SCIENCE

CONTENTS

ELECTROMERISM, A CASE OF CHEMICAL ISOMERISM RESULTING FROM A DIFFERENCE IN DISTRIBUTION OF VALENCE ELECTRONS[1]

RECENT advances in our knowledge of the structure of matter have made it possible for an organic chemist to address a group of non-organic chemists and of physicists upon this subject without apologizing. During a period which is not far behind us in the past, not only the validity, but, possibly, even the utility of employing structure conceptions requiring atoms and their arrangements was brought into question; so that the organic chemist, who has maintained an abiding faith in atoms and a confidence in his ability to decipher something of their arrangements in molecules, became aware of an indulgent smile whenever he broached this subject except in the company of his own confrères.

With this inheritance, it is natural to expect that the organic chemist would welcome any discoveries which make our conception of atoms and of the mechanism by which atoms combine to form molecules more concrete; and that he would be among the first to seek to apply these concepts to special problems in his own field.

With a feeling of keen satisfaction, therefore, we learn through the work of Bragg that, in a diamond crystal, each carbon atom is surrounded by four other carbon atoms placed equidistant from it. These atoms are grouped around the central carbon atom as the four corners of a

[1] An address prepared for the symposium on the "Structure of Matter," held at the meeting of the American Association for the Advancement of Science in New York City, December, 1916.

regular tetrahedron are arranged around its center. Thus, the tetravalent character of the carbon atom manifests itself clearly. Furthermore, when a model of a diamond crystal is examined, it is discovered that the atoms appear to arrange themselves in rings of six. These relationships suggest at once well known fundamental theories of the organic chemist.

Through the writings of J. J. Thomson,[2] Stark,[3] Abegg[4] and many others, the conviction has been reached, that the forces which hold the atoms together, commonly called chemical affinity, are chiefly, if not wholly, electrical in character. The impetus to this interpretation has come from the discovery that electricity itself possesses an atomic structure, and that our material atoms appear to be composed of units of positive and negative electrical atoms nicely balanced in the neutral atom. As Carl Barus says:[5]

Not only has energy possessed herself of inertia, but with ever stronger insistence she is usurping the atomic structure once believed to be among the very insignia of matter. Contemporaneously matter, itself, the massive, the indestructible, endowed by Lavoisier with a sort of physical immortality, recedes ever more into the background among the shades of velocity and acceleration.

Electrochemical theories have not been lacking in the development of chemistry. For many years the electrochemical theory of Berzelius was a guide in the interpretation of chemical phenomena. There is, perhaps, no greater tragedy recorded in the annals of science during the past one hundred years than that which overtook Berzelius at the close of his active career as leader of chemical thought. We of to-day know best why this theory failed, and why we are now busily engaged in formulating a new electrochemical theory, as well as a new electrophysical theory. In fact, J. Stark in his recent work, "Die Elektrizität im chemischen Atom," gives a eulogy of Berzelius, and points out the many striking qualitative resemblances which the theory of Berzelius bears to his own.

The special purpose of my remarks to-day precludes any detailed discussion of the various theories concerning the structure of the atom. This phase of the subject has already been presented in the morning meeting of this symposium. It may be said that all theories agree upon a positive core or nucleus associated with negative electrons, the atoms of negative electricity. Thomson presents hypotheses concerning the possible arrangements within the atom, while Stark limits his treatment chiefly to the surface layer. The surface layer, he says, contains an excess of positive electricity. In the neutral atom one or more electrons, called valence electrons, are held close to the surface of the atom by this positive charge. Compounds are formed, when the lines of force from one or more of these valence electrons reach out and end on the positive areas of other atoms. In the case of strongly polar compounds, an electron is almost wholly drawn over to the atom which it then holds combined.

Lewis[6] classifies compounds into polar and non-polar, but in a footnote remarks:

It must not be assumed that any one compound corresponds wholly, and at all times, to any one type.

He distinguishes between valence number and polar number. Valence number he defines as the number of positions, or regions, or points (bond termini) on the

[2] J. J. Thomson, *Phil. Mag.*, March, 1904, 27, 757 (1914), etc.

[3] J. Stark, "Die Elektrizitut im Chemischen Atom," Leipzig, 1915.

[4] Abegg, *Z. Anorg. Chem.*, 39, 330 (1904); 50, 309 (1906).

[5] SCIENCE, N. S., Vol. XL., 727, 1914.

[6] G. N. Lewis, *J. Am. Chem. Soc.*, 38, 762 (1916).

atom at which attachment to corresponding points on other atoms may occur. Polar number is the number of negative electrons which an atom has lost (in an algebraic sense).

The evidence of, perhaps, indeed, the cause of the mobility of polar compounds is the freedom of one especially important atom, the atom of electricity, or the electron, to move from one position to another.

From a study of the reactions of chemical compounds, and in particular of organic compounds, it seems doubtful whether the classification into polar and non-polar based upon physical values, such as the dielectric constants[7] of compounds in the gaseous state, is of any more significance than the terms electrolyte and nonelectrolyte were to the older supporters of the theory of Arrhenius. In time, it came to be known that it was no easy matter to draw the dividing line between these two classes, and that one class seemed to merge imperceptibly into the other. So, with polar and non-polar compounds, it seems theoretically probable that there is no perfectly non-polar compound, unless it be a molecule composed of two like univalent atoms, such as hydrogen;[8] and that other

[7] Stark ("Die Elektrizität im Chemischen Atom," p. 29) says: "Between the properties 'dielectric' and 'conducting' there is a connection. In a dielectric medium, since there are positive and negative 'Quanten' bound to one another, it follows that the medium may become conducting when, through proper application of energy from without, the 'Quanten' pairs become partially dissociated, or ionized; that is, into freely moving positive and negative 'Quanten.' Conversely, the ions of a conducting medium by mutual union to form 'Quanten' pairs may make the medium dielectric; and in general a material medium is at the same time dielectric and conducting, so that by assigning a dielectric constant and a specific conductivity, the medium is characterized for a finite electric field and a finite electrical current."

[8] Bohr concludes that the hydrogen molecule consists of two hydrogen nuclei (at a distance apart of 0.60×10^{-8} cm.), and two electrons which

compounds are polar in varying degrees, depending upon the mutual attractions between valence electrons and the positive surfaces or cores of the atoms combined, and upon the distances to which these electrons, in forming such compounds, are deflected from their normal positions relative to the positive areas of the uncombined atoms themselves.

Even before the electron theory had been proposed, an application of the theory of ion formation and charges upon ions led to the recognition of polar characteristics in compounds not known to be ionogens.

In a study of chloroamines, $RNHCl$ and R_2NCl, Seliwanow[9] observed that, during hydrolyses, the chlorine in these compounds was replaced by hydrogen; and that they interacted with hydrogen iodide with the liberation of two equivalents of iodine for each equivalent of combined chlorine,

$$R_2NCl + 2 \ HI = R_2NH + HCl + I_2.$$

Usually, during hydrolysis, combined chlorine in organic compounds is exchanged for hydroxyl and has no tendency to liberate iodine from hydriodic acid. Seliwanow ascribed this peculiar behavior of the chlorine atom in chloroamines to the fact that, *even in combination,* it existed as *"hypochlorous chlorine."* He pointed out that the chlorine atoms in nitrogen trichloride, NCl_3, also showed the same peculiar behavior.

In 1901, Noyes and Lyon,[10] in performing Hofmann's well-known lecture experiment for demonstrating the composition of ammonia, observed that, under certain favorable conditions, the amount of nitrogen liberated as free nitrogen was about one sixth, instead of one third, the volume

revolve in an orbit in a plane perpendicular to the line joining the nuclei.

[9] Seliwanow, *Ber.*, 25, 3612 (1892).

[10] W. A. Noyes, A. C. Lyon, *J. Am. Chem. Soc.*, 23, 460 (1901).

of the chlorine used. They explained this reaction by the following equation:

$$12\,NH_3 + 6\,Cl_2 = N_2 + NCl_3 + 9\,NH_4Cl.$$
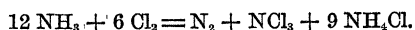
This observation led them to study the chemical properties of nitrogen trichloride. They found that each chlorine atom present in nitrogen trichloride was equivalent to two atoms of "available chl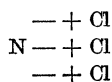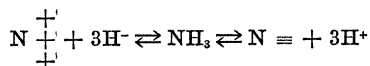orine," or, as Seliwanow had put it, the chlorine is hypochlorous in character. Noyes and Lyon represented nitrogen trichloride as follows:

$$\begin{array}{c} -+\,Cl \\ N-+\,Cl \\ -+\,Cl \end{array}$$

and, to account for the reaction between ammonia and chlorine, assumed that ammonia may *ionize* in two ways,

$$\overset{+}{\underset{+}{N}} + 3H^- \rightleftarrows NH_3 \rightleftarrows N \equiv +\,3H^+$$

and, furthermore, that the chlorine molecule may ionize to give both positive and negative chlorine ions.

In the same number of the *Journal of the American Chemical Society*, Stieglitz[11] commented upon the work of Noyes and Lyon, and put forth arguments to show that this reaction,

$$H_2O + Cl_2 \rightleftarrows HCl + HOCl,$$
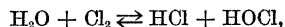
a reversible reaction, was, at the same time, an *ionic reaction*. In other words, hypochlorous acid may ionize in two ways, amphoterically,

$$HOCl \rightleftarrows H^+ + OCl^-$$
$$HOCl \rightleftarrows HO^- + Cl^+.$$
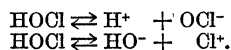
The chlorine molecule, therefore, must yield negative chlorine ions, Cl⁻, and, also, positive chlorine ions, Cl⁺.

These deductions, expressed originally by Noyes and Lyon, as well as by Stieglitz, in terms of ion formation, have since been translated into the language of the electron theory of valence. Thus, the chlorine mole-

[11] Stieglitz, *J. Am. Chem. Soc.*, 23, 797 (1901).

cule may be represented electronically by the symbol, Cl — + Cl.

The striking difference in behavior of derivatives of positive chlorine and of negative chlorine may be illustrated by comparing the two compounds, nitrogen trichloride and phosphorus trichloride, which, by virtue of the family relationship of nitrogen and phosphorus in the periodic system, and the similarity in the formulas of the two chlorides, would be expected to resemble one another in chemical behavior about as closely as any two compounds could. At the same time, the illustration will serve to explain the significance of the statement made in an earlier part of this paper, viz., that the polar characteristics of compounds may be revealed by a study of their chemical interactions.

If the electronic formulas,

$$\begin{array}{cc} -+\,Cl & +-\,Cl \\ N-+\,Cl & P+-\,Cl \\ -+\,Cl & +-\,Cl \end{array}$$

are assigned to these two substances, we obtain formulas which, unlike those in general use, show why it is that the two compounds are most dissimilar in chemical deportment; why nitrogen trichloride, when hydrolyzed, gives ammonia and hypochlorous acid, while phosphorus trichloride yields phosphorus acid and hydrogen chloride; why the chlorine atom in nitrogen trichloride possesses oxidizing properties, while the chlorine in phosphorus trichloride does not. The oxidizing value of a positive chlorine atom corresponds to a gain of two negative electrons, if a negative chlorine ion is the final stage in the change.

$$Cl^+ \rightarrow Cl \rightarrow Cl^-.$$
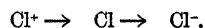
Certain other halogen compounds have been found to show similar polar differences. Thus, Nef[12] observed that chlorocyanogen, upon hydrolysis, gave hydrogen chloride and cyanic acid, while iodocyanogen gave hypoiodous acid and prussic acid,

[12] Nef, *Ann.*, 308, 320 (1899); *ibid.*, 329 (1899).

$$Cl - + CN + H + - OH =$$
$$H + - Cl + HO - + CN,$$
$$I + - CN + H + - OH =$$
$$HO - + I + H + - CN.$$
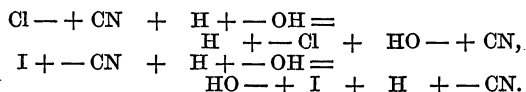
Tetrabromomethane and tetraiodomethane, when hydrolyzed, give bromoform and iodoform, respectively:

$$Br_3C - + Br + \overset{+}{H}O\overset{-}{H} =$$
$$Br_3C - + H + HO - + Br,$$
$$I_3C - + I + \overset{+}{H}O\overset{-}{H} =$$
$$I_3C - + H + HO - + I.$$

Iodine monochloride reacts as follows:

$$I + - Cl + H^+ - OH = HO - + I + H + - Cl.$$
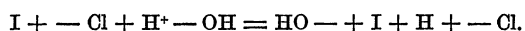
In fact, there is no difficulty in finding among organic compounds countless cases in which the polarity manifests itself clearly during chemical changes. Thus, in the case of alkyl cyanides, RCN, it may be asked what indication there is in the formula itself to lead chemists to predict, unerringly, that the products of hydrolysis of such a compound are always ammonia and a carboxylic acid. Pure speculation would suggest that at least four different sets of products are possible:
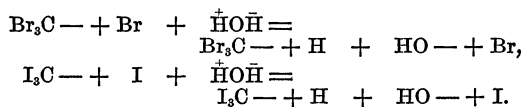
(a) $RC(OH)_3$ and NH_3;
(b) $RCH(OH)_2$ and NH_2OH;
(c) RCH_2OH and $NH(OH)_2$;
(d) RCH_3 and $N(OH)_3$.

But the substances expressed under (a) are the only ones ever realized. That this decision is not inherent in the formula is emphasized all too forcibly by the fact that these four sets of products are the very ones which beginning students offer to explain the hydrolysis of an alkyl cyanide. In terms of the electron conception valence, the explanation lies in the fact that the nitriles are polar compounds of the formula:

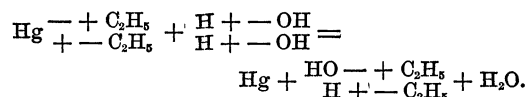$$RC \overset{+}{\underset{+}{+}} \overset{-}{\underset{-}{-}} N$$
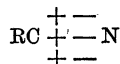
In this connection, some recent experiments on mercury dialkyls carried out with Mr. Werner in our laboratory have led to the observation that, upon complete hydrolysis in the presence of acetic acid, the products formed are *metallic mercury,* an *alcohol,* and a *hydrocarbon.* At about 200°, mercury diethyl decomposes to give mercury and butane. This dissociation implies that the mercury atom in these dialkyls either possesses, or readily assumes, the condition of reduction which it has in the metallic state, viz., with an equal number of positive and negative "charges." This suggests, also, that the two ethyl groups may be one negative and the other positive:

$$Hg \overset{-}{\underset{+}{+}} \overset{+}{\underset{-}{-}} \begin{matrix} C_2H_5 \\ C_2H_5 \end{matrix} = Hg + C_2H_5 + - C_2H_5.$$
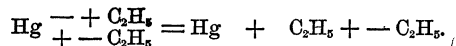
When mercury diethyl is heated with acetic acid, further evidence in support of this inference is furnished; a quantitative yield of metallic mercury is found, and in addition, ethane and ethyl alcohol (or acetic ethyl ester). These changes may be expressed in terms of the electron conception of valence as follows:

$$Hg \overset{-}{\underset{+}{+}} \overset{+}{\underset{-}{-}} \begin{matrix} C_2H_5 \\ C_2H_5 \end{matrix} + \begin{matrix} H + - OH \\ H + - OH \end{matrix} =$$
$$Hg + \begin{matrix} HO - + C_2H_5 \\ H + - C_2H_5 \end{matrix} + H_2O.$$

If these reactions of mercury diethyl are compared with those of zinc alkyls and of oxygen alkyls, the significance of the statement that the polar characteristic of compounds becomes manifest during chemical changes will be apparent. Thus, zinc alkyls are hydrolyzed to give exclusively *zinc hydroxide* and a *hydrocarbon;* oxygen alkyls give exclusively *alcohols.*

$$Zn \begin{matrix} + - C_2H_5 \\ + - C_2H_5 \end{matrix} + \begin{matrix} H + - OH \\ H + - OH \end{matrix} =$$
$$Zn \begin{matrix} + - OH \\ + - OH \end{matrix} + \begin{matrix} H + - C_2H_5, \\ H + - C_2H_5, \end{matrix}$$

$$O \begin{matrix} - + C_2H_5 \\ - + C_2H_5 \end{matrix} + \begin{matrix} H + - OH \\ H + - OH \end{matrix} =$$
$$O \begin{matrix} - + H \\ - + H \end{matrix} + \begin{matrix} HO - + C_2H_5, \\ HO - + C_2H_5. \end{matrix}$$
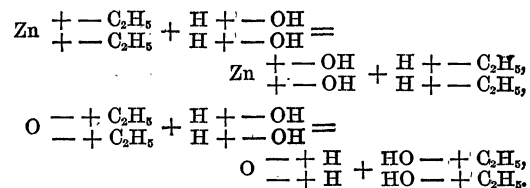
If, therefore, the atoms in compounds may function positively or negatively, in general a univalent atom, *A,* may be represented by two electronic symbols, *A +* and

A — ; and an atom whose valence is n may function in $(n+1)$ ways electronically. Thus:

$$O \overset{+}{\underset{+}{}}, \quad O \overset{-}{\underset{+}{}}, \quad O \overset{-}{\underset{-}{}},$$

$$N \overset{+}{\underset{+}{+}}, \quad N \overset{+}{\underset{-}{+}}, \quad N \overset{+}{\underset{-}{-}}, \quad N \overset{-}{\underset{-}{-}}.$$
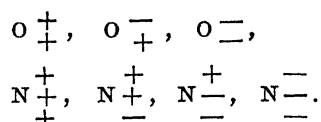
A compound formed by the union of the univalent atoms, A and B, may be represented by two electronic formulas:

$$A + - B \text{ and } A - + B.$$

These two formulas represent isomers in a peculiar sense, quite unlike structural isomers. The difference lies solely in the distribution of valence electrons. Two or more compounds related in this manner have been called electronic isomers, or *electromers*.[13]

There is a certain resemblance between electromers and structure tautomers. While the transformation of one tautomer into another is accompanied by a wandering of an atom from one position in the molecule to a new position, the transformation of one electromer into another depends upon a more subtle change, viz., of electrons, or negative atoms of electricity, from one position to another within the molecule. Furthermore, it would be expected that, like tautomers, one electromer would be more stable than the other, and, in the majority of cases, that only one form might be capable of isolation, but that under certain favorable conditions, both electromers might be realized.

Moreover, between two electromers there might exist a condition of equilibrium similar to that which exists between tautomers and desmotrops, viz.,

$$A + - B \rightleftarrows A - + B.$$

Many cases requiring an assumption of such a relationship have been observed. One simple illustration will suffice. When

benzene sulphonic acid is subjected to the action of superheated steam, it yields benzene, C_6H_6, and sulphuric acid. But if the same sample is heated with caustic alkalies, the products are phenol, C_6H_5OH, and sulphurous acid (or sulphites). Since benzene and phenole, as well as sulphurous acid and sulphuric acid, are related as oxidation-reduction products, the question arises what is the electronic formula of benzene sulphonic acid? To account for the substances formed in the two reactions, it must be assumed that two electronic formulas may be assigned to benzene sulphonic acid, and that the two substances represented by these formulas are in equilibrium as *tautomeric electromers*[14]

$$C_6H_5 - + SO_3H \rightleftarrows C_6H_4 + - SO_3H.$$
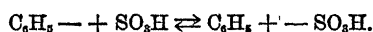
It is self-evident that the problem of preparing two or more electromers presents far greater experimental difficulties than the separation of structure tautomers has offered in the past. When, therefore, it is recalled that von Baeyer observed the first case of tautomerism while studying isatin, and that many years elapsed before two compounds related as tautomers were actually separated as distinct substances (desmotrops), it should not be a matter of surprise that the preparation of actual electromers has not been more successful so far.

The first set of experiments, and practically the only ones, carried out with the express purpose of preparing electromers, are those of W. A. Noyes.[15] Noyes tried to prepare a nitrogen trichloride in which the chlorine atoms, like those in phosphorus trichloride, are negative

$$\begin{array}{c} + - Cl \\ N + - Cl \\ + - Cl. \end{array}$$
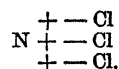
No conclusive evidence in support of the

[13] Fry, *Z. Physik Chem.*, 76, 387 (1911).

[14] L. W. Jones, *Am. Chem. J.*, 48, 26 (1912).

[15] W. A. Noyes, *J. Am. Chem. Soc.*, 35, 767 (1912).

existence of such an electromer could be found.

In an article[16] published in the *Journal of the American Chemical Society*, I presented evidence, which I believe to be conclusive, to show that the certain derivatives of hydroxylamine, prepared by Meisenheimer, represent the first known cases of electromers, viz., compounds identical in structural formulas, but dissimilar in chemical and physical properties by virtue of a different arrangement of valence electrons, and the concomitant differences in force fields within the molecules.

A consideration of the properties of hydroxylamine, and its various derivatives and, in particular, the peculiar behavior of the hydroxyl group in such compounds, led me to conclude that this hydroxyl group could not be regarded as identical with negative hydroxyl, — OH. This opinion was expressed by Stieglitz.[17]

The similar behavior of hydroxlamine and halogen amines, of hydroxylamine and hydrogen peroxide, still more the fundamental similarity existing between hydroxylamine and ammonia, and between their salts, and above all, the fact that, as far as the writer is aware, no hydroxylamine derivative has been found to exchange hydroxyl for halogen by treatment with halogen acids, or phosphorus halides, are facts upon which the writer's views are based. (According to a later private communication from Dr. Jones, he has now reached the same conclusion in this question and has discovered further evidence supporting it.)

These facts all imply that the hydroxyl group in hydroxylamine may be positive, $+ O \leftrightharpoons + H$,

$$\begin{array}{l} -+\,H \\ N -+\,H \\ -+\,OH. \end{array}$$
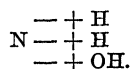
Compounds of the formula $R_3N(OH)X$[18] are found among the products which result

when hydroxlamine is treated with halogen alkyls. Moist silver oxide converts these substances into hydrated amine oxides, $R_3N(OH)_2$, H_2O. The same hydrated amine oxides may be prepared by the action of hydrogen peroxide[19] upon tertiary amines, R_3N. In fact, Hantzsch and Hillard[20] suggested that hydrogen peroxide might react with tertiary amines by addition and that the reaction may be reversible.

$$(CH_3)_3N + HOOH \rightleftarrows (CH_3)_3N(OH)_2.$$
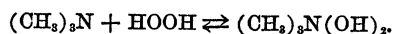
By careful dehydration of hydrated amine in vacuo, amine oxides, R_3NO, are formed.

These amine oxides and their hydrates are oxidizing agents, and in this property show a striking resemblance to hydrogen peroxide. In fact, Dunstan and Gaulding, in summing up their behavior, say:

We conclude that the oxygen is in an ''active'' condition analogous to the oxygen atom in hydrogen peroxide.

Thus, trimethylamine oxide rapidly decomposes in two ways:

$$2(CH_3)_3NO = 2(CH_3)_3N + O_2,$$
$$(CH_3)_3NO = (CH_3)_2NH + CH_2O.$$
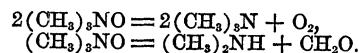
These changes, looked at from the point of view presented by the electron theory, would lead to the inference that the oxygen atom in amine oxides should be represented as follows: $R_3N \mathrel{\overset{-}{+}} O$; and that the hydrated amine oxides, or their salts, should receive the following formulas: $R_3N \mathrel{+}{}^{'} \dfrac{OH}{X}.$

If the hydroxyl group in hydroxylamine be regarded as positive, and if this condition of the hydroxyl group be retained in the alkyl (aryl) derivatives, two inferences concerning the behavior of substituted hydroxylamines must follow logically.

In the first place, compounds containing in their formula the group N — OH, or the

[16] L. W. Jones, *J. Am. Chem. Soc.*, 36, 1268 (1914).

[17] *J. Am. Ch. Soc.*, 36, 288 (1914).

[18] Dunstan and Goulding, *J. Chem. Soc.*, 69, 839 (1896); 75, 1005 (1899).

[19] Merling, *Ber.*, 25, 123 (1892); Wernick Wolffenstein, *Ber.*, 31, 1553 (1898); Mainlock and Wolffenstein, *Ber.*, 33, 159 (1900).

[20] Hantzsch and Hillard, *Ber.*, 31, 2058 (1898).

group N — OR, should show different physical and chemical properties, depending upon the nature of the hydroxyl, or alkoxyl group; *i. e.*, whether it is negative (I.) or positive (II.).

$$N + - O - + R, \qquad N - + O - + R.$$
$$\text{(I.)} \qquad\qquad \text{(II.)}$$
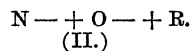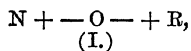
Then, again, provided one of the hydroxyl groups is positive and the other negative, compounds of the type, $(R)_3 N(OH)_2$ should exist in two isomeric forms (electromers) when one of the hydrogen atoms is replaced by a single radical R; and, furthermore, there should be two distinct isomers (electromers) if two of the hydrogen atoms are replaced simultaneously by dissimilar radicals, R and R'.

$$(R^+)_3 \equiv N \begin{matrix} + - O - + H \\ - + O - + R \end{matrix},$$

$$(R^+)_3 \equiv N \begin{matrix} - + O - + H \\ + - O - + R \end{matrix},$$

$$(R^+)_3 \equiv N \begin{matrix} - + O - + R \\ + - O - + R' \end{matrix},$$

$$(R^+)_3 \equiv N \begin{matrix} - + O - + R' \\ + - O - + R \end{matrix}.$$

In the second place, compounds of the formula R, R', R'', $N(OH)_2$, in which there are three different alkyl (or aryl) radicals linked to the nitrogen atom, should exist in *stereoisomeric modifications,* provided one hydroxyl group is *negative* and the other one is *positive.* By the action of an optically active acid, *e. g.*, d-bromocamphorsulfonic acid, or d-tartaric acid, a racemic compound obtained by synthesis should be resolved into a dextro- and a levo-modification. Optical activity might even persist in the corresponding amine oxides R, R', R'', $N \overset{+}{\underset{-}{\rightleftharpoons}} O$. Although the two hydroxyl groups are *structurally* alike, they are totally different *electronically.* Consequently, the nitrogen atom is linked to five different radicals, and, in this respect, compounds of these types may be compared to substituted ammonium derivations of the formula R, R', R'', R''', N — X, which have

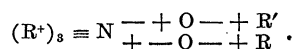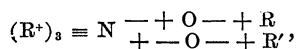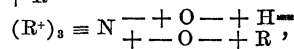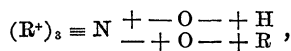been resolved into optically active forms[21] repeatedly. Experimental evidence supporting both of these deductions has been presented quite recently.

1. *Electromers.*—In an article concerning the "Non-equivalence of the Five Valences of Nitrogen," Meisenheimer[22] describes the preparation of two isomeric compounds of the type

$$(R)_3 N(OCH_3)(OH).$$

The *first* isomer was obtained by the action of methyl iodide upon trimethylamine oxide, and the subsequent replacement of iodine by hydroxyl. Thus:

1. $(CH_3)_3 N = O + CH_3I = (CH_3)_3 N = \begin{matrix} OCH_3 \\ I \end{matrix},$

2. $(CH_3)_3 N \begin{matrix} - OCH_3 \\ - I \end{matrix} + NaOH =$

$$(CH_3)_3 N \begin{matrix} - OCH_3 \\ - OH \end{matrix} + NaI.$$
$$(A)$$
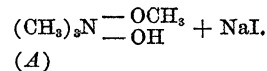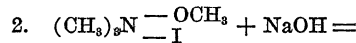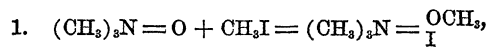
The *second* isomer was secured by the action of sodium methylate upon the salt obtained by treating trimethylamine oxide with hydrogen chloride.

1. $(CH_3)_3 N = O + HCl = (CH_3)_3 N \begin{matrix} - OH \\ - Cl \end{matrix},$

2. $(CH_3)_3 N \begin{matrix} - OH \\ - Cl \end{matrix} + NaOCH_3 =$

$$(CH_3)_3 N \begin{matrix} - OH \\ - OCH_3 \end{matrix} + NaCl.$$
$$(B)$$
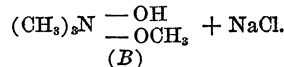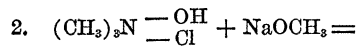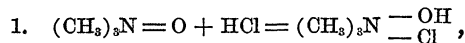
The two forms, (A) and (B), are identical *except for the order in which the hydroxyl groups and the methoxyl groups were introduced.* In (B), as Meisenheimer said, the methoxyl group is linked to the *"fifth* valence," or the one which usually engages the *acid radical;* while it is linked to the *"fourth* valence" in formula (A). But

[21] Le Bel, *Compt. rend.*, 112, 724 (1891); 129, 548 (1899); *Ber.*, 33, 1003 (1900); Wedekind, *Ber.*, 32, 517, 3561 (1899); 35, 766 (1902); 36, 3791 (1903); 38, 1838 (1905); Wedekind and Oberheide, *ibid.*, 37, 2712, 3894 (1904); Wedekind and Froelich, *ibid.*, 38, 3438 (1905); Pope and Peachey, *J. Chem. Soc.*, 75, 1127 (1899); Pope and Harvey, *ibid.*, 79, 828 (1901).

[22] *Ann.*, 397, 273 (1912).

these two substances are fundamentally different. This is easily demonstrated by a study of their solutions. When a water solution of trimethylmethoxyammonium hydroxide (A) was heated, it decomposed quantitatively in accordance with the following equation:

$$(A) \quad (CH_3)_3 N \genfrac{}{}{0pt}{}{-OH\ (5)}{-OCH_3(4)} = $$
$$(CH_3)_3 N + CH_2 O + H_2 O.$$

While trimethylhydroxyammonium methylate (B) showed a totally different behavior

$$(B) \quad (CH_3)_3 N \genfrac{}{}{0pt}{}{-OH\ (4)}{-OCH_3(5)} = $$
$$(CH_3)_3 N = O + CH_3 OH.$$

In addition to these compounds, Meisenheimer prepared a number of isomeric mixed dialkyl compounds, with methyl, ethyl and propyl radicals, e. g.,

$$(CH_3)_3 N \genfrac{}{}{0pt}{}{-OCH_3}{-OC_2H_5} \quad \text{and} \quad (CH_3)_3 N \genfrac{}{}{0pt}{}{-OC_2H_5}{-OCH_3}.$$

In every case, water decomposed compounds of this type to give a tertiary amine, an alcohol and an aldehyde; but, invariably, the radical which was eliminated as aldehyde was the radical which occupied "position four (4)" and the group eliminated as alcohol always occupied "position five (5)." Meisenheimer stated that he never obtained even recognizable traces of the aldehyde which should have resulted if the group attached in position five had separated in that form. His conclusions may be stated in his own words:

> Durch diese Reaktion ist bewiesen dass die beiden Alkoxygruppen nicht in gleicher Weise an das Stickstoffatom gebunden sind.

The key to these disputed relations is easily furnished in terms of the electronic conception, by assuming that the one hydroxyl (or alkoxyl group) is positive and the other negative; thus:

$$(A) \quad (CH_3^+)_3 \equiv N \genfrac{}{}{0pt}{}{-+O-+CH_3(4)}{+-O-+H\ (5)} = $$
$$(CH_3^+)_3 \equiv N \genfrac{}{}{0pt}{}{-+H}{+-O-+H} + H_2 C_{+-}^{+} O,$$

$$(B) \quad (CH_3^+)_3 \equiv N \genfrac{}{}{0pt}{}{-+O-+H\ (4)}{+-O-+CH_3(5)} = $$
$$(CH_3^+)_3 \equiv N_{+-}^{+} O + CH_3 +-O-+H.$$

It will be observed that the two groups, or, in the final analyses, the two oxygen atoms, upon which the electromerism depends, are not linked directly, but through a third atom, nitrogen.

$$RO+-\overset{||}{N}+-OH \quad \text{and} \quad HO+-\overset{||}{N}+-OR.$$

This is undoubtedly responsible for the relative stability of these electromers as compared with others in which the atoms of different polarity are directly connected; e. g.,

$$A+-B \quad \text{and} \quad A-+B.$$

Here, again, the analogy to structure tautomers appears. Chemists have failed to prepare desmotrops of prussic acid, and of many other compounds in which the wandering atom passes from one atom in the molecule to another directly linked to it.

$$HCN \rightleftharpoons CNH.$$

The majority of successful separations of desmotrops lie among compounds in which, similar to the electromers described above, tautomeric changes involve two atoms not directly linked, but connected by a third atom. Thus, in the keto-enol and in the nitro-nitronic acid desmotrops,

$$O = \overset{|}{C} - \overset{|}{C}H_2 \rightleftharpoons HO - \overset{|}{C} = \overset{|}{C}H$$
$$O = N - CH \rightleftharpoons HON = C -$$

the wandering hydrogen atom passes from carbon to oxygen not directly linked.

2. *Stereomers.*—Meisenheimer[23] was the first to observe that amine oxides with three different radicals R R' R''N = O, could be resolved into enantiomorphous modifications. Amine oxides of this kind were prepared by oxidizing tertiary amines with hydrogen peroxide, or Caro's acid. Meis-

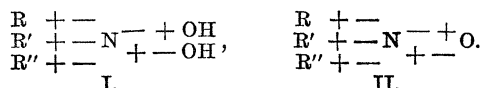23 Meisenheimer, *Ber.*, 41, 3973 (1908); *Ann.*, 385, 117 (1911); 399, 371 (1913).

enheimer and his coworkers prepared methylethylaniline oxide, methylethyl-β-naphthylamine oxide and other similar compounds,

$(CH_3)(C_2H_5)(C_6H_5)N = 0$
$(CH_3)(C_2H_5)(C_{10}H_7)N = O.$

The racemates were resolved by means of d-bromocamphorsulfonic acid or d-tartaric acid. After fractional crystallization and separation, each salt was converted into the active picrate, which was changed to the corresponding active chloride and finally into the active amine oxide itself.

Previous attempts to resolve compounds with two like radicals, Na_2bcd, have been fruitless. Even compounds more closely allied to these amine oxides in form, such as N-methylpicolinium salts, N-methylquinolinium salts, could not be resolved by H. O. Jones.[24] Meisenheimer takes it for granted that an explanation of the stereoisomerism is provided when he has called attention to the fact that, in the amine oxides, the doubly bound oxygen engages the valence which usually holds the acid radical, while in the case of the compounds studied by H. O. Jones, only non-ionizable valences have been satisfied by doubly bound carbon.

It seems that a more consistent explanation may be offered in terms of the electronic viewpoint, if the amine oxides and their hydrates are assigned the following formulas:

$$\begin{array}{cc} \begin{matrix} R & +- \\ R' & +- \\ R'' & +- \end{matrix} N \begin{matrix} -+OH \\ +-OH \end{matrix}, & \begin{matrix} R & +- \\ R' & +- \\ R'' & +- \end{matrix} N \begin{matrix} -+O. \\ +- \end{matrix} \\ \text{I.} & \text{II.} \end{array}$$

It must be assumed that the linking in formula II. is similar to the grouping in formula I., in so far as its effect upon the asymmetry of the molecule is concerned, since amine oxides dissolved in benzene often show large rotations. The nitrogen atom, in either even, *does not hold two like groups,* since the properties of positive and

[24] H. O. Jones, *J. Chem. Soc.,* 83, 1400 (1903).

negative hydroxyl are as divergent as those of positive and negative chlorine. In this respect, the conditions are not the same as those in ammonium compounds of the form, Na_2bcd, but are comparable to the condition existing in ammonium compounds of the general type, $Nabcde$.

In conclusion, permit me to express the belief that chemists will soon come to realize more fully that the recent investigations into the structure of the atom have a practical bearing upon their particular problems. The study of electromers, and the investigations of the conditions under which they may be prepared, certainly furnishes an inviting field of research, which, in my opinion, is worth tilling, and can not fail to be productive of results of far-reaching importance to chemists. Furthermore, with our present limited knowledge of the subject, no one can predict in what manner the discoveries, sure to be made, may react to modify and clarify our theories concerning the structure of matter, and, in particular, our vague notions of "chemical affinity."

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RECENT PHYSIOLOGY AND THE WAR[1]

THIS theme, kindly suggested by Professor Sir James Dewar, is sufficiently large to preclude more than a succinct treatment of some outstanding points in the time permissible in a single lecture. But these points are of considerable interest and have a more than fleeting importance.

The first is that of fatigue, its measurement and incidence in factory employees. The indices taken have been speed of output and quantity of output by groups of workpeople working under the conditions of a munitions factory. An inference of

[1] Address before the Royal Institution of Great Britain, February 2, 1917.