relation between any one of the colligative properties and the concentration of the solution for any given solvent and solute will obviously depend upon the degree of association, dissociation and solvation of the solute.[5] Since the magnitude of these effects and their dependence upon

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[3] The derivations of these relations and a more detailed discussion of them are given in a previous paper, "A Simple System of Thermodynamic Chemistry Based upon a Modification of the Method of Carnot" (THIS JOURNAL, 32, 467 (1910)). For convenience in reference these equations are given the same number here as in the previous paper where the significance of the quantities appearing in the equations is explained in detail.

[4] Proposed by van der Waals to distinguish heat capacities, latent heats, heats of reaction, etc., from colligative properties.

[5] It is hardly necessary to remark that this statement tacitly assumes that the desired relation is to be one which involves the number of mols of the solute.

the concentration are in general unknown quantities, the problem is too complex for any complete solution. In general, therefore, it is necessary to make a separate investigation for every solvent and solute in order to establish the desired relation connecting some one of the colligative properties with the concentration. To leave the problem in this condition, however, is naturally not very satisfactory, and the course usually followed by science when confronted with a problem which is too complex is first to simplify the problem. Let us try to trace the process of simplification which has been followed by science in the present instance.

Since association or dissociation of either solvent or solute molecules introduces complications, the first step in the process of simplification is obviously to consider the simple case of a solution in which neither takes place. Since the union of a portion or all of the solute molecules with the solvent molecules (solvation) is also a complicating factor, the next step in the process of simplification would naturally be to eliminate this factor also by assuming no solvation. After making these simplifications our problem would read as follows: What are the relations connecting the colligative properties with the composition in the case of a solution in which the number of molecular species present is equal to the number of components?[6] Let us call such a solution, provisionally, an "ideal solution," postponing until later a more definite and accurate description of the properties of the type of solution to which the term "ideal" should be applied.

There is, however, another method by which the complicating factor of solvation can also be eliminated. Willard Gibbs, in his monumental work on thermodynamic chemistry, has taught us that the proper way to represent the composition of any phase is by the means of the mol fractions of its several components.[7]

Now in the case of a solution, the mol fraction of the solute (for example) will be altered if it becomes solvated on going into solution, owing to the consequent change in the number of solvent molecules. Such a complication can be eliminated from our problem, as explained above, by assuming no solvation; or it can be likewise eliminated *by taking the solution sufficiently dilute*. For, as the solution becomes more and more dilute, the limit approached by the mol fraction of the solute is the same whether solvation occurs or not.[8]

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[6] For example, in the case of two components, a solvent and one solute, there would be only two different kinds of molecules; for a solvent and two solutes, only three different kinds of molecules, etc.

[7] This system has been consistently followed by all investigators who use systems of thermodynamics based upon Gibbs' thermodynamic potential. The reason that it has not been followed by others is because they have confined themselves to the region of dilute solutions, where it is possible to use one of the limiting forms approached by the mol fraction of the solute, as the concentration approaches zero.

[8] To illustrate, if we put n' mols of a solute in n mols of a solvent and no solvation (or dissociation or association) occurs, then the mol fraction of the solute is $\frac{n'}{(n' + n)}$. If, however, on the average x mols of solvent are combined with each mol of solute, the mol fraction of the (solvated) solute is $\frac{n'}{[n' + n - n'x]}$ or $\frac{n'}{[n'(1-x) + n]}$. As the

Owing to an "historical accident" the latter method of eliminating the complication of solvation has been the one followed by science, instead of the former and more logical one. The "historical accident"[9] in this instance was van't Hoff's brilliant discovery of the remarkably simple equation connecting osmotic pressure with temperature and concentration in very dilute solutions. Starting with this equation as a basis and using the principles of thermodynamics, he showed us how to construct a complete theory of dilute solutions.

As the field of dilute solutions became more and more developed, both from the experimental and theoretical side, investigators began to turn their attention to the subject of concentrated solutions. Investigation in this direction has usually taken the direction of attempts to extend the osmotic pressure equation by the introduction of quantities corresponding to the a and b of van der Waals' *condition equation* for gases, upon the basis of kinetic conceptions derived from an assumed analogy between osmotic and gas pressure. Other investigators have sought to attribute all of the deviation of concentrated solutions from the equations of dilute solutions, to solvation, and have even gone so far as to compute on this basis the approximate degree of hydration in some very concentrated aqueous solutions, for example. Still other attempts have been taken in the direction of an extension of our present equations by the addition of a series of terms containing a number of constants intended to express the influence of the solute molecules upon one another and upon the solvent.

Attempts to obtain a satisfactory theory of concentrated solutions in any of these directions give no promise of success. An attempt to "explain" why, as a solution becomes more and more concentrated, it deviates more and more from the equations of very dilute solutions is somewhat analogous to an attempt to explain why the sine of angle, which for sufficiently small angles is equal to the angle, deviates more and more as the angle grows larger. The reason is, of course, a purely mathematical one. Similarly in the case of solutions there is first of all a purely mathematical reason why concentrated solutions should deviate from the equations of the infinitely dilute solution. The equations of dilute solutions are the limiting forms assumed by more general equations, owing to the fact that certain terms become negligible as the concentration approaches zero. In other words we have in our dilute solution laws only a portion, the residue, so to speak, of a more general set of laws for solutions of all

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solution becomes more and more dilute, both expressions approach $\frac{n'}{n}$ as their limit. This is the familiar ratio which appears in our boiling point and freezing point equations. In the case of our osmotic pressure equation, instead of writing it $\pi = \left(\frac{n'}{n}\right)\left(\frac{RT}{V}\right)$, where V is the molecular volume of the solvent, it is customary to substitute $V_s = nV$ and write $\pi V_s = n'RT$. Here again, if the solution is *sufficiently* dilute, it is obviously immaterial whether we understand V_s to mean the volume of the solution or the volume of pure solvent in which the n' mols of solute were dissolved in preparing the solution.

[9] The expression, "historical accident," is, of course, used in the philosophical sense.

concentrations. Consequently before science can hope to make any progress in the region of concentrated solutions she must go back to the point where the simplifying assumption of a dilute solution was unconsciously introduced, and, in place of it, make the simplifying assumption of an "ideal solution" as we have defined it above. We come, therefore, to

2. The Laws of the Ideal Solution.

Owing to the simplicity of the thermodynamic treatment of solutions by what we may call the osmotic-cyclical-process method and the fact that it uses conceptions which are comparatively easy to grasp and processes which can be readily pictured in the mind, it has been the favorite system among physical chemists. The fact that the theories developed by the advocates of this method have been confined almost entirely to the domain of the dilute solution is not due to any inherent fault in the method. In addition to this method we have the systems of thermodynamics based upon the Gibbs thermodynamic potential and its related functions. These systems have been the favorite ones among physicists and those who by training and inclination were accustomed to the use of potential functions, and it is among the advocates of the thermodynamic potential that we find the first successful attempt to formulate a theory of solution which is free from the assumption that the solution must be dilute.

This theory has been developed in Holland by van der Waals and his associates, especially by van Laar. The first attempt was made in 1893 by Hondius Boldingh[10] in an Amsterdam Dissertation which so far as I have been able to learn has never been published elsewhere. In the following year van Laar[11] published two papers in which he derived a set of "exact formulae for osmotic pressure, change in solubility, freezing point, boiling point, etc." His results were expressed in a series of equations in which the concentration of the solution appeared in a term, $\ln(1-N')$, in which N' represents the mol fraction of the solute. The equations contained, in addition, an undetermined function of the molecular thermodynamic potentials of the constituents. In numerous subsequent publications van Laar has advocated with great warmth and zeal, the use of the thermodynamic potential method and the introduction of the concentration of the solution into the equations by means of the expression $\ln(1-N')$, instead of assuming that the solution is dilute. Van Laar has in fact advocated a theory of solution which is entirely free from the assumption that the solution must be dilute. The foundations for this theory have existed in the literature for the last fifteen years. If it occurs to any one to wonder why the theory has not come into general use in the chemical world, he has only to glance through some of van Laar's papers, especially his earlier ones, and the reason will be more or less obvious.

It is my present purpose to free this theory from the language of the thermodynamic potential and to develop it in the so-called "osmotic language."[12] Stated in this language, our problem is to determine the

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[10] Boldingh, "De Afwijkingen van de Wetten voor Verdunde Oplossingen." Dissertation, Amsterdam, 1893.

[11] van Laar, *Z. physik. Chem.*, 15, 457 (1894).

[12] The "language of the colligative properties" would be a better term. Too much importance is usually ascribed to osmotic pressure in our solution theory.

functional relation between some one of the colligative properties of the solution and its concentration in the case of an ideal solution. Theoretically we can start with any one of the colligative properties we choose, but since our present theory of dilute solutions is usually assumed to start with the osmotic-pressure-concentration relation, it will perhaps be more interesting to develop our theory of the ideal solution from the same standpoint.

Let us, therefore, turn to the equation which expresses the osmotic pressure[13] for a very dilute solution:

$$\pi = \frac{n'RT}{V_s} = \frac{n'RT}{nV} \tag{100}$$

In this equation, n' is the number of mols of solute in n mols of solvent and V is the molecular volume of the pure liquid solvent. Let us now make use of the method, introduced by Willard Gibbs, of expressing the composition of the solution by means of the equation $N' + N = 1$, where N' is the mol fraction of the solute and N that of the solvent. The above equation can now be written:

$$\pi = \frac{\frac{n'}{n+n'}RT}{\frac{n}{n+n'}V} = \frac{N'RT}{NV} \tag{101}$$

We have long recognized the fact that our osmotic pressure equation expresses *strictly* only the limit approached by the osmotic pressure as the concentration of the solution approaches zero. Let us therefore write the equation itself so that it will indicate this fact. This gives us

$$\Delta\pi = \left(\frac{\Delta N'}{N}\right)\left(\frac{RT}{V}\right). \tag{102}$$

Seeing the equation in this form it is natural to suspect that the real relation might possibly be

$$d\pi = \left(\frac{dN'}{N}\right)\left(\frac{RT}{V}\right), \tag{103}$$

or since by definition—$dN' = dN$,

$$d\pi = \left(\frac{-RT}{V}\right) d \ln N. \tag{104}$$

Stated in words, this means that not only would the addition of dN' mols of solute to a pure solvent involve an increase (*i. e.*, from 0 to $\Delta\pi$) of osmotic pressure which satisfies equation (104) but that it would also involve the *same* increase in osmotic pressure when added to a solution whose osmotic pressure is π. If such proves to be the case (and we shall see that in many cases, at least, it does), our Modern Theory of Solutions

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[13] Throughout this paper, we shall understand by the term "osmotic pressure," the pressure difference π as defined by the equation $\pi = P - P_A$, where P_A is the pressure upon the pure liquid solvent A when it is in equilibrium (through a membrane or medium permeable only to itself) with the solution under the constant pressure P. This has been discussed more fully in the previous paper (THIS JOURNAL, 32, 478 (1910)).

has remained a theory of infinitely dilute solutions, because we have failed to recognize the fact that we have been working with true differential equations, and that in order to obtain the "theory of concentrated solutions" which we have been seeking, the *only thing we needed to do was to integrate our equations.*

In the case of osmotic pressure, for example, if we integrate equation (104), we shall obtain an equation which contains no assumption whatever regarding the concentration. The solution may be infinitely dilute or infinitely concentrated or may have any concentration between these limits. In order to do this we have only to put $V = V_0(1 + \alpha\pi)$, where V_0 is the molecular volume of the pure solvent under the standard pressure P and α is its coefficient of compressibility, and on integration we obtain the Boldingh-van Laar[14] equation for osmotic pressure:

$$\pi + \tfrac{1}{2}\alpha\pi^2 = \left(\frac{-RT}{V_0}\right)\ln(1 - N') \qquad (105)$$

Having come to the conclusion that the integral of equation (104) should represent the osmotic pressure for an "ideal solution," whatever its concentration, we naturally seek for experimental confirmation before adopting it finally.[15] Owing to the great difficulty of making accurate and

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[14] The history of this equation (105) is very interesting. The differential form as expressed by equation (104) was obtained by van der Waals as early as 1890 (*Z. physik. Chem.*, 5, 163) but no attempt was made to integrate it, only the case of dilute solutions being discussed, for which case it assumes the form of equation (102) or (100). In 1893 Hondius Boldingh, a student of van der Waals, making use of the thermodynamic potential of Gibbs, derived equation (105) in the following form (Diss., Amsterdam, 1893, p. 57):

$$\pi V_0 = -RT \ln(1 - N') + aN'$$

This differs from equation (105) as we have obtained it above, only in the fact that the compressibility of the liquid is neglected and a small correction term aN' is added, a being a quantity which, according to the molecular theory of van der Waals, expresses the mutual influence of the components of the solution upon each other. For "ideal solutions" it is negligible.

Boldingh apparently made no attempt to apply his equation. The same equation was obtained the following year by van Laar (*Loc. cit.*) and in numerous publications since then, this investigator has given various derivations of this equation usually by methods involving the thermodynamic potential (cf., however, note 15). In 1897 an osmotic pressure equation in its essential points practically identical with equation (105) was derived by Willard Gibbs (*Nature*, 60, 461 (1897)) by a method of balanced columns. Finally G. N. Lewis, in a recent paper (THIS JOURNAL, 30, 675 (1908)), has obtained equation (105) by a derivation involving his "activity" function and based upon the assumption that the "activity" of the solvent is proportional to its mol fraction. Both van Laar (*Proc. Acad. Sci.*, Amsterdam, 9, 55 (1906)) and Lewis (*Loc. cit.*) have discussed the relation of this equation to the van't Hoff equation and have made comparisons of the values of osmotic pressure given by it with those obtained by Morse and Frazer by direct measurement, in the case of aqueous solutions.

[15] In view of the fact that the van't Hoff equation for osmotic pressure is usually regarded as derivable from the kinetic theory by methods analogous to those used in the kinetic derivation of the perfect gas laws (that is, on the assumption that osmotic pressure is caused by the molecular bombardment of the solute molecules), it may

reliable osmotic pressure measurements, it would be an unnecessary waste of time and effort to seek experimental confirmation in this direction, especially as the equation can be tested *just as satisfactorily* by means

not be without interest to include here a brief kinetic derivation of the differential form of equation (105). For this purpose I shall modify slightly the derivation given by van Laar (*Sechs Vorträge*, p. 20).

Consider two solutions of the same solute in the same solvent, both under the external pressure P and separated from each other by a membrane permeable only to the molecules of the solvent. According to a theorem of Boltzmann, the number of solvent molecules which diffuse per second through a unit surface of the membrane in the two directions is given by the expressions:

(*a*) From the weaker solution to the stronger,

$$n_w = (1 - N'_w)e^{\frac{\lambda+PV_w}{RT}}. \qquad (107)$$

(*b*) From the stronger solution to the weaker,

$$n_s = (1 - N'_s)e^{\frac{\lambda+PV_s}{RT}}. \qquad (108)$$

In these equations e is the base of natural logarithms, N'_w and N'_s are the mol fractions of solute in the weaker and the stronger solutions respectively, V is the volume of the solution, R the gas constant, T the absolute temperature and λ a quantity which is a function of the temperature and which depends upon the units of measurement. By adjusting the pressure on the two solutions we can make the number of molecules of solvent which pass in the two directions equal; in other words the two solutions will be in equilibrium as respects the passage of the solvent from one to the other. Under these conditions the right-hand members of the above equations can be placed equal to each other, giving us the equation:

$$(1 - N'_w)e^{\frac{\lambda+P_wV_w}{RT}} = (1 - N'_s)e^{\frac{\lambda+P_sV_s}{RT}} \qquad (109)$$

Let us now impose the condition that the "weaker solution" shall be the pure solvent and that the "stronger solution" shall be an infinitely dilute solution in this solvent and shall be under an external pressure P. Under these conditions the above equation assumes the form

$$e^{\frac{[\lambda+(P+d\pi)V]}{RT}} = (1 - dN')e^{\frac{(\lambda+PV)}{RT}}. \qquad (110)$$

Dividing through by $e^{\frac{(\lambda+PV)}{RT}}$ and using the logarithmic instead of the exponential nomenclature, we obtain equation (104):

$$d\pi = \left(\frac{-RT}{V}\right) d\ln(1 - N') \qquad (104)$$

After giving a kinetic derivation for equation (105), van Laar follows it with what he terms a "rein thermodynamischer" proof. Such a proof is of course impossible, if by "purely thermodynamic" we are to understand that the equation can be shown to be a necessary consequence of the two laws of thermodynamics and nothing else. In his papers on the subject, van Laar does not distinguish carefully between purely thermodynamic relations and relations which involve additional assumptions. This makes it difficult for the reader, who has not had considerable experience in the use of the thermodynamic potential, to appreciate just what assumptions he is making and what grounds he has for making them. Van Laar also falls into the error of attributing the failure of the modern theory of solutions in the region of concentrated solutions, to an inherent weakness in the osmotic method which he condemns severely, at the same time advocating with great zeal the thermodynamic potential as the *only* quantity of its thermodynamic derivatives. Of these we will consider first, the vapor pressure derivative. The thermodynamic relation connecting osmotic pressure and vapor pressure is

$$d\pi = \left(\frac{-v}{V}\right)dp. \qquad (77)$$

Combining this with equation (104) so as to eliminate π we obtain

$$Vdp = RTd\ln N. \qquad (111)$$

If the vapor can be regarded as a perfect gas we can put $v = \frac{RT}{p}$ and obtain

$$d\ln p = d\ln N \qquad (112)$$

which on integration gives

$$p = p_0 N \qquad (113)$$

where p_0, the integration constant, is the vapor pressure of the pure solvent. Since the terms solvent and solute are quite arbitrary, we can state therefore in general that the partial vapor pressure of any constituent of an "ideal solution" is proportional to its mol fraction, if the vapor obeys Boyle's law. We have therefore in equation (113) an excellent means of testing our fundamental osmotic equation.

which is in a position to completely solve the problem (*Sechs Vorträge*, p. 19). This point of view is absolutely unjustified and is doubtless partially responsible for the fact that the many excellent and valuable features of this investigator's contributions to this problem have not received from the chemical world the consideration which they deserve. Whether we should adopt a system of thermodynamic chemistry based upon the entropy function (as worked out by Horstmann), or upon one of the thermodynamic potentials of Gibbs or Planck, or upon the "fugacity" and "activity" as defined by Lewis or upon the "osmotic pressure" and its related colligative properties, is largely a philosophical question in which the personal equation is an important factor. The "best" system from one point of view is not the "best" from another, and instead of adopting one of these systems and severely condemning the others, we should rather rejoice that the problems of our science are being attacked from these different points of view.. All of these systems rest upon the common ground of the first and second laws of thermodynamics and any chemical problem which can be solved in terms of one of them can be solved in terms of all. I cannot therefore agree with van Laar, that the so-called "osmotic" system "läuft auf seinen letzen Beinen" and "nach wenige Jahre wird abgereist sein."

Van Laar also attacks the so-called "gas theory" of solutions, that is, the theory that what we call "osmotic pressure" is a real pressure which exists within an isolated solution due to a molecular bombardment by the solute molecules. On this question, I sympathize largely with van Laar's point of view. His exposition of the difficulties in the way of such a theory is clear and convincing and I shall not, therefore, attempt any further discussion of the question at this time. In this connection, however, it is interesting to recall the views held by Willard Gibbs upon this point. In speaking (*Loc. cit.*) of the osmotic pressure in the case of a solution A, containing a solute, D, he says:

"But we must *not* suppose in any *literal* sense, that this difference of pressure represents the part of the pressure in A which is exerted by the D-molecules, for that would make the total pressure calculable by the law of Boyle and Charles."

The next question which confronts us is, where are we to look for solutions whose characteristics approach most closely those which we have assumed for our "ideal solution," or in other words where can we find solutions for which we have reason to believe that we know the mol fractions of the constituents in the solution? Our attention is naturally directed towards mixtures of the so-called "normal" liquids of which many examples are to be found among the hydrocarbons of the benzene series and their substitution products. These liquids possess the property of mixing with each other in all proportions, the process of solution being accompanied by little if any heat effects or volume changes, such as would, in general, necessarily occur, if the process of solution were accompanied by chemical reactions such as solvation or changes in the degree of association or dissociation of any of the components. In general the physical properties of these solutions are additive with respect to the constituents. This behavior is, however, just what we should expect in the case of the "ideal solution" which we have assumed. We may therefore expect to find experimental confirmation of our osmotic pressure equation in the case of these solutions. Fortunately data are at hand in the vapor pressure measurements of Zawidski and others. These data show most conclusively that equation (113) expresses the partial vapor pressure for *both* constituents throughout the total concentration range from zero to infinity for some dozen or fifteen different mixtures.[16] Freezing point data furnish additional confirmation of the correctness of our fundamental equation. Van Laar finds, for example, that the "freezing point" curve for solutions of mercury in tin, throughout its entire range (from $t = 232°$ C., $N' = 0$ to $t = -19°$, $N' = 0.9964$), is satisfactorily represented by an equation which rests on the same basis as our fundamental osmotic pressure equation.

This perfect experimental confirmation, combined with the light which is thrown upon the subject by the historical criticism, constitutes a most convincing array of evidence in favor of the adoption of the Theory of the Ideal Solution, as the best provisional *General Theory of Solution*. Before turning to a more detailed consideration of the equations of the Ideal Solution, let us state clearly the general characteristics of such a solution. They are as follows:

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[16] The mixtures which obey this vapor pressure law are as follows:

(1) CO_2—CH_3Cl; (2) C_6H_{14}—C_8H_{18}; (3) $C_2H_4Cl_2$—C_6H_6; (3) $C_2H_4Br_2$—$C_2H_6Br_2$; (2) CH_3OH—C_2H_5OH; (2) $CH_3COOC_2H_5$—$C_2H_5COOC_2H_5$; (2) C_6H_6—$C_6H_5CH_3$; (4) C_6H_6—C_6H_5Cl; (4) C_6H_6—C_6H_5Br; (2) $C_6H_5CH_3$—$C_6H_5C_2H_5$; (4) $C_6H_5CH_2$—C_6H_5Cl; (4) $C_6H_5CH_3$—C_6H_5Br; (2) C_6H_5Cl—C_6H_5Br.

References:

[1] Kuenen, *Z. physik. Chem.*, **11**, 38 (1893).

[2] Young, *J. Chem. Soc.*, **81**, 768; **83**, 68 (1903).

[3] von Zawidski, *Z. physik. Chem.*, **35**, 129 (1900).

[4] Linebarger, THIS JOURNAL, **17**, 615, 690 (1895).

This experimental confirmation of the theory of the ideal or "perfect" solution was pointed out in a recent paper by G. N. Lewis (*Loc. cit.*) who has computed some tables which exhibit in a very striking manner the excellent agreement of equation (105) with the experimental data, even in the most concentrated solutions.

I. The number of molecular species present is equal to the number of components.

II. The physical properties of the solution are connected with the physical properties of its components in the pure state by the equation

$$X = xN + x'N' + x''N'' + \ldots \qquad (114)$$

in which X is the molecular property in question (*e. g.*, molecular heat capacity, molecular volume, molecular refraction, molecular internal energy, etc.), x (x', x'', etc.) the molecular property of a constituent in the pure state and N (N', N'', etc.) its mol fraction in the solution.

III. The third and most important characteristic is that which describes the thermodynamic relations. The manner of stating this characteristic depends upon what system of thermodynamics one chooses to make use of. I shall therefore state it in three different "languages."

(*a*) *The Gibbs Thermodynamic Potential System.*—According to van Laar the thermodynamic characteristics of the "ideal solution" are expressed by the equation

$$\mu = \mu_0 + RT \ln N \qquad (115)$$

in which μ is the molecular thermodynamic potential of a constituent in the solution, μ_0 the molecular thermodynamic potential of the same constituent in the pure state and N its mol fraction in the solution.

(*b*) *The Fugacity-Activity System of Lewis.*—Lewis uses a system of thermodynamic chemistry based upon two quantities, the "fugacity" ψ, and the "activity" ξ, whose relation to each other is expressed by the equation

$$\psi = \xi RT \qquad (116)$$

and which are connected with the thermodynamic potential by the equation

$$\mu = C + RT \ln \psi \qquad (117)$$

where C is a function of the temperature only. According to Lewis the "perfect solution" is defined by the equation

$$\xi = \xi_0 N \qquad (118)$$

or what amounts to the same thing,

$$\psi = \psi_0 N. \qquad (119)$$

That van Laar's and Lewis' methods of describing the "ideal" or "perfect" solution are identical is made evident by writing equation (119) in the form

$$RT\ln\psi = RT\ln\psi_0 + RT\ln N, \qquad (120)$$

and combining it with equation (117) when we obtain at once equation (115).

(*c*) *The Colligative Property System or the So-called Osmotic System.*—According to this system, the relation between the colligative properties of the Ideal Solution and its composition is expressed by a set of equations which is composed of the equation

$$d\pi = \left(\frac{-RT}{V}\right) d\ln N \qquad (104)$$

and its thermodynamic derivatives.[17]

Having established fundamental equations for the Ideal Solution, let us now derive a set of equations for such a solution similar to our present equations for dilute solutions, but free from any assumptions as to the concentration of the solution. In deriving such a set of equations we could start either with our osmotic pressure equation (104) or the vapor pressure derivative (112). In either case we should obtain the same set of equations. There is not much reason for choosing one of these equations rather than the other as a starting point. Each possesses certain advantages for this purpose. In the following derivations, however, I shall start with the osmotic pressure equation (104) in each case. This procedure will allow of direct comparison with our corresponding derivations for dilute solutions and it moreover avoids the necessity of using the gaseous phase in the derivation of a relation which is independent of the properties of the vapor. The procedure for obtaining our set of equations is very simple. In each instance, it consists simply in combining equation (104) with the proper purely thermodynamic relation and then integrating the result. The purely thermodynamic relations have all been obtained by the author in the previous publication[3] to which the reader is referred for their derivation. For convenience in reference these equations will be designated by the same numbers as in the preceding publication. All numbers below 100 refer to the previous paper.

3. Vapor Pressure.

We have already derived this equation for which the integrated form is

$$p = p_0 N \qquad (113)$$

where p is the partial vapor pressure of any molecular species from an ideal solution in which its mol fraction is N, and p_0 is its vapor pressure in the pure liquid state at the same temperature. For a single non-volatile solute whose mol fraction is N' this can also be written in the form

$$\frac{\Delta p}{p_0} = N' = \frac{n'}{(n + n')}. \qquad (121)$$

If in a mixture of say two liquids, polymerization of one or both constituents, or chemical combination between them occurs, we can obviously make use of equation (113) to determine the exact nature and extent of these processes if we know the necessary partial vapor pressure data. Derivatives of equation (113) for special cases of association and of chemical combination have been applied recently with considerable success

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[17] Regarding the general characteristics of the Ideal Solution as stated above, it should be noted that although *in general* the *absence* of heat effects or volume changes on mixing two liquids may be taken as evidence for the absence of accompanying chemical reactions, the reverse is not necessarily the case. Heat effects and volume changes *may* and doubtless do occur in the absence of any chemical reaction, although in such a case the heat effect will in the majority of cases be of quite a different order of magnitude from that which is caused by a chemical reaction.

by Ikeda[18] and by Dolezalek[19] to the elucidation of the chemical condition of several pure liquids and of their mixtures. The accumulation of accurate and reliable vapor pressure data is of the highest importance to a clearer and more complete knowledge of the nature of solutions. For reasons which I have stated elsewhere,[21] the vapor pressure equation is the relation best adapted to serve as a basis for the experimental attack on the problem of concentrated solutions.

4. The Freezing Point Equation.

If we combine the purely thermodynamic equation

$$d\pi = \left(\frac{-L_F}{V}\right)\frac{dT_F}{T_F} \tag{82}$$

with our fundamental equation

$$d\pi = \left(\frac{-RT}{V}\right) d\ln N \tag{104}$$

so as to eliminate π, we obtain the desired equation[20]

$$dT_F = \left(\frac{RT_F^2}{L_F}\right)\left(\frac{dN}{N}\right) = \left(\frac{-RT_F^2}{L_F}\right)\left(\frac{dN'}{N}\right). \tag{122}$$

For *very dilute* solutions, we *can* of course substitute the freezing point lowering Δt_F in place of $-dT_F$ and $\frac{n'}{n}$ in place of $\frac{dN'}{N}$ and obtain the familiar law of Raoult-van't Hoff for freezing point lowering in dilute solution:

$$T_0 - T_F = \Delta t_F = \left(\frac{RT_0^2}{L_F}\right)\left(\frac{n'}{n}\right) \tag{124}$$

It is preferable, however, to integrate our differential equation and thus obtain a general equation for an ideal solution of any concentration. Before doing this we will substitute in equation (122)

$$T_0 - \Delta t_F = T_F,\ 1 - N' = N \text{ and } -d(\Delta t_F) = dT_F$$

where Δt_F is the freezing point lowering in centigrade degrees and T_0 is the freezing point of the pure solvent on the absolute scale. This gives us

$$\frac{dN'}{d(\Delta t_F)} = \frac{L_F(1-N')}{R(T_0 - \Delta t_F)^2}. \tag{125}$$

In order to integrate, we must first express L_F as a function of Δt_F which is done by the following purely thermodynamic equation:

$$L_F = L_{F_0} - \Delta C_{P_0}\Delta t_F - {}^1/_2\alpha(\Delta t_F)^2 - {}^1/_3\beta(\Delta t_F)^3 - \ldots. \tag{85}$$

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[18] Ikeda, *J. Coll. Sci. Imp. Univ. Tokyo*, 25, Art. 10 (1908).

[19] Dolezalek, *Z. physik. Chem.*, 64, 730 (1908); see also Möller, *Ibid.*, 69, 449 (1909).

[20] This equation was obtained by Boldingh (*Loc. cit.*, p. 61) in the following form:

$$\left(\frac{L_F}{R}\right)\left(\frac{dT_F}{T_F^2}\right) = \left[\frac{1}{(1-N')} + 2aN'\right] dN' \tag{123}$$

where *a* has the meaning explained in note (14). Boldingh integrated his equation under the assumption that L_F is independent of T.

In this equation L_{Fo} is the molecular heat of fusion of the pure solvent at its freezing point T_o, ΔC_{Po} is the attendant decrease in the heat capacity of the system and α, β, etc., are constants expressing the dependence of ΔC_P upon the temperature. Combining (85) with (125) we obtain finally (neglecting β):

$$\frac{dN'}{d(\Delta t_F)} = \frac{[L_{Fo} - \Delta C_{Po} - {}^1/_2\alpha(\Delta t_F)^2](1 - N')}{R(T_o - \Delta t_F)^2} \tag{126}$$

This equation can now be integrated. A convenient way to do this is to integrate into a power series in the desired variable by applying McLaurin's theorem directly to the differential equation, carrying the series only so far as the accuracy of the experimental data warrant for the particular case under consideration. For example, in the case of water solutions if Δt_F be known to 0.001°, then for values of Δt_F which do not exceed 7°, the terms containing α, β, etc., are negligible and the application of McLaurin's theorem gives us the equations[21]

$$N' = \frac{L_{Fo}}{RT_o^2}\left[\Delta t_F - {}^1/_2\left(\frac{L_{Fo}}{RT_o^2} + \frac{\Delta C_{Po}}{L_{Fo}} - \frac{2}{T_o}\right)(\Delta t_F)^2\right] \tag{127}$$

and

$$\Delta t_F = \frac{RT_o^2}{L_{Fo}}\left[N' + {}^1/_2\left(1 + \frac{RT_o^2\Delta C_{Po}}{L_{Fo}} - \frac{2RT_o}{L_{Fo}}\right)N'^2\right], \tag{128}$$

the remaining terms in the expansion not being significant.

If we desire to follow a freezing point curve through a considerable range of temperature, the general integral of equation (126) is more advantageous. The general integral is

$$R\ln(1 - N') = (\Delta C_{Po} + \alpha T_o)\ln\frac{(T_o - \Delta t_F)}{T_o} - \frac{[L_{Fo} - (\Delta C_{Po} + \alpha T_o)\Delta t_F + {}^1/_2\alpha\Delta t_F^2]}{(T_o - \Delta t_F)} + \frac{L_{Fo}}{T_o}. \tag{129}$$

Equations of this general character have been derived by several observers[22] and the corresponding theoretical curves have been compared with the experimental curves for a number of systems with good agreement. In these comparisons, however, the constants of the theoretical equation have been evaluated from the freezing point data themselves, so that the agreement loses a good deal of its significance.

5. The Boiling Point Equation.

By combining the purely thermodynamic equation

$$d\pi = \left(\frac{L_v}{V}\right)\left(\frac{dT_B}{T_B}\right) \tag{90}$$

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[21] The application of equation (127) to the data for aqueous solutions and the interpretation of the results obtained have been discussed by the author in a previous paper (*Technology Quarterly*, 21, 370 (1908)). This application was made on the assumption that the molecular weight of liquid water is 18. Although the results obtained on this assumption were fairly satisfactory up to a concentration of 1 molal, it is clear that a complete study of the behavior of aqueous solutions from the standpoint of the laws of the Ideal Solution must take into account the degree of association of the solvent. Further investigations along this line are now in progress in this laboratory.

[22] *e. g.*, van Laar (*Versl. K. Akad. van Wet.*, Amsterdam, 1903 and 1904; several papers) Roozeboom (*"Die Heterogene Gleichgewicht,"* 2, 267 *et. seq.*), and Yamamota (*J. Coll. Sci. Imp. Univ. Tokyo*, 25, Art. 11 (1908)).

with equation (104) so as to eliminate π we obtain the desired equation

$$dT_B = \left(\frac{RT_B{}^2}{L_v}\right)\left(\frac{dN'}{N}\right). \qquad (130)$$

which for very dilute solutions takes the familiar form

$$T_B - T_{Bo} = \Delta t_B = \left(\frac{RT_{Bo}{}^2}{L_v}\right)\left(\frac{n'}{n}\right). \qquad (131)$$

In order to integrate the differential equation (130) we have only to express L_v as a function of the temperature. The First Law of Thermodynamics gives us the rigorous equation

$$\frac{dL_v}{dT} = c_p - C_P + \frac{L_v}{T} - \left(\frac{L_v}{v}\right)\left(\frac{\partial v}{\partial T}\right)_p \qquad (132)$$

by means of which we can calculate the temperature coefficient of L_v. If the vapor behaves as a perfect gas this equation becomes

$$\frac{dL_v}{dT} = \Delta C_P \qquad (133)$$

and the methods of integration of equation (130) become perfectly analogous in every respect to those followed in the case of the freezing point equation in the preceding section. It is not necessary therefore to discuss them in detail. The final equations have the same form as the corresponding ones for the freezing point lowering.

6. Chemical Equilibrium.

Two examples will be sufficient to illustrate the method of derivation of the laws which regulate chemical equilibrium in the ideal solution. Let the equilibrium be expressed by the equation:

$$a\mathrm{A} + b\mathrm{B} + \ldots\ldots \rightleftarrows m\mathrm{M} + n\mathrm{N} + \ldots \qquad (134)$$

(*a*) *The Effect of Concentration.*—The purely thermodynamic equation for the effect of concentration upon chemical equilibrium in a liquid phase at constant temperature and pressure is

$$-aV_{\mathrm{A}}d\pi_{\mathrm{A}} - bV_{\mathrm{B}}d\pi_{\mathrm{B}} - \ldots\ldots + mV_{\mathrm{M}}d\pi_{\mathrm{M}} + nV_{\mathrm{N}}d\pi_{\mathrm{N}} + \ldots = 0. \qquad (30a)$$

According to equation (104) the osmotic pressure for each substance taking part in the equilibrium is

$$V_{\mathrm{X}}d\pi_{\mathrm{X}} = -RTd\ln N_{\mathrm{X}}. \qquad (135)$$

Combining these two equations we obtain the relation

$$\frac{N_{\mathrm{A}}^{a} \cdot N_{\mathrm{B}}^{b} \cdots}{N_{\mathrm{N}}^{n} \cdot N_{\mathrm{M}}^{m} \cdots} = K_N \qquad (136)$$

where K_N is a constant. This expression differs from the Guldberg-Waage Law only in the substitution of the mol fraction N, in place of the volume concentration C. Equation (136) was obtained by Planck[23] as early as 1887, and the reasons for adopting it in place of the Guldberg-Waage form and for expressing the composition of solutions in terms of mol fractions instead of mols per liter were clearly stated by him at the same time.

(*b*) *The Effect of Temperature.*—The purely thermodynamic relation is

$$-aV_{\mathrm{A}}d\pi_{\mathrm{A}} - bV_{\mathrm{B}}d\pi_{\mathrm{B}} - \ldots + mV_{\mathrm{M}}d\pi_{\mathrm{M}} + nV_{\mathrm{N}}d\pi_{\mathrm{N}} + \ldots = \frac{Q_{\pi}dT}{T}. \qquad (38a)$$

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[23] Planck, *Wied. Ann.*, 32, 489 (1887).

Combining this with equations (136) and (135) and introducing the First Law of Thermodynamics we obtain the equation

$$\frac{d\ln K_N}{dT} = \frac{U}{RT^2} \qquad (137)$$

which is identical with the van't Hoff Law, with the substitution of K_N in place of the Guldberg-Waage constant K_C. In general it may be stated that the laws for chemical equilibrium in an ideal solution may be obtained from our present dilute solution laws by substituting mol fractions in place of volume concentrations. This applies also to heterogeneous equilibrium. The Solubility Product Law, for example, for a saturated solution of the solute BC which dissociates into B and C becomes[24]

$$N_B \cdot N_C = const. = K_S. \qquad (138)$$

7. Concluding Discussion.

Lest any one from the perusal of the foregoing pages should gain the impression that the problem of a satisfactory general theory of solutions may be regarded as completely solved, it will be well to examine for a moment, in a general way, the characteristics of the Theory of the Ideal Solution with respect to its advantages and disadvantages when regarded as the basis for a general theory of solutions. When compared with the Theory of Dilute Solutions we must acknowledge that it constitutes a distinct and decided step forward. One requirement of a satisfactory general theory of solutions is that it shall represent the facts throughout the whole range of concentrations for some type of solution, at least. This requirement is fulfilled by the Theory of the Ideal Solution and we may feel considerable certainty that any deviation from the requirements of this theory, in a given case, is due to physical or chemical causes and capable of a physical or chemical explanation and is not simply the result of attempting to apply a set of incomplete laws which do not and could not be expected to hold for any kind of a concentrated solution no matter how simple its character.

The success of the Theory of the Ideal Solution as an instrument for throwing light upon the processes occurring in solutions has already been demonstrated in several instances. In the case of several solutions which apparently exhibit a behavior contrary to the requirements of the Theory, Dolezalek[19] has shown that perfect agreement between theory and experiment exist if the assumption be made that a simple compound is formed between the two constituents or that one of them is partially associated. In the case of acetone and chloroform for example, the assumption of a single compound, $CHCl_3 \cdot (CH_3)_2CO$, and the introduction of the corresponding equilibrium constant into the equations sufficed to produce complete agreement between theory and experiment. It is true that the value of the constant was computed from the vapor pressure data themselves, but in a recent paper[19] Möller has shown that the values of such constants may be obtained independently of the vapor pressure data of the solution under consideration and that they therefore possess

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[24] This is obtained by combining equations (51) and (104). It does not involve the Mass Action Law [*i. e.*, equation (136)], which is usually assumed as the basis for the derivation of the Solubility Product Law. This point, which was brought out in the previous paper, has been overlooked in all of the textbooks of physical chemistry, although it was explained clearly by Planck as early as 1887 (*Loc. cit.*).

the physical significance ascribed to them and are not simply empirical constants of an interpolation formula.

In all the cases studied by Dolezalek he found that agreement between experiment and theory is produced if the assumption be made that what appears to be a deviation from the theory is simply due to the fact that the numbers assumed as the mol fractions of the two constituents in the solution are incorrect and that when the proper mol fractions are used, the apparent discrepancy disappears. If we were justified in assuming that *all* solutions are really ideal solutions and that what appear to be exceptions are merely due to our inadequate knowledge of the number and kind of the various molecular species present and their respective mol fractions, then the Theory of the Ideal Solution would constitute a general theory including all solutions and all concentrations and would enable us to ascertain just what occurs chemically, when the solution is formed out of its constituents. Unfortunately such is not the case, for it can be easily shown mathematically that if certain liquids form an ideal solution with one another they must be miscible in all proportions. The solutions in a system composed of two or more liquid phases in equilibrium with one another cannot therefore be governed to the laws of the Ideal Solution. Moreover, these exceptions are not merely apparent but are real and cannot be explained on the grounds of association, dissociation or chemical combination. The explanation must be looked for in a radical difference in the physical nature of the medium.

To illustrate by an extreme case, let us consider a system composed of a solution of benzene in mercury and a solution of mercury in benzene, both solutions in equilibrium with each other. The vapor pressure of benzene from the mercury layer is equal to its vapor pressure from the benzene layer and yet the mol fraction of benzene in the mercury layer is probably so small that we could not detect it by any analytical means, while in the benzene layer it is equal to 1, within the limits of our ability to measure it. The equality of the vapor pressure from the two layers can only be due, therefore, to the fact that the nature of the medium between the molecules of mercury is such that the benzene molecules can penetrate it only with the greatest difficulty. This effect of the physical nature of the medium is therefore one which must be taken account of in all applications of the Theory of the Ideal Solution. In order that the laws of the Ideal Solution shall apply, the nature of the medium or the field of force in which the molecules find themselves in the solution must not be *very* different from that of the pure liquid itself. Although this restricts somewhat the sphere of usefulness of the theory, there still remain a large number of cases where it should prove of the greatest value in the elucidation of the chemical nature of solutions. Even in cases where the theory cannot be extended over all concentrations because of a consequent radical change in the physical nature of the medium, we may still hope to obtain valuable results with its aid in solutions of moderate concentrations. At all events, I believe that the Theory of the Ideal Solution is the one which should be adopted as the basis for reference, classification an interpretation of the experimental data on solutions in place of our present Theory of the Infinitely Dilute Solution which is only a special, though very important, case of the former theory.

URBANA, ILLINOIS, Feb. 1, 1910.

A REVIEW OF SOME RECENT INVESTIGATIONS IN THE QUINAZOLINE GROUP.[1]

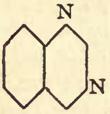
By Marston Taylor Bogert.

Received March 31, 1910.

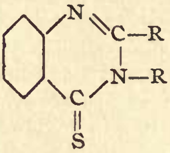
For several years past, the Organic Laboratory of Columbia University has been engaged in the synthesis and study of compounds belonging to that group of organic heterocycles known as quinazolines or phenmiazines.

To us, the work has been most interesting and enjoyable. The compounds obtained have been generally crystalline solids, quite readily purified, stable, and very satisfactory to work with.

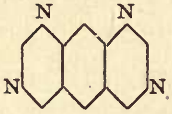
Our investigations have included—A. Quinazolines, B. Thioquinazolines, and C. Naphthotetrazines of quinazoline structure:



(Quinazoline)



(Thioquinazoline)



(1,3,7,9-Naphthotetrazine)

Incidentally, a great many new preparatory, intermediate and subsidiary products have been obtained. From the standpoint of new substances, the field has been an unusually fruitful one.

It is, therefore, not only an honor but also a pleasure to present on this occasion a brief synopsis of the major lines of the work to date.

A. Quinazolines.

Colby and Dodge,[2] as the result of their investigations of the interaction of nitriles and organic acids, under conditions of heat and pressure, came to the following conclusions:

I. Fatty nitriles and aromatic acids give fatty acids and aromatic nitriles.

II. Aromatic nitriles and fatty acids give mixed secondary amides.

III. Aromatic nitriles and aromatic acids give secondary amides, unless the temperature is very high, when the nitrile of the higher radical may form.

Mathews,[3] in continuation of this work, heated acetonitrile and anthranilic acid together under pressure, hoping thereby to obtain the

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[1] Presented at the Twentieth Anniversary Celebration of Clark University, Worcester, Mass., Sept. 14, 1909.

[2] *Am. Chem. J.*, 13, 1 (1891).

[3] This Journal, 20, 654 (1898).

anthranilic nitrile. On examining the contents of the tube, he found not the nitrile desired but a colorless crystalline compound, melting at 232° (uncor.), which was not identified at the time.

Later, Bogert and Gotthelf[1] made a more careful study of this reaction and found that the crystalline substance melting at 232° was identical with the 2-methyl-4-ketodihydroquinazoline first described by Weddige,[2] and later obtained by Bischler and Burkart,[3] Bischler and Lang,[4] and Niementovskii.[5] By varying the nitrile, they obtained other quinazolines of analogous structure.

Continuing this work, Gotthelf[6] heated anthranilic acid under pressure with a:

IV. Fatty nitrile alone (using aceto-, propio-, *n*-butyro-, *i*-valero- and *i*-capronitriles).

V. Fatty nitrile and the corresponding fatty acid (acetonitrile and acetic acid, propionitrile and propionic acid, etc.).

VI. Fatty nitrile and a higher fatty acid (acetonitrile and propionic acid, *n*-butyronitrile and capric acid, etc.).

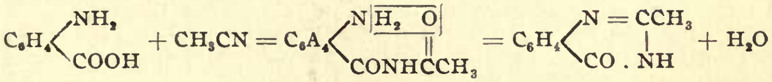
VII. Fatty nitrile and a lower fatty acid (isocapronitrile and propionic acid, etc.).

VIII. Fatty nitrile and the corresponding acid anhydride (propionitrile and propionic anhydride, valeronitrile and valeric anhydride, etc.).

IX. Fatty nitrile and higher acid anhydride (acetonitrile and propionic anhydride, etc.).

X. Fatty nitrile and lower acid anhydride (acetonitrile and formic acid, etc.).

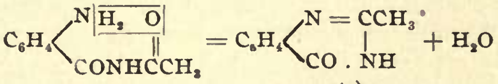
In considering case IV, Bogert and Gotthelf at the time thought it probable that the production of a quinazoline was due to the formation of an intermediate secondary amide.



$$C_6H_4\left\langle\begin{array}{l}NH_2\\COOH\end{array}\right. + CH_3CN = C_6A_4\left\langle\begin{array}{l}N\boxed{H_2\quad O}\\CONH\overset{\|}{C}CH_3\end{array}\right. = C_6H_4\left\langle\begin{array}{l}N = CCH_3\\ \quad\ \ |\\CO\ .\ NH\end{array}\right. + H_2O$$

just as acetonitrile and acetic acid when heated under pressure give diacetoamide.[7]

One objection to this explanation of the course of the reaction lies in the fact that it involves a lactam condensation, whereas Weddige's investigations in this very field have made it quite clear that these condensations follow preferably the lactim course. If the intermediate secondary amide assumed by us passes directly into the quinazoline by loss of water, two different quinazolines should result according to whether the condensation is of lactam or lactim type:



$$C_6H_4\left\langle\begin{array}{l}N\boxed{H_2\quad O}\\CONH\overset{\|}{C}CH_3\end{array}\right. = C_6H_4\left\langle\begin{array}{l}N = CCH_3\\ \quad\ \ |\\CO\ .\ NH\end{array}\right. + H_2O$$

(*a*)

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[1] THIS JOURNAL, 22, 129 (1900).

[2] *J. prakt. Chem.*, [2] 31, 124 (1885).

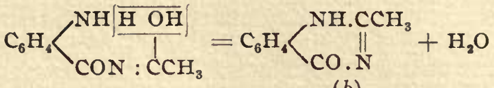
[3] *Ber.*, 26, 1350 (1893).

[4] *Ibid.*, 28, 282 (1895).

[5] *J. prakt. Chem.*, [2] 51, 564 (1895) and *Ber.*, 29, 1360 (1896).

[6] THIS JOURNAL, 23, 611 (1901).

[7] Kekulé, *Lehrbuch* (1st ed.), 1, 574; Gautier, *Ztschr. Chem.*, 1869, 127.



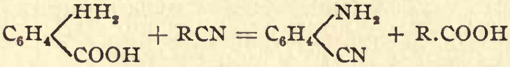
$$C_6H_4\left\langle\begin{array}{l}NH\boxed{H\ OH}\\ \quad\quad\ \ |\\ CON:CCH_3\end{array}\right. = C_6H_4\left\langle\begin{array}{l}NH.CCH_3\\ \quad\quad\ \|\\ CO.N\end{array}\right. + H_2O$$

(*b*)

As a matter of fact, the product obtained by us is identical with (*a*).

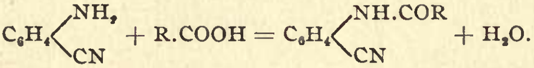
Another objection is that it is not in harmony with the conclusions of Colby and Dodge[1] cited above. According to their experiments, the first products of the action of a fatty nitrile upon an aromatic acid at high temperature and pressure are the aromatic nitrile and the fatty acid, which may and often do subsequently combine to a mixed secondary amide. That the secondary amide is not the first product seems established by their results, for in no case where a fatty nitrile acted upon an aromatic acid was the secondary amide found unaccompanied by aromatic nitrile, while in many cases aromatic nitrile and fatty acids were found unaccompanied by any secondary amide. Thus, acetonitrile and benzoic acid at 220° gave no acetobenzamide, but only benzonitrile and acetic acid, whereas when the latter two were heated together at 220°, only acetobenzamide was formed.

It therefore seems probable that the first phase of the reaction between anthranilic acid and a fatty nitrile is as follows:



$$C_6H_4\left\langle\begin{array}{l}HH_2\\COOH\end{array}\right. + RCN = C_6H_4\left\langle\begin{array}{l}NH_2\\CN\end{array}\right. + R.COOH$$

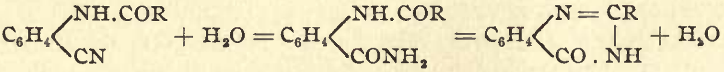
As aniline when heated to sufficiently high temperatures with fatty acids yields the corresponding anilides,[2] the second phase of the reaction is probably



$$C_6H_4\left\langle\begin{array}{l}NH_2\\CN\end{array}\right. + R.COOH = C_6H_4\left\langle\begin{array}{l}NH.COR\\CN\end{array}\right. + H_2O.$$

As the ease with which this acylation takes place decreases with increase in the molecular weight of the fatty acid, the higher nitriles should give smaller yields of the quinazoline, and this was found to be the case. The yield with propionitrile, for example, was 22.5 per cent., while with valeronitrile it was only 5 per cent. of the theoretical.

The acylanthranilic nitrile may then pass into the quinazoline by either of the following reactions:

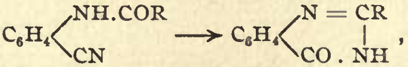


$$C_6H_4\left\langle\begin{array}{l}NH.COR\\CN\end{array}\right. + H_2O = C_6H_4\left\langle\begin{array}{l}NH.COR\\CONH_2\end{array}\right. = C_6H_4\left\langle\begin{array}{l}N=CR\\ \quad\ \ |\\CO.NH\end{array}\right. + H_2O$$

or

$$C_6H_4\left\langle\begin{array}{l}NH.COR\\CN\end{array}\right. + R.COOH = C_6H_4\left\langle\begin{array}{l}NH.COR\\CONHCOR\end{array}\right. = C_6H_4\left\langle\begin{array}{l}N=CR\\ \quad\ \ |\\CO.NH\end{array}\right. + R.COOH.$$

That a simple molecular rearrangement of the acylanthranilic nitrile occurs,



$$C_6H_4\left\langle\begin{array}{l}NH.COR\\CN\end{array}\right. \longrightarrow C_6H_4\left\langle\begin{array}{l}N=CR\\ \quad\ \ |\\CO.NH\end{array}\right.,$$

seems unlikely, for the reason that when acetoanthranilic nitrile was heated for some time above its melting point, or when its solution in dry toluene was heated to high temperatures in sealed tubes, no change

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[1] *Loc. cit.*

[2] Williams, *Ann.*, 131, 288; Pebal, *Ibid.*, 91, 152.

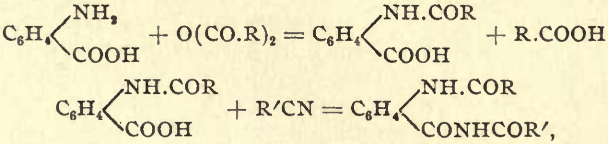
whatever occurred.[1] Moisture was, of course, rigidly excluded in these experiments, since a small amount of water, by successive addition and splitting off, would suffice to convert an indefinite amount of the nitrile to the quinazoline.

In further support of the assumption that the acylanthranilic nitrile is an intermediate product, are the following facts: (1) Acetanilide is found as a by-product in the tubes.[2] (2) The presence of a small amount of acetic anhydride greatly increases the yield of quinazoline. (3) The same quinazoline results when acetoanthranilic acid is heated in a sealed tube with acetonitrile as when anthranilic acid itself is used.[3] (4) Acetoanthranilic nitrile on partial hydrolysis changes immediately to the quinazoline.[4]

The by-products observed in the experiments were carbon dioxide, aniline, anilides, amides and ammonia. Of these, carbon dioxide and aniline are normal decomposition products of anthranilic acid at high temperatures. Partial hydrolysis of the nitrile accounts for the presence of amide. Aniline acting on the latter,[5] or upon the fatty acid present, yields the anilide, the by-product in the former case being ammonia.

In those cases (V, VI and VII) where the anthranilic acid was heated with both the fatty nitrile and the fatty acid, the results are confusing and the interpretation obscure. Quinazolines were formed, but the course of the reactions is not clear and additional work is needed before any satisfactory conclusions can be reached.

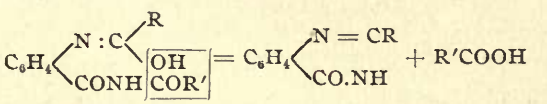
When an acid anhydride was added to the tubes containing the anthranilic acid and fatty nitrile (VIII, IX and X), the anhydride used determined the quinazoline formed in practically every case. In these experiments, the reaction is therefore probably as follows:



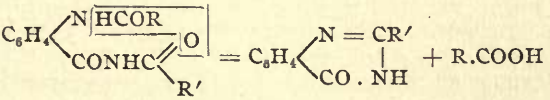
$$C_6H_4\left\langle\begin{array}{l}NH_2\\ COOH\end{array}\right. + O(CO.R)_2 = C_6H_4\left\langle\begin{array}{l}NH.COR\\ COOH\end{array}\right. + R.COOH$$

$$C_6H_4\left\langle\begin{array}{l}NH.COR\\ COOH\end{array}\right. + R'CN = C_6H_4\left\langle\begin{array}{l}NH.COR\\ CONHCOR',\end{array}\right.$$

the latter then condensing in either of the following ways:



$$C_6H_4\left\langle\begin{array}{l}N:C\left\langle\begin{array}{l}R\\ \boxed{OH}\end{array}\right.\\ CONH\,\boxed{COR'}\end{array}\right. = C_6H_4\left\langle\begin{array}{l}N=CR\\ CO.NH\end{array}\right. + R'COOH \quad (a)$$



$$C_6H_4\left\langle\begin{array}{l}N\,\boxed{HCOR}\\ CONHC\left\langle\begin{array}{l}\boxed{O}\\ R'\end{array}\right.\end{array}\right. = C_6H_4\left\langle\begin{array}{l}N=CR'\\ \quad\;\,|\\ CO.NH\end{array}\right. + R.COOH \quad (b)$$

The nitrile was used with the corresponding acid anhydride (VIII), with a higher acid anhydride (IX), and with a lower anhydride (X). Of these, types VIII and IX invariably yielded pure quinazolines according to reaction (*a*) above. Only when a lower anhydride was used with the

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[1] Bogert and Hand, THIS JOURNAL, 24, 1034 (1902).

[2] Bogert and Gotthelf, *Ibid.*, 22, 528 (1900).

[3] Bogert and Gotthelf, *Loc. cit.*

[4] Bogert and Hand, *Loc. cit.*

[5] Kelbe, *Ber.*, 16, 1200 (1883).

nitrile (X), were products encountered which were mixtures of quinazolines.

Of these different sealed-tube reactions, much the best was that in which the anthranilic acid was heated with the fatty nitrile and the corresponding acid anhydride (VIII). The yield by this process was fair (30 to 50 per cent. of the theory) and, unless the heating was too high, the tube contents were invariably light-colored and crystalline.

In the foregoing, it is assumed that the secondary amide is an intermediate product in the formation of the quinazoline. Such an amide, R.CO.NH.CO.R′, being symmetrical, should be producible either from R.COOH and R′CN, or from R′COOH and RCN. In other words, since the formation of the —CO.NH.CO— group is due solely to the combination of the CN and COOH, it should make no difference which radical carries the CN and which the COOH. The same secondary amide and, therefore, the same quinazoline, should result whether the acylanthranilic acid is heated with the fatty nitrile, or the acylanthranilic nitrile with the fatty acid (or its anhydride). On testing this practically,[1] such was indeed found to be the case, and a number of quinazolines were thus obtained from the acylanthranilic nitriles by heating them in sealed tubes with the fatty acid or, better, its anhydride.

In experimenting with these acylanthranilic nitriles, a method of converting them into the quinazolines, far superior to any of the methods described above, was discovered. It consists in digesting the acylanthranilic nitrile for a few minutes with a warm alkaline dioxide solution, and is really a beautiful method, being very rapid, simplicity itself in execution, and giving large yields of practically pure quinazolines. It depends upon the hydrolysis of the nitrile to the amide, the acylanthranilamide then condensing to the quinazoline, as shown by Weddige.[2]

In those cases where the *o*-amino acid is best obtained from its nitrile by saponification, it is convenient to be able to pass direct from the nitrile to the quinazoline. Thus, homoanthranilic nitrile is readily prepared from *m*-nitro-*p*-toluidine, through *m*-nitro-*p*-toluonitrile, and from the acyl derivatives of this homoanthranilic nitrile and an alkaline dioxide solution (hydrogen dioxide solution made alkaline with sodium hydroxide), the 7-methyl-4-quinazolones were prepared.[3]

By a number of different processes, including those already mentioned, starting with brominated anthranilic acdis, bromoquinazolines were prepared.[4]

Our attention was next turned to the nitroquinazolines, and many were made from nitroanthranilic acids by the methods already described, and also by heating the ammonium salt of the nitroanthranilic acid with formamide,[5] by the direct action of heat on the ammonium salts of nitroacylanthranilic acids,[6] and by the action of primary amines on nitroacetoanthranils.[7] The last is a very fine method indeed, and one we have developed quite extensively.

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[1] Bogert and Hand, THIS JOURNAL, 24, 1031 (1902).

[2] *J. prakt. Chem.*, [2] 31, 124 (1885); 36, 141 (1887).

[3] Bogert and Hoffman, THIS JOURNAL, 27, 1293 (1905).

[4] Bogert and Hand, *Ibid.*, 25, 943 (1903); 28, 94 (1906).

[5] Niementovskii, *J. prakt. Chem.*, [2] 51, 564 (1895).

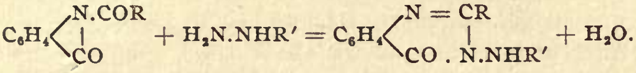
[6] Bischler and Burkart, *Ber.*, 26, 1349 (1893).

[7] Anschütz, Schmidt and Griffenberg, *Ber.*, 35, 3480 (1902).

By these various methods, we prepared 5-nitro-,[1] 6-nitro-[2], and 7-nitro-4-quinazolones.[3] Of the four possible types of benzoylnitroquinazolines, representatives of the 6-nitro,[4] and 8-nitro,[5] were already known. The preparation of the 5-and 7-nitro derivatives completed the series.

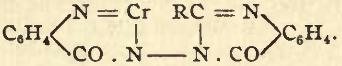
Reduction of the nitroquinazolines yielded the corresponding benzoylaminoquinazolines,[6] in which, as might have been expected, the amino group shows the usual aniline reactions.

Aminoquinazolines with the amino group on the miazine side of the nucleus were produced by condensing simple or substituted acylanthranils with primary hydrazines,[7]



$$C_6H_4\left\langle\begin{matrix}N.COR\\ |\\ CO\end{matrix}\right. + H_2N.NHR' = C_6H_4\left\langle\begin{matrix}N = CR\\ |\\ CO\,.\,N.NHR'\end{matrix}\right. + H_2O.$$

With hydrazine itself, it was also found possible to condense two molecules of the anthranil with one of the hydrazine, thereby giving 3,3'-diquinazolonyls,



$$C_6H_4\left\langle\begin{matrix}N = Cr & RC = N\\ | & |\\ CO\,.\,N & \text{——}\ N\,.\,CO\end{matrix}\right\rangle C_6H_4.$$

The same result can be accomplished, though less satisfactorily, by condensing the 3-aminoquinazoline with a second molecule of the anthranil. The di-quinazolonyls so far isolated are all very difficultly soluble and inert.

The 3-aminoquinazolines proved interesting because of their unsymmetrical secondary hydrazine structure, $>N.NH_2$. In the main, their properties coincide with those of other N-amino heterocyclic compounds. Thus, nitrous acid does not diazotize the amino group, but replaces it by hydrogen; with diacetosuccinic esters, they often yield pyrrole derivatives;[8] with aromatic nitroso bodies, they do not give azo compounds; nor are they oxidized to tetrazones by mercuric oxide. On the other hand, they do not usually condense with ketones, while they do occasionally yield phenyluramino derivatives with phenyl isocyanate.[9] In the elimination of the N-amino group by the action of nitrous acid, there must be some unstable intermediate product formed, for if immediately after the addition of the nitrous acid the mixture be poured into an alkaline solution of alpha- or beta-naphthol, dyestuffs are formed of considerable tinctorial power, the structure of which has not been elucidated.

Further experimentation with the acylanthranils showed that they

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[1] Bogert and Chambers, THIS JOURNAL, 27, 649 (1905); Bogert and Seil, *Ibid.*, 27, 1305 (1905) and 29, 532 (1907).

[2] Bogert and Cooke, *Ibid.*, 28, 1449 (1906).

[3] Bogert and Steiner, *Ibid.*, 27, 1327 (1905); Bogert and Seil, *Ibid.*, 29, 532 (1907); Bogert and Klaber, *Ibid.*, 30, 807 (1908).

[4] Dehoff, *J. prakt. Chem.*, [2] 42, 347 (1890); Thieme, *Ibid.*, 43, 441 (1891).

[5] Zacharias, *Ibid.*, 43, 441 (1891).

[6] Bogert and Chambers, THIS JOURNAL, 28, 207 (1906); Bogert and Klaber, *Ibid.*, 30, 807 (1908).

[7] Bogert and Seil, *Ibid.*, 28, 884 (1906); Bogert and Cook, *Loc. cit.*; Bogert and Klaber, *Loc. cit.*

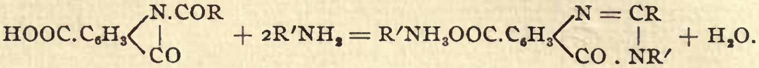
[8] Bülow, *Ber.*, 35, 4312 (1902); 39, 2621 and 3372 (1906).

[9] Bogert and Gortner, THIS JOURNAL, 31, 943 (1909).

could also be condensed with amino nitrils or amino esters to the corresponding quinazolines.[1]

The ease with which acylanthranils condense with primary amines to crystalline quinazolines suggests the utilization of this reaction for the separation and identification of easily soluble or sirupy amines difficult to handle otherwise.

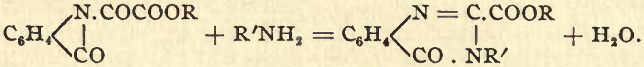
The same reaction was employed for the preparation of quinazoline carboxylic acids from acylanthranil carboxylic acids,[2]



$$HOOC.C_6H_3\left<\begin{matrix}N.COR\\ |\\ CO\end{matrix}\right. + 2R'NH_2 = R'NH_3OOC.C_6H_3\left<\begin{matrix}N = CR\\ |\\ CO\,.\,NR'\end{matrix}\right. + H_2O.$$

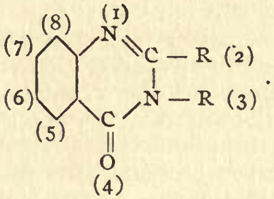
These quinazoline benzoylcarboxylic acids are colorless crystalline solids, melting with decomposition above 300°, more or less soluble in alcohol, but very difficultly soluble in other neutral organic solvents.

From the oxalyl anthranils, quinazolinecarboxylic acids were prepared carrying the carboxyl group on the miazine side of the nucleus,[3]

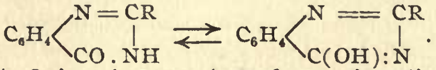


$$C_6H_4\left<\begin{matrix}N.COCOOR\\ |\\ CO\end{matrix}\right. + R'NH_2 = C_6H_4\left<\begin{matrix}N = C.COOR\\ |\\ CO\,.\,NR'\end{matrix}\right. + H_2O.$$

The particular quinazolines described in the foregoing are for the most part of the type designated as 4-ketodihydroquinazolines or, more simply, 4-quinazolones,



When there is an H at position 3 instead of a radical, there arises the possibility of keto-enolic tautomerism,



$$C_6H_4\left<\begin{matrix}N = CR\\ |\\ CO\,.\,NH\end{matrix}\right. \rightleftarrows C_6H_4\left<\begin{matrix}N = CR\\ |\\ C(OH):N\end{matrix}\right..$$

(4-Quinazolone) (4-Hydroxyquinazoline)

All those 4-quinazolones (4-hydroxyquinazolines) which carry a hydrogen at position 3 are easily soluble in aqueous solutions of the caustic alkalies and re-precipitable from such solutions by carbon dioxide or acetic acid. When these alkali salts are treated with alkyl halides, the 3-(*N*)alkyl derivative is the chief product.[4] The nitro derivatives furnish an apparent exception to this, in that the product with the higher alkyl halides is reported as chiefly the oxygen ether (*i. e.*, the 4-(*O*)alkyl, or -OR compound).[5] We are somewhat skeptical, however, of the accuracy of these results and feel that they should not be fully accepted until the pure oxygen ethers have been prepared by other processes and the two

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[1] Bogert and Klaber, *Loc. cit.*

[2] Bogert, Wiggin and Sinclair, THIS JOURNAL, 29, 82 (1907); Bogert and Jouard, *Ibid.*, 31, 489 (1909).

[3] Bogert and Gortner, *Ibid.*, 32, 119 (1910).

[4] Bogert and May, *Ibid.*, 31, 507 (1909).

[5] Bogert and Seil, *Ibid.*, 29, 517 (1907).

products compared. One reason for this skepticism on our part is that certain of these suppositious oxygen ethers could not be hydrolyzed with concentrated mineral acids (hydrochloric), a result contrary to our experience and to that of others working with true oxygen ethers.

Pure 3-(*N*)alkyl derivatives are easily obtained by the acylanthranil reaction already described. For the isomeric 4-OR derivatives, the best method appears to be the treatment of the 4-chloroquinazolines with sodium alcoholates.[1] In the case of the simple alkyl derivatives of unsubstituted 4-quinazolones (4-hydroxyquinazolines), the (3)-NR compounds are colorless, odorless solids, quite soluble in water, generally very difficultly volatile with steam, of higher melting point than the 4-OR isomers, and are not hydrolyzed by strong hydrochloric acid. On the other hand, the 4-OR compounds are oily liquids or low-melting solids, usually of pleasant odor, readily volatile with steam, less soluble in water but more soluble in hydrochloric acid than the NR isomers, and are readily hydrolyzed by mineral acids to the hydroxyquinazoline (4-quinazolone) again. Some of the lower ones can even be distilled undecomposed at ordinary pressure.

In the preparation of the 4-chloroquinazolines from the 4-hydroxyquinazolines (4-quinazolones),[1] a methyl or ethyl group in position 2 exerts a peculiar influence upon the course of the reaction with phosphorus halides or similar halogenating reagents. In all such cases, it was found impossible to replace the OH at 4 by chlorine without simultaneously introducing three chlorine atoms in the benzene part of the nucleus. Even when 2,3-dimethyl-4-quinazolone was heated with phosphorus penta- and oxychlorides,[2] the 3-methyl group was split off, a Cl attached itself at 4, but again three Cl's entered the benzene nucleus.

Our investigations in this 4-quinazolone group have led to the synthesis and study of derivatives carrying the following substitutions:

1. At position, 2-, methyl, ethyl, normal and isopropyl, isobutyl, isoamyl, phenyl, *m*- and *p*-nitrophenyl, benzyl, *p*-tolyl, COOH, and various complex radicals and residues.
2. At position, 3-, methyl, ethyl, normal and isopropyl, iso- and secondary butyl, isoamyl, allyl, phenyl, *o*-tolyl, *p*-anisyl, benzyl, beta-naphthyl, CH_2COOR, CH_2CONH_2, CH_2CN, C_6H_4COOR, $C_6H_4CONH_2$, C_6H_4CN, the amino group and its derivatives, quinazolonyls, and dimethyl dicarbethoxypyrrole.
3. At position, 4-, OH, Cl, and OR.
4. On the benzene nucleus-, alkyls, halogens, nitro, amino (and derivatives), and COOH.

In the various series, where homologs of analogous structure are compared, it will be found that the melting point falls quite steadily with rise in molecular weight, the iso compounds melting higher than the isomers carrying normal alkyls. This is perhaps not so surprising since many series of anthranilic compounds (for example, the alkyl and acylamino anthranilic acids, the acylanthranilic nitriles, etc.) exhibit a similar behavior.

In addition to the 4-quinazolones, our studies have included also the 2-quinazolones (2-hydroxyquinazolines), 2,4-dihydroxyquinazolines (2,4-

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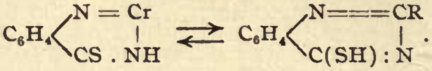
[1] Bogert and May, *Loc. cit.*

[2] Compare Fischer, *Ber.*, 32, 1297 (1899).

diketotetrahydroquinazolines, or benzoylene ureas), and a few other types.

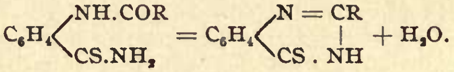
B. Thioquinazolines.

The work in the domain of the oxygenated quinazolines led quite naturally to the production of bodies of analogous structure carrying sulphur instead of oxygen, and known as the 4-thioquinazolone or quinazolthion (4) type,[1]



$$C_6H_4\left\langle\begin{array}{l}N=Cr\\ \quad\;|\\ CS\,.\,NH\end{array}\right. \rightleftarrows C_6H_4\left\langle\begin{array}{l}N=CR\\ \qquad\;|\\ C(SH):N\end{array}\right. .$$

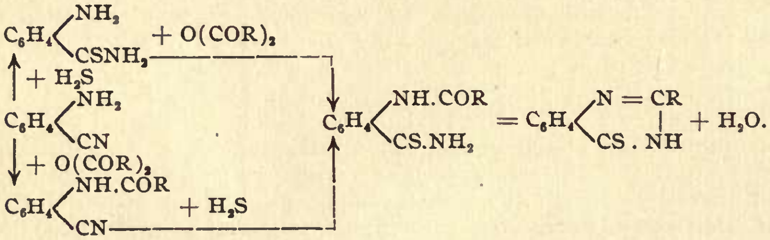
Since anthranilamides, as noted, easily condense to quinazolines by loss of water, it seemed probable that the corresponding thioamides would yield thioquinazolines.



$$C_6H_4\left\langle\begin{array}{l}NH.COR\\ CS.NH_2\end{array}\right. = C_6H_4\left\langle\begin{array}{l}N=CR\\ \quad\;|\\ CS\,.\,NH\end{array}\right. + H_2O.$$

and the results corroborated this fully.

The acylanthranilic thiamide was prepared either by first converting the anthranilic nitrile to the amide by the direct addition of hydrogen sulphide and then acylating, or by first acylating and then adding the H_2S:



$$C_6H_4\left\langle\begin{array}{l}NH_2\\ CSNH_2\end{array}\right. + O(COR)_2$$

$$\uparrow + H_2S$$

$$C_6H_4\left\langle\begin{array}{l}NH_2\\ CN\end{array}\right. \qquad C_6H_4\left\langle\begin{array}{l}NH.COR\\ CS.NH_2\end{array}\right. = C_6H_4\left\langle\begin{array}{l}N=CR\\ \quad\;|\\ CS\,.\,NH\end{array}\right. + H_2O.$$

$$\downarrow + O(COR)_2$$

$$C_6H_4\left\langle\begin{array}{l}NH.COR\\ CN\end{array}\right. + H_2S$$

By the use of thiol acids (for example, thioacetic acid) in sealed tubes, the thioquinazoline was obtained direct. The thiol acid first acylates the amino group. The by-product of this acylation, H_2S, cannot escape from the tube and is thus forced to attach itself to the CN, thereby changing it to the thioamide. The acylaminothioamide then passes to the thioquinazoline by loss of water.

As comparatively few thiol acids are readily available, we made our reaction more widely applicable by substituting the acid anhydride with sodium sulphide for the thiol acid. Thus, when anthranilic nitrile is heated with acetic anhydride and sodium sulphide in open flasks or, better, in sealed tubes, the anhydride first acetylates the amino group with formation of acetic acid as the by-product. The latter then attacks the sodium sulphide, setting free hydrogen sulphide and forming sodium acetate. The hydrogen sulphide converts the acetoanthranilic nitrile to the thioamide, which then splits out water and gives the quinazoline, the sodium acetate possibly assisting in the elimination of this molecule of water.

These thioquinazolines crystallize in beautiful yellow needles or prisms when alcohol is used as the solvent. By virtue of the —CS.NH— $\rightleftarrows$ —C(SH) : N— group, they dissolve freely in solutions of the caustic

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[1] Bogert, Breneman and Hand, THIS JOURNAL, 25, 372 (1903); Bogert and Hand, *Ibid.*, 25, 935 (1903).

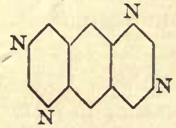
alkalies and are reprecipitated therefrom by carbon dioxide or by acetic acid.

Like the corresponding oxygen compounds, the melting point of the 2-alkyl derivatives steadily falls with rise in molecular weight, the iso compounds melting higher than the isomers of normal structure.

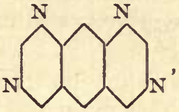
In the course of the investigation, we have used both simple and substituted anthranilic acids.

C. Naphthotetrazines.

Our syntheses of the simple quinazolines having resulted so satisfactorily, we decided to attempt the synthesis of compounds of the following types,



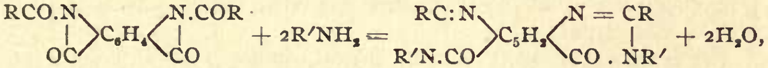
(1,3,6,8-Naphthotetrazine)



(1,3,7,9-Naphthotetrazine)

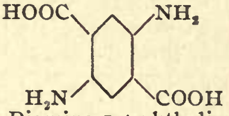
and in this were equally fortunate.

Naphthotetrazines of both types were prepared from the bis-acylanthranils of the appropriate diaminophthalic acid and various primary amines,[1]

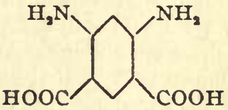


$$\begin{matrix}\mathrm{RCO.N} & & \mathrm{N.COR}\\ | & \rangle C_6H_4\langle & | \\ \mathrm{OC} & & \mathrm{CO}\end{matrix} + 2R'NH_2 = \begin{matrix}\mathrm{RC:N} & & \mathrm{N=CR} \\ & \rangle C_5H_2\langle & | \\ \mathrm{R'N.CO} & & \mathrm{CO\,.\,NR'}\end{matrix} + 2H_2O,$$

as well as from the diaminophthalic acids themselves by reactions similar to those employed for the synthesis of the simple quinazolines. The diaminophthalic acids used, which must be, of course, of anthranilic structure, were



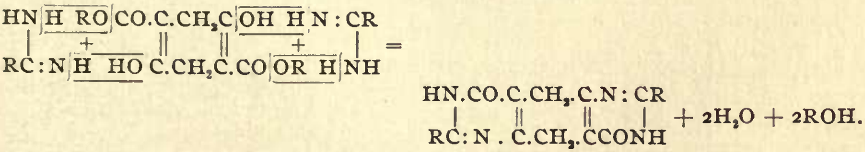
(3,6-Diamino-1,4-phthalic acid)



(4,6-Diamino-1,3-phthalic acid)

These acids, as can be seen by a glance at their graphic formulas, are only double anthranilic acids, and undergo similar reactions, the former yielding the 1,3,6,8-naphthotetrazines, and the latter the 1,3,7,9-isomers.

1,3,6,8-Naphthotetrazines were also obtained by condensing succinylosuccinic esters with amidines:[2]



$$\begin{array}{l} \mathrm{HN|\overline{H\ RO}|CO.C.CH_2C|\overline{OH\ H}|N:CR} \\ |\qquad + \qquad \| \qquad \| \qquad + \qquad | \qquad = \\ \mathrm{RC:N|\underline{H\ \ HO}\,C.CH_2C.CO|\underline{OR\ H}|NH} \end{array}$$

$$\begin{array}{l} \mathrm{HN.CO.C.CH_2.C.N:CR} \\ |\qquad \| \qquad \| \qquad | \\ \mathrm{RC:N\,.\,C.CH_2.CCONH} \end{array} + 2H_2O + 2ROH.$$

All of these naphthotetrazine derivatives so far obtained by the above processes are either infusible or melt very high. They are insoluble in the ordinary neutral organic solvents. When they carry the —NH.CO—

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[1] Bogert and Nelson, THIS JOURNAL, 29, 729 (1907); Bogert and Kropff, *Ibid.*, 31, 1071 (1910).

[2] Bogert and Dox, *Ibid.*, 27, 1127 and 1302 (1905).

$\rightleftarrows$ —N : C(OH)— group, they dissolve readily in solutions of the caustic alkalies, whence they are reprecipitated by carbon dioxide or by acetic acid.

The naphthotetrazine prepared from guanidine and succinylosuccinic ester gives a sodium salt crystallizing in beautiful yellow needles or prisms which have a magnificent greenish fluorescence.

This, in a very hasty and imperfect way, indicates the main lines along which this particular field of investigation has been developed. It would only weary you to refer even hurriedly to the many subordinate lines of investigation radiating from these main ones, necessitating or resulting in the synthesis of many hundreds of new organic substances. I can only say, as I did at the outset of this address, that it has all been most interesting to us, and that we are still carrying on the work.

The articles published in the progress of these researches are listed below. They all have appeared in *The Journal of the American Chemical Society*, to which the volume numbers refer:

1900 1. A new synthesis in the quinazoline group. M. T. Bogert and A. H. Gotthelf, THIS JOURNAL, 22, 129.

2. The direct synthesis of ketodihydroquinazolines from orthoamino acids. M. T. Bogert and A. H. Gotthelf, *Ibid.*, 22, 522.

1901 3. The synthesis of alkyl ketodihydroquinazolines from anthranilic acid. A. H. Gotthelf, *Ibid.*, 23, 611.

1902 4. The synthesis of alkyl ketodihydroquinazolines from anthranilic nitrile. M. T. Bogert and W. F. Hand, *Ibid.*, 24, 1031.

1903 5. The synthesis of alkyl thioketodihydroquinazolines from anthranilic nitrile. M. T. Bogert, H. C. Breneman and W. F. Hand, *Ibid.*, 25, 372.

6. 3,5-Bibrom-2-aminobenzoic acid; its nitrile and the synthesis of quinazolines from the latter. M. T. Bogert and W. F. Hand, *Ibid.*, 25, 935.

1905 7. The synthesis of 5-nitro-4-ketodihydroquinazolines from 6-nitro-2-aminobenzoic acid, 6-nitro-2-acetylaminobenzoic acid, and from the corresponding nitro acetylanthranil. M. T. Bogert and V. J. Chambers, *Ibid.*, 27, 649.

8. The condensation of succinylosuccinic acid diethyl ester with guanidine. A derivative of 1,3,5,7-naphthotetrazine, a new heterocycle. M. T. Bogert and A. W. Dox, *Ibid.*, 27, 1127.

9. Some acyl derivatives of homoanthranilic nitrile, and the 7-methyl-4-ketodihydroquinazolines prepared therefrom. M. T. Bogert and A. Hoffman, *Ibid.*, 27, 1293.

10. The condensation of succinylosuccinic acid diethyl ester with acetamidine: 2,6-dimethyl-4,8-dihydroxy-9,10-dihydro-1,3,5,7-napthotetrazine. M. T. Bogert and A. W. Dox, *Ibid.*, 27, 1302.

11. The synthesis of 2-methyl-5-nitro-4-ketodihydroquinazolines from 6-nitro acetanthranil and primary amines. M. T. Bogert and H. A. Seil, *Ibid.*, 27, 1305.

12. The synthesis of 7-nitro-2-alkyl-4-ketodihydroquinazolines from 4-nitro acetanthranilic acid and from 4-nitro acetanthranil. M. T. Bogert and S. H. Steiner, *Ibid.*, 27, 1327.

13. 5-Brom-2-aminobenzoic acid and some of its derivatives. M. T. Bogert and W. F. Hand, *Ibid.*, 27, 1476.

1906 14. The preparation of 6-brom-4-ketodihydroquinazolines from 5-brom-2 aminobenzoic acid and certain of its derivatives. M. T. Bogert and W. F. Hand, *Ibid*,, 28, 94.

15. On 5-amino-4-ketodihydroquinazolines and 5-amino-2-methyl-4-ketodihydroquinazolines. M. T. Bogert and V. J. Chambers, *Ibid.*, 28, 207.

16. On the condensation of succinylosuccinic esters with amidines. M. T. Bogert and A. W. Dox, *Ibid.*, 28, 398.

17. On a 3-aminoquinazoline and the corresponding 3,3′-diquinazolyl, from 6-nitro acetanthranil and hydrazine hydrate. M. T. Bogert and H. A. Seil, *Ibid.*, 28, 884.

18. Synthesis of 6-nitro-2-methyl-4-ketodihydroquinazolines from 5-nitro acetanthranil and primary amines. M. T. Bogert and E. P. Cook, *Ibid.*, 28, 1449.

1907 19. The synthesis of quinazoline carboxylic acids from 4-aminoisophthalic acid and from aminoterephthalic acid. M. T. Bogert, J. D. Wiggin and J. E. Sinclair, *Ibid.*, 29, 82.

20. A strange case of poisoning. M. T. Bogert, *Ibid.*, 29, 239.

21. On 2,3-dialkyl-4-quinazolones and the products obtained by alkylating 2-alkyl-4-quinazolones (2-alkyl-4-hydroxyquinazolines). M. T. Bogert and H. A. Seil, *Ibid.*, 29, 517.

22. The synthesis of 1,3,6,8-naphthotetrazines from paradiaminoterephthalic acid and from certain of its derivatives. M. T. Bogert and J. M. Nelson, *Ibid.*, 29, 729.

1908 23. On certain 7-nitro-2-methyl-4-quinazolones from 4-nitroacetanthranil. M. T. Bogert and W. Klaber, *Ibid.*, 30, 807.

1909 24. 3-Amino-*o*-phthalic acid and certain of its derivatives. M. T. Bogert and F. L. Jouard, *Ibid.*, 31, 483.

25. On certain quinazoline oxygen ethers of the type —N:C(OR)— and the isomeric —NR.CO— compounds. M. T. Bogert and C. E. May, *Ibid.*, 31, 507.

26. On some amino and nitroamino derivatives of benzoic, metatoluic and metaphthalic acids. M. T. Bogert and A. H. Kropff, *Ibid.*, 31, 841.

27. On 2-methyl-3-amino-4-quinazolone and certain of its derivatives. M. T. Bogert and R. A. Gortner, *Ibid.*, 31, 943.

28. On 6-methyl-7-aminoquinazolones, 7-nitroquinazolone-6-carboxylic acids, and 1,3,7,9-naphthotetrazines. M. T. Bogert and A. H. Kropff, *Ibid.*, 31, 1071.

1910 29. On oxalyl anthranilic compounds and quinazolines derived therefrom. M. T. Bogert and R. A. Gortner, *Ibid.*, 32, 119.

HAVEMEYER LABORATORIES, COLUMBIA UNIVERSITY,
March 23, 1910.

A REVIEW OF DISCOVERIES ON THE MUTAROTATION OF THE SUGARS.[1]

By C. S. HUDSON.

Received May 9, 1910.

Dubrunfaut[2] discovered in 1846 that the specific rotation of a freshly prepared cold solution of crystalline glucose decreases from an initial value of about 110° to become constant at 52°. This phenomenon he named *birotation* but later discoveries have shown the name to be inappropriate and the better term *mutarotation*, which was introduced by Lowry[3] in 1899, has generally replaced it, though the word *multirotation*

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[1] Presented at the Second Decennial Celebration of Clark University, Worcester, Mass., Sept. 15, 1909.

[2] *Ann. chim. phys.*, 18, 99–107 (1846); 21, 178–80 (1847); *Compt. rend.*, 23, 38–44 (1846).

[3] *J. Chem. Soc.*, 75, 212–5 (1899).

is also in use. In addition to glucose the following crystalline sugars have been found to show mutarotation: lactose,[1] galactose,[2] arabinose,[3] maltose,[4] xylose,[5] fructose,[6] fucose,[7] rhamnose,[8] mannose,[9] rhodeose,[10] gentiobiose,[11] melibiose,[12] perseulose,[13] and several rare synthetic sugars. All of these sugars reduce Fehling's solution and combine with phenylhydrazine, proving that they are aldoses or ketoses and contain the carbonyl group; on the other hand such sugars as sucrose, raffinose, gentianose, and stachyose, and the polysaccharides starch, inulin, mannan, etc., and the glucosides salicin, amygdalin, helicin, arbutin, etc., none of which show the characteristic reactions for the carbonyl group, do not exhibit mutarotation. This proves that the mutarotation is in some way dependent upon the carbonyl group.

After Dubrunfaut's great discovery the next important observation on mutarotation was made by E. O. Erdmann[14] in 1855, who noticed that lactose occurs in two crystalline modifications, one having a higher rotation (86°) than that of the stable solutions (52°), and the other a lower rotation (36°), and each form showing mutarotation towards the same final rotation (52°). Erdmann measured the rates at which each form changes in rotation to that of the stable solution, but did not notice that the rates are the same in value and that this fact is of much theoretical significance. Many years later, after the principles of chemical dynamics became better known, the author[15] showed that these equal rates prove that the two changes of rotation are not different reactions but are opposite parts of one balanced reaction. In this way the mutarotation of lactose, and what is true of this sugar is doubtless true of all which show mutarotation, was proved to belong to the great class of balanced reactions.[16]

In 1859 Anthon[17] noticed that crystalline glucose forms its saturated solutions in cold water very slowly even when the mixing is vigorous; this fact was discovered for lactose by Mills and Hogarth[18] in 1879. It is now known that this slowness of the process of solution is caused by the same slow balanced chemical reaction, involving the carbonyl group,

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[1] E. O. Erdmann, *Fortschritte Physik.*, p. 13; *Fortschritte Chemie*, p. 671 (1855).

[2] Pasteur, *Compt. rend.*, 42, 347–51 (1856).

[3] Parcus and Tollens, *Ann.*, 257, 160–78 (1890).

[4] Soxhlet, *J. prakt. Chem.*, 21, 283 (1880).

[5] Koch, *Pharm. Ztg. Russland*, 25, 619, 635, 651, 667, 683, 699, 730, 747, 763 (1886).

[6] Jungfleisch and Grimbert, *Compt. rend.*, 107, 390–3 (1888).

[7] Guenther and Tollens, *Ber.*, 23, 2585–6 (1890).

[8] Parcus and Tollens, *Loc. cit.*

[9] Van Ekenstein, *Rec. trav. chim.*, 15, 221–4 (1896).

[10] *Z. Zuckerind. Böhmen*, 25, 297 (1902).

[11] Bourquelot and Hérissey, *Ann. chim. phys.* 27, 397–432 (1902).

[12] *Z. Ver. d. Zuckerind.*, 53, 1050–9 (1903).

[13] Bertrand, *Compt. rend.*, 147, 201–3 (1908).

[14] *Loc. cit.* Also *Ber.*, 13, 2180–4 (1880).

[15] *Z. physik. Chem.*, 44, 487–94 (1903).

[16] Using the same method Meyer later proved this for glucose, *Z. physik. Chem.*, 62, 74 (1908). Cf. also Roux, *Ann. chim. phys.*, 30, 422–32 (1903).

[17] *Dingler's poly. J.*, 151, 213–23 (1859); 155, 386–8 (1860); 166, 69–71 (1862).

[18] *Proc. Roy. Soc. London*, 28, 273–9 (1879).

which causes the mutarotation, and that it is a general property of all the aldehyde and ketone sugars.[1]

The first attempt to find the physical law which governs the rate of the mutarotation was made by Mills and Hogarth[2] in 1879, but the result was only an empirical formula and must be regarded as unsatisfactory. It is to Urech[3] that we owe the first real progress in this line. He showed by a series of experiments during 1882–5 that the mutarotation follows the law of unimolecular reactions. It is interesting, and to some minds instructive, to note that this correct beginning in the physico-chemical study of the long unsolved mutarotation reaction was coincident in time with the beginning of the modern theory of solutions and chemical dynamics. There can be little doubt that Urech's experiments, which are the starting point of all exact work on mutarotation, were suggested by the advances that were being made at that time in the study of chemical dynamics by the new physico-chemical school.

In 1888 Brown and Morris[4] and Arrhenius[5] observed that the freezing temperatures of glucose solutions remain unchanged during the process of mutarotation, which proves that the reaction which causes mutarotation is not a polymerization or dissociation of the sugar. More recently Roth[6] has detected a slight change in freezing temperature of concentrated solutions of anhydrous glucose on standing but this is doubtless due to hydration and does not alter the conclusion from the work of Brown and Morris and Arrhenius, because a polymerization or dissociation would also affect the freezing point of dilute solutions, and the investigators are all agreed that such an effect is not discernible.

In 1890 O'Sullivan and Tompson[7] noticed that the invert sugar which is produced by the hydrolytic action of the enzyme invertase on sucrose shows mutarotation; this fact was later investigated by E. F. Armstrong[8] and has been precisely studied lately by the author.[9] These researches have shown that the glucose which is liberated from sucrose is α-glucose and the fructose is a hitherto unknown form of this hexose, α-fructose; these facts show that sucrose has the constitution α-glucose $<>$ α-fructose. The new form of fructose has not as yet been obtained crystalline. This method for determining the constitution of the polysaccharides by studying the mutarotation of the sugars which are formed by their enzymotic hydrolysis was first used by E. F. Armstrong[2] in his correlation of the α- and β-methylglucosides with the α- and β-glucoses. In applying the method to other substances such as cane sugar where two mutarotating sugars are formed at the same time it is necessary to extend the theoretical considerations; a mathematical theory of the modified method of Arm-

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[1] Hudson, *Z. physik. Chem.*, 44, 487–94 (1903); THIS JOURNAL, 26, 1065–82 (1904).

[2] *Loc. cit.*

[3] *Ber.*, 15, 2130–3 (1882); 16, 2270–1 (1883); 17, 1547–50 (1884); 18, 3047–60 (1885).

[4] *J. Chem. Soc.*, 53, 610–21 (1888).

[5] *Z. physik. Chem.*, 2, 491–505 (1888).

[6] *Ibid.*, 43, 539–64 (1903).

[7] *J. Chem. Soc.*, 57, 920 (1890).

[8] *Ibid.*, 83, 1305–13 (1903).

[9] THIS JOURNAL, 30, 1160–6, 1564–83 (1908); 31, 655–64 (1909).

strong and an experimental demonstration of it has recently been published by the author.[1]

In 1895 Charles Tanret[2] discovered a new form of crystalline glucose which was found to have a specific rotation lower than that of the stable solution (52°), though its value increased to this on standing. This discovery is the complement to Dubrunfaut's and the two must cause chemists the world over to be grateful to French science, because more fruitful single discoveries in the chemistry of the carbohydrates have hardly been made. Tanret found the final rotation of glucose solutions to be the same whether the solution is made from the higher or the lower initially rotating form. He interpreted his results as proving that three forms of glucose exist, one of high rotation, one of low, and the third the form to which each of these changes in aqueous solution. About the same time Tanret isolated similar new crystalline forms of rhamnose, galactose and arabinose, and obtained Erdmann's lower rotating form of lactose practically pure. Tanret's striking discoveries immediately caused new interest to be taken in the problem of mutarotation. In 1899 Lowry[1] advanced the view that the mutarotation of glucose is caused by a balanced reaction between the highest and lowest rotating forms of the sugar, a view which may be expressed by the equation *α-glucose* $\rightleftarrows$ *β-glucose.* This explanation is essentially different from any that preceded it and later investigations have proved it to be entirely correct. On the other hand, Lowry did not support this hypothesis with any direct proof and it remained without such proof for several years. In 1902[3] the author published the same view as an explanation of the mutarotation of lactose, being at that time unacquainted with the publication of Lowry. The explanation may be expressed by the equation α-lactose $\rightleftarrows$ β-lactose, and experimental evidence for the view was given by measurements on the heats of solution of the three forms of lactose, which showed that the stable form to which α- and β-lactose change in solution is not a chemical individual, as Tanret had supposed, but is a mechanical mixture of α- and β-lactoses. In 1903 the author[4] measured the slow maximum rate of solution of α-lactose and showed that the slowness of dissolving, which had been discovered by Mills and Hogarth,[1] is caused by the balanced reaction which produces the mutarotation. By quantitative measurements the hypothesis of the balanced reaction was tested and proved, and the explanation which these measurements gave of the mutarotation of lactose was immediately accepted by such an authority as Nernst.[5] In the same year Lowry[6] published similar experiments on glucose and proved the suggestion which he had advanced in 1899. These questions of priority are here stated for the reason that E. F. Armstrong[7] has recently claimed for Lowry the discovery of the balanced reaction which causes the mutarotation, a claim which in the opinion of the author is entirely too broad.

[1] *Loc. cit.*

[2] *Bull. soc. chim.*, 15, 195–205, 349–61; 17, 802–5.

[3] Princeton Univ. *Bull.*, April, 1902.

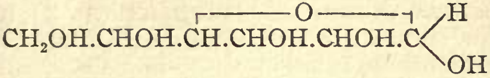
[4] *Z. physik. Chem.*, 44, 487–94 (1903).

[5] "Theoretische Chemie," ed. 1904.

[6] *Proc. Chem. Soc.*, 19, 156–7 (1903); 20, 108–9 (1904).

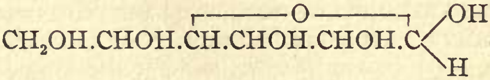
[7] "The Simple Carbohydrates and Glucosides," p. 8.

A very fruitful idea was advanced by Lippmann[1] in 1895 in the suggestion that the lactonic formula for glucose predicts two possible forms of the sugar on account of the asymmetry of the end carbon atom, the two structures being



$$\mathrm{CH_2OH.CHOH.}\overbrace{\mathrm{CH.CHOH.CHOH.C}}^{\mathrm{O}}\!<^{\mathrm{H}}_{\mathrm{OH}}$$

and



$$\mathrm{CH_2OH.CHOH.}\overbrace{\mathrm{CH.CHOH.CHOH.C}}^{\mathrm{O}}\!<^{\mathrm{OH}}_{\mathrm{H}}.$$

This suggestion, after a slight development by Simon,[2] was made more probable by Armstrong's discovery,[3] that the α- and β-forms of methyl glucoside are hydrolyzed by enzymes to give methyl alcohol and the α- and β-forms of glucose respectively. As the methyl glucosides show no aldehyde reactions the lactonic formulas have always been chosen for them, the hydroxyl of the end carbon atom in the structures shown above being replaced by the group OCH_3. Armstrong's discovery indicates that similar structures probably apply to the forms of glucose. This suggestion received final proof in 1909 when the author[4] showed that certain numerical relations which can only be explained by the assumption of such lactonic structures for the two forms of the sugar, hold all through the sugar group. If the rotation of the end carbon atom is B for one structure it must be —B for the other, and if A is the rotation of the remaining asymmetric carbon atoms, which are common to both structures, the total rotation of the one structure is $A + B$, and of the other structure $A - B$, the difference between the two total rotations being then $2B$. This rotation B applies to all the aldoses because they contain the same end asymmetric carbon, therefore the difference between the molecular rotations of the α- and β-forms of all the aldose sugars should be a constant quantity if the sugars have the two isomeric lactonic structures. The molecular rotatory powers of the two forms of lactose, glucose, arabinose and galactose were found indeed to differ by the quantities 17600, 16000, 16200, and 15700, which are sufficiently alike to show that the theory is correct and that the two forms of each of the mutarotating sugars have the stereomeric lactonic structures. Certain other similar conclusions from the same theory were also found to agree with the rotatory powers of the sugars and their glucosidic derivatives.

The catalytic action of various substances on the mutarotation reaction has been investigated by various chemists.[5] These researches have shown that only acids and alkalies have a strong action. Osaka[6] made the first quantitative study of the relation between acidity or alkalinity and catalytic action and found that the catalysis is proportional to the concentration of the hydroxyl ions and proportional to the square root

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[1] "Die Chemie der Zuckerarten," ed. 1895, pp. 130, 990, 992.

[2] *Compt. rend.*, 132, 487–90 (1901).

[3] *Loc. cit.*

[4] THIS JOURNAL, 31, 66–86 (1909).

[5] Levy, *Z. physik. Chem.*, 17, 301–24 (1895); Trey, *Ibid.*, 18, 193–218 (1895); 22, 424–63 (1897); 46, 620–719 (1903); Simon and Bénard, *Compt. rend.*, 132, 564–6 (1901); Lowry, *J. Chem. Soc.*, 83, 1314–23 (1903).

[6] *Z. physik. Chem.*, 35, 661–706 (1898).

of that of the hydrogen ions. Later the author[1] showed that the proportionalities are somewhat different from this and that the rate of the mutarotation of glucose is related to the acidity and alkalinity of the solution by the expression *rate* $= A + B(H^{\cdot}) + C(OH')$, where A, B, and C are constants at constant temperature. This formula has lately been used as the basis of a new method for measuring the electrolytic dissociation of water.[2] A satisfactory explanation of the fact that acids and alkalies are enormously powerful catalysts of the mutarotation while all other substances are without comparable action is lacking.

The sugars glucose, lactose, galactose, rhamnose, melibiose, arabinose, maltose, xylose and some others occur as monohydrates and these have generally been regarded as hydrated aldehydes without lactonic structure and thus intermediate forms between the two lactonic α- and β-forms of the sugars. The freshly prepared solutions of these monohydrates are identical in properties with such solutions of one of the anhydrous lactonic forms of the sugars and it is therefore to be concluded that the equilibrium between this lactonic form, whichever it may be, and the monohydrate is established instantly. For most of the sugars the lactonic form which is thus in instantaneous equilibrium with the monohydrate is the α-form, but for one sugar at least, maltose, it is the β-form. The mutarotation reaction may then be considered to be the slow change of the monohydrate into the other lactonic form by a reversible reaction, or in the form of an equation,

$$\alpha\text{-sugar} + H_2O \underset{(1)}{\rightleftharpoons} \text{monohydrate} \underset{(2)}{\rightleftharpoons} \beta\text{-sugar} + H_2O.$$

For most of the sugars the reaction 1 is instantaneous in comparison with 2, which is therefore the mutarotation reaction, but for maltose the relations are reversed. Why the monohydrate should change instantly to the α-form for some sugars, but to the β-form for others is entirely unknown and is a most interesting problem.

The mutarotation reaction is general to all the aldehyde and ketone sugars. It may indeed be called the fundamental reaction of the sugar group. While its cause remained unknown during the half century following its discovery, the last decade has brought a full explanation of it. The principal facts regarding it have been accurately measured and correlated. On the other hand the application of these facts to the elucidation of the chemical and biological reactions of the sugars, in every one of which mutarotation plays a part, has just begun, but it is even now apparent that the unfolding chemistry of the polysaccharides is to be largely a development of the mutarotation reaction.

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[1] THIS JOURNAL, 29, 1571–6 (1907).

[2] *Ibid.*, 31, 1136–8 (1909).

OUTLINE OF A THEORY OF ORGANIC CHEMISTRY FOUNDED ON THE LAW OF ENTROPY.[1]

BY ARTHUR MICHAEL.

Received June 27, 1910.

There appears to be no generalization in science more firmly established than the second law of thermodynamics, which demands that every spontaneous chemical change shall be accompanied by an increase of entropy, and that the system shall endeavor to realize this increase to its maximum extent.

Since the law of entropy represents the fundamental principle, underlying and regulating all chemical phenomena occurring in nature, it must necessarily be the correct scientific basis for the theory of organic chemistry. But it is a curious fact that there has been as yet little attempt to use this basic chemical principle in connection with organic theory; this theory has been developed along lines so mechanical in their character that it is perhaps no exaggeration to speak of them as essentially pictorial. This unilateral, mechanical development is due largely to the interpretation of the phenomenon called valency; and, if we are to incorporate the law of entropy into chemical theory, it is here that our theoretical conceptions will require a radical modification.

Before entering a discussion of the subject of valency, we shall mention a conception of the chemical genesis of matter, since it prepares the way for the theoretical views which follow. A simple hypothesis is to assume that cosmos was originally made up of two kinds of matter, which were the carriers of two kinds of chemical energy,[2] and that the temperature of the system was inconceivably low. Chemical energy, as it now appears to us, exists in two conditions. One of these is freely and perfectly convertible into less active chemical energy and into various forms of physical energy; and this less active chemical energy can be reconverted into the active form only partially and then with comparative difficulty. We shall designate the active form free, the relatively inactive form, bound *chemical* energy,[3] and, as the transformations of chemical energy must have obeyed the law of entropy since the beginning of cosmos, the original corpuscles were exclusively carriers of free *chemical* energy, and the accumulation of bound *chemical* energy and the various forms of physical energy now existing have been gradually evolved from it.

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[1] Address delivered at the Second Decennial Celebration of Clark University, Worcester, Mass., September 15,1909.

[2] To distinguish between them they will be called positive and negative, but this does not imply any connection with positive and negative electricity.

[3] The terms free and bound *chemical* energy, as here used, are not to be confused with the terms free and bound energy as used in physical chemistry, with which they are not identical.

The permanence of the law of entropy justifies the conclusion that the chemical relations which existed between the corpuscles at the beginning were similar to those which now exist between the atoms and the molecules. We may, therefore, assume that the free *chemical* energy of unlike and like corpuscles united to form aggregations in which the corpuscles were held together by bound *chemical* energy. At first the chemical evolution of matter must have been accompanied by an enormous rise of temperature, but later, owing to the decreasing amount of free *chemical* energy in the cosmical system, a period must have come when the loss of heat through radiation was greater than its formation, and then the temperature of the system must have begun to decrease. We may assume, too, that the atoms of those elements, the molecules of which now show the greatest stability toward heat, were formed first and during the hottest period of cosmical evolution. Hence, the atoms of hydrogen, and those of the non-metals, with small atomic weight, represent the earliest forms of atomic matter.

If we suppose that in the formation of the atoms of certain elements the free *chemical* energy of the corpuscles was very largely converted into bound *chemical* energy and heat, their atoms would be extremely inert toward other atoms and incapable of uniting with each other. Such elementary matter is represented by the so-called noble gases, in the atoms of which the relation of free corpuscular to free atomic *chemical* energy is analogous to that of free atomic to free molecular *chemical* energy in the atom and molecule of nitrogen. Further, if we suppose that thermic, or other conditions, toward the end of the corpuscular period of chemical evolution no longer permitted a sufficient conversion of free into bound *chemical* energy, we get a glimpse into the genesis of radioactive matter, the atoms of which contain so much free corpuscular *chemical* energy that they represent a reversible system and are, therefore, gradually breaking down into smaller parts, which then rearrange according to the changed conditions of cosmos.

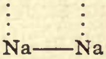
Kekulé,[1] in his memorable paper, "Ueber die Constitution und die Metamorphosen der chemischen Verbindungen," assumed that the first phase in chemical union consists in molecules attracting each other through their chemical affinity, and that a sort of loosely joined, larger molecule is thus formed. It is obvious that the formation of this "Kekulé polymolecule"[2] is due to the attraction between the free *chemical* energy in the constituent molecules, and that it proceeds with the conversion of more or less free into bound *chemical* energy and heat—the extent of this change determining its stability.

Let us represent the free *chemical* energy in an atom by a point

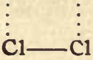
[1] *Ann.*, 106, 141.

[2] Michael, *Ber.*, 34, 4028; 39, 2140, 2570. *Am. Chem. J.*, 39, 3; 41, 120.

and the bound by a line, and let the number of the points and the length of the lines be a rough indication of the changes in the energy values occurring during the reaction. If we assume that the energies of unlike character in a molecule of sodium and of chlorine are approximately equal in value, we may represent the energy relations in sodium and chlorine by

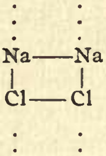


$$\overset{\vdots}{\mathrm{Na}}\text{——}\overset{\vdots}{\mathrm{Na}}$$



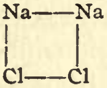
$$\overset{\vdots}{\mathrm{Cl}}\text{——}\overset{\vdots}{\mathrm{Cl}}$$

and the "polymolecule," representing the first phase in their interaction, by



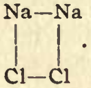
$$\begin{array}{ccc} \vdots & & \vdots \\ \mathrm{Na} & \text{——} & \mathrm{Na} \\ | & & | \\ \mathrm{Cl} & \text{——} & \mathrm{Cl} \\ \vdots & & \vdots \end{array}$$

which indicates that some of the free has been converted into bound *chemical* energy. The free *chemical* energies of unlike character would then strive to neutralize each other as completely as possible, a phase of the reaction that may be represented by



$$\begin{array}{ccc} \mathrm{Na} & \text{——} & \mathrm{Na} \\ | & & | \\ | & & | \\ \mathrm{Cl} & \text{——} & \mathrm{Cl} \end{array}$$

and then, certainly facilitated by the enormous "internal maximum heat of reaction,"[1] the bound *chemical* energies between Na and Na and Cl and Cl would be converted into bound *chemical* energy between Na and Cl and Na and Cl; finally, to realize a phase which may be represented by



$$\begin{array}{ccc} \mathrm{Na} & - & \mathrm{Na} \\ | & & | \\ | & & | \\ \mathrm{Cl} & - & \mathrm{Cl} \end{array}.$$

At this point, the bound *chemical* energy between the atoms of like nature may be inadequate to hold them together, and the complex would then break down into two molecules of NaCl.[2]

What happens if we substitute magnesium in the place of sodium; that is, an element the atom of which contains much less positive energy? The formation of a "polymolecule," then the conversion of the free *chemical* energy in the metallic and non-metallic atoms into bound between metal and halogen; but, although the energy in the sodium molecule suffices to neutralize that in the chlorine to an extent that the complex breaks down into two molecules, that in the much less positive mag-

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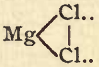
[1] Wohl, *Ber.*, 40, 2290. That part of the free and bound *chemical* energy is converted into heat has not been indicated.

[2] The energies in two unlike atoms are never capable of exactly neutralizing each other, so that a certain content of free *chemical* energy is invariably present in the atoms of every molecule.

nesium molecule is insufficient to convert enough of the bound energy between the chlorine atoms into bound energy between metal and halogens, therefore the latter atoms separate. On the other hand, the greater energy in the chlorine atoms is capable of using up that in the magnesium to an extent that these fall apart. In magnesium chloride, therefore, the halogen has a considerably greater content of free *chemical* energy than it has in sodium chloride, and bound *chemical* energy exists not only between it and the metal, but between the chlorine atoms. We may represent these relations by:



While the energy in a molecule of magnesium is not sufficient to separate the chlorine atoms, it obviously may be able to do so with the less negative oxygen, and, if the opposite energies in magnesium and oxygen approximately neutralize each other, two molecules of magnesium oxide should be formed. But, if we take oxygen and a metal with considerably more positive energy than magnesium, say lithium, the oxygen is not able to separate the metallic atoms, while the latter can separate the oxygen atoms, thus leading to the formation of Li_2O, in which the Li atoms are held together by bound *chemical* energy. The valency of an element, according to this interpretation, represents the resultant of the intramolecular chemical forces acting on the atom in terms of *bound chemical* energy, whether the action takes place directly, that is through direct union of the atoms or through space; or indirectly, that is, through other atoms. In as far as the free *chemical* energy in the atoms is not so converted into bound *chemical* energy, it will be able to exert readily a chemical attraction for such other atoms, either in the same or other molecules, for which it shows a chemical affinity.

Although a spontaneous chemical change can proceed only with increase of entropy, the increment depends on free *chemical* energy and chemical affinity existing between those atoms, which in the reaction enter into direct union with each other. The atoms in a molecule are held together *solely* by bound *chemical* energy and, if their chemical nature is such that their free *chemical* energy has very largely disappeared in the formation of the molecule, the substance must be chemically inert; if not, it will be more or less chemically active. Thus, the well neutralized condition of NaCl and Al_2O_3, the superabundant positive energy in Na_2O, and the negative in $AlCl_3$, is reflected in the properties of those substances.

Let us suppose that we could isolate and experiment with elements other than the noble gases in atomic condition, and could prevent the formation of molecules by the union of like, but not unlike, atoms. In such a system free *chemical* energy would be amply present and chemical union would therefore depend alone on the affinity relations of the atoms. Moreover, if an isomeric substance could be formed, it would be that particular isomer which would represent the maximum entropy of the system under the prevailing conditions.

For instance, the present structure theory indicates the existence of two isomeric cyanogen chlorides, *i. e.*, ClNC and ClCN, but leaves us entirely in doubt why only one is known. So great is the uncertainty in regard to its constitution that this has long been a subject of active discussion and investigation.[1] Chlorine, nitrogen and carbon in atomic condition would possess ample free *chemical* energy for union and the question which isomer would be formed would depend on the increase of entropy connected with the affinity relations of Cl for N and for C. Since we know that the affinity between Cl and N is exceedingly slight, and that between Cl and C is large, it is absolutely certain that the isomer in which the halogen is united directly to the C, *i. e.*, ClCN, would be the direct product. Furthermore, a consideration of the energetic conditions enables us to predict the properties of the isomeric form (ClNC); it could exist only at a very low temperature and under ordinary condition the rearrangement $\mathrm{ClNC} \longrightarrow \mathrm{ClCN}$ would occur so quickly, and with such a great increase of heat that the substance would be a violent explosive.[2] The matter we actually deal with is, however, in a molecular condition and all chemical changes that do not proceed *solely* through expenditure of free *chemical* energy involve an expenditure of energy due to overcoming bound *chemical* energy between atoms in the molecule. Chemical action is dependent, therefore, on a third factor, which constitutes a chemical hindrance, and it can proceed spontaneously only when the increase of entropy due to changes of free *chemical* energy and affinity is greater than the expenditure of energy necessary to overcome the chemical hindrance. That is, when the value of the equation: chemical affinity plus free chemical energy divided by chemical hindrance, is positive.

To ascertain quantitative values for the various factors that determine an organic reaction is at present impossible, but it is of the greatest importance for the development of organic theory to be able to connect

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[1] See Michael and Hibbert, *Ann.*, 364, 69.

[2] It is evident that the content of free *chemical* energy in ClNC would be vastly greater than that in ClCN, which implies a better condition of intramolecular neutralization of the chemical forces of the atoms in the latter structure. Since such chemical neutralization proceeds with increase of entropy, we may substitute chemical neutralization in the place of entropy in the second law of thermodynamics. Further, we may apply the Carnot principle to the activity of free *chemical* energy of unlike kinds, and conclude that the increase of entropy will be greatest when the chemical forces are able to neutralize each other exactly. This law of chemical neutralization has the advantage over that of entropy in a much wider application to organic reactions (Michael, *J. prakt. Chem.*, [2] 60, 293; 68, 489. *Ber.*, 38, 23).

changes in these values with modifications in structure. This done, we shall then be able to predict relative changes in the factors that contribute to the entropy values and thus be able to understand and explain organic reactions to a degree at present impossible.

What are the properties of carbon on which the existence of this wonderful and intricate organic world mainly depend? First, its capacity to polymerize, to form stable chains of astonishing length; second, the extreme sensitiveness of its properties to the influence of other elements,[1] which is shared in a like degree only by hydrogen, and which has been called its "chemical plasticity";[2] and third, its high valence combined with its marked affinity for hydrogen and for most of the non-metals, to form more or less stable derivatives.

The first of these properties stands clearly in a close relation to the position of the element in the periodic system. In the halogen group, the tendency to form greater than diatomic molecules is not shown, with the exception perhaps of iodine; in the oxygen group it is shown by that element, but in a far greater degree by the other members. From analogy, a similar tendency to form large molecules by conversion of free into bound *chemical* energy should be expected in passing from oxygen to nitrogen, but the latter element acts anomalously, although in the formation of its diatomic molecule its free is converted into bound *chemical* energy to a remarkable extent.

The next member of this group, phosphorus, shows a marked capacity to polymerize to large molecules, and the conversion of ordinary into red phosphorus, which is accompanied by the evolution of only 19 calories, is one of the most salient illustrations in chemistry of how a change of free into bound *chemical* energy will radically change the properties of a substance. The very existence of organic life depends on carbon not sharing with nitrogen the property of polymerizing to a diatomic molecule, which is poor in free *chemical* energy. The actual change in passing from N to C is similar to that in going from N to P, but it is in a degree much more highly developed, and carbon represents among elements the greatest capability to use the free *chemical* energy in its atom to form molecules containing a large number of atoms. The midway position of carbon in the second series of the periodic system indicates that there is an approximate balance of positive and negative corpuscles in the make-up of its atom. And, as the polymerizing capacity of non-metallic atoms increases, generally speaking, with a tendency toward this constitution of their atoms, it seems reasonable to connect this all-important property of the carbon atom with its corpuscular composition.

A relation which is hardly less important for organic theory than the

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[1] Van't Hoff, Ansichten über organische Chem., I, 280; II, 242.

[2] Michael, *J. prakt. Chem.* [2], 60, 325.

foregoing, is to what extent the polymerizing power of carbon is modified by the presence of other elements in the molecule, and the influence which they exert on the affinity of carbon for hydrogen and for non-metals. Without exception, every element joined to carbon decreases its polymerizing capacity, *i. e.*, its affinity for itself, and the influence is in the order, H, halogen, N, S and O. To the influence of the last element carbon is so exceedingly sensitive that, through direct union with a single atom of oxygen, the enormous combining capacity of the carbon atom for itself is completely destroyed.

Notwithstanding the considerable content of free *chemical* energy in the atoms of CO, this substance shows practically no tendency to polymerize, but the characteristic property of carbon reappears at once, when the influence of oxygen is neutralized by the presence of other elements. Thus, the action of potassium on CO leads not to COK, but to a polymerized product, derived from benzene.

Not only does O decrease the affinity of C for C, but of C for H and for any non-metal to which carbon may be joined, whether the atoms are directly or indirectly joined. This is true to a degree directly proportionate to the extent of such negative influences acting on the atoms.[1] The capacity of hydrogen to decrease the affinity of carbon for carbon is far less than that of oxygen, but it plays, nevertheless, an important role in many organic reactions. Thus, the pinacone ⟶ pinacoline rearrangement: $(H_3C)_2 = C(OH) — (HO)C = (CH_3)_2 \longrightarrow (CH_3)_3 \equiv C—CO—CH_3 + H_2O$, takes place on boiling with dilute mineral acid, and the

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[1] Michael, *J. prakt. Chem.*, **37**, 473; **60**, 286. *Ber.*, **38**, 28, 3221. The writer is unaware of any facts in organic chemistry which are not strictly in accordance with the above stated rule. W. A. Noyes (THIS JOURNAL, **31**, 1371) believes that the greater instability of acetoacetic acid ($CH_3COCH_2CO_2H$) over pyrotartaric acid (CH_3COCO_2H) "is some slight indication that the separation of the carbon atoms is ionic in character, taking place more readily when there is a greater contrast between the atoms united together." In the first-named acid, the group $C—CO_2H$ is under the influence of H_2 and a negative, acidic radical (CH_3CO), in the second under a positive radical (CH_3) and O and it is quite in agreement with the above rule that acetoacetic acid splits off CO_2 much more readily than pyrotartaric acid. The writer, also, knows of no satisfactory evidence in favor of the view that any strictly organic reaction is ionic in character (see Michael, *Ber.*, 38, 29; *Am. Chem. J.*, **43**, 322; Michael and Hibbert, *Ber.*, **31**, 1090); or of any facts that are more easily understood than otherwise by such an assumption. The formation of ethyl chloride from ethyl alcohol and phosphorus pentachloride, while phenol gives partly chlorobenzene, partly phenyl phosphate, is mentioned by Noyes (*loc. cit.*, 1370) as confirming this view. However, when we consider that the chemical hindrance to the formation of a chloride, *i. e.*, the energy necessary to separate hydroxyl from the hydrocarbon radical, is much greater with phenol than with ethyl alcohol, it is obvious that such assumptions as that phenol can ionize to the phenyl and hydroxyl group, and that ethyl alcohol can ionize to ethyl and hydroxyl, do not contribute in any way to make the subject more clear.

reaction apparently should lead, with loss of water, to the formation of tetramethylethylene oxide.

This compound contains a three-membered, cyclic chain, which is formed under considerable tension, and, besides, a large number (12) of hydrogen atoms, exerting in a very important position (3) their positive influence on the cyclic carbons. Such a structure cannot represent a very stable substance. On the one hand, there is considerable tension, representing energy in a potential condition; on the other, an extremely insufficient, intramolecular chemical neutralization of the positive by the negative energy in its atoms. The compound may, indeed, be compared to sodium oxide, and shares with that substance a capacity to unite with water, most energetically, and with great increase of entropy. It is apparent that the oxide cannot possibly be formed from pinacone under the conditions of the reaction, but, if a rearrangement may lead to the formation of an intramolecularly well neutralized substance, this may be formed, provided the increase of entropy due to the intramolecular neutralization is greater than the decrease that is due to the chemical hindrance, *i. e.*, the energy necessary to effect the migration of a methyl group. These conditions are possible, for pinacoline represents a fairly well neutralized structure and has, consequently, a considerable heat of formation;[1] and the expenditure of energy accompanying the migration of a methyl in pinacone is comparatively small, owing to the *decrease of the affinity of carbon for carbon by the influence of the numerous hydrogens.*

That phenyl exerts an extremely strong positive influence on any atom joined directly to it[2] is evident from the fact that two such groups united directly with iodine, give that non-metal a metallic character. It might, therefore, have been expected, that the accumulation of phenyl groups would facilitate rearrangements of the nature of the pinacone ⟶ pinacoline reaction, as this has been especially proven by the investigations of Tiffeneau. We have, moreover, direct experimental evidence that hydrogen diminishes the affinity of carbon for carbon in the observation of Acree,[3] that in the rearrangement with di-*p*-tolyldiphenylpinacone it is the more positive tolyl radical that migrates.

Another interesting illustration of this influence of hydrogen is found in that much-discussed substance "triphenylmethyl" (hexaphenylethane). Tshitshibabin[4] has shown that replacement of five of the hydrogens in ethane by phenyl groups materially lessens the affinity of the ethane carbon atoms for each other. It is, therefore, not surpris-

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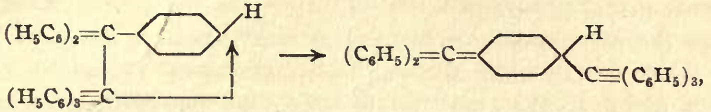
[1] Zoubuff, *Chem. Centralbl.*, 99, I, 516.

[2] Michael and Leighton, *Ber.*, 39, 2792.

[3] *Am. Chem. J.*, 33, 180.

[4] *Ber.*, 40, 367.

ing that when the remaining hydrogen is likewise replaced, the mutual affinity of these carbons is so greatly diminished that the substance easily dissociates into two molecules of triphenylmethyl,[1] and that these carbons, or the carbon, in "triphenylmethyl" joined to the three phenyl groups, have chemical properties similar to those of a very positive metal, for instance, sodium.[2] Nor is it surprising that hexaphenylethane may undergo easily a desmotropic rearrangement into the quinoid form:



or, since the difference in the entropy values of these two forms is slight, that the existence of one or the other form, or a derivative, will depend on the nature of a reagent or even of a solvent.[3]

The remaining fundamental properties of carbon, its high valency and its capability to combine not only with hydrogen but with most of the non-metals to form stable derivatives, are also related to the position of the element in the periodic system. An element acts as monovalent towards H, or Cl, when its energy suffices to neutralize that of H, or Cl, to an extent that the system is incapable of uniting with further

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[1] Since the above was written Schlenk (*Ann.*, 372, 1) has shown that with a more positive radical than phenyl, *i. e.*, biphenyl, the affinity of carbon for carbon is reduced to such an extent that tribiphenylmethyl exists in solution in mono-molecular condition, which is a further confirmation of the above explanation.

[2] Michael, *J. prakt. Chem.*, [2] 60, 423, 428; 64, 107; *Ber.*, 39, 2791.

[3] Michael and Hibbert, *Ber.*, 41, 1091. A thermochemical investigation on *intramolecular* rearrangement will be published later; it may be stated that all our present experimental data on this subject confirm the view that the fundamental reason of the phenomenon is the increase of entropy proceeding with the change. In *intramolecular* changes it is the formation of an isomer with a greater heat of formation and in *intermolecular* rearrangements the increase of entropy is connected with a change in composition and the reagent uniting with a product of decomposition; in either case, slight chemical or physical forces may bring about the change, if the chemical hindrance is inconsiderable (see Michael and Hibbert, *Ber.*, 41, 1091). The rearrangements of camphor on treatment with P_2O_5 and H_2SO_4, to which W. A. Noyes (THIS JOURNAL, 31, 1372) recently called attention, may be understood from the point of view here presented. In camphor the affinity of the central carbon to those with which it is directly joined has been diminished considerably by the influence of hydrocarbon radicals and the central ring appears to exist in a condition of tension; moreover, such reduced benzene derivatives show a tendency to pass over into benzene derivatives, as the formation of the para-bonds in benzene is connected with a considerable increase of entropy (Michael, *J. prakt. Chem.*, [2] 79, 418). Phosphoric anhydride is a *powerful dehydrating agent* and the formation of a benzene derivative (cymene) with the elimination of water and rupture of a central carbon bond represents the maximum increase of entropy. In its action on camphor sulphuric acid acts not only as a *hydrolyzing*, but also as an *oxidizing agent*; the formation of *p*-acetyl-*o*-xylene undoubtedly represents the maximum entropy under such conditions.

atoms of these elements. In passing from F to O, from O to N, and from N to C, the valency for H, or Cl, increases, because the amount of energy in these atoms, able to neutralize that of H, or Cl, is successively decreasing. CH_4 or CCl_4 represent stable substances, because the energy and affinity relations between C and H, or Cl, are such that, in the combination of four atoms of hydrogen or chlorine among themselves and with one atom of carbon, comparatively little free *chemical* energy remains in any of the atoms.[1]

Like the polymerizing capacity and the "chemical plasticity" of carbon, its power to unite not only with hydrogen, but with most non-metals, is due to the approximate balance of the positive and negative corpuscular energies in its atom. The direction in which the affinity of carbon for such elements will vary under the influence of other atoms in the molecule must be toward those of elements adjacent to it in the periodic system. Thus, the effect of increasing the influence of H on C in relation to H, or to a non-metal, joined to it, must be to shift its affinity values toward those of silicon, *i. e.*, there should be a decrease in the value for H and an increase for that of a non-metal. On the other hand, increasing the influence of O should shift them towards those of N, *i. e.*, decrease the values both for H and a non-metal. Further, the effect of such changes on the content of free *chemical* energy of C, and of any atom joined to it, must stand in a direct relation to the changes in the affinity values; in fact, the free must respond to such changes before the bound *chemical* energy.

According to van't Hoff,[2] two atoms in a molecule acting through direct union or through space, or indirectly, that is through intermediate atoms. This idea has been further developed[3] and shown to be of great importance in explaining organic reactions. If we number a certain atom in any fatty compound with a normal carbon chain by the figure 1, our present knowledge of the combined mutual influence between this atom and others in the molecule is expressed by the following "scale of combined influence," the numbers indicating the degree of removal and the extent of the influence decreasing in the order given: 2—3—5—6—4—7—

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[1] Replacement of an H in CH_4 by Na gives a substance with preponderance of positive energy, and which is, therefore, poorly neutralized intramolecularly. Carbon, a weak non-metal, in uniting with very positive metals, tends to form compounds of the type C_2Me, in which the accumulated negative energy of several carbon atoms endeavors to neutralize the positive energy of the metal. Only with a weak positive metal like Al are metallic derivatives of methane formed, and it is doubtless owing to this relation between the energies of C and Al, the compounds of which are so widely distributed in nature, that we owe the occurrence of such enormous deposits of *saturated* hydrocarbons.

[2] Ansichten üeber die organische Chemie, I, 284–285; II, 252–254.

[3] Michael, *J. prakt. Chem.*, [2] 60, 331. *Ber.*, 39, 2138–2157, 2780–2790; 40, 141.

(9—10—11)—8. It is to be strongly emphasized that the effect of an atom in position 2 or 3 is *far greater* than that of any similar atom less closely connected, and, in the case of atoms farther removed, the influence must be largely direct, *i. e.*, spatial.

The principles developed above form a new basis for the theory of organic chemistry and may be applied to any problem arising in the science.

Several important organic questions will be discussed from the new point of view. One of the weakest sides of the present structure theory is that it indicates the existence of a countless number of compounds, which are incapable of existence. One instance, that of an isomeric chloride of cyanogen (ClNC) has been already discussed, but this question is of such importance that it will be considered with substances of a different type. Nitrosomethane (H_3CNO) does not exist, as it passes over spontaneously into the isomeric oxime: $H_3C—NO \longrightarrow H_2C=N(OH)$. If we add an oxygen to the nitroso group, we obtain nitromethane (H_3CNO_2), which is perfectly stable, but the tautomeric form of which ($H_2C=NO(OH)$) is so unstable, that its existence can be proven only by indirect means. The thermochemical equation, $2NO + O_2 = 2NO_2 + 26.9$ cal. proves conclusively that the nitroso group contains much more free *chemical* energy than the nitro, which is the reason why the nitroso group in nitrosobenzene is so much more reactive than the nitro group in nitrobenzene. In nitrosomethane, then, the following energetic and affinity relations exist: the oxygen has much free *chemical* energy and a strong affinity for the H of the methyl group, and by the change into the oxime, the great content of free *chemical* energy in the nitroso group is largely converted into bound *chemical* energy and heat. The transformation therefore proceeds with increase of entropy and the oxime represents an intramolecularly well neutralized structure, which agrees with its amphoteric properties and the slight additive capacity at the double bond. Since the nitro group in nitromethane has less free *chemical* energy than the nitroso in nitrosomethane, its oxygen has less capability to overcome the bound *chemical* energy holding the hydrogen to the carbon. A rearrangement to isonitromethane is barred for a second reason, *viz.*, that it would proceed with a degradation of entropy, for it is evident that the *neutral* nitromethane, the nitro group of which carries but little free *chemical* energy, is vastly poorer in such energy than the strongly *acidic*, unstaturated isonitromethane.[1]

In order that a rearrangement should proceed spontaneously, the atom which receives the migrating atom, or group, must have sufficient affinity for it to be able to overcome the bound *chemical* energy between the migrating atom, or group, and the atom to which it is already joined.

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[1] See *Ann.*, 363, 21.

If we increase through a structural change the bound *chemical* energy more than we do the affinity and free *chemical* energy factor; or if we decrease the latter without essentially altering the former, we obviously increase the relative stability of the new derivative and it may show an existence in a free state. Through certain structural changes the difference between the entropy values of the isomeric forms may be lessened, and we may arrive in this way to desmotropic substances, the energy relations of which are so evenly balanced that the existence of one or the other form may be determined by a slight expenditure of extraneous chemical, or physical energy.[1]

Before 1887 the substitution process in organic chemistry was universally supposed to consist of the direct replacement of an atom, or group, by another. It was then shown, by an investigation on the constitution of acetoacetic ester and its sodium derivative,[2] that this view could be upheld no longer and that apparent substitution is often the result of a combination of an addition and elimination process. Subsequent researches[3] have shown that substitution, as represented by the old view is of comparatively rare occurrence, and that a rational interpretation of the process may be based on the entropy principle. Thus, by the use of a metal like sodium, which has considerable free *chemical* energy and a strong affinity for oxygen, the hydrogen in $CH_2=NOH$ attached directly to oxygen may be driven out, with the formation of $CH_2=NONa$.[4] This change is only apparently a direct replacement of hydrogen by sodium, for what actually occurs is, that the energy and affinity values of the metal are such that it is able to overcome the bound *chemical* energy between the oxygen and hydrogen and that the latter element is *driven out*, not replaced.

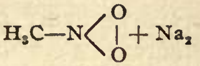
The distinction between replacing and driving out may seem from the above instance to be unimportant, but it is in reality of fundamental importance in organic reactions. Let us consider, for instance, the behavior of nitromethane and hydrocyanic acid towards sodium from the new point of view! In the system

[1] Michael, *Ann.*, 363, 27.

[2] Michael, *J. prakt. Chem.* [2], 37, 473.

[3] Michael, *Loc. cit.*, 60, 316. *Ber.*, 33, 3739; 34, 4028; 38, 22, 1922–1938, 2083, 2097, 3218. *Amer. Chem. J.*, 43, 330.

[4] It does not follow from the formation of this sodium derivative that the change as represented by $CH_2=NOH \longrightarrow CH_2=NONa$ designates an increase of entropy; indeed, a consideration of the well neutralized, amphoteric character of the oxime and the strong basic, easily hydrolyzed character of the sodium derivative, leaves no doubt that the free *chemical* energy in the latter is much greater than in the former structure. In the reaction much of the free *chemical* energy in sodium is converted into bound; it is the total change ($2CH_2=NOH + Na_2 = 2CH_2=NONa + H_2$) that proceeds with increase of entropy.



$$H_3C{-}N\Big\langle\begin{matrix}O\\ |\\ O\end{matrix} + Na_2$$

the metal may be attracted either by the C or the O, but not only is the free *chemical* energy in the O larger than that in the C, but also the chemical affinity for Na. Moreover, according to the law of entropy, the system must strive to realize the maximum condition, which will be the formation of a sodium derivative, in which the free *chemical* energy existing in nitromethane and in sodium is converted as completely as possible into bound *chemical* energy and heat. This condition is realized by the direct union of Na with O, since then an almost neutral salt will be formed, while the derivative containing the metal joined directly to C would be strongly basic and have positive energy in great excess. Indeed, if such a derivative as $NaCH_2NO_2$ could be obtained at a low temperature, it would pass over at ordinary temperature spontaneously and with an enormous in, crease of entropy into $CH_2{=}N(ONa)O$.[1] The intramolecular hindrance-which nitromethane offers to attack, of the Na on the O is the energy necessary to overcome the bound *chemical* energy between a hydrogen and the carbon, which, owing to the strong negative character of the nitro group, is very considerably less than in methane and the reaction therefore proceeds readily.

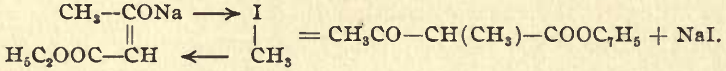
According to the old substitution theory, the action of Na on HCN[2] proceeds by the direct replacement of the hydrogen by the metal, forming NaCN; according to the new theory, the Na may be attracted by the C or the N, and a salt may be formed if the metal is able to overcome the bound *chemical* energy between the H and the C and the reaction proceeds with an increase of entropy. The properties of the cyano group leave no doubt as to the existence of considerable free *chemical* energy in the C and the N, and there is also no doubt that Na has a greater affinity for N than for C: furthermore, N, being an element with more negative *chemical* energy than C, the energy of the metal in NaNC is much better neutralized than it would be in NaCN. The energy and affinity conditions permit, therefore, in the *direct* formation of $CH_2{=}NO(ONa)$ and NaNC, the maximum possible increase of entropy, and any other conception of the structures of these salts, is as inconceivable from the new theory, as the older view leaves us wholly in the dark in regard to them.

[1] Although a "double" bond is usually an indication of the accumulation of free *chemical* energy, its symbolistic use for this purpose would be misleading. The free *chemical* energy in an atom must vary with the extent of intramolecular neutralization; *i. e.*, in $CH_2{=}NO(ONa)$ the free *chemical* energy at C and N is used up indirectly to a very considerable extent in neutralizing the positive energy of the sodium. An approximate idea of the free *chemical* energy in the atoms of a molecule can usually be formed by a consideration of their chemical nature, the structure and the properties of the substance.

[2] Michael and Hibbert, *Ann.*, 364, 64.

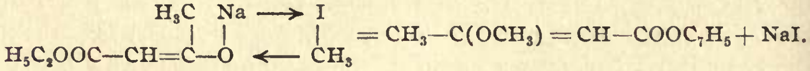
We have seen that the positive energy in sodium has been largely converted into bound *chemical* energy, when the metal is introduced into nitromethane and that neither at the unsaturated carbon or nitrogen of $H_2C{=}N(ONa)O$ is there much free *chemical* energy. It follows from these energy conditions that this salt should not easily react with a reagent, unless the latter contains atoms with much free *chemical* energy and a large affinity value for certain atoms in the salt. Hence, sodium isonitromethane is comparatively inert toward methyl iodide: but, if we make a change in the structure of the salt, so that the metal is less well neutralized, we shall facilitate the reaction; for, by doing so, we increase not only the free *chemical* energy of the unsaturated atoms, but the difference between the heats of formation of sodium iodide and the sodium salt, which is one of the largest factors in determining the entropy of the reaction. The conditions for an easy reaction are fulfilled, for instance, in sodium acetoacetic ester ($CH_3{-}CONa{=}CH{-}COOC_2H_5$), for in this derivative the positive energy of the metal is very inadequately neutralized by the weakly acidic organic radical to which it is joined, and the unequal balance between the positive and negative chemical forces must leave considerable free *chemical* energy in the unsaturated atoms. The reaction may proceed in two directions:

I.



$$\begin{matrix} & \mathrm{CH_3{-}CONa} & \longrightarrow & \mathrm{I} & \\ & \| & & | & = \mathrm{CH_3CO{-}CH(CH_3){-}COOC_7H_5} + \mathrm{NaI.} \\ \mathrm{H_5C_2OOC{-}} & \mathrm{CH} & \longleftarrow & \mathrm{CH_3} & \end{matrix}$$

II.



$$\begin{matrix} & \mathrm{H_3C} & \mathrm{Na} & \longrightarrow & \mathrm{I} & \\ & | & | & & | & = \mathrm{CH_3{-}C(OCH_3){=}CH{-}COOC_7H_5} + \mathrm{NaI.} \\ \mathrm{H_5C_2OOC{-}CH{=}} & \mathrm{C} & \mathrm{{-}O} & \longleftarrow & \mathrm{CH_3} & \end{matrix}$$

It is of interest to analyze the energy and affinity relations of the unsaturated carbon joined directly to the carbethoxyl group and those of the oxygen joined to sodium, since they determine the course of the reaction. Sodium iodide is formed in either case, and, as the heat of formation of the C- is greater than that of the O-methyl derivative,[1] its formation represents the maximum entropy of the system. The introduction of sodium into acetoacetic ester ($CH_3{-}CO{-}CH_2{-}COOC_2H_5$) has the following effect on the energy and affinity relations of the carbonyl oxygen (in CO) and the methylene carbon (in CH_2):

First, the free *chemical* energy in the O has been greatly decreased through direct union with the metal, while part of the bound *chemical* energy of the C (used before in holding the eliminated H) has been converted into free; second, the affinity of the O for CH_3 has been greatly reduced by the positive influence of the metal, which, on the other hand, has neutralized the effect of the two negative radicals (CH_3CO and $COOC_2H_5$) and given the unsaturated α-C a large affinity value for methyl. It is evident that when we take the entropy, energy and affinity relations

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[1] Experimental proof will be published later.

into consideration, the conversion of the O-sodium salt into the C-methyl derivative, *i. e.*, the reaction represented by I, is not an abnormal, but a perfectly normal, reaction,[1] as, indeed is every chemical change in which the condition of maximum entropy is realized.

Finally, we shall discuss another fundamental organic process, that of addition, from the standpoint of the second law of thermodynamics.

If we remove one hydrogen from two adjacent hydrocarbon groups in propane a compound is formed ($CH_3—CH=CH_2$) in which part of the bound *chemical* energy previously holding the eliminated hydrogen atoms in chemical union appears as free *chemical* energy at the unsaturated C-atoms.[2] In the addition of a reagent to such a compound, the free *chemical* energy of the unsaturated atoms is more or less completely converted into bound *chemical* energy and heat, and the second law of thermodynamics compels the addition to take place in such a manner that the maximum entropy will be realized, unless there is some chemical hindrance, which prevents this attainment of the ultimate goal of free *chemical* energy.

The structure theory teaches us that in the addition of hydrobromic acid to propene, two isomers (propyl and isopropyl bromide) may be formed, but it fails altogether to give us any indication which of these products, or whether both of them, should result. The chemical hindrance in this reaction is the energy necessary to overcome the bound *chemical* energy between the H and the Br of HBr to the extent to which it exists between them in the bromopropane that will be formed in the addition.[3] This hindrance is obviously quantitatively the same in the formation of either isomer. The maximum entropy in this addition will be attained, therefore, in the formation of the isomeric bromopropane with the greater heat of formation.

Obviously, it is of great importance in this and in many other organic reactions to be able to trace the relation between the structure of isomers and their heat of formation. This is enabled by the following "thermochemical law of structure."[4] In isomers with normal chains and which contain a common negative radical as a nucleus, that isomer will have the largest heat of formation, the positive radicals of which to the greatest extent are under the influence—direct and indirect—of the negative nucleus. Thus, in propyl and isopropyl bromide the common negative nucleus is CBr, which in the last compound is under the direct influence of two methyl groups, while in propyl bromide only one methyl is directly, the other indirectly, joined. The intramolecular neutraliza-

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[1] Michael, *Ber.*, 38, 129.

[2] *J. prakt. Chem.*, [2] 60, 298.

[3] Michael, *Am. Chem. J.*, 43, 333 (foot-note).

[4] Michael, *J. prakt. Chem.*, [2] 68, 499; 79, 418; *Ber.*, 39, 2140.

tion, which finds an expression in the heat of formation, is therefore larger in the iso than in the normal bromide, and, since the thermic value of direct is very much greater than that of indirect chemical union, the heat of formation of the former compound is considerably larger than that of the latter.

Not only does the system, propene and hydrobromic acid, realize its maximum condition of entropy in the formation of isopropyl bromide, but the affinity relations at the points of maximum concentration of the free *chemical* energy, *i. e.*, at the unsaturated carbons, are such as to favor the course of the reaction in this direction, since the influence of methyl in this substance is positive to that of hydrogen in the same position.[1] This relation causes in propene a greater accumulation of positive energy at the middle than at the end unsaturated carbon and the middle carbon must have, therefore, the greater affinity for the strongly negative halogen of the acid. It seems theoretically probable that this coincidence of affinity and entropy values should lead exclusively to the formation of the iso derivative, as, indeed, it would if chemical change depended solely on the free energy and the affinity values. When a mixture, containing an acid with a very large and a very small acidity constant, is brought together with a quantity of a strong base inadequate for complete neutralization of the acids present, there is always an appreciable amount of salt derived from the weak acid formed. The chemical force in each acid endeavors to its utmost capacity to contribute its share toward the increase of entropy, which depends not only on the values of the affinity constants but, although to a very much smaller degree, on the actual mass, by weight, of acid present.

If the formation of normal propyl bromide from propene and hydrobromic acid proceeds with an increase of entropy, which it undoubtedly does, we have in this addition reaction two chemical forces, each striving to increase the entropy, but, in this case, the mass by weight cannot be changed and the struggle is between energies.[2] Furthermore, since there is no difference in the chemical hindrance to the addition in either direction, it is extremely probable that the relative amounts of salts, or isomeric bromides, formed will stand in a direct relation to the increase of entropy, and as this is very much greater with the formation of isopropyl bromide, it agrees with the theory that the normal bromide is formed only to a very slight extent.[3]

The principle here involved was first used by Thomson[4] to determine the relative acidity constants, and has been called the "*principle of*

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[1] Michael, *J. prakt. Chem.*, [2] 60, 332; *Ber.*, 39, 2142 (footnote).

[2] There is no practical difference, as matter from a chemical point of view should be considered only as a carrier of chemical energy.

[3] Michael and Leighton, *J. prakt. Chem.*, 60, 443.

[4] *Pogg. Ann.*, 138, 497.

partition";[1] it may be applied to every organic reaction where two or more isomers may be formed.[2] Let us take, as illustrations of the application of this principle, the addition of water by means of sulphuric acid to hexine–1 and –2. In hexine–1 ($\mathrm{CH_3{-}CH_2{-}CH_2{-}CH_2{-}C{\equiv}CH}$), we have practically the same conditions as in propene, that is, the difference between the energy and affinity values of the unsaturated carbons are due to the difference between the direct influence of an alkyl group and a hydrogen; hexanone–2 ($\mathrm{CH_3{-}CH_2{-}CH_2{-}CH_2{-}CO{-}CH_3}$) and probably a very slight amount of hexanal ($\mathrm{CH_3{-}CH_2{-}CH_2{-}CH_2{-}CH_2{-}CHO}$) are formed. The relations in hexine–2 ($\mathrm{CH_3{-}CH_2{-}CH_2{-}C{\equiv}C{-}CH_3}$) are quite different; the unsaturated carbons are both joined directly to alkyl groups, and the change in their energy values is due not to direct, but to indirect, influences, which are largely spatial. This relation must cause the heats of formation of the products that may result, hexanone–2 and –3, to be much nearer together than the isomers that may be formed in the addition to hexine–1; also an approximation in the energy and affinity values at the unsaturated carbons.

According to the "principle of partition," the relative amounts of hexanone–2 and –3 formed should not fall very far apart. Moreover, we can approximately estimate the energy values of the unsaturated carbons in relative terms by the use of the "scale of combined influence" mentioned above. Applying this scale to the relations in hexine–2, omitting those atoms the influences of which on the unsaturated carbons are equal,[2] or very nearly so, we find that Δ^{β}—C[3] (joined directly to methyl) is under the influence of one carbon in the 4th, one hydrogen in the 3rd, and three hydrogens in the 5th position, and Δ^{γ}—C (joined directly to butyl) has one carbon acting in the 3rd and 4 hydrogens in the 4th position. Since atoms in the 3rd and 5th positions exert a greater influence than those in the 4th, it is obvious that the positive energy at Δ^{β}—C is greater than that at Δ^{γ}—C, and that a larger proportion of that ketone should be formed, when the negative part of the addenda adds to it, *i. e.*, hexanone–2. A re-investigation[4] of the reaction shows indeed that about 60 per cent. of hexanone–2 to 40 per cent. of –3 are formed in the reaction.

The present structure theory has been, and always will be, of inestimable service to organic chemistry: it has taught us, until recently,[5] the possible number of isomers that may exist of a given formula, and it has been a guide in determining the constitution of most of the substances that

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[1] Michael, *J. prakt. Chem.*, [2] 60, 341–354; *Ber.*, 39, 2138–2156, 2569, 2786–2795; 40, 140.

[2] See *J. prakt. Chem.*, 60, 341. *Ber.*, 39, 2141.

[3] The capital "Delta" denotes unsaturation (Baeyer, *Ann.*, 245, 112).

[4] Michael, *Ber.*, 39, 2133.

[5] *Ber.*, 39, 203.

have been discovered. But its weakness and limitations are inherent in its foundation on a mechanical conception of valency and an almost exclusive theoretical development along similar lines, for surely in nature there are no forces more intimately and indissolubly connected with changes in energy than the chemical.

Largely for this reason, the structure theory fails to offer explanations for many of the simplest organic reactions and, for many years, it has failed in explaining and co-ordinating with theory much of the wonderful experimental progress that has been made in the science.

It is true that innumerable attempts have been made to amplify or change the idea of valency and the structure theory so as to remedy these deficiencies, but they have always been along mechanical lines and have led to such impossible theoretical conceptions as new brands of valencies, dissociated and partial valencies, oxonium and carbonium theories, steric hindrance due to size of the atoms, etc., etc.

All the forces in nature, whether mechanical or chemical, have the same goal in view, which is the realization of the maximum condition of entropy, and a scientific theory of chemistry must inevitably have this law as its basis. The present aim of organic theory is not to abandon the structure theory, but so to broaden and develop it that it becomes a consistent and harmonious part of nature.

NEWTON CENTRE, MASS.

PROGRESS IN SYSTEMATIC QUALITATIVE ORGANIC ANALYSIS.[1]

BY S. P. MULLIKEN.

Received June 29, 1910.

A general procedure in organic qualitative analysis that may be trusted to lead to the discovery of the proximate composition of any unknown organic substance whatever, whether this be a simple compound or a mixture, is demonstrably incapable of practical realization. Before proceeding to the discussion of the main subject of this paper, it therefore behooves us to pause for a moment to note certain limits which Nature seems to have set against the too curious advances of the analyst.

The most clearly insuperable of these limitations are associated with high molecular weight. If a paraffin hydrocarbon of the formula $C_{35}H_{72}$ were to be isolated in a state of perfect purity and in large quantity from some natural product, it would be impossible to absolutely identify it as a compound corresponding to any particular structural formula by any combination of methods of investigation now known, or whose future discovery appears probable. Such a hydrocarbon would not differ by one one-hundredth of one per cent. in its hydrogen or its carbon content from its adjoining homologues, while in chemical and physical properties there would be no measurable differences between it and

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[1] An address delivered at the Second Decennial Celebration of Clark University, Worcester, Mass., Sept. 16, 1909.

thousands of its four million undiscovered structural isomers, which, according to the calculations of Cayley, are theoretically possible. Indeed, in the case of the discovery of such a high hydrocarbon by any process other than one of simple synthesis, no proof could be contrived which would show that the substance might not well be a mixture of many isomers and neighboring homologues; for all finite methods of purification by fractional separation based on differences in properties must inevitably fail when the numerical odds against them are so great, and we have no choice in such a case but to resign ourselves with the best grace possible to an inevitably partial solution of our problem.

But without having ascended to such an altitude in the homologous scale as in the instance just cited, it is often necessary or expedient to accept incomplete answers in qualitative inquiries because of our thraldom to the rule that unknown compounds in mixtures cannot in general be fully identified without previous isolation in a state of purity. It is for this reason that it is so common a practice in technical analysis to express the quantitative composition of familiar and important products in conventional or collective terms. Long and thoroughly as the animal fats have been studied, for example, there is probably no instance on record of a quantitative examination of any natural fat in which it could be safely claimed that the structural identity of all its fatty acids containing less than eighteen carbon atoms had been irrefutably established. Nor would it be surprising under the circumstances if such a result were never accomplished.

Thus handicapped, systematic qualitative organic analysis has developed slowly when compared with the simpler qualitative analysis of the inorganic elements and salts. Yet, if we contrast the difficulties to be overcome in constructing an orderly scheme for the separation and identification of the list of less than one hundred elements with the difficulties to be met in any corresponding scheme for the organic compounds, and then recall what has already been accomplished in overcoming them, and also the imperfections which present-day inorganic qualitative schemes still exhibit when the rarer elements are included, the organic chemist will find little cause for pessimism. The greater part of the contributions to organic qualitative analysis have been made, however, without much thought of the part which they might be made to play in any comprehensive scheme of procedure, and have often owed their origin to incidental observations made during the execution of investigations of broader scope and different purpose. Fischer's numerous characterizations of compounds in the sugar, purine and protein groups, by well chosen reactions and derivatives, and his ingenious separations for the amino acids formed in proteolysis are illustrations of this fact. Among the rather numerous handbooks of organic analysis, although many devote much space to qualitative testing, the speaker recalls only one whose author (Barfoed, 1878) has been sufficiently venturesome to incorporate the phrase "Organic Qualitative Analysis" in its title. Of the many commendable partial schemes for the isolation and identification, or the detection in certain classes of mixtures, of carbon compounds belonging to restricted groups, we owe the origin of a large proportion to an acute need of special analytical assistance in some department of industry, research, or governmental control. To such cause we owe much of what is most valuable in Allen's "Commercial Organic Analysis," Post's "Chemisch-technische Analyse," and the works of Vortmann, Dragendorff, Hoppe-Seyler, König, Leach, Sherman, and others. The investigation of methods for the detection and determination of constituent radicals has also proved a fruitful source of valuable material, much of which has been made accessible for ready reference in H. Meyer's "Analyse und Konstitutionermittelung organischer Verbindungen."

The resolution of mixtures is usually the first, and often the most difficult part of a qualitative analysis. Definite plans for correlation in a broad general procedure of the methods of separation that have proved effective in the study of restricted classes of mixtures have yet to be proposed. The speaker is not in accord with the rather prevalent view that it is useless to strive for broader and more systematic separation procedures. But, on the other hand, as he is unprepared to play the prophet's rôle, it may be more profitable for him to confine the following discussion to the topic of systematic procedures for the identification of pure compounds, this being an important division of the qualitative problem whose solution seems nearer accomplishment.

Prior to 1831, the date of the inauguration of those revolutionary improvements in organic combustion methods by Liebig, which rendered it possible to determine the percentage composition of any carbon compound with considerable accuracy and comparative convenience, it does not appear that any comprehensive systematic methods for identifying previously described organic compounds had been formulated, or that the lack of them had been felt as a serious inconvenience. The number of pure compounds that had been described was comparatively small, the possibility of laboratory syntheses for organic compounds having only just become recognized, and the descriptions of such compounds as were known were not scattered as to-day through an almost endless list of special journals and treatises. A chemist of this earlier period, if a man of extended practical experience, well read, and having access to a good library, rested more or less content in the knowledge that he could probably accomplish by a purely eclectic procedure, based on his miscellaneous sources of information, ingenuity, and common sense, all that was then analytically possible.

Thanks to Liebig's writings and the influence of the students who passed from his Giessen laboratory, his simplified methods of ultimate analysis were not long in becoming widely known. In scientific laboratories they were everywhere welcomed and adopted. This welcome was richly deserved; for, besides serving as a means to determine percentage composition values—which will perhaps always remain the most fundamental of chemical constants—their use, in connection with the later widely adopted vapor density molecular weight determination methods, furnished all information required for the calculation of empirical formulas. These, if we add knowledge of genetic relations and chemical behavior, become structural formulas with all the added information as to chemical characteristics and individuality which are inherent in the latter. The vapor density molecular weight determination methods reached their climax for the organic chemist in the air displacement form proposed by Victor Meyer in 1878. The prestige of the empirical formula as an aid in compound identification was soon still further enhanced by the discovery of Raoult's principle, followed by the invention of the Beckmann thermometer in 1888, these aids to molecular weight determination finally enabling the inclusion among the compounds of directly determined empirical formulas of a large share of the non-volatile compounds. Other causes about to be mentioned also conspired to bring the analytical importance of the empirical formula to extreme prominence.

During the two decades closing in 1880, the unprecedented increase in newly described organic compounds had already begun to assume the dimensions of a threatening deluge. The synthesis responsible for the creation of a new species, being aware of its genetic relations, and having determined its empirical formula, was usually in a position to correctly interpret the chemical identity of his progeny; though to prove that his discovery was really an original one by a search through the swollen literature had become a task to be undertaken with fear and trembling. The time rapidly approached when the healthy future development of organic research seemed likely to receive a serious check from the confusion and discouragement in store for investigators who could only hope to escape plagiarism in recounting their alleged discoveries by well-nigh interminable bibliographical delvings. Those of us in the younger generation of organic chemists are not in a position to even faintly appreciate the sigh of relief that must have been breathed by hundreds of workers in many lands when these chaotic conditions were ameliorated in 1882 by the completion of the first edition of Friedrick Beilstein's great handbook of organic chemistry. With rare foresight Beilstein had in season anticipated the mission which this remarkable work had to fulfil, and its publication after twenty years of incessant labor, occurring as it did at this critical period in the development of organic chemistry, is of epoch-making importance to organic qualitative analysis as well as to all other departments of the science.

Beilstein's "Handbuch" was a digest of the complete literature of the modes of formations, properties and reactions of all the analyzed compounds of carbon. It did not purport to be an analytical guide, and in its introduction the possibility of a qualitative organic analysis at all comparable to the inorganic is categorically denied. Nevertheless, because of the completeness and orderly arrangement of its concise descriptions, its importance as an aid in the identification of organic compounds may be fairly estimated as greater than that of all the special analytical treatises which have ever been issued. Its general classification for the compounds has sometimes been criticized as clumsy and confusing, but the division of species according to chemical function, saturation, and in homologous series, has, on the whole, served the interests of the analyst well; and the invention of a simple device for locating in its pages the description of any desired compound of known empirical formula, which has been more recently made available through the ingenuity and coöperation of M. M. Richter, the manager of the Prinz Dye Works in Carlsruhe, has now long served in case of compounds of this class to greatly facilitate their identification.

Richter's "Tabellen der Kohlenstoff-Verbindungen" with its 20,000 brief references to the literature and properties of the analyzed organic compounds was issued in 1884. The first volume of the second edition appeared in 1900 under the altered title of "Lexikon der Kohlenstoff-Verbindungen." In its present completed form this edition registers more than one hundred thousand compounds of determined empirical formulas, and gives direct access to the full description and literature of each by citation of the proper volume and page number of Beilstein. As a bibliographical index for compounds of known empirical formula it is hard to imagine anything simpler or more complete than the Richterian classification. The exact position of every possible compound (if we exclude the arrangement of isomers with reference to one another) is automatically fixed by its formula alone, and is as easily found, and in much the same manner, as a word in a dictionary through a knowledge of the relative positions of its letters in the alphabet. The completeness of the tabulation is suggestively indicated by the author's remark that his guiding thought during its preparation was "Das Unwesentliche, d. h. die weniger bekannten Verbindungen, stets in erster Linie und vollstandig hervorzuheben." On the other hand, its use as the basis for a method of identification for unknown organic compounds is often attended with serious or prohibitive difficulties.

It has been already pointed out that an absolute determination of species among the carbon compounds is theoretically impossible by any combination of tests in the case of compounds of extremely high molecular weight, and that the unavoidable errors of ultimate organic analysis with such substances are large enough to prevent analysts from making any selection between a large number of seemingly possible and equally probable empirical formulas. This unfortunate circumstance prohibits the use of the Richterian system in large and important fields where quantitative investigation by other methods may be conducted with good prospect of success. For example, the dyestuff tables of Schultz and Julius describe a hundred distinct tetra-azo dyestuffs having molecular weights above 500, and some of them exceeding 1000. These colors are many of them important, their constitutions well established by synthesis, and their identification through their physical and chemical properties, or at least their approximate identification—which is often all that is required—is not especially troublesome. The absurdity of an attempt to identify an unknown color of this class through its empirical formula—which would usually involve the quantitative determination of at least six elements with an impossible degree of precision—is so patent from the mere mention of the stoichiometric conditions that it may be hoped it has never been made by any rational being.

A second defect in the method of the empirical formula, which in the ordinary laboratory curtails its actual application even more than the absolute limitation just mentioned, is the fact that much special manipulation, skill and apparatus are necessary to insure trustworthy results in elementary organic analysis, and that so much time is always consumed in the preliminary arrangements for a combustion and in its conduct. In the larger organic laboratories where the combustion of new synthetic products is an almost daily incident of the routine of investigation, and the equipment of the combustion room is maintained at all times in a state of perfect preparedness for emergency calls, so that no time need ever be lost in the mobilization for an analysis, the organic combustion is not formidable to the initiated. But under other circumstances—and they are the prevalent ones—chemists do not resort to the method of the empirical formula except under rather strong compulsion, and many identifications which ought to be made are not even attempted.

In view of these defects and inconveniences, it is natural to inquire whether there is hope of securing in the future any scientific substitute for the method of the empirical formula. In the comprehensiveness and simplicity of its classification of compounds, it must be admitted that it will be vain to expect anything but loss from radical changes in the Richterian arrangement; but, if we accept the logician's definition of a scientific classification as "Nothing more than a system of division carried out in such a way as to best serve a given purpose," and if our purpose is convenience and effectiveness in general qualitative investigation, the possibility of other and more scientific classifications is not to be denied; and it has seemed to the speaker that the discovery of such methods of classification is at present one of the important and attractive fields for organic chemical research. What the final outcome of this quest will be—if we have the right to speak of a final outcome in a problem which from its nature permits of only progressive partial solution—no one can as yet speak with full authority. Some of the general considerations bearing on the subject may, however, be brought to your attention.

Scientific classifications are chiefly concerned with relations of resemblance and contrast. To answer the question what points of resemblance and contrast must be regarded, and in what order, if we are to make a classification scientific, is to say that no basis of classification ("*fundamentum divisionsis*") is *per se* better than any other. All depends on the ultimate object. If the object of a classification is ready diagnosis of natural objects, it is evident that the characteristics used as *differentiae* for distinguishing between groups should permit of easy as well as certain determination; and it is also a good quality in such a division to collect individuals in the lowest group for comparison which are on the whole most alike. Methods of subdivision which aim at discovering something without regard to whether the resemblances of adjacent species are fundamental or accidental, like the classification of words in a dictionary according to the accidental alphabetical sequence of their letters, are called artificial systems. The Linnaean and Richterean systems belong to this category. No comprehensive system of division in natural science is free from many artificial features. But these are more likely to be prominent in the early than in the later stages of the development of a classification, the pioneer in such work having to first bridge his rivers with such structural materials as lie nearest at hand.

To the observant mind the discovery of possible *differentiae* for the classification of natural objects is an easy and fascinating pastime, though to make a wise selection may often be quite the reverse. Thus we read in the quaint diary of the botanist Linnaeus under the date of June 12, 1632, in his "*Lapland Observations*": "Close to the road hung the under jaw of a horse, having six front teeth, much worn and blunted, two canines, and at a distance from the latter twelve grinders, six on each side. If I knew how many teeth and what peculiar form, as well as how many udders, and where situated, each animal has, I should perhaps be able to contrive a most natural methodical arrangement of quadrupeds." As with Linnaeus' quadrupeds, so with organic compounds—we find a multitude of easily determined properties from which we may choose the *differentiae* for our classification, and by the exact coincidence of a sufficient number of these characteristics of different orders with those of an unknown compound, the identity of the latter may be proved. Qualitative elementary composition, color, melting and boiling point, specific gravity, odor, taste, solubility, refractive index, specific optical rotation, electrical conductivity, absorption spectra, color reactions, precipitations, and general chemical behavior—especially simple chemical reactions that throw light on the nature of dominant atomic groups and structural peculiarities—may all be thus used.

Regarding the chemical compound, or individual, as the *species* of a chemical system, it appears most natural to group these species in such a way as to make the next higher unit or *genus* contain species which are most similar in general chemical behavior. This would, for example, tend to make congeners of members of all homologous series containing the aldehyde radical, provided we could find sufficiently reliable and simple chemical tests for showing the presence of the CHO group. Recent chemical literature abounds in suggestions for tests suitable for generic *differentiae*, though much additional work will be required in every instance to determine the real value and exact boundaries of the genera that their employment would create, there being ever-present danger that overconfidence in the constancy of behavior of a reagent towards a given radical in different structural environments may lead to false conclusions. Thus it is not safe to assume that under certain specified conditions all ketones will form oximes; all acids and phenols will dissolve in alkali; all esters will be saponified; or all unsaturated compounds will add bromine. In first delimiting a genus such assumptions may be adopted, after preliminary experiments, as tentative working hypotheses; but the contents and existence of the genus must be held to be strictly provisional and dependent on the positive outcome of the proposed genetic reaction when applied to a larger number of its carefully selected species, and to its negative outcome when tried with numerous members of all genera of higher numerical designation in the same classificatory *order*. It will also be the duty of the classifier to indicate, in a manner that will leave no doubt in the minds of readers, all descriptions, or parts of descriptions, for which he is personally responsible; for unless some means is given for distinguishing between data which he has verified, and others which he has not, the authority is liable to be more or less implicated in the mistakes of others for which he need have assumed no responsibility, but which will now tend to vitiate the value of his classification as a whole.

It would be premature at this time to present in all its minutiae any plan for such a classification as has just been suggested in its outlines. Details in illustration of the speaker's original conception and partial execution of such a plan are to be found in the already published first and third volumes of his "*Method for the Identification of Pure Organic Compounds.*" All that is desired here is to lead to a discussion of the advantages in the plan for Chemistry; and if it is sound, to arouse interest with a view to eventually bringing about a wider coöperation for furthering its future development. The difficulties to be overcome are considerable. Recorded descriptions of organic compounds, while frequently very complete for a few properties like melting and boiling points, are commonly equally deficient concerning others—especially in exact data showing the extent of the influence of slight variations in chemical constitution on the results of the selected differential tests. The occasion hence arises for an investigation or partial reexamination of a considerable proportion of the species receiving locations. If one has the pure compounds with which to experiment, the tests are easily made. But as only a few thousand pure compounds can be procured through commercial channels, and most of these require some purification, sucess in the construction of a comprehensive diagnostic classification implies assistance from private collections throughout the world; for to synthesize any considerable part of the rarer species would overtax the facilities of the largest and best equipped of laboratories.

To bring a majority of the carbon compounds referred to in Richter's Lexikon into an essentially "natural" classification of the kind suggested would, assuming the study of tests and revision of constants to be thoroughly done, perhaps involve a labor as great as the transformation of the "artificial" botanical classification of Linnaeus into the modern "natural" system as it was left by de Candolle. An undertaking of this magnitude and character might presumably in the present century be accomplished with greater benefit to science under the direction of some such organization as the committee entrusted with the periodical revision of Beilstein's "Handbuch" and the Richter "Lexikon" than under private auspices.

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BOSTON, MASS.

THE OUTLOOK FOR A BETTER CORRELATION OF SECONDARY SCHOOL AND COLLEGE INSTRUCTION IN CHEMISTRY.[1]

If the question "Should more credit be allowed by institutions of college grade for work in chemistry done by pupils in secondary schools?" were asked of any considerable number of teachers in those schools it is easy to believe that the majority would make an affirmative reply, and that all would at least be inclined to add to the query the traditional language of the examination paper, "If not, why not? Give reasons for your answer." Inasmuch as the present conditions with respect to the correlation of the work in the two grades of schools is admittedly unsatisfactory, and since these conditions are essentially determined by decisions on the part of the colleges, it is fitting that the situation should be occasionally reviewed, with the purpose of finding out, on the one hand, how far the present situation can be defended and, on the other hand, of seeking means by which better results can be attained. Others have dealt with this subject from various standpoints, and the statements which follow are made less with the expectation that anything like a final word will be said, than the hope that a contribution of the experiences of the teachers in one more laboratory, and a few of the conclusions which they have reached, may do something to aid in the comprehension of one of the most perplexing problems which confront the teacher of elementary chemistry to-day.

The experiences here recorded have been gathered from the routine of instruction in a technical school, and it may be considered doubtful by some whether observations made in the laboratory of a technical school in which the instruction in chemistry becomes a part of a "step up" system of requirements (that is, one in which successful work in subjects of later years is directly dependent upon a thorough grounding in earlier subjects to a degree that does not obtain in the less rigid sequence of studies in the college) should be taken as a basis for conclusions bearing also upon college work; but, while such doubts may be justified in the case of a limited number of institutions in which chemical instruction is merely a part of a general college course, it is increasingly true that more and more students from all colleges are seeking the technical schools to complete some of the professional courses which they offer. In the case of the university the technical school may well be a part of its own system; in the case of the college it means that its reputation for efficiency in teaching is to be unexpectedly tested by some other group of instructors, and it should be as much a matter of concern to them to see that their students have an adequate preparation in the sciences as to see that they are soundly taught in mathematics or the humanities. Many of the colleges have much room for improvement in this respect.

Let us first look at the situation as it apparently exists at present in some of our typical institutions as indicated by the following brief summaries. The term "entrance requirement" is assumed to represent the work of a year with the ordinary time allotment for chemistry in the preparatory schools. The data have been obtained through direct correspondence with representatives of the institutions mentioned.

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[1] Presented at the second decennial celebration of Clark University, Worcester, Mass., September 17, 1909.

1. *Yale College.*—Does not require chemistry for entrance. Students may take an examination for advanced standing, but rarely do so.

2. *Harvard College.*—Those who have passed the entrance requirement take the same lecture as those who have had no chemistry, but they have special laboratory work and more advanced instruction in a special division. They are also allowed to take a first course in organic chemistry in the freshman year. Admission of such students to work in qualitative analysis has not proved successful. Those who present more chemistry than the entrance requirement are individually considered, but are rarely excused from college work on the basis of secondary school work.

3. *Cornell University.*—The entrance requirement is nearly the same as that of the College Entrance Examination Board, but the passing of this examination does not secure credit for introductory inorganic chemistry in the university. The student may take an examination for advanced standing if he desires.

4. *Columbia University.*—Those who pass the College Entrance Examination Board examination are admitted to a special course in lectures in chemistry, including a somewhat advanced treatment of the subject.

5. *Syracuse University.*—For one year of chemistry in a normal school credit is given for elementary chemistry in college, provided the student takes another course in chemistry and passes well. After one year of chemistry in a secondary school, pupils are allowed to take the regular examination in elementary chemistry, and if they pass, credit is given for that course. If chemistry is accepted for admission the student is admitted to second-year classes, but no credit is given for elementary chemistry.

6. *Washington and Lee University.*—Students from secondary schools with the equivalent of Remsen's "Briefer Course" are admitted to a course including physico-chemical topics and to qualitative analysis. If they do well, they are excused from the former at Christmas, and continue with analytical chemistry; otherwise they continue the course in inorganic chemistry through the year. A few students from selected schools are admitted at once to qualitative analysis, but no college credit is given.

7. *Washington and Jefferson University.*—Students from a few selected schools are given credit for the first year of chemistry in college, provided they take a later course in chemistry and attain a high pass record. Others are required to pass an examination before any credit is given. Chemistry is given in the sophomore year in this institution.

8. *Wellesley College.*—An advanced course is provided for those students who have had a year of chemistry. Smith's "College Chemistry" is used, and a somewhat exacting line of experiments is required. Some quantitative experiments, some volumetric analysis and some inorganic preparations are included.

9. *Chicago University.*—Students who have completed one year of chemistry in an accredited school are admitted to special courses and complete the work preparatory for qualitative analysis, or elementary organic chemistry, in about two-thirds of the time required by beginners; that is, they complete two majors in chemistry in place of three. The work of these two majors is carefully adapted to utilize and clarify the knowledge already gained.

10. *University of Michigan.*—For a year of chemistry at an accredited school four hours of university credit are allowed (sixteen hours per semester is full credit). These students are admitted to a course somewhat less elementary than that given to beginners.

11. *University of Illinois.*—A full year of chemistry in a secondary school is accepted in place of one semester in the university, provided no more chemistry is taken (and provided chemistry is not offered for entrance). When the student continues in chemical subjects he is advised to take the regular course of lectures in chemistry, but spends less time in the laboratory.

12. *University of Wisconsin.*—Credit is given for entrance chemistry to the extent of one or two units out of fourteen. These students enter the same classes as the others, but have a slightly different laboratory course. In the course of two months they appear to be on about the same footing as those taking the subject anew.

13. *Lehigh University.*—Up to two years ago certain certificates were accepted from secondary schools but the results were so unsatisfactory that an examination has been substituted. Those who fail take elementary chemistry; those who pass are admitted to a course in theoretical chemistry.

14. *Sheffield Scientific School.*—If the student passes entrance chemistry, he is allowed to take an examination to pass off the elementary course in the scientific school, and if successful he is admitted to qualitative analysis. Very few students are thus admitted.

15. *Stevens Institute of Technology.*—Students pass an entrance examination like that of the College Entrance Examination Board, but the instructor finds that he cannot make use of the earlier work, and all students take a course in elementary chemistry.

16. *Worcester Polytechnic Institute.*—Earlier attempts to examine upon a limited portion of elementary chemistry with the purpose of definitely eliminating this from the college course were not successful. Notebooks are now examined, and when these indicate a satisfactory course, the students are placed in separate divisions and given a different laboratory course. They attend the same courses of lectures as the beginners.

17. *Massachusetts Institute of Technology.*—Students who have satisfied the entrance elective requirement are admitted to a special class during the first term, and the lecture and class-room instruction, as well as the work in the laboratory, are designed to take advantage of the work already completed by the student in the preparatory school. The effort is made to introduce new lines of experimentation, as well as to reawaken interest in earlier work by encouraging the student to interpret the phenomena which he now studies in the light of his more extended experience, and with the aid of such additional concepts as have been introduced into the lectures and recitations. The two divisions of the class are united for the work of the second term.

Of these seventeen institutions one does not recognize chemistry for entrance, two make no specific provision for students who have had chemical instruction in the preparatory schools, three provide special laboratory instruction, but give no definite college credit, six provide special instruction in both lecture room and laboratory, but without giving college credit, while two give some college credit on certificate, and four excuse students from elementary college courses after special examination.

These institutions are sufficiently varied as to locality and type to justify the assertion that they represent the present practise on the part of thoughtful college teachers. That there is apparently much duplication of effort is at once evident, and that this must result in some loss of time, energy and enthusiasm hardly requires argument. Why, then, have we so long tolerated this apparent waste, and why do we not immediately take steps to avoid it? The answer seems to me to be this: It appears to be impossible to select any point in the chemical instruction received by the members of a college entering class at which they have such a sound understanding of the facts and principles already studied that this knowledge may safely be accepted as a foundation for further college instruction; or, if such a point may be selected, it lies so near to the beginning of the college course as to make a definite excuse from this small amount or work practically meaningless. There is, of course, a small proportion of students to whom this statement is not applicable, but it holds true to so large a proportion that it determines the character of the instruction which is given to all students who have had any previous chemical instruction. The situation does not appear to be appreciably better in institutions having a definite entrance requirement in chemistry than in others.

Some of the reasons for this state of affairs we will try to consider presently, but let us first look at the conditions as they confront the college teacher who has an earnest desire to enable his students to utilize every advantage which they have gained, remembering, however, that in these days it is not a question of individual but of class instruction, so far as the main features of a course are concerned. The college teacher or the teacher in a technical school will find among the members of a single class students of each of the following types, with many variations:

Student A.—An intelligent, reasonably thoughtful pupil from a school where there are small classes, a well-arranged one-year course and a judicious, helpful teacher. Such a student is a source of constant pleasure, and much can be done for and with him.

Student B.—The chemical enthusiast who, during a course of one or two years' duration has been permitted, because of his enthusiasm, to work extra hours or to assist his teacher. He has won high praise and occasionally merits it, but too often the college teacher learns to dread the expenditure of energy and tact which is necessary to retain the good will of such a student while bringing him to realize that a more profound knowledge than his own may be possible; yet, when the battle has been won, perhaps half of these men make excellent students.

Student C.—The student who has had two years of chemistry, in a course of ordinary excellence, under average conditions as to equipment and teaching. He feels, with some reason, that all this should count for a great deal, and no argument will wholly displace this notion. He works without interest, and generally badly, and is a heavy load to carry. You ask, Why not transfer him to the work of the higher years? We reply, Because experience has shown that he probably lacks adequate preparation for it, and will fail in it. The only practicable alternative lies in so arranging his laboratory practise that he shall have as large a measure of new work assigned him as it is possible to oversee without disproportionate attention on the part of the instructors.

Student D.—A student of moderate ability from an average school with a year of experience. His credentials are clear, but he has perhaps had little personal instruction and his knowledge is ill-arranged and vague, as to both fact and principle. He has no confidence in himself, and there is very little which is final in his preparatory work. His is one of the most difficult cases to provide for at the start, but often turns out well in the end.

Student E.—A student who has spent a year, or more rarely two years, under inadequate instruction, which has been worse than useless. An entrance examination may exclude him, but under other systems he becomes a troublesome factor in the complex problem and it may require some weeks to discover or be sure of his trouble. His place is with those students who take up the study of chemistry as beginners and his exclusion from the more advanced class is logical; but a transfer to elementary classes when these are provided is almost certain to breed discontent in the individual, and often disarranges other work of the term which, by that time, is well advanced.

But the confusion of interest does not end here! The types just referred to have been selected essentially along the lines of general efficiency of instruction and length of courses. It must further be recalled that even efficient teachers vary widely in their conceptions of the ground to be covered, and the college receives students who, during a single year of chemical instruction, have had the chief emphasis laid upon descriptive chemistry; others where it has been laid chiefly on "theoretical chemistry;" again others where the course is largely one of physics rather than chemistry; and, finally, where considerable qualitative analysis has been included even in this brief time.

The conditions appear, then, to be these, briefly stated: Experience indicates that the pupils who have had even two years of instruction in secondary schools are, in general, not in a condition to take up work in chemistry which is more advanced than that of the first year in the college, and for students who have had but a single year there is at present so little that can be regarded as common knowledge that the present apparent duplication of work seems unavoidable. Regarding this duplication more will be said presently.

Let us next face the question, Why is it that secondary-school courses have failed, and, as it seems to me, are likely to fail, to serve as substitutes for any considerable amount of college instruction in chemistry? The reasons are far from simple, and they need some analysis. We may distinguish, I think, at once between certain factors which, since they are inherent in the nature of our science or in the period in the pupil's life in which the instruction is given, are common to all schools, and those elements in the situation which are the outcome of varying fitness on the part of the instructors.

Is it not true that chemistry itself presents some peculiar difficulties? It is often said that "physics is taught better in the secondary schools than chemistry." I am inclined to think that, as a general statement, it is essentially true. But might not the full truth be better stated in this form: "Physics is more effectively taught than chemistry in the secondary schools because physics is an easier science to teach?" It is true that chemical phenomena are plentifully at hand, and that our very life processes are dependent upon them; yet they are not recognized as such and are essentially unfamiliar. The teacher of chemical science, and the practitioner who seeks recognition for his achievements, are alike forced to realize that the tools which he employs, the working conditions which he establishes and the terms in which the results of his labors are to be expressed are unusual and strange and, because of this, more difficult of comprehension by his fellow-men.

The beginner in chemistry is at a similar disadvantage as compared with the beginner in physics. In his work in physics the pupil handles, for example, the balance, the mirror, the pendulum or the battery, and he makes his measurements in units which are largely familiar to him; and the phenomena which he observes are not foreign to his daily life. On the other hand, the very test-tube and beaker to which the student of chemistry is immediately introduced are unaccustomed objects, the bottle of acid is still more so, and we often accentuate the situation by asking him to don breast-plate and armor for his personal protection, in the shape of aprons or rubber sleeves. While, on the other hand, the concepts and laws of physics may not be properly alluded to as "easy," yet it seems to me evident that they make less demands upon the intellect and the imagination than the fundamental principles of chemistry, if these principles are to mean more to the pupil than mere memorized statements.

With the growth of the holes in the pupil's clothing the strangeness of the beaker, test-tube and acid bottle lessens, to be sure, but he is coincidently introduced to increasingly complicated phenomena; he is asked to conceive of molecules, atoms, ions, even of electrons; he is asked to form some notion of valence, to construct chemical equations, and to "state all that they express"—a thing which you and I with our greater wisdom and experience may well hesitate to attempt. He must master the principles of stoichiometry, that branch of chemical science which seems to baffle the human intellect to a degree that never ceases to amaze even experienced teachers. It may even happen that his course includes such concepts as those of chemical equilibrium, the mass law, or the phase rule which, in their relation to the proper subject matter of a secondary-school course, somehow remind one of the records of those early chemical processes found in the first chapter of Genesis in which it is quite incidentally stated that near the close of the fourth day the Lord created "the stars also." It is easier to forgive the ancient recorder for his lack of a due sense of proportion than to excuse the twentieth-century instructor.

Keeping in mind, then, the newness of the chemical processes and chemical concepts, and the fact that the latter necessarily make considerable demands upon immature imaginations, may we not fairly ask whether it is actually reasonable to expect that a young boy or girl of fifteen to seventeen will gain a really clear insight into chemical science in one year; such an insight as will serve as a safe foundation for a chemical superstructure without further strengthening through review? I think I can hear teachers answering warmly in the affirmative. But, again, do they not have in mind the exceptional rather than the average pupil? It seems to me that experience indicates that the most that it is wise to attempt in the case of the large majority of pupils of the ages named is to broaden their horizon by teaching them to interpret common phenomena in the terms of chemistry, and with the aid of only the simplest fundamental principles to help in the understanding of those terms, leaving the meaning of the more abstract conceptions to be learned in a college course, or by later and more mature reading if the pupil is not destined for college, but has an inquiring mind. I believe that the disparity between the immaturity of mind of the pupil and the demands of the subject matter assumed to be taught has been far too much ignored. I think this is the more true in these days when it seems evident that our educational system, through its multiplicity of subjects and the over-prominence of the baneful influence of the examination paper, tends to remove nearly all opportunity for concentrated or independent thought on the part of the pupil, or of originality in methods of instruction on the part of the teacher.

I believe, then, that even the competent teacher, with adequate equipment and the usual time allotment must find great difficulty in teaching chemistry to even the more receptive pupils at the secondary-school age so thoroughly as to permit the college to substitute it for any considerable part of the college course, at least under present conditions. For, let it be said with all humility, we college teachers too often made a sad mess of it even with the advantages as to maturity and environment, which we presumably possess.

The statement is sometimes made by college teachers that they would prefer to receive students without previous chemical experience, and the question may be raised whether or not it would be better to abandon entrance requirements in chemistry. I believe it is the opinion of the majority of college teachers, especially of those who have given the problem the most careful thought, that this would be very unfortunate. I should consider it so far at least two important reasons: first, because, while formal excuse from a definite portion of the college work is not yet generally practicable, the experience already acquired by the student can be made very helpful if judiciously utilized, and second, because it is mainly through increased coöperation between the schools and the colleges in an effort to secure better working conditions for the teacher, and the adoption of a rational course of instruction in the secondary schools, which will take into account all of the pupils, rather than those alone who propose to enter college, that we may hope to attain better results.

It is noticeable in the statements quoted above regarding the present practise in the various institutions, that the state colleges are apparently giving a greater amount of definite credit for work in the secondary school than the others. This is frankly stated by some of the college teachers to be due to the closer organic connection of the state university with the general school system, and is admittedly done under slight pressure. On the other hand, these institutions have, through the system of school inspection on the part of the state universities, a more direct means of influencing instruction in the preparatory schools. The outlook for better conditions in the future is generally regarded as favorable.

Perhaps we may ask just here, What would these better conditions be like? It is probably fair to say that they would be such as to avoid duplication of work. Obviously repetition and duplication should be reduced to a minimum, and no one would welcome changes which tend to bring this about more than I. But I think it is possibly true that there is less actual duplication of work than is commonly supposed in those institutions in which the students who have had a year or more of chemical instruction are segregated in separate divisions. Let us take a concrete case by way of illustration. The pupil in the secondary school prepares chlorine, using salt, sulphuric acid and manganese dioxide, or hydrochloric acid and manganese dioxide. The time available rarely permits the use of any other method, and the chemical changes involved are sufficiently complex to present some little difficulty for their complete comprehension. Few pupils, as experience shows, really understand that this is a typical, and not an isolated or unique procedure, and the rôle played by the manganese dioxide is but vaguely grasped. It *is* true that such students are asked to again prepare chlorine from these materials in the college laboratory, but they are at the same time required to study the action upon hydrochloric acid of such agents as lead dioxide, barium dioxide, hydrogen dioxide, potassium permanganate or potassium dichromate, and to discuss the changes involved from the common point of view of the oxidation of the acid, and the proportion of actual duplication of work is really small. Similarly, in the study of the action of acids upon metals, while it is desirable to ask the student for the sake of completeness to repeat the familiar process for the preparation of hydrogen from zinc and sulphuric acid, this becomes a mere incident in the series of experiments and in the broader discussion of all phenomena observed which may well go so far as to include the principles of solution tension, in the case of such students.

It is, apparently, work of this general character which many college teachers are offering to those who have had earlier chemical training. The laboratory work is, as we have seen, frequently accompanied by lecture demonstration and recitations of a corresponding grade, and while it does not, of course, appeal to the student as a step in advance, as would some other procedure which seemed to give a stamp of finality to his earlier studies, it may well be questioned whether it does not better foster his intellectual welfare than the more alluring plan could do. It should, however, be the purpose of the college teacher to keep closely in touch with the actual and probably increasing average attainments of the pupils sent to him, in order that he may take all proper advantage of the instruction already given, and it is probably true that a larger number of institutions should offer such moderately advanced courses than is at present the case.

I propose next to refer briefly to one or two specific points at which it appears to me that the instruction in the secondary schools might be improved. I do this with much hesitation, for I realize that those very details or methods which perhaps fail to appeal to me may well be very dear to another, and I realize that I should be loath indeed to have the actual efficiency of my own instruction judged by certain alleged quotations on the part of some of my students, or even by the subsequent acts of many of them. A conspicuous instance of the failure of some of our hopes was afforded by a statement made by one of our students in a recent written test that "nitroglycerine is used as a lubricant."

A question which many find difficult to answer is this: How far, taking into account existing and not idealized conditions, is it just to regard note-books as an index of the efficiency of the instruction as given in a particular school, or college? I shall not be rash enough to undertake to answer this beyond expressing a conviction that while a note-book which is well kept and carefully corrected probably indicates careful, efficient teaching, a relatively poor note-book may represent more accurately an overburdened condition of the teacher, which prevents adequate inspection and correction, than actual inefficiency in instruction. For it is often true that much of apparent error in the records may have been actually corrected in conference or class-room. This does not, however, apply to some of the atrociously bad specimens which are occasionally met with, nor, on the other hand, does it ignore those note-books which are obviously not records of work done, but studiedly prepared exhibits, executed through connivance of teacher and pupil at the expense of a fundamental principle of all scientific work, rigid honesty.

Is it not true that too many teachers are contented to have their students perform more or less perfunctorily the magic "forty experiments" which are said by some one else to represent a suitable course, rather than to vitalize their instruction by devising ten, twenty-five, fifty-five or any other number of experiments of their own to illustrate the facts or principles which they themselves desire to fix in the pupils' minds, and to see that these are actually discerned. The busy, often overburdened teacher, will not always find time or energy to devise an entire course of instruction, but the introduction of even a limited amount of well-considered experiments or class-room instruction which represents the personal equation of the individual teacher does much to maintain enthusiasm for the teaching which is often reflected in the work of the pupils as well.

The deadening tendency of a mere following of a course of experiments laid down by others shows itself also in a disposition to regard each experiment as a thing apart, the nominal completion of which is a cause mainly for relief, is also reflected in many instances in the notes submitted, which are long and minutely descriptive of really insignificant details, but miss the real point of the experiment. This, in turn, comes from the fact that the pupil is not sufficiently informed why he is asked to perform the experiment at all, and in the strangeness of the work he naturally confuses the important and the unimportant. For example, he is often apparently left to think that a description of "the apparatus used" is as essential when he pours silver nitrate solution from a bottle into a test-tube containing a halide solution, as when he is preparing nitric acid from saltpeter, and he elaborates his descriptions with the same fidelity in the former case as in the latter, with a very considerable aggregate loss of good energy on his part and that of his instructor. But that is not the worst of it, for he gains an idea that all experiments are to be treated with similar uniformity in other respects, even including his search for their hidden meanings. I do not, of course, advocate telling the student what is to happen and then asking him to say that it did occur, adding, possibly, the color of a precipitate; but I do believe that a great deal would be gained if nearly all experiments, or groups of experiments, were more carefully prefaced in the laboratory directions by a brief statement regarding the principles or the types of changes involved, and if, then, the student were encouraged to make his observations with reference to these statements and were required to show that he under-stands how the given experiment actually confirms the points in question. This would do much to avoid what is at present a wasteful expenditure of time, muscular energy and eyesight—all of which could be used to increase the pupil's experience, and it would partially, at least, eliminate the vague groping which results as those appalling scientific monstrosities which follow the words "I conclude" in the note-book of many a conscientious student. Have you ever recalled the bewilderment of your student days, when you had no idea what to look at among so many phenomena? Have you ever taken a half dozen experiments and candidly asked yourself what *you can legitimately conclude* from what has been performed? It is very much like trying to answer some of one's own well-sounding examination questions: a procedure which often causes them to lose their attractiveness.

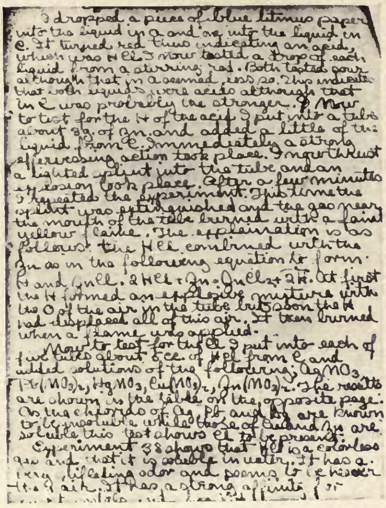
Do we not then, tend to lay too much stress upon mere performance of experiments, and devote too much time to the making and reading of descriptive notes which are often copies of the experiment manual, and too little time to helping the pupil, through judicious suggestions regarding the experiments and through questioning at the work-table and in the recitation room, to comprehend what it is all about, and the relation of a given experiment to others already performed?

In order that the perplexities of the college instructor may be brought more clearly to mind, and in order to illustrate certain types of note-books, I reproduce here a few pages from the books presented in connection with the entrance elective requirement of the Massachusetts Institute of Technology. The first (Fig. 1) is a representative of a rather small number of superior books. The observations are carefully recorded, the deductions are valid and well expressed and there is evidence (not shown in the cut) that the note-book had been inspected and corrected. Under existing conditions as to numbers of pupils to be taught it is probably too much to expect that all will attain a standard which this note-book appears to represent. To all appearances the records are original and the instruction efficient.

The pages reproduced in Figs. 2 and 3 are of a not uncommon type. The first leaves one in doubt as to what part of the work has been performed by the pupil, since the statements made regarding the physical properties could have been copied from a book, the records of experiments performed are distinctly wrong and, in the case of the alleged preparation of chlorine, would, if ever followed, lead more directly to a residence at a hospital than to any worthy scientific end. Fig. 3 shows a page which makes no pretense of being anything more than a mere record of a useless mixing of a few solutions, and moreover these records are also entirely wrong.

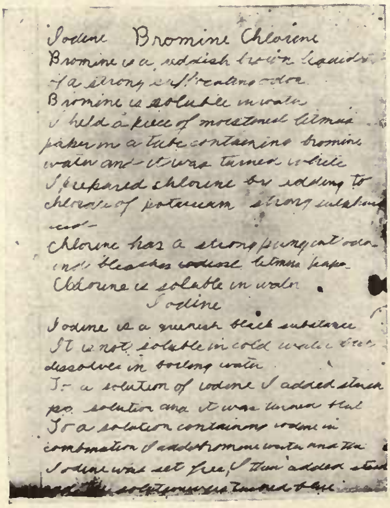
The two pages just commented upon did not bear any evidence of inspection on the part of the teacher; that shown in Fig. 4 bore the stamped legend "approved," but a careful inspection leaves one in doubt as to what particular feature of the record warranted this, unless it may be the evidence of sympathy (?) on the part of the pupil with the tendency towards spelling reform.

These are not exceptional pages; they are representatives of many that pass under our inspection each year, and I ask you, with all sympathy for the teachers concerned, what evidence does any but the first give that one may safely omit a review of the ground supposed to be



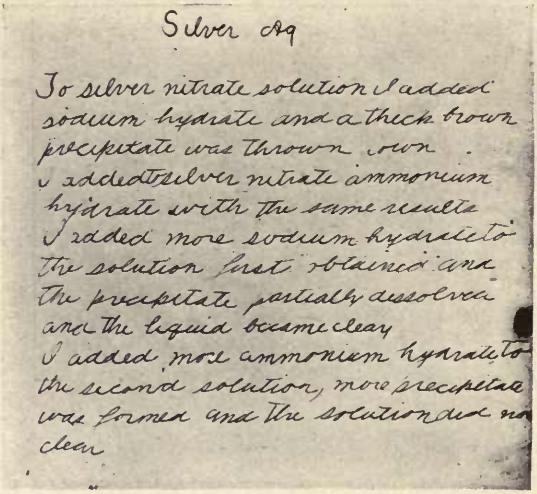
I dropped a piece of blue litmus paper
into the liquid in a and one into the liquid in
C. It turned red thus indicating an acid,
which was HCl. I now tasted a drop of each
liquid from a stirring rod. Both tasted sour
although that in a seemed less so. This indicates
that both liquids were acids although that
in C was probably the stronger. ¶ Now
to test for the H of the acid I put into a tube
about 3g. of Zn. and added a little of the
liquid from C. Immediately a strong
effervescing action took place. I now thrust
a lighted splint into the tube and an
explosion took place. After a few minutes
I repeated the experiment. This time the
splint was extinguished and the gas near
the mouth of the tube burned with a faint
yellow flame. The explaination is as
follows: the HCl combined with the
Zn as in the following equation to form
H and ZnCl. $2HCl + Zn = ZnCl_2 + 2H$. At first
the H formed an explosive mixture with
the O of the air in the tube but soon the H
had displaced all of this air. It then burned
when a flame was applied.
Now to test for the Cl I put into each of
five tubes about 5 cc. of HCl from C and
added solutions of the following: $AgNO_3$
$Pb(NO_3)_2$, $HgNO_3$, $Cu(NO_3)_2$, $Zn(NO_3)_2$. The results
are shown in the table on the opposite page.
As the chlorides of Ag, Pb and Hg are known
to be insoluble while those of Cu and Zn are
soluble this test shows Cl to be present.
Experiment 38 shows that HCl is a colorless
gas and that it is soluble in water. It has a
very stifling odor and seems to be heavier
than air. It has a strong affinity for
[illegible]

Fig. 1.



Iodine Bromine Chlorine
Bromine is a reddish brown liquid
of a strong suffocating odor.
Bromine is soluble in water
I held a piece of moistened litmus
paper in a tube containing bromine
water and it was turned white
I prepared chlorine by adding to
chlorate of potassium strong sulphuric
acid
Chlorine has a strong pungent odor
and bleaches moist litmus paper
Chlorine is soluble in water
Iodine
Iodine is a greenish black substance
It is not soluble in cold water but
dissolves in boiling water
To a solution of iodine I added starch
paste solution and it was turned blue
To a solution containing iodine in
combination I added bromine water and the
Iodine was set free, I then added starch
and the solution was turned blue

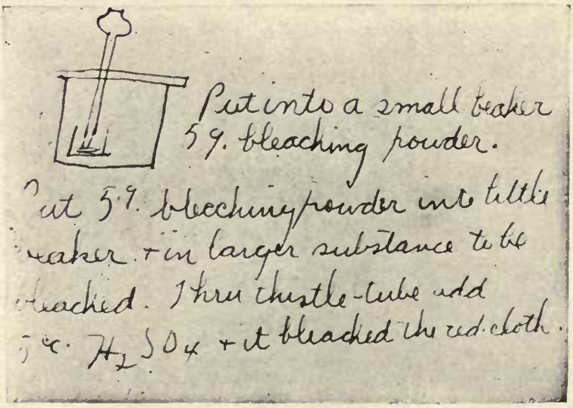
Fig. 2.



Silver Ag

To silver nitrate solution I added
sodium hydrate and a thick brown
precipitate was thrown down.
I added to silver nitrate ammonium
hydrate with the same results
I added more sodium hydrate to
the solution first obtained and
the precipitate partially dissolved
and the liquid became clear
I added more ammonium hydrate to
the second solution, more precipitate
was formed and the solution did no
clear

Fig. 3.



Put into a small beaker
5 g. bleaching powder.
Put 5 g. bleaching powder into little
beaker + in larger substance to be
bleached. Thru thistle-tube add
5 cc. H_2SO_4 + it bleached the red cloth.

Fig. 4.

covered by this work in a college course which is primarily expected to furnish a safe foundation on which there is afterwards to be erected a very considerable superstructure of chemical knowledge? Are we not justified in our perplexities?

I should like also to appeal to the teachers in the preparatory schools to encourage the pupils to better economize their laboratory time. Too many are allowed to placidly watch a crucible heat, or a solution boil, when other experiments might be in progress at the same time, and these habits are difficult to overcome. I should like to suggest, too, that some of the most promising pupils are often seriously harmed by allowing them to work too much by themselves, or by encouraging them to go beyond their depth in a particular line in which they appear to be specially interested, to the detriment of their fundamental work. Some pupils usually come to college with an exaggerated sense of their own attainments and it frequently requires long and tactful persuasion on the part of the college instructor before they can be reduced to reasonable humility.

On the other hand, I venture to plead that all proper encouragement be given to pupils to take advantage of such special privileges as the colleges offer. It is not an infrequent occurrence to find a pupil who tells us that he has been advised by his teacher to take the elementary course for beginners as one in which he will incur less risk of failure. Were the examination the goal of the course, there obviously would be little to criticize in this suggestion; its effect upon the student as an embryo scientist is seldom happy.

In conclusion let us ask, how can we make the work in chemistry in the various institutions more mutually helpful?

1. By a more extensive coöperation on the part of the colleges and technical schools in the way of separate courses for those who have taken chemistry before entrance, a closer study of the problem on the part of all, and a readiness to recognize improved conditions.

2. By an intelligent delimitation of the secondary-school course, so that it will only offer what the pupil can best assimilate at the age and in the environment in which he works. This is too large a topic for discussion in this connection, and it is sadly complicated by the necessity for furnishing a course which shall be alike useful for the pupil who expects to enjoy college opportunities and his less fortunate associate. I plead, as I have often done, for a course which is fundamentally descriptive in its character. I do not mean a mere catalogue of facts, but a course in which selected facts are taught for some specific reason, which is invariably explained to the pupil, and in which these facts are interpreted for him in terms of the simplest of the fundamental principles and concepts, so often repeated and constantly utilized that they may ultimately mean more than memorized paragraphs from what he may later remember only as "a book with a green cover." I think there can be no greater mistake than to suppose that such a course is a less worthy one than such as is often pointed to with pride as a "theoretical course," and no teacher should consider that it will demand less than his best efforts, supplemented by all his knowledge, to utilize the opportunities for helpful and thorough instruction which such a course affords. It is, of course, difficult to determine whether or by how much the instruction of the boy or girl destined for college should be differentiated from that of their fellow-students, but I venture to hope that a decision may yet be reached, through coöpera-

tion, which may permit us to select a limited field which shall be so well covered as not to necessitate repetition in college, and that this may be done without prejudice to the candidate or non-candidate for college credits. How soon this will come, or how large this field may be, I do not venture to predict.

3. By increasing the time allotted to chemistry in the secondary schools until it is more nearly commensurate with the dignity and difficulty of the subject. Whether such increase should amount to one third, or some larger fraction of the present time allotment is a point which those actively concerned in the teaching can best determine. The increase in time should be asked for mainly in the interests of those who will not pursue the study of chemistry further, but it will also presumably hasten the time when a definite point of articulation with the college work, as just suggested, can be fixed.

Finally, there is the urgent need of decreasing the demands made upon the teacher of chemistry in the secondary school for duties other than those of chemical instruction, and also a critical need for relatively more instructors. I believe that a very large proportion of the unsatisfactory results now noticeable are due to the fact that in most of our schools it is not humanly possible for the teaching force to accomplish what should be expected of them, or to be at the desk of the pupil when he reasonably needs assistance. In some schools which have come under my observation the distribution of supplies must be attended to by the senior (or often the only) instructor, an operation which consumes a half hour or more.

Probably no science demands for its understanding by the beginner more individual instruction in laboratory and class-room than chemistry, and the school authorities should realize this. When they do we shall have much cause for rejoicing, and much of the present groping and bewilderment on the part of the young student will give place to enjoyment in the study of a science which is really second to none in its attractiveness or value when pursued under favorable conditions.

It is a pleasure, in closing, to say that I feel that too much praise can hardly be given to the loyal, hard-working, intelligent and inspiring teachers who are accomplishing so much in behalf of our science in the training of the beginners. No thoughtful college teacher can fail to recognize the good work done in very many schools throughout the country, and while many feel that more definite recognition in the college curriculum can not wisely be given to this work at the present time, I am sure from the messages which have recently come to me from many colleagues in many institutions that there is an increasing appreciation of the fact that the way to better things lies through a sympathetic appreciation and study of our common problem and our common difficulties.[1]

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[1] In a discussion which followed the presentation of this and other papers on educational topics, a statement was made by a secondary school teacher of recognized standing to the effect that many such teachers had become indifferent to the opinions of college instructors, since it is "impossible to satisfy them any way." While I heartily sympathize with the thoughtful teacher who desires to teach his subject in his own way and with his own ideals in view, and deplore any attitude of the colleges, collectively or individually, which tends to interfere with this, it seems to me that the common cause of greater total efficiency in instruction can hardly be served by ignoring

If there can be a determination, on the one hand, to undertake only so much as can be well taught and to give the largest practicable vitality to the instruction, and, on the other hand, a disposition to promptly recognize and utilize every bit of ground gained which offers a secure foundation for later work, a more satisfactory situation than that which exists at present can hardly fail to result, even though the degree of recognition of secondary school instruction may fall short of that which some desire. H. P. TALBOT.

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HIGH SCHOOL CHEMISTRY: THE CONTENT OF THE COURSE.[1]

Every teacher in the high school of to-day finds himself in stimulating circumstances. He is obliged to question himself closely as to the part that his subject plays in the curriculum, for, at least in the large cities, the long-discussed change in the character of the high school is upon us. The reason for the change is found in a realization of the facts that in the past, high school education has been enormously wasteful; that eighty to ninety per cent. of our pupils do not complete the course; that only a small part of the remaining per cent. achieve the purpose for which the whole course has been framed, that of entering college. The evidence that the change has actually begun is found in the establishment of trade and vocational schools, in the frequent discussion of questions pertinent to these points, and in the statements of principals and superintendents that something must be done to stop the enormous educational waste; and in their declaration that the high school must meet real needs, must give the boy or girl the education that is best for him or her, as a member of the human group, with little reference to college entrance.

Among the changes that are coming from a recognition of these facts, we find the importance of science in the high school largely increased. The fact that it is science that has produced the great material advance of the past century makes it certain that in the further turning from formal to practical education, science will play a larger part. It is the purpose of this paper to inquire into the manner in which these changing conditions are reacting on the high school course in chemistry, and to discuss some of the considerations that are determining, or should determine, a new course of study. The speaker wishes also to discuss, in general, the problem of high school chemistry, presenting personal and perhaps even extreme points of view.

We may classify the various forces that are shaping the new course as external and internal. In the first class we find: (*a*) a lessening of the college influence, due to a realization of the necessity of educating for other purposes than college entrance; (*b*) a tendency to put chemistry

the opinions of the colleges, even if they are mistaken. May it not be true that the secondary school teachers lack some courage, or at least some persistence, in forcing their convictions upon the college teacher? They have the privilege of speaking from a fullness of experience with the young pupil which the college instructor usually lacks.

[1] Presented at the second decennial celebration of Clark University, Worcester, Mass., September 16, 1909.

earlier in the course and to give a second year of it; (*c*) what we may call the lay demand for practical education.

The lessened college influence will give to the body of secondary teachers not only greater freedom in the selection and arrangement of their material, but what is of even more importance, because it serves as a stimulus to their creative ability, a realization of the importance of their own great work and their responsibility for it. The lack of this kind of freedom is in part responsible for the condition that exists to-day when the high school, paying comparatively high salaries, can not get enough good men, while the college apparently has more than it needs at a smaller compensation. This is not the least of the evils that have resulted from the college domination of the high school. Others have often been pointed out and are well known. The course of study can never be adapted to the real needs of the high school so long as it is framed by the college, at the best a force operating at a distance, at the worst a power acting for needs it cannot know. The college, as far as the high school was concerned, always had the idea of preparation, not growth, in mind. A thousand boys went through a course in chemistry whose nature was determined solely by the needs of the three or four who were to be trained to be expert chemists. It is often said at this point that the course which best prepares the pupil for advanced work is also best for every other boy. It is nearer the truth to say that the education which best meets the needs of the growing member of the human whole ought to be the best preparation for college.

Chemistry earlier in the course and perhaps a second year of it; the first of these conditions may bring dismay to many teachers; the second, delight to all, surely. Certainly some changes in the traditional course are necessary in teaching chemistry in the second year. On this point the speaker can refer to an experience covering nearly seven years. During all that time chemistry has been taught to some second-year students. At times fourth-year students and second-year students have been taking nearly the same course simultaneously in separate classes; at other times the two terms of students have been mixed in the same class. In both cases a certain degree of success with the second-year students has been obtained, even if we judge by no other standards than results of college entrance and state board examinations. Speaking for the moment from the standpoint of the college entrance syllabus, but little change is necessary to adapt the chemistry to second-year students. A less rigorous insistence on the philosophical development of the atomic and other hypothesis seems to be the most necessary item of change. In any case, as far as the ability of the student to comprehend is concerned, the difference between individuals is much greater than the difference between second- and fourth-year classes. The general average of work is considerably better in fourth-year classes, but this is explained largely by the dropping out of weak material.

To meet the demand for practical education, we find that there is a decided tendency to introduce into the high school a great deal more of chemical technology than there was in the older course. There are some who go so far as to say that the high school ought to give the pupil a means of earning his living; that chemistry should be taught so as to fit him for some direct employment in practical occupations. While admitting this as a possible ideal, the view implies such an extreme change in the character of the high school that it is not advisable to take it into consideration in the present discussion, except to admit that, given time, it would be possible to accomplish this result. Along with the demand for technical education, we find a tendency to fill the course with a great deal of matter that is associated with the home and every-day life. These two demands have come largely from without. They have done great good and have added much to the human interest of our science. We teachers are very prone to an academic point of view, and the stimulus has been a needed one. Yet with the good, there is some danger. There is a tendency in some quarters to emphasize the technological details of processes, to fill the discussion with technical terms, so that the pupils' talk bristles with tuyères and downcomers and the particular names of the many towers that find application in manufacturing chemistry. The chief evil of this kind of instruction is that it produces rather showy results, it seems to indicate more knowledge than really exists. Moreover, a technical process of to-day is a very complicated thing. It is improved every year and we find to our discomfiture, on visiting the factory, that the process we have so carefully learned from the textbook differs in a hundred details from that actually employed.

The chemical interpretation of the ordinary phenomena of the household is a very interesting matter. Unfortunately many of these interpretations are very complex, others are unknown. Some are simple enough to be comprehended by a beginner, and certain food tests and the like can be taught so that the pupil can go through them in a more or less mechanical fashion. But surely these do not constitute a suitable vehicle for the transmission of that highly organized mass of knowledge and way of thinking which we know as chemistry. The intellectual and material advance that our science has brought to the world has not come from the knowledge of isolated test-tube reactions, but from the brilliant imaginings of the authors of its great hypotheses, from the realizations of its tremendous generalizations, from the perceptions of most deeply hidden relationships among the things that we call matter. If this that we teach our pupils is to bear the name of chemistry, it must give them at least a glimpse of these deeper things. Technological chemistry and household chemistry have a very proper place in the high school course, but they should never be over-emphasized. They afford the illustrative material which the good teacher will constantly use to give interest to his work by showing what good the science has brought to mankind. But a course composed almost wholly of such material, as has been proposed, would not be chemistry, and it would probably not be science. There would be an absence of principles of relationships. A pupil might indeed learn that there exists a simple process for the manufacture of soda, but he would not share in any degree the kind of thinking that has made this and a thousand other processes possible. I hold that it is our chief duty to give him this kind of knowledge.

Coming then to the internal considerations which shall help shape our new course of study, we must inquire what high school chemistry should seek to accomplish for the pupil. One way of answering this question is by asking ourselves what it has done for us as individuals. We know that it has made us broader men and freer human beings, and it is fitting that we should seek to have our pupils attain in some degree this high end. Again, it is certain that one who has been through a good course in chemistry, who has learned the principles of chemical action, and comprehended the great laws that the science has revealed, looks upon the world about him in an altogether new way, so much so that with the increase in the general knowledge of science there is being produced a new type of world mind. Our pupils must be taught so that they shall share in this new world mind.

THE LABORATORY ASPECT OF THE COURSE.

The course will continue to be based on experiment, the amount of laboratory work being limited only by the physical possibilities of the situation. The experiment will precede the class discussion in order that the pupil may conceive the things that he is talking about as realities. Chemical thinking cannot go far without these definite conceptions. It requires images of real things, and it is this point of view that should determine the character of our laboratory work. There seems to be considerable difference of opinion, if not confusion, on this point.

There is the point of view which assumes that it is the purpose of the experiment to prove the statement of the teacher or the text. Because there was so much that was bad in reliance upon authority in older types of education, it is felt that science must have none of this, but must accompany everything by rigorous proof. Following this method at its worst, the pupil is stimulated into a condition of perpetual doubt. He meets every statement with a but, and has rather the air of believing that some scientific charlatanry is being imposed on him. This is wrong; science does not have this attitude of perpetual doubt. It requires the most rigorous proof from discoverers of new things, but if each of us had demanded ocular demonstration at each step in our advancing knowledge, we should probably still be somewhere in the realm of descriptive inorganic chemistry. Moreover, it is a serious scientific mistake to let the pupil think that a single experiment performed under the ordinary condition of the beginner's laboratory proves much of anything. If it does, the speaker has seen many curious things proved in his time. Let us be frank: these experiments show at best the line of thought by which the proof is obtained. They illustrate the proof—they do not give it.

Nor does the theory that the pupil should, in the laboratory, rediscover the fundamental truths of the science, give us a right basis for experimental work. Followed to the extreme, this method soon reduces itself to an absurdity. Take, for example, the experiments of Lavoisier, which afford such an excellent starting point in the teaching of the subject. The pupil is given some metals and a balance, and is supposed, in an hour and a half, to rediscover what it took the best minds the world then possessed several centuries to accomplish. The fact the pupil's laboratory record, duly attested by the teacher, indicates that he independently accomplished this prodigious feat is a comment on the system. All that is done in this method at its best, is the arousing of the pupil's curiosity, which is later gratified by judicious suggestions at the proper moment from the teacher. There is no rediscovery; the line of thought has simply been retraced, and the big steps have ever been taken by the teacher. To be a discoverer you must be the author of your own curiosity. Another trouble with this method is that once committed to it the teacher is driven to curious round-about expedients to prevent the pupil's having knowledge in advance of the thing he is going to see. There are hundreds of instances where the pupil should have this knowedge in advance.

The speaker is more and more convinced that while the laboratory should to a certain extent seek to accomplish the things which the holders of two points of view consider desirable, its real purpose is to afford illustrative material, and by illustrative material he means that which will give concrete ideas—images—of things and processes. One might read hundreds of pages about chlorine, but if he had never seen it he would never know it. This is the great work of the laboratory method, to teach things and not literal symbols for them. We should seek this end, and let other considerations give way to it.

And we shall not neglect to exercise the pupil's scientific imagination. Chemical thinking requires this faculty. After he has been well grounded in the method of the laboratory, we shall want the pupil to learn to foresee chemical possibilities. The progress of the science has been by the working together of experiment and imagination, the one reacting upon the other and each suggesting in turn new steps in the advancing knowledge.

THE CLASS-ROOM ASPECT OF THE COURSE.

It is no longer being framed exclusively for the college entrance requirement; our course will not require us to cover so much material as it did formerly. Discussion of the rare elements and their compounds will give way to a more intensive study of those that show typical chemical actions, and establish the main lines of thought. We shall prefer to do this by reference to the things of the practical life where we can, but we will not go into the chemistry of foods, dyes, textiles and the like, knowing that this matter is far too complex for us to use in establishing the laws and relationships that are necessary for a comprehension of the science. We shall draw from every aspect of chemistry in our effort to establish the principles of chemical action. Our teaching may grow less descriptive and more dynamic. We may find it better to study types of chemical action than to study elements and compounds. As suggestion along this line, we might proceed, after reaching the definitions of chemical action, element and compound, to the general study of simple decompositions, using many experimental illustrations. We would bring in the ideas of stability and heat of formation. We would then proceed to direct combinations, simple replacements, and so on, until finally the pupil would have a very good idea of the comparatively few types of chemical action. He would acquire incidentally a very practical descriptive knowledge.

Our course will necessarily continue to pay a large amount of attention to chemical theories, in order that we may have the means of seeing analogies and interpreting results. The mechanism of chemical changes is so far removed from direct observation by the senses that any attempt to comprehend these must be largely by aid of the imagination. The atomic theory has given us a splendid instrument for this purpose. We should retain it even if it had done nothing more than give us a system of chemical formulas, or made it possible to represent chemical actions by equations. Only one who has attempted to teach chemistry without the use of these symbols can fully appreciate what a tremendous aid they are. We shall therefore want to establish the atomic theory rationally, and to show how formulas are determined. This is perhaps the most difficult part of our work, but the fact that many pupils fail utterly to comprehend this matter is no ground for its omission from the course. There are many who succeed, and we must not forget that those who fail at least learn that such knowledge was acquired by human reasoning and patient experimenting. We should make our pupils feel that these theories are very practical things indeed, since it is largely by their aid that the science has advanced and brought material benefits to mankind.

We have in the past been given to considerable drill in certain types of chemical problems, largely because of the demands of college entrance examinations. There has been a good deal of mental gymnastics in the matter. These calculations should be taught in a less formal way; the laboratory is the best place to do it. Let the pupil calculate from the equations the quantities of substances he needs for his reaction, and then actually mix them in these proportions. Let him get practise in correcting gas volumes in the course of experiments involving simple gas measurements. Knowledge acquired in this way has a far greater staying quality than that obtained in formal class-room drill.

As we have already said, chemical technology will find a place in the course, but it must be taught by principle too. In the Solvay process, for example, it is more important that the pupil should get the idea of precipitation by differences in solubility than that he should know the mechanical details of the carbonating towers. It is more important he should know that the process is only commercially profitable because the ammonia is recovered, thus getting hold of the principle of the utilization of by-products, than that he should know the factory terms for the machinery and operations. A good course in manufacturing equipment, in which different types of furnaces, towers and the like were grouped and compared, might be of great practical and educational importance. But isolated bits of such information have no such value.

Our high school chemistry might well include a treatment of more organic compounds than it has in the past. This knowledge can readily be acquired by reference to inorganic types. So many of the simpler derivatives of the hydrocarbons are things of every-day life that in order to include them we can afford to sacrifice some of the things of the traditional elementary course. The pupil needs, moreover, some intimation of the character and extent of the organic branch of the science.

In conclusion, the speaker feels that the best hope for the improvement of high school chemistry lies in discussions of the kind we are engaged in this morning. The experimental end of our work has been so new and interesting that much of our time has been spent on these matters. But the time is at hand when a reconsideration of the course as a whole in its general relations would be of benefit to the teaching of the elementary science.

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CHEMISTRY IN SECONDARY SCHOOLS.[1]

It is not necessary in a gathering such as this to recount the stages in the history of chemistry teaching in secondary schools—how, from the

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[1] Presented at the second decennial celebration of Clark University, Worcester, Mass., September 16, 1909.

purely descriptive natural philosophy of the early college we finally assayed the teaching of chemistry and physics as sciences; how the miscellaneous encyclopedic instruction has been replaced by courses, designed, in these latter days, to develop power for the pupil rather than to impart knowledge.

The changes in content and method of formal secondary-school instruction have been brought about by the colleges; by advice, by supplying the teachers and most drastically, by the requirements for admission. While the bulk of the class might pass from the school and not be heard from again, the failure of a pupil to pass the college examination is quickly brought home to the teacher, so that the entrance examinations have become the standard of the school.

During the last fifteen years four syllabuses have been published which have decidedly affected the teaching of chemistry in schools; in 1894 that of the Committee of Ten, descriptive and general; in 1898 a Harvard syllabus, largely quantitative and scientific in method; in 1900, the syllabus of the College Entrance Examination Board, a plan for a course I hesitate to classify; in 1905, the last revision of the syllabus of the New York Department of Education, a historico-systematic course.

There is almost nothing in common to these four courses, and although the College Entrance Examination Board maintains and strengthens its hold upon the schools it has never, fortunately for the pupils, conducted its chemistry examination in accordance with its syllabus.

If we examine the texts to find what is being taught in high schools we find the chemistry text-books to be descriptive or theoretical; very few have successfully combined the two. The descriptive texts usually become encyclopedic, try to include all the elements, strange compounds, the latest processes and weird discoveries, often curtailing or entirely displacing those common things we are too liable to take for granted that every one knows. The theoretic texts are largely the product of college men. These tend to become too abstract and sacrifice the pupil to the subject. One elementary text of very wide use devotes two pages to a discussion of the action of bleaching powder, but does not state how it is used or for what goods.

If a subject is to be treated as a science many facts must be given and understood in order that the pupil may acquire a comprehensive idea of the subject. It is folly to expect thorough understanding of a part without a general knowledge of the whole. The high schools cannot train chemists or engineers. Time and cost do not admit of such intensive science teaching, even if it is desirable. Such teaching should be left to the college.

If we take the pupils as we find them in our large city high schools they are not well informed and have little opportunity to be. They live in a complex environment. The city boy or girl is brought in contact with but few simple phenomena; a push of a button—a bell is rung; another push—a door is unlocked; another push—a light appears. The modern apartment is a complicated structure operated by buttons. If we look for chemical actions within this pupil's sphere we find them to be rather few, too familiar to hold the attention or too complicated to tempt analysis. He comes in contact with but few elements and but few pure compounds. Steel is to him a specially pure iron, zinc is the metal used in batteries, tin—used for cans, sulphur smells bad. He has often been told that soda water contains no soda. Soap is useful in cleaning, as it eats dirt as an acid "eats metal." A material involving electric means is necessarily superior.

The tendency to centralization in driving our small industrial establishments has narrowed the child's opportunities for observation. The shops of the blacksmith, carpenter and soap-maker where he learned the art of critical observation and learned some things not taught in school have been withdrawn behind doors marked "no admission."

The classes of our large schools are mixed as to sex, race and ability. It is often said with pride that our urban population is cosmopolitan, but that the second generation from the emigrant is acquainted with American ways. Admitting that the second generation may be somewhat acquainted with American ways, we must also admit that the population of our large cities is becoming mongrel. The mongrel is never stable and is rarely successful. The psychology of the mongrel is analogous to that of the mob. Is it not then asking too much that children of one or two generations from barbarity should be put through the same course and be expected to meet the same educational standards as the natives of Massachusetts?

The tendency of education at present is the development of *power*, of ability to reason, to think. We may, indeed, ask if the drill along this line has not been pushed so far at times as to neglect giving something to think about. The school, unlike the college, works by the clock, the work must be cut to fit the time, thus we often find a few facts or questions are presented in such a way that but one conclusion is possible. This is called inductive teaching—teaching to reason.

It makes the work easier for the teacher if the work can be made to follow a mathematical model, so problems come to take an important place. The work becomes quantitative and is now held to develop thought, originality and logical reasoning. But the problem in elementary chemistry is usually of type form, and is not the teacher largely sponging on the power drilled into the pupil by the mathematics teacher? The English of the schools is criticized by college and business men alike. I believe a clear, concise exposition of phenomena in correct language will be of more benefit to the pupil than any number of problems in chemical arithmetic.

The pupils I have in mind are the ordinary ones in large schools, thirteen to sixteen years of age, girls and boys. Only a small percentage will go to college, some will go to business, some to be clerks, some home makers, some teachers. They have been herded in elementary schools taught *at* in bulk. They are deficient in English and any correct notions of the activities of the world. It is the business of the high school to supplement the elementary school and by its specialization correct the errors of the grades and systematize the instruction. College preparation is only incidental.

A large amount of knowledge is not needed in practical life so much as the power to do things, but knowledge certainly increases power. While we must be able to do one thing well even a superficial knowledge of many things is not to be despised. Good judgment, ability to arrive at accurate conclusions from given data is most essential, but if we look closely a large part of what is commonly called reasoning is but rehearsing of formulae. Good judgment cannot be taught. So few of our pupils will ever be so situated that they need reason independently concerning chemical phenomena that it is scarcely justifiable to foist the time and cost of such instruction on the public.

Where and how can chemistry accomplish the most good in the school? If the object of education is to develop a youth most completely, to make a well-rounded individual, to make him feel an intelligent interest in the activities of the world, it is not necessary that each factor in such a total should be well rounded. A number of smooth, well-rounded sticks will make a very insecure bundle, but if some of the tricks are somewhat rough the bundle may not appear so elegant but it will be more firm. Chemistry touches every phase of human activity. It requires language for its expression, mathematics for its determination, physics for its operation. Its history is the history of the world.

It would be impossible to find a better subject than chemistry to bind together the school work, to systematically furnish splinters to make the bundle strong. The domestic science teacher, the biology teacher and the physics teacher give some splinters of information which they call chemistry and build their work upon this basis, usually indigestible definitions. A systematic course in elementary science should be placed in the first year of the high school, designed to impart that information of things and processes we might well expect every one to know. This might be followed later by a course more thorough.

We now expect our pupils to specialize as soon as they leave the elementary schools and to prepare for some life work. He or she knows nothing of human activities out in the every-day world; there is practically no place in the school curriculum where this is taught. We have trade schools, vocation schools, commercial schools, not to mention others all of which require him to specialize before showing him any general plan from which to choose or guiding his choice.

The pupil who will receive no further school instruction can in a year be given a good knowledge, by a teacher with adequate equipment, of many of the facts of elementary chemistry relating to our daily life and its activities—a knowledge sufficient in most cases to excite a lasting interest in natural phenomena and to cause the student to seek explanation. There is a multitude of chemical facts which concern the boy who goes into the shop or office or behind the counter, and which he should know. The girl who will stop at home or teaches others' children is also concerned with chemical phenomena, chemical information which has been crowded out of her curriculum to make room for more cultured and less mussy subjects.

Adhering to traditional procedure, our science courses have become pseudotheoretical or pseudotechnical; it is time we had one systematically informational and practical. Facts are as important as explanations and should precede them. Such a course need not pretend completeness in any line. It might be comparative rather than critical. It would not attempt to rediscover or verify natural laws, but would aim to cultivate the powers of observation and of accuracy of description, to express ideas of phenomena in simple, direct English rather than to hide incoherent thought behind a big name or a slang expression.

In a first course in chemistry, atoms, molecules, ions and many other terms might be omitted altogether. They are but words, the modern idea of an atom is incomprehensible to one without a wide knowledge of chemistry. Theory should be eliminated as much as possible, making the course treat of facts, their sequence and relation to one another. Numerical problem solving should take but a small part in recitation work. No more can come out of an equation than we put into it. It cannot develop originality.

Such a course for children of twelve to thirteen years would need simplicity in its treatment. Faraday's lectures to children are a model in this respect. Ostwald's "Conversations" show how some complicated things may be dealt with simply.

I would have such a course give information concerning natural phenomena and the work of man, show what is being done, and how, without technical detail.

I would give the pupil something to *know*. Facts that are worth knowing in and of themselves—facts that concern himself, his food, his clothing, his shelter and his work. Concerning the things he or she will meet in life, no matter whether the future be as a chemist, a bookkeeper or in the kitchen. The material is ample.

The subject might be systematized by its applications rather than the traditional order. Study topics rather than elements; study detergents, not soap; study bleaching rather than peroxide or bleaching powder. The development of the race through the stone, bronze and iron age has depended largely upon his chemical knowledge. Let us study the metals in their metallic aspects rather than according to the periodic table.

Foods, clothing, materials of utility and convenience or of commerce often can not be rationally treated by the present systems of our texts, but a suitable systematization might easily include these; what they are, how they are produced and what they do.

In its effects upon the pupil and school, we may be sure that pupils who have seen something of the general trend of the instruction through a systematic preliminary course will feel more interest to continue study and will accomplish more and better work in later courses.

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RADIOACTIVITY.[1]

By Andre Debierne.[2]

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Radioactivity comprises to-day a very large number of facts and theories of which it would not be possible to give a complete survey in a brief address. Nevertheless, I shall make an effort to bring out all the chief points of interest of the new science, the birth of which may be considered without exaggeration as the most important scientific event of the past few years.

Not only has this new science revealed the existence of extremely curious substances and brought a rich harvest of new natural phenomena, but it has led us to the attack of a problem which seemed absolutely chimerical only a few years ago—the problem of the transmutation of atoms or of the chemical elements; for it is now demonstrated that the phenomena of radioactivity are concomitants of the disintegration of atoms. Radioactivity may now be defined as the science of atomic transformations; it is not impossible that in time radioactivity may become the art of changing chemical elements into one another. The facts known at present leave no doubt as to the reality of atomic disintegrations; if as yet these transformations are entirely beyond our control, possibly some day we may learn how to bring them about and to control them.

The fundamental phenomenon, which was discovered by Henri Becquerel and has served as the point of departure for the development of radioactivity, is as follows: Certain substances emit spontaneously a peculiar radiation whose properties are analogous to those of the rays obtained in a Crookes tube. The new rays render gases conductors of electricity, act on a photographic plate, and produce fluorescence in certain substances. This spontaneous emission of rays was first observed in the case of uranium and its compounds, later also in the case of thorium compounds. Then were discovered new substances possessing the same property in a very high degree. All these substances are said to be *radioactive*. They constitute a new source of energy.

An apparently essential characteristic of the phenomenon of radio-

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[2] Translated from the French by M. A. Rosanoff.

activity is its spontaneity: the emission of rays takes place without visible external cause. This characteristic permits of distinguishing the phenomena of radioactivity from those that take place in the course of certain chemical reactions. For instance, the oxidation of phosphorus is accompanied by phosphorescence and by electrical conductivity of the gases surrounding the phosphorus. The same phenomena may be brought about by the action of heat upon the sulfate of quinine. But in all such cases the phenomenon is not spontaneous; it is brought about by external causes which are easy to detect. Therefore, phosphorus and quinine sulfate are not considered as radioactive substances.

Another essential characteristic was brought out by the early researches of Madame Curie. Radioactivity is an atomic property. The spontaneous emission of rays is connected with the radioactive *atom*, and is not in the slightest degree influenced either by changes of state of aggregation of by chemical combination with the atoms of other elements. Thus, the intensity of the Becquerel rays emitted by the substances containing uranium, and measured by the conductivity of the surrounding gases, is always proportional to the number of uranium atoms contained in the substance and is independent of the form in which uranium may be present. Among the numerous other properties of matter, mass alone is so distinctly atomic in its nature.

Our realization of the atomic character of the radioactive property has had a directing influence on the science of radioactivity and has led to the establishment of its present theories. But first of all it had led to the discovery of radium itself and of the other strongly radioactive substances. I shall review briefly the genesis of the discovery of radium, which forms one of the most beautiful investigations ever carried out in the physical sciences, both as regards the logical keenness with which the research was carried on and as regards the material difficulties which had to be overcome. The novel method employed has since been constantly used in researches in radioactivity.

Among the elements that had previously been known, only uranium and thorium were radioactive, and the activity of any substance containing one of these elements was found to be proportional to the quantity of the active element present. Certain minerals, however, containing uranium showed a greater activity than metallic uranium itself. Pierre Curie and Madame Curie, thoroughly convinced of the atomic nature of radioactivity, assumed that these minerals contained new chemical elements, endowed with greater activity than uranium, and although physicists by profession, and with only rudimentary laboratory means at their disposal, they undertook a search after the new hypothetical elements.

I cannot depict here all the difficulties that presented themselves in the search, which involved the chemical treatment of tons of material. Suffice it to recall the results obtained by Pierre Curie and Madame Curie after several years of uninterrupted effort. Those results fulfilled their expectations entirely. The minerals studied do contain strongly radioactive compounds, whose radioactivity is due to the presence of new chemical elements. In the case of one of these elements, namely radium, it has been possible to prepare a series of pure salts; further, its spectrum has been studied, its atomic weight determined and a place has been assigned to it in the periodic classification of the elements. Radium has become a marvelous instrument of research, and to it we owe all the most important discoveries in radioactivity.

It was soon recognized that radioactive substances may differ from one another, not only in intensity of radiation, but also in the character of radiation and in certain peculiarities in the mode of emission of the rays. On the basis of these properties it is as easy to recognize a given radioactive element with certainty as it is to recognize one of the older elements with the aid of spectrum analysis.

The principal new radioactive substances are polonium and radium, discovered by Pierre Curie and Madame Curie; actinium, discovered by myself shortly afterwards; radio-thorium, discovered by Hahn; and ionium, discovered by Rutherford and Boltwood. However, certain of these substances are really complex mixtures containing entire families of chemical elements: namely, the thorium family, the radium family, and the actinium family.

The rays emitted by radioactive substances may be subdivided into three groups, *viz.*, the α rays, the β rays, and the γ rays, which are analogous to the three groups of rays emitted in a Crookes tube, *viz.*, canal rays, cathode rays, and Roentgen rays. The α rays are constituted by the projection of positively charged particles; the β rays by a projection of negatively charged particles; the γ rays are not charged at all.

The particles of β rays are *electrons*, and the rays are easily bent out of their path by a magnetic field. Certain β rays are constituted by electrons projected with an extremely great velocity, a velocity approaching that of light, and it has been possible to verify on these rays an important deduction from the electron theory. For very great velocities, namely, the inertia of a particle ceases to be a fixed quantity; it may greatly increase with increased velocity of motion, and so the particle no longer obeys the laws of Newtonian mechanics. Finally, comparing β rays and cathode rays, one finds them analogous, only the particles of β rays move with greater velocity and are capable of penetrating a much thicker layer of matter (for instance, a plate of aluminium one mm. thick).

The α rays are constituted by the projection of *material particles*, charged electro-positively, having the dimensions of atoms, and moving with a smaller velocity than the particles of β rays. The α rays are bent by a magnetic field with considerable difficulty, and can penetrate only a very thin layer of matter (aluminium foil $^1/_{20}$ mm. thick absorbs them completely). They have the peculiarity of suddenly stopping after having traversed a certain well-determined path in a given medium. The length of this path in air is a very important quantity, for it permits of distinguishing from one another the different species of α rays and consequently also the different radioactive substances. The α particles play a very important part in radioactive transformations, and their nature seems now to be clearly understood.

The γ rays are not charged, and therefore are not deflected by a magnetic field. They suffer but slight absorption in matter (a considerable proportion of the γ rays from radium passes through a lead plate one centimeter in thickness).

These several rays excite fluorescence in a number of substances (platinocyanide of barium, sulfide of zinc, uranyl salts, glass, paper, diamond, etc.). The action of α rays upon zinc sulfide produces the very peculiar phenomenon generally designated by the term *scintillation*; in this, the luminosity of the zinc sulfide screen is caused by an infinity of brilliant little points which appear and disappear continually and which are clearly distinguishable when the screen is examined with a lens.

The radioactive substances constitute a new source of energy; but during the earlier researches both the origin and the mechanism of this production were entirely unknown. Pierre Curie and Madame Curie advanced two distinct hypotheses to explain the production of this energy. The first hypothesis assumed that the energy was furnished from outside in the form of a special radiation, causing in the radioactive substances a phenomenon analogous to phosphorescence. According to the second hypothesis, the energy comes from the active substance itself, and hence the emission of energy must be accompanied by a change in the substance. Pierre Curie and Madame Curie, who had demonstrated the atomic character of the new property, believed thoroughly, even before radium had been discovered, that the transformation takes place in the radioactive atom itself, which must therefore change into a different atom and, consequently, gradually disappear in course of time. It is this hypothesis of atomic transmutation that has proved to be most fruitful and has formed the basis of the theories accepted at present.

The principal fact which has led to these theories is as follows: With the aid of radioactive substances, whose activity appears constant and permanent, it is possible to produce phenomena of radioactivity whose intensity diminishes in time. These phenomena of temporary activity may be observed under various circumstances. Thus, if any substance whatever is placed near a salt of radium, thorium, or actinium, the surface of the substance becomes radioactive, and this activity diminishes more or less rapidly in time. This is the phenomenon of induced radioactivity discovered by Pierre Curie and Madame Curie. Similarly, any gaseous atmosphere surrounding radium, thorium, or actinium, becomes itself radioactive, and its activity likewise diminishes in time. Rutherford, the discoverer of this last phenomenon, gave the name "emanation" to the cause of the temporary activity of the gases. Finally, as first observed by myself, in the case of actinium, substances temporarily radioactive may also be obtained through certain chemical separations in mixtures containing permanently radioactive substances.

These temporary radioactivities often follow complex laws of decrease. The study of these laws has shown that there exist really several different kinds of radioactivity succeeding one another in time. When one kind of activity has died out, another replaces it, and this may gradually cease to exist in its turn. Each kind of radioactivity is characterized by its own velocity of decrease and by a radiation peculiar to itself. Extraordinarily great temporary radioactivities may accumulate in an extremely slight quantity of matter.

Applying to these temporary radioactivities the idea which had guided to the discovery of radium, namely, that radioactivity is an atomic property of the elements exhibiting it, one is led to think that the temporary radioactivities which have been separated from radium, thorium, and actinium characterize new radioactive atoms. And, accepting the hypothesis of atomic transmutation as an explanation of the origin of radioactive energy, the decrease of a given radioactivity appears to result from the gradual disappearance of a radioactive element and its transmutation into another element.

The present theory of radioactive phenomena is based on these considerations. It was proposed by Rutherford and Soddy, who have published numerous observations in complete accord with it. At present the theory is accepted by all investigators of radioactivity. An extremely precious guide in research, it has again and again been confirmed by discoveries of great importance.

The various phenomena exhibited by radium may, then, be interpreted as follows: The radium atom, which emits a certain α radiation, produces continually a radioactive emanation. This emanation is considered to be a radioactive gaseous element resulting from the transmutation of radium, and hence the latter must gradually disappear in time. The emanation emits an α radiation different from that of radium and disappears quite rapidly (the decrease follows a simple exponential law and amounts to one-half in 3.8 days). The emanation produces deposits of induced radioactivity, which are considered as new elements resulting from the transmutation of the emanation. In these deposits it has been possible to identify a series of stages which have received the names of Radium A, Radium B, Radium C, and which succeed one another, radium A changing into radium B, which in turn changes into radium C. These different members of the group emit different radiations and undergo destruction with considerable velocities.

Following radium C is another sequence of terms, characterized by a much smaller rate of disappearance, *viz.*, Radium D, Radium E_1, Radium E_2, and Radium F. The last-named has been shown by Rutherford to be identical with polonium. Polonium itself disappears little by little, but the element succeeding it is as yet unknown.

It has been possible to determin with much precision the laws of formation and destruction of the different transition terms of the series. These laws are exponential expressions analogous to those which hold for monomolecular chemical reactions. Most of the terms have been isolated (by means of chemical reactions, electrolysis, heating, condensation at low temperatures, etc.), and the several exponential formulas followed by their rates of destruction have been determined separately, the formula corresponding to each term having a characteristic exponent, λ, of its own. The rate of destruction of a given term is frequently characterized by specifying the time T required to diminish by one-half the original intensity of its radiation. The quantity $1/\lambda$ may be considered as the mean duration of life of an atom of the substance under consideration; it is denoted by the symbol Θ and is usually referred to briefly as "the mean life." We have, then, $\Theta = 1/\lambda$ and $T = \Theta \ln 2$.

The numerous researches which have been carried out on radioactive substances have resulted in fairly complete knowledge concerning the series of radioactive transformations in the several families, the properties of the different terms, and the properties of the rays emitted during the transformations. The knowledge gathered up to the present time is reproduced in the accompanying tables.

Active substance.	Destruction period T.	Radiation.	Path of α rays.	Absorption coefficient of β rays.	Absorption coefficient of γ rays.	Various properties.
Uranium	6×10^9 years (order of magnitude)	α	3.5 cm.			At. wt. 238.5. Well known chemical properties.
↓						
Radio-uranium						Partly carried down by barium sulfate.
↓						
Uranium X	20.7 days	β,γ		2 groups: $\mu_1 = 14.4$ $\mu_2 = 510$	$\mu = 7.4$	Prepared from uranium with iron hydroxide and bone-black, more soluble in water than in ether.
↓ ? ↓						
Ionium	1500 years (?)	α	2.8 cm.			Properties identical with those of thorium.
↓ ? ↓						
Radium	2000 years	α	3.5 cm.			At. wt. 226.5. Group of alkaline earths. Luminous salts. Evolves heat (1 gram of radium in radioactive equilibrium evolves 118 calories per hour; 20 per cent. of this is produced by radium itself). The principal rays of the characteristic spectrum of radium are 4340.6; 3814.7; 3649.6. One gram of radium in equilibrium evolves 0.37 cubic millimeters of helium per day. The ionization produced by 1 gram of Ra in equilibrium equals that produced by 7,300,000 grams of uranium.
↓						

Radium emanation	3.86 days	α	4.23 cm.		Inert gas. Principal lines of the characteristic spectrum: 4349.8; 4166.6; 3981.6. The emanation in equilibrium with 1 gram of Ra occupies 0.60 cubic millimeter under a pressure of 1 atmosphere.
↓					
Radium A	3.0 minutes	α	4.83 cm.		The deposit of induced activity is volatil at 800–900°. Soluble in strong acids.
↓					
Radium B	26.7 minutes	β		from 13 to 890	The deposit of induced activity is volatil at 600–700°. Precipitates together with $BaSO_4$.
↓					
Radium C	19.5 minutes			13 to 53	The deposit of induced activity is volatil at 1000–1300°. Is deposited on nickel and copper in acid solution. Radium B and radium C can be separated by electrolysis.
↓					
Radium D	12 years (?)	No rays			Properties identical with those of lead. Volatil below 1000°.
↓					
Radium E_1	6.3 days	No rays			Can be separated from radium D by boneblack and also by electrolysis.
↓					
Radium E_2	4.8 days	β		40	
↓					
Radium F or polonium	140 days	α	3.86 cm.		Is deposited on Bi, Cu, Sb, Ag, and even Pb. Sulfide insoluble. Carried down with basic salts of bismuth. Precipitated by $SnCl_2$. Volatil toward 1000°. The substance known as radio-lead is a mixture of radiums D, E_1, E_2, F.
↓					
? (unknown term)					

Active substance.	Destruction, period T.	Radiation.	Path of α rays.	Absorption coefficient of β rays.	Absorption coefficient of γ rays.	Various properties.
Thorium.	3×10^{10} years	α	3.5 cm.			At. wt. 232.4. Known chemical properties.
↓						
Mesothorium I.	5.5 years					
↓						
Mesothorium II.	6.2 hours	β,γ		20 to 39	0.5	
↓						
Radiothorium.	2.0 years	α	3.9 cm.			
↓						
Thorium X.	6.64 days	α	5.7 cm.			Partly soluble in ammoniacal solutions.
↓						
Thorium emanation.	53 seconds	α	5.5 cm.			Inert gas. Condenses toward —120°.
↓						
Thorium A.	10.6 hours	β		140		The deposit of induced activity is soluble in strong acids.
↓						
Thorium B.	55 minutes	α	5.0 cm.			Deposit of induced activity. Is deposited upon nickel from acid solution. Carried down by boneblack. May be separated from thorium A by distillation or by electrolysis.
↓						
Thorium C.	very short	α,β,γ	8.6 cm.	15.7	0.5	
↓						
Thorium D.	3.7 minutes.	β		very penetrating		
↓						
?						
(unknown term)						

Actinium..................	very long	No rays				Group of rare earths.
↓						
Radioactinium..............	19.5 days	α	4.8 cm.			May be separated by electrolysis or by fractionation with ammonia.
↓						
Actinium X................	10.5 days	α,β	6.55 cm.	170		Soluble in ammoniacal solutions; can be separated by electrolysis.
↓						
Actinium emanation.........	3.9 seconds	α	5.8 cm.			Inert gas. Condenses between —120° and —150°.
↓						
Actinium A................	36.1 minutes	β		highly absorbable		Deposit of induced activity. Soluble in strong acids. Volatil at 400°.
↓						
Actinium B................	2.1 minutes	α	5.5 cm.			Can be separated from the preceding by electrolysis. Volatil at 700°.
↓						
Actinium C................	5.1 minutes	β,γ		29	2.0 to 3.6	Carried down by boneblack or by platinum sponge.
↓						
? (unknown term)						

Remark I.—The absorption coefficients of the β and γ rays refer to aluminium and are expressed in cm.$^{-1}$ units.

Remark II.—Potassium salts possess a slight radioactivity, which seems to come, not from radioactive impurities, but from the potassium atom itself; β rays are emitted.

The inter-relation between the different terms of one and the same family is not the result of theoretical interpretation. It is a thoroughly established experimental fact. According to present-day theory, each term represents a certain chemical element which differs from the ordinary elements only by its ephemeral existence and by its emitting a special radiation. The disappearance of the radioactive atom is the result of its transformation into another atom, the special radiation representing the energy which accompanies that transformation. According to this theory, then, the study of radioactivity has led to the discovery of some thirty new elements.

The theory outlined above permits of an easy interpretation of all phenomena thus far known. Still, it was a matter of great importance to obtain a direct experimental demonstration of the reality of atomic transformations, and of the existence of chemical atoms having a very short life, corresponding to the ephemeral radioactivities. Such direct experimental demonstrations have actually been produced, and hence the theory rests on an extremely solid basis.

The reality of atomic transformations accompanying the phenomena of radioactivity has been demonstrated by the experiments of Ramsay and Soddy on the production of helium from radium. Radium, whose character as a chemical element is established by its chemical properties, by its atomic weight, and by its spectrum, continually produces the gas helium, which is itself a well characterized chemical element. This production of helium cannot be reasonably interpreted in any other way than by recognizing atomic transformation.

Some time after Ramsay and Soddy, I showed that the same phenomenon takes place in actinium, which also continually produces helium gas. Recently, Soddy has discovered the production of helium also from uranium and from thorium.

The production of helium from radioactive substances is the first case ever discovered of the transformation of chemical atoms.

That an ephemeral radioactivity is due to the existence of a corresponding chemical element has been experimentally demonstrated in the case of the radium emanation. This emanation has been isolated in a pure state, its spectrum determined, and its volume measured. Somewhat numerous experiments were first carried out by Ramsay and his collaborators, and though the published results are not in perfect agreement, they still leave no doubt whatever as to the material existence of the emanation, which is characterized by a spectrum of its own. The isolation of the substance was effected by utilizing its property of easily condensing at low temperatures. These experiments were later repeated by Rutherford and Royds, who obtained agreeing measurements of the volume occupied by the pure emanation produced by a given quantity of radium, and who described completely the spectrum of the emanation. Recently, I have carried out analogous experiments: my volume measurements agree perfectly with Rutherford's, and my spectrophotographs are identical with those of Rutherford and Royds. I have observed besides that the volume of gas produced does not increase proportionally to the time, owing to the spontaneous destruction of the substance. The observed volume is invariably proportional to the radioactivity of the emanation, no matter what the duration of its production from radium. In the experiments mentioned above, all investigators have observed the production of helium from the emanation: the spectrum of helium gradually appears, while that of the emanation disappears. Finally, Rutherford, and also Ramsay, have succeeded in determining the point of liquefaction and the point of solidification of the emanation.

It thus appears entirely certain that the emanation is a material gas—a fact which corroborates very strongly Rutherford and Soddy's theory.

The production of helium by radioactive substances is directly related to the emission of α particles, and the hypothesis early advanced by Rutherford, that each α particle is an atom of helium, is to-day confirmed. In fact, Rutherford has shown that the α rays and the helium produced by the radium emanation pass through thin layers of matter in a similar manner. Other properties of the α particles are in complete accord with this conception of their nature.

Now, if we assume that in all transformations accompanied by the emission of α particles each radioactive atom changes into the next in order by loss of a single α particle or helium atom, it becomes possible to calculate the atomic weights of the several transition elements of the radium series. The atomic weight of helium being 4, we have, namely: Radium 226.5 ⟶ Emanation 222.5 ⟶ Radium A 218.5 ⟶ Radium B 214.5 ⟶ Radium C 214.5 ⟶ Radium D 210.5 ⟶ Radium E 210.5 ⟶ Radium F, or Polonium, 210.5 ⟶ a last unknown substance 206.5. This last number represents exactly the atomic weight of lead, which suggests the idea that this element is the final product of the transformation of radium. It is probable that this idea can be subjected to experimental verification.

The mother substances, uranium, radium, actinium, and thorium, ought to gradually disappear in course of time, as they are transformed into other elements. But the destruction is certainly very slow, and no diminution of their activity has been directly detected. The laws of their destruction may, however, be determined indirectly. Since the transformation of each radioactive atom produces an emission of rays, it is natural to assume that the more intense the radiation produced by a gram-atom of the substance, the more rapid is the transformation. Thus, radium ought to have a much shorter life than uranium or thorium. The comparison of the radiations may be carried out quantitatively, and thus the ratio of the mean lives of two radioactive substances may be readily obtained.

On the other hand, if it is assumed that the emission of a single α particle corresponds to the transformation of a single atom, it will suffice to determin the number of particles emitted per second by a given mass of the active substance under consideration, in order to ascertain its velocity of transformation. Indirect determinations were first made by measuring the total positive charge emitted in the form of α rays by the active substance and making an assumptiion concerning the charge of a single particle. The results so obtained have been confirmed by directly counting the α particles emitted by a certain quantity of active substance.

The first direct results were yielded by the scintillations produced by α particles on a screen of zinc sulfide. Each scintillation being assumed to be produced by a single α particle, the number of scintillations was determined, produced in a given time by a known quantity of the active substance. This gave the number of α particles emitted by the substance, and consequently the number of atoms transformed in a given time. Another, and very ingenious, method was first employed by Rutherford and Geiger, who utilized the ionization produced in a gas by α particles. These investigators succeeded in determining the ionizing effect produced in a rarefied gas by each α particle by making use of the phenomenon of ionization by shock. The entrance of each single α particle into the gas affects the electrometer, and all that is necessary is to count the number of disturbances produced in a given time. The two methods have yielded well agreeing results, which indicate that radium ought to be one-half destroyed in about 2000 years.

The destruction of radium is too slow to be capable of being detected by direct experiment. Nevertheless, in order to account for the presence of radium in minerals, it is necessary to assume that radium is continually produced in those minerals, the destruction being thus partly compensated for. The element which appears evidently to be the most capable of changing into radium is uranium.

In fact, radium is always found in uranium minerals and, furthermore, uranium is radioactive and hence in a state of decomposition. Since the radioactivity of uranium is much less intense than that of radium, its duration of life must be much greater than that of radium, and this explains the occurrence of uranium in considerable quantities in nature.

An extremely important argument in support of the accepted relationship between uranium and radium lies in the constant ratio of the quantities of the two elements found in minerals. The constancy of this ratio, which has been principally affirmed by the experiments of Boltwood, is readily explained if we assume that radium is produced from uranium, and that the destruction of radium is much more rapid than that of uranium. The ratio permits of calculating the mean life of uranium.

Attempts to demonstrate directly the formation of radium from uranium have shown that this transformation is certainly not immediate, and that there ought to exist at least one substance intermediate between uranium and radium. This has been confirmed by Rutherford and Boltwood's discovery of a new substance capable of producing radium. This new substance has been named ionium. The mean life of ionium being probably long, there is hope that this substance will be isolated without much difficulty.

The question of the relationship between uranium and radium seemed to be definitly settled, when recently Mlle. Gleditsch announced that the ratio of the quantities of uranium and radium was *not* the same in all minerals, contradicting the earlier results of Boltwood. While the ratios found by Mlle. Gleditsch are of the same order of magnitude, they nevertheless differ very materially from one another. The hypothesis of the formation of radium from uranium furnishes so simple an explanation of the presence of radium in minerals that one can hardly abandon it. As a matter of fact, however, the conditions of formation of radium appear to be complex and not yet completely elucidated. Unquestionably, further study of the relative quantities of the different active substances in minerals will yield new and important results. Such study will also be of great usefulness in geology.

If the phenomena of radioactivity indicate atomic transformation, one expects to find radioactive energy, corresponding to the transformation of atoms, to be far greater than the energy changes generally accompanying the transformation of molecules. That this is true is shown by Pierre Curie and Laborde's discovery of the enormous quantity of energy given off by radium. One gram of radium in radioactive equilibrium would produce about 120 calories of heat in an hour. The quantity of heat that would be set free by the complete transformation of one gram of radium is nearly the same as that produced by the combustion of a ton of coal. Most of this heat has been shown to come from the kinetic energy of the α particles. Heat has also been shown to be developed by actinium, thorium, and polonium. Radioactivity thus constitutes an extremely important source of energy. A very slight proportion of radium in the sun (about 1 gram per cubic meter) would be sufficient to account for all the energy radiated by it. The energy radiated by our own planet seems to be more than compensated for by the radium contained in its crust, so that the progressive cooling of the earth, once generally accepted, now seems to be problematic. It seems legitimate to assume that radioactivity constitutes one of the principal sources of the energy radiated in the universe. No other hypothesis is based on an equally serious experimental foundation.

The atomic transformation of radioactivity takes place under very peculiar conditions. As already stated, the phenomenon is spontaneous, apparently causeless. Moreover, no method is as yet known by which such transformations might be brought about or stopped, or even in the least degree hastened or slowed up. Elevation of temperature, which is so sure to increase the velocity of chemical reactions, seems to have no effect whatever on radioactive transformations. Thus, the characteristic constant of the destruction of radium emanation is the same at high temperatures as at the temperature of liquid air. Neither does the nature of an inactive chemical element combined with the radioactive atom seem to have any influence upon the velocity of its destruction. As yet, we are mere spectators, observing the transformation of atoms, but unable to interfere with it in any way.

The transformation follows a probability law identical with the law of mass action followed by chemical reactions: the number of atoms transformed per unit of time is at any instant proportional to the total number of atoms present. No simple and satisfactory hypothesis, however, has been advanced explaining this fact. In the case of mono-molecular chemical reactions, the fact that the transformation takes place gradually is explained on the assumption that all the molecules present are not in the same condition, either owing to collisions between the molecules or because of differences in whatever motion may be going on within the molecules themselves. The transformation of a given molecule is instantaneous, but the molecule will not undergo transformation unless it happens to get into a certain condition necessary for it. The probability law must then remain the same as long as the number of molecules remains very great and the external conditions of the reaction remain the same. In the case of radioactive transformations, external conditions (*e. g.*, of temperature) and intermolecular collisions ought to have no effect. Therefore, only the motion within the interior of the atom can be invoked in an effort to explain why, in one and the same substance, some atoms break down immediately after being formed, while others are destined to live hundreds or even thousands of years before undergoing transformation.

It is imaginable that there exists in space a special field of force which influences intra-atomic motion and is therefore capable of causing the disintegration of atoms. The action of such a force must then be independent of any translatory motion of the atoms. There is, however, at present absolutely no indication of the existence of such a force in space.

If the transformation is *not* brought about by an external force, and if external conditions of pressure, temperature, etc., have really no influence upon the progress of radioactive changes, one is led to assume that the destiny of a given atom is completely determined at the very moment of its formation, that at that moment it is already in such a state that its transformation must take place after exactly a certain interval of time. In that case a radioactive element must be considered as made up of atoms of different nature, some destined to very speedy destruction, others to a more or less prolonged existence. It is not unthinkable that these different atoms of one and the same radioactive element may some day be separated.

In order to account for the exponential law of spontaneous destruction, it is necessary, in that case, to assume that the distribution of life durations among the atoms at the moment of their formation is represented by a simple exponential function, the atoms of short life being much more numerous than those of long life. It is, however, difficult to imagine what can possibly be the cause of such a law of distribution, and considerations like the above only show that while the laws of radioactive transformations have been determined with precision and are well known, the initial cause of the phenomena is as yet altogether obscure.

In concluding this summary, I will mention the attempts that have been made with a view to artificially bringing about atomic transformations with the aid of radioactive energy. Some results in this connection have been published by Ramsay and Cameron. They believed that by the action of radium emanation upon water they had succeeded in producing neon. They further believed that by the action of the emanation upon a salt of copper they had produced alkali metals: the formation of lithium appeared to have been especially well demonstrated.

These results have, unfortunately, been shown to be erroneous. Mme. Curie and Mlle. Gleditsch repeated the experiments on the formation of lithium and found that when no other than platinum vessels were used, the appearance of lithium could not be detected; in Ramsay and Cameron's experiments the lithium came from the glass of the apparatus employed. Similarly, Rutherford and Royds have re-investigated the effect of emanation upon water and have failed to obtain any neon. I, too, have failed to find neon in the gases evolved by a solution of radium. The neon found by Ramsay and Cameron must have come from a small quantity of air introduced by accident.

So it may be said that up to the present time no atomic transmutation has been produced artificially. All we can do is to subject to inquiry spontaneous transmutations which we cannot control. A long step, therefore, remains to be taken before the dream of the alchemists has been realized.[1]

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[1] New results have been published by Ramsay and Gray. According to these investigators, carbon dioxide may be produced by the action of radium emanation upon compounds of thorium, zirconium, silicon, etc. But inasmuch as carbon compounds may easily find their way into apparatus by accident, it is difficult to establish beyond doubt a transformation of the elements thorium or zirconium into carbon. The authors themselves admit that their experiments are not conclusive.