of Radiology, American Society for the Control of Cancer, Memorial Hospital in New York City and the Massachusetts Health Department.

It is probable that many months will have to be devoted to the solution of the problem engaging the interest of these experts. That the most advanced thought and the ablest advice will be brought to bear upon the questions under study goes without saying. Regardless of the time spent, we may confidently expect a satisfactory clarification of the perplexities connected with terminology and clinical records in the cancer field.

That the health of the people is a responsibility of government is no longer a question. Educators, statesmen and business men realize *now* that our greatest national assets are the human resources of the nation. Again and again, health departments, insurance companies and private agencies have demonstrated that no investment yields surer returns than expenditures for the prevention of disease and the care of the sick. For example, the Metropolitan Life Insurance Company has spent over a period of 30 years, 120 million dollars in health education, in nursing the sick and in the general prevention of disease. "We who are used to actuarial methods," says Dr. Louis I. Dublin, vice-president of the company, "are entirely satisfied with our investment. Year in and year out we have increased our investments in the preservation of health because we felt that these investments paid."

What the National Cancer Institute will eventually mean to the nation in the saving of lives may only be conjectured at this time. This will depend upon the extent to which it merits the confidence and cooperation of the scientific institutions, the medical profession and the people themselves. It is hoped that the benefits to the people, however, will be both direct and indirect; not limited to the present, but promising much for the future. The provision of a more adequate supply of radium for the treatment of present and future sufferers from cancer; the training of personnel for the correct diagnosis and appropriate treatment of the disease in its early stages are the more tangible and immediate benefits.

We have not the slightest doubt that some day, maybe soon, the cancer problem will be solved. There is no reason to be pessimistic about cancer research. It is not likely that any individual worker will singlehandedly conquer cancer. Scientific knowledge has increased and become so complex, that only through close coordination of research in the biological sciences with other disciplines can future advances in our knowledge of cancer be made. The National Cancer Institute of the Public Health Service hopes to demonstrate by the soundness of its policies, the extent of its cooperation and help, that it can attain an important place in this concerted warfare against the disease.

What we are discussing is no academic problem; cancer represents one important sector of a people's fight for life. You are engaged in a long-time struggle against one of mankind's oldest and most resourceful enemies; malignant growth of cells. If from this congress with its clashes of intellect and ideas, there should be generated the spark of understanding as to a means of ridding the world of the cancer menace, your contribution to humanity—to its happiness and future prosperity—might equal or even exceed the human losses of another world war.

On behalf of our government, therefore, I welcome your presence here. I wish you success in your deliberations. The one in ten of us in this country who, under the present rates, is doomed to die of cancer, pray that at least a beginning may be made toward unravelling the tangled skein, toward eradicating the menace of cancer.

A NEW REACTION IN ORGANIC CHEMISTRY: THE REDISTRIBUTION REACTION

By Dr. GEORGE CALINGAERT

DIRECTOR OF CHEMICAL RESEARCH, ETHYL GASOLINE CORPORATION, DETROIT, MICHIGAN

THE chief difference between typical organic and inorganic compounds is the complete sharing of pairs of electrons in the bonds of the former, in contrast to the presence of electrostatic bonds in the latter. This results in profound differences in the behavior of these compounds. Electrostatic or ionic bonds are readily loosened in a suitable dielectric medium, such as water, for instance, and solutions result in which the two ions of opposite signs are in mass equilibrium with one another but where any one ion does not remain paired with one individual ion of the opposite sign. As a result, when two or more kinds of positive ions are introduced in a solution with two or more negative ions, separation of the salts from the solution will not necessarily yield back the particular salts which were originally introduced: the pairing of anions with cations will be governed primarily by solubility relationships, and appropriate manipulations of the conditions, primarily concentrations and temperatures, will effect predictable changes in the composition of these precipitated salts. Accordingly, we should not think of a solution as containing, say, sodium ions in equilibrium with chlorine and bromide ions:

$$NaCl + KBr \rightleftarrows Na^+ + K^+ + Cl^- + Br^- \rightleftarrows NaBr + KCl.$$

The covalent bond, as the sharing of a pair of electrons is called, is not readily dissociated either by solution in a dielectric solvent or by heat or other means. Thus, a solution of ethyl acetate and methyl butyrate still contains these two compounds in the proportions in which they were introduced, and they can be readily recovered unchanged by any appropriate method such as fractional distillation. In order to separate the two groups forming such a molecule, namely, the acid group and the alcohol group, it is necessary to resort to chemical means whereby one of these groups is replaced by one of similar chemical nature but of greater reactivity; for instance, treatment of an ester with sulfuric acid will liberate the organic acid, while the more reactive sulfuric acid then becomes combined with the alcohol. If it is preferred to liberate the alcohol, a base such as sodium hydroxide may be used, in which case it is the organic acid which is obtained in combined form:

$$EtOAc + H_2SO_4 = EtOSO_3H + HOAc$$
$$EtOAc + HaOH = EtOH + NaOAc.$$

A new reaction has now been found whereby the alcohol and acid groups present in such a mixture of esters can be caused to exchange freely between the two or more groups of the opposite type which are present in the solution. Thus, the above mixture will yield two new compounds, namely, methyl acetate and ethyl butyrate.

$$EtOAc + MeOBt \rightleftarrows MeOAc + EtOBt^1$$

This reaction takes place by the simple use of a catalyst without the observable expenditure or production of energy, and practically without side reaction of any kind. The result, therefore, bears a striking similarity to the distribution of ions in an aqueous solution.

The reaction is not limited to esters, and similar observations have been made in the case of alkyl halides such as ethyl chloride and ethylene dibromide, and even more strikingly in the case of organo-metallic compounds. The latter case is all the more remarkable because these compounds, in general, behave very much like hydrocarbons, and their organic radicals can hardly be called functional groups, like the acid and alkyl groups in esters, or the halogens in alkyl halides, which are all susceptible of being removed or reintroduced at will by the use of appropriate strong chemical reagents. Typical examples of this reaction are illustrated in Figs. 1, 2 and 3, which show the distillation curve of mixtures containing originally two compounds, and after reaction all the possible combinations of the two kinds of radicals or atoms present.

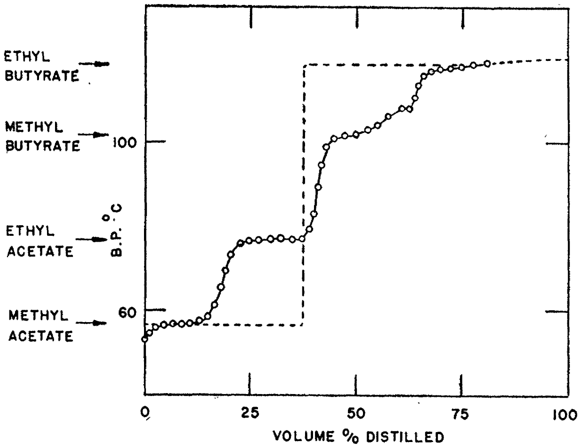

FIG. 1. Distillation of the reaction product of methyl acetate + ethyl butyrate. Dotted line represents distillation of same mixture before reaction.

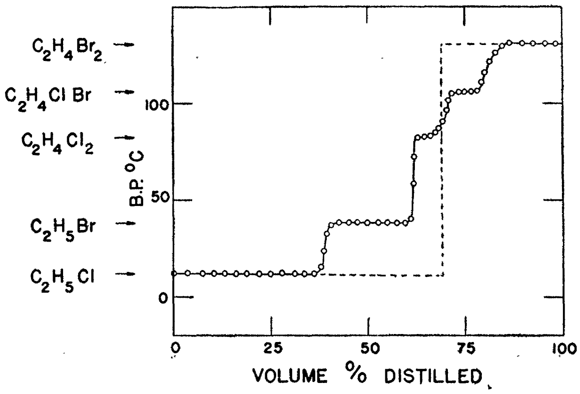

FIG. 2. Distillation of the reaction product of ethyl chloride + ethylene dibromide. Dotted line represents distillation of same mixture before reaction.

The organic chemist is apparently so steeped in the tradition that no reaction can take place between

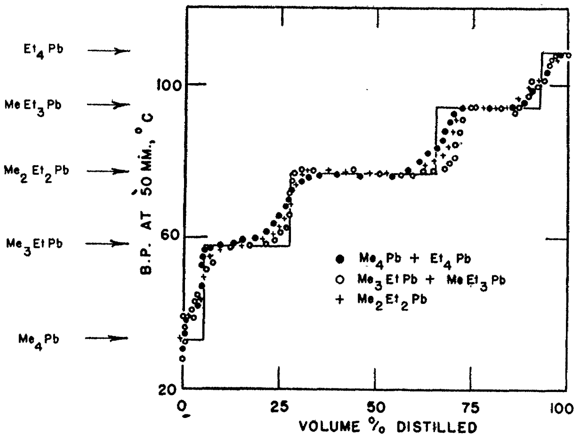

FIG. 3. Distillation of the reaction product of methyl and ethyl lead compounds. Solid line calculated for random equilibrium mixture having $r = 0.5$.

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[1] Ac = acetyl: $CH_3 \cdot CO-$; Bt = butyryl: $CH_3 \cdot CH_2 \cdot CH_2 \cdot CO-$.

molecular groupings of the same type that no statement to that effect is found in the text-books; the notion becomes so obvious on the basis of our general chemical knowledge that it is subconsciously accepted. The present discovery seemed to strike so deeply at the foundation of our conception of organic chemistry that the investigation was soon directed toward an attempt to discern order in this seeming chaos. Systematic investigations have established the following characteristics of this unusual reaction:

(1) As far as has been ascertained, the reaction appears to be general within the classes of compounds investigated.

(2) The reaction is quantitative, and in some cases the most elaborate and precise methods of detecting by-products failed to find any.

(3) Little or no energy change is involved.

(4) The reaction is reversible, that is, the same final composition is obtained from any one or more starting materials as long as the bulk composition of the system is unchanged.

(5) The equilibrium composition is not appreciably affected by dilution with inert solvents, by temperature or any other commonly recognized independent variable in a chemical equilibrium, but is a function only of the gross composition of the system.

In view of the above observations, the simplest assumption was made regarding the nature of this equilibrium, namely, that it corresponded to the complete random distribution of the groups involved. The laws of probability express in simple form the expected proportions of all the possible combinations in systems of this kind. In the particular case which has been used most extensively for quantitative investigation in this field, namely, the case of tetraalkyllead compounds containing only methyl and ethyl groups, if we call r the mole fraction of methyl groups in the mixtures of methyl and ethyl groups, *i.e.*, Me/(Me + Et), the concentration of the five possible compounds will be expressed by:

Me_4Pb	r^4
Me_3EtPb	$4\ r^3(1-r)$
Me_2Et_2Pb	$6\ r^2(1-r)^2$
$MeEt_3Pb$	$4\ r(1-r)^3$
Et_4Pb	$(1-r)^4$

Fig. 3 shows, as a solid line, the calculated distillation curve for such a system containing equal proportions of methyl and ethyl groups, *i.e.*, $r = 0.5$, and the three series of experimental distillation curves superimposed correspond to three systems for which $r = 0.5$ or nearly so, but in which the starting materials in each case were quite different, namely: $Me_4Pb + Et_4Pb$, $Me_3EtPb + MeEt_3Pb$ and Me_2Et_2Pb. Fig. 4 likewise gives corresponding calculated and observed distillation curves for two systems with high and low values of r, namely, $r = 0.345$ and $r = 0.776$. In each case, the agreement is remarkably good, showing that the distribution truly takes place completely at random.

These novel characteristics for a chemical reaction suggest the advisability of coining some new chemical terms and, accordingly, the reaction has been named "The Redistribution Reaction" and its final product a "Random Equilibrium Mixture."

The further investigation of the reaction was carried on principally in the field of organic metallic compounds, because these compounds react readily and with little or no side reaction and because the identity and exact concentration of the constituents of such systems are easily established.

Extended investigation of the reaction has shown it to take place in the case of alkyl or aryl groups, as well as with other metals than lead, such as tin, silicon and mercury, and complete random interchange of the radicals has been found to take place.

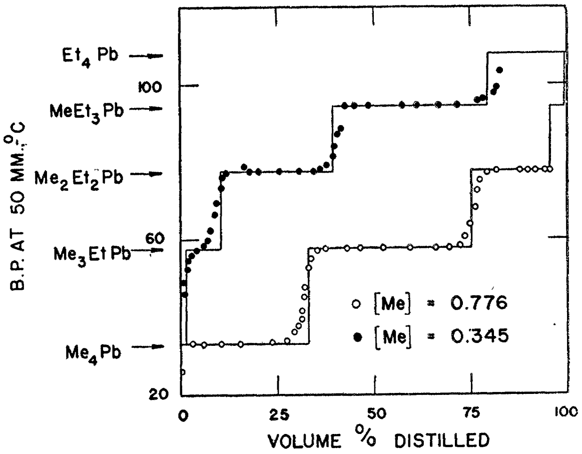

FIG. 4. Distillation of the reaction product of tetramethyllead + tetraethyllead. Solid lines calculated for ○ $r = 0.776$; ● $r = 0.345$.

Considering what we know of the instability of free radicals and their tendency to react with molecules or to rearrange yielding saturated and unsaturated hydrocarbons, it is remarkable to observe here a complete random mobility, without any loss of these groups through side reactions. This observed random distribution signifies that the bond strengths of the linkages involved are independent of the nature of the other linkages in the same molecule, that is, that the strength of a Me-Pb bond, for instance, is the same whether the other three linkages of the Pb are to methyl or to ethyl. This unexpected conclusion is likely to attract the attention of the chemists who spend considerable effort in attempting to determine bond strengths in atomic linkages. The systematic use of the redistribution reaction will be of considerable help in solving this key problem of molecular chemistry.

Another interesting application is in the study of relative affinities. When a system is investigated in which two or more groups of one kind, say alkyl radicals in organo-metallic compounds, are redistributed between two or more different "acceptors," as we shall call them, such as lead and mercury, a new factor enters into play. In this case, methyl and ethyl radicals wander not only from one lead atom to another, but also from a lead atom to a mercury atom. Although, as it has just been stated, when only one metal is involved, the methyl bonds are not affected by the presence of ethyl bonds and conversely, there seems to be no reason to assume that the same will hold when two metals are present. In this case, a methyl radical attached to a lead atom may interchange with an ethyl radical attached to a mercury atom, and the two metals need not necessarily have the same relative affinity for the two alkyl radicals involved. This can be tested experimentally: If a random equilibrium mixture is made, for instance, containing equivalent quantities of methyl and ethyl radicals, on the one hand, and mercury and lead atoms on the other, in the absence of different affinity relationships, the observed methyl-ethyl distribution on each metal will be equal to the over-all distribution, namely, $r = 0.5$. A greater relative affinity of one metal for one radical will be reflected by a shift of the value of r up for one metal and correspondingly down for the other. The equilibrium so obtained will obey the mass action law and give an equilibrium which is expressed by:

$$K = \frac{[\text{Me}-\text{Pb}]\ [\text{Et}-\text{Hg}]}{[\text{Me}-\text{Hg}]\ [\text{Et}-\text{Pb}]},$$

where the brackets denote the concentration of the corresponding bonds in the total product. The result of such an investigation on the Me-Et-Pb-Hg system is illustrated in Fig. 5, where the same final equilibrium was reached from either end, that is, starting with $Me_4Pb + 2\,Et_2Hg$ as well as with $Et_4Pb + 2\,Me_2Hg$. By careful fractional distillation supplemented by analysis of each distillation cut for Pb and Hg, it was possible to tabulate the exact amount of each of the five lead and three mercury compounds formed. This corresponded in each case to a value of $r_{Pb} = 0.32$ and $r_{Hg} = 0.68$, giving a value of $K = 4.5$, showing that lead has a greater affinity for ethyl radicals, as compared to methyl, than has mercury.

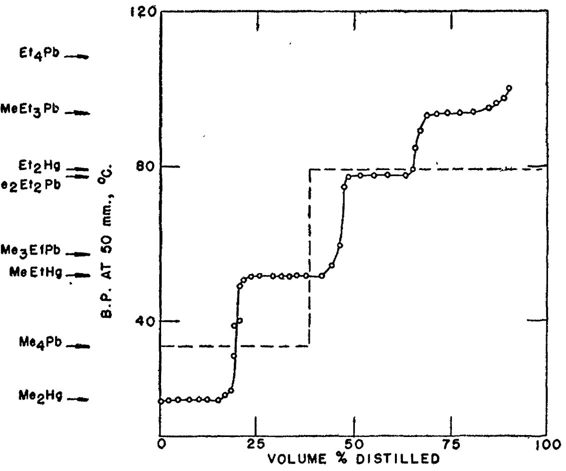

FIG. 5. Distillation of the reaction product from $Me_4Pb + 2\,Et_2Hg$, or $2\,Me_2Hg + Et_4Pb$. Dotted line represents distillation of the same mixture before reaction.

Thus it is now possible by using the redistribution reaction to effect a direct measurement of the relative strengths of two kinds of bonds by actual observation under conditions of rigid equilibrium between the bonds involved, rather than by inference from the comparison of separate measurements, such as rates of reaction or the displacement of one radical by another.

The above quantitative observations clearly show the nature of the equilibrium. They throw, however, no light on the reasons for its existence or the mechanism involved. Reasoning by similarity with inorganic compounds, one might expect the mechanism to be through the formation of ions, while, on the other hand, the known existence of free radicals suggests the possibility of their playing a role in the redistribution reaction. Too much, however, is known about ions and free radicals as well as about the electronic nature of the covalent bond to make such explanations tenable. The organic compounds involved here are definitely not ionizable under the conditions used, and free radicals, if formed at all, would be bound to react with one another as well as with undissociated molecules, leading to the formation of large amounts of secondary products which are remarkably absent here.

The catalysts used in each case, although they may vary appreciably in chemical formulae, seem to have two characteristics in common, namely, (*a*) they contain one or more of the groups or atoms the redistribution of which they are capable of effecting, and (*b*) they are known or expected, on account of their electronic structure, to be capable of readily forming addition compounds with complete molecules of some kinds. This suggests that the mechanism of the redistribution reaction may be the reversible formation of a loose complex between a molecule of the catalyst and one or more molecules of the compounds to be redistributed. In this complex, the atoms or radicals to be redistributed are no longer identified with the particular molecule which has supplied them to the complex, but are shared in common by the residual parts of the catalyst as well as of the other molecule. When the complex breaks up, which probably occurs very frequently, each molecule, that is, the catalyst and the other compound, is reformed with its proper complement of groups, but these groups are taken at random from the common supply, and the final result of the repetition of this process is then the mathematical equilibrium corresponding to complete random redistribution. This is represented schematically by the equation:

$$R_2R'_2M + R'C \rightleftharpoons [R_2R'_3]\ [MC] \rightleftharpoons R_3R'M + RC$$

in which R and R′ are the groups to be redistributed, M is the carrier, such as Pb in the case of alkyllead compounds, and R′C or RC is the catalyst.

The information obtained so far on the redistribution reaction is in accord with such a mechanism, but does not yet include data which confirm its correctness. Kinetic studies of the reaction and investigation of the physical and chemical characteristics of the catalyst are, however, expected to throw light on this point. It seems fair to expect that a closer scrutiny of the mechanism of the reaction will lead to a better understanding of the exact nature of the covalent bond and particularly of the exact mechanism whereby it is loosened and reformed in ordinary chemical reactions.

Beyond these positive studies one may well speculate whether this heretofore unsuspected reaction does not often take place spontaneously in natural systems containing several kinds of similar compounds. It may well be that the aging of alcoholic beverages is due at least in part to the redistribution of the esters to which they owe their flavor, while some of the little understood changes which take place in the living cell may correspond to the random interchange of the amino acid groups between the molecules of protein.

Practical applications should also not be overlooked. Two groups already suggest themselves at first sight. One is the preparation of mixed compounds such as mixed esters of polybasic acids, for instance: instead of preparing these by successive esterification, they can now be prepared directly by redistribution between the two corresponding symmetrical esters. A second and perhaps less obvious line would be the opening of new fields of use for materials heretofore considered too inert to be of practical value in chemical syntheses. For instance, organic bromides are not usually thought of as brominating agents because the bromine can not be removed by ordinary methods. As shown in Fig. 2, appropriate double decomposition between ethylene dibromide and an organic chloride will yield the corresponding bromide. Bearing in mind the availability and ease of handling ethylene dibromide, it seems probable that its use will prove advantageous in the preparation of some organic bromides, especially where the corresponding chloride is readily available.

The scientific reader who is not directly concerned with organic chemistry will be interested to note that this discovery carries a lesson which reaches well beyond the confines of its field. The concept of the absence of reaction between similar organic compounds has been accepted without challenge because of its usefulness in introducing order in our chemical knowledge. The experimental evidence reported above proves once more that we should ever bear in mind that the validity of any concept depends on how strictly we have been able to subject it to experimental verification and not on how long we have had it or how easily it fits our mental processes.[1]

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[1] A complete technical report on the subject will appear in the *Journal* of the American Chemical Society beginning in October, 1939.

OBITUARY

WITMER STONE[1]

(1866–1939)

WITMER STONE was born a naturalist, nurtured a naturalist, and a naturalist he lived to the end of his days. Most of the many activities that filled his busy life flowed from his profound interest in nature. An instinctive collector, he loved to gather about him the objects that excited his admiration and curiosity. In naming and classifying his specimens he became a systematist and a scientist. Inevitably as he made and mastered collections his keen perceptions discovered new kinds of animals and plants and new facts relating to kinds previously known. He wrote of his discoveries so wisely and so well that he became editor of the foremost ornithological journal of America. As a master editor and through his technical papers he became known throughout the world and added to his fame and that of the institution which was his scientific home.

Stone's association with the Academy of Natural Sciences of Philadelphia was practically life-long. It began in a boyish fascination following a visit to the museum when he was eight or nine years old and became closer year by year until 1888, when he assumed charge of the bird collections for the Ornithological Section. From this nominal official connection he succeeded step by step through curatorial positions from conservator to director of the museum. His life became so merged with that of the academy that for many years it was difficult to think of them apart. During the half-century of his official connection the collections of the academy grew greatly. The number of birds alone increased from 26,000 in 1888 to 143,000 in 1939.

Apart from his curatorial duties but more or less closely linked with them Witmer Stone's activities may be placed under four heads: namely, (1) scientific research, (2) nomenclatural, (3) editorial and histori-

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[1] Based on a Minute of Appreciation presented to the council of the Academy of Natural Sciences of Philadelphia, October 3, 1939.