though the precipitate is a hydrogel and hard to wash. Other compounds of osmium, as the osmates, are also precipitated by alcohol but here again the precipitate is difficult to free from alkalies, if they are present. No method, which can be considered thoroughly satisfactory, is known by which osmium can be quantitatively precipitated. The same is even more true of ruthenium, for no method is yet known by which this metal can be completely precipitated from solution.

WASHINGTON & LEE UNIVERSITY,
LEXINGTON, VA.
January 1, 1908.

ON THE NON-EQUIVALENCE OF THE FOUR VALENCES OF THE CARBON ATOM.[1]

BY J. U. NEF.

Received January 8, 1908.

Three assumptions are made with reference to the carbon atom in our present system of organic chemistry: first, that the valence of this atom is invariably four; second, that the four valences are equivalent; and third, that they are distributed in three dimensions and act in the direction of the axes of a tetrahedron.

If we believe, as many at present are inclined to do, that the chemical forces are analogous to or identical with the electrical forms of energy, it at once becomes improbable that the four valences of the carbon atom can be equivalent. Had Berzelius, for example, realized that the molecules of hydrogen and oxygen were each composed of two atoms he would have developed his electrochemical theory from a different standpoint; he would have concluded, as have Clausius, Schönbein, and many others in more recent times, that the forces holding the two atoms of oxygen or hydrogen together in these molecules must be alternately positive and negative.

Let us first analyze critically, however, the evidence which has led us, for some fifty years past, to assume that the four valences of a carbon atom are equivalent. In the last analysis the fact that up to the present moment every one of the great number of monosubstitution products of methane has been found to exist in one modification only is all we have to justify our assumption. There is but one acetic acid, one nitromethane, one aniline, one acetaldehyde, etc., etc. It is evident that we are here drawing positive conclusions from negative evidence—always an unreliable and dangerous process of reasoning. How can we ever be certain when we have a monosubstitution product before us that it is not always one and the same hydrogen atom of marsh gas which has been replaced?

A Belgian chemist, Henry,[2] has spent a number of years in trying to prove by experiment that any one of the four hydrogen atoms of methane, *a*, *b*, *c* or *d*, may be replaced by the carboxyl or nitro group and yet give thus one and the same acetic acid or nitromethane respectively. Such experiments can not conceivably be decisive, for they necessitate the unjustifiable assumption that the various atoms or radicals bound to the

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[1] See THIS JOURNAL, **26**, 1549–1577. Read at the Chicago meeting of the American Chemical Society.

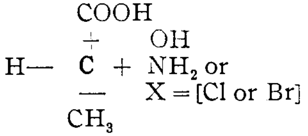
[2] Bull. acad. royal de Belgigue (3), **12**, 644; **15**, 333.

four different valences of a carbon atom hold their places. A study of the optically active α-brompropionic acids, the brom-phenylacetic and succinic acids (see below) shows for instance very decisively that such an interchange of radicals is continually taking place at ordinary temperature.

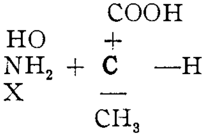
The present situation with reference to the nature of the four valences of the carbon atom may therefore very properly be summed up in the following words; we assume their equivalence until there is proof to the contrary.

During the past ten years or more there has accumulated quite a mass of evidence pointing unquestionably to the conclusion that the four affinity units of carbon are equivalent in pairs only, as shown by the following expression, $\substack{+\\-}\substack{+\\-}C\substack{+\\-}\substack{+\\-}$, in which the plus and minus signs do not necessarily mean positively and negatively charged valences, but are simply used to discriminate between two different kinds of affinity units.

Allow me to call your attention to certain reactions shown by the following optically active, space isomeric, α-substituted propionic acids.



$$\begin{array}{ccccl} & & COOH & & \\ & & + & & OH \\ H- & & \mathbf{C} & + & NH_2 \text{ or} \\ & & - & & X = [Cl \text{ or } Br] \\ & & CH_3 & & \end{array}$$

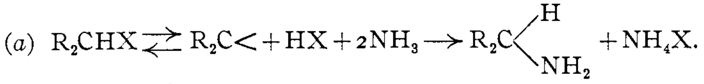


$$\begin{array}{lccc} & & COOH & \\ HO & & + & \\ NH_2 & + & \mathbf{C} & -H \\ X & & - & \\ & & CH_3 & \end{array}$$

d-lactic acid.	*l*-lactic acid.
d-alanine (aminopropionic acid).	*l*-alanine.
d-brompropionic acid, etc.	*l*-brompropionic acid.

When *d*- or *l*-brompropionic acid, or its ester, is treated with ammonia we always obtain the *corresponding*, optically active, α-amino acid, *d*- or *l*-alanine, or its ester. Similarly when these same brom acid esters are treated with various metallic hydroxides, the *corresponding*, optically active, *d*- or *l*-lactic acid derivatives are obtained.

During the past twelve years an enormous amount of evidence has accumulated which shows that the interaction of the primary and secondary alkyl halides, RCH_2X and R_2CHX, with ammonia, metallic hydroxides, or with silver salts of various acids proceeds through the following successive stages:

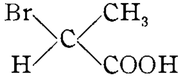


$$(a)\ R_2CHX \rightleftarrows R_2C< + HX + 2NH_3 \longrightarrow R_2C\begin{smallmatrix} \diagup H \\ \diagdown NH_2 \end{smallmatrix} + NH_4X.$$

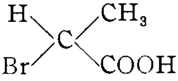
$$(b)\ R_2CHX \rightleftarrows R_2C< + H{-}X + M{-}OH \longrightarrow R_2C< + MX + H{-}OH \longrightarrow R_2CHOH + MX.$$

$$(c)\ R_2CHX \rightleftarrows R_2C< + H{-}X + Ag{-}A \longrightarrow R_2C< + AgX + H{-}A \longrightarrow R_2CHA + AgX.$$

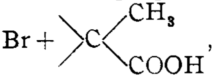
Now the two space isomeric α-brompropionic acids, named above, may be regarded as α-carboxylated ethyl bromides,

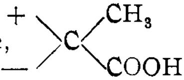
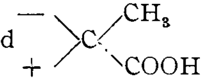


and



; they must therefore be entirely analogous in their reactions to the secondary alkyl bromides. It is furthermore evident at a glance that if the four valences of carbon were equivalent both *d*-

and *l*-brompropionic acid must give by loss of hydrogen bromide, HBr +  $\genfrac{}{}{0pt}{}{\diagdown}{\diagup}C\genfrac{}{}{0pt}{}{\diagup CH_3}{\diagdown COOH}$, through dissociation, one and the same ethylidene carboxylic acid; this substance must theno bviously absorb ammonia, H—NH_2, water, H—OH, or the acid H—A, to give equal amounts of both *dextro*- and *laevo*-alanine or lactic acid derivatives respectively.

This can, however, *not* be the result provided the two valences of carbon in ethylidene carboxylic acid are unlike; the two methylene derivatives obtained from *d*- and *l*-brompropionic acid by loss of hydrogen bromide must then in fact not be identical but represent two isomers of space as shown by the formulae,  $\genfrac{}{}{0pt}{}{+\diagdown}{-\diagup}C\genfrac{}{}{0pt}{}{\diagup CH_3}{\diagdown COOH}$ and  $\genfrac{}{}{0pt}{}{-\diagdown}{+\diagup}C\genfrac{}{}{0pt}{}{\diagup CH_3}{\diagdown COOH}$. These substances then obviously absorb the dissociated ammonia, H—NH_2, or water, H—OH, present to give *d*- or *l*-alanine or the corresponding *d*- or *l*-lactic acid derivative—which agrees with the facts.[1] The moment, therefore, we admit the correctness of the interpretation given of the action of alkyl halides with ammonia, water, etc., the facts presented above prove with precision that two of the four valences of carbon can not be equivalent.

This conclusion also enables us to comprehend in a more simple manner the phenomenon of autoracemation, and especially to understand why optically active substances can maintain their independent existence notwithstanding the fact that the various groups or radicals bound to the different valences of carbon are also continually dissociated from them; thus *d*- or *l*-lactic acid, *d*- or *l*-alanine, *d*- or *l*-brompropionic acid although partially dissociated at ordinary temperatures into *d*- or *l*-ethylidene carboxylic acid and water, ammonia or hydrogen bromide respectively, maintain their identity for a long period of time. Nevertheless the optically active brompropionic acids, as well as their esters, and the corresponding monobromsuccinic and phenylacetic acid derivatives go over as Walden has shown,[2] on long standing (two to five years) at ordinary temperatures into a mixture of equal amounts of the *d*- and *l*-compounds. *Dextro* and *laevo* lactic acid, on the other hand, can be kept indefinitely without change at ordinary temperatures and yet each changes very quickly, in two to three days, at 140° into racemic, *i. e.*, *d*-*l*-lactic acid.

The analogous *d*- and *l*-iodopropionic acids are as yet unknown, but it is certain that they must transform themselves with great speed at ordinary temperatures into racemates so that their actual isolation is problematical. Why are there these remarkable differences in the stability of quite analogous optically active compounds? It is due simply to a difference in the relative amount of existing dissociation. The alkyl iodides are relatively far more dissociated into $C_n\ H_{2n}$ and HI than the

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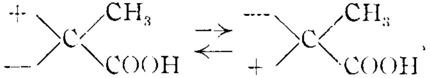
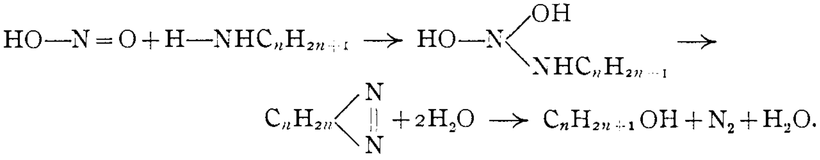
[1] I am purposely avoiding here a discussion of the remarkable optical inversion observed by Walden [(*Ber.*, 32, 1833-55) and by Fischer (*Ibid.*, 40, 489)] in a few isolated instances in the malic and lactic acid series—a reaction which all admit is abnormal and one which, in my opinion, when better understood, will also lead to the conclusion that the four valences of carbon are not equivalent.

[2] *Ber.*, 31, 1420.

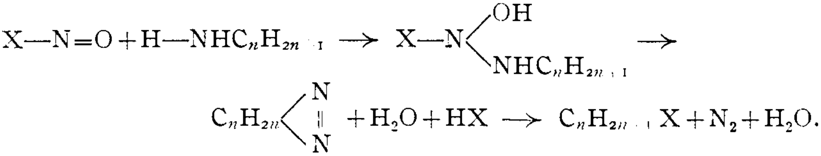
corresponding bromides, chlorides or fluorides—hence the well-known far greater activity of the alkyliodides, alkylsulphates, etc. Furthermore it is obvious in the case of the α-substituted propionic acids under discussion, that as soon as the percentage of dissociation in these compounds into *d*- and *l*-ethylidenecarboxylic acid reaches a certain definite limit, then a very slow transformation of these two space isomeric methylene derivatives into each other, , must automatically take place—hence the phenomenon of autoracemation.

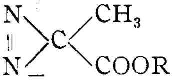
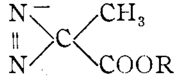
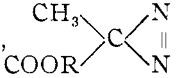
Finally, and this is important, since the above interpretation of the reactions of the alkyl halides is not yet generally accepted by chemists, we may reach the same conclusion, namely, that the four valences of carbon are not equivalent, from an entirely different standpoint by considering another series of reactions shown also at ordinary temperatures by optically active amino acids. When *d*- or *l*-alanine ester is treated with nitrous acid, nitrosyl bromide or chloride respectively we always obtain the *corresponding*, optically active *d*- or *l*-lactic, brom- or chlorpropionic ester. Now the well-known conversion of primary amines into alcohols or alkyl halides by means of nitrous acid or nitrosyl halide has been shown to proceed, in the aliphatic series, through the following stages, *a* or *b*:

(*a*)

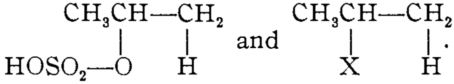


(*b*)



i. e., through an intermediate formation of a fatty diazo compound. Consequently *d*- as well as *l*-alanine ester must go over, when treated with the reagents named, into the two space isomeric *d*- and *l*-α-diazopropionic esters,  and ; the first of these must give with water or haloid acid *d*-lactic or *d*-halogenpropionic acid, whereas the second one is necessarily converted, with evolution of nitrogen, into the corresponding antipodes. It is of course at once apparent that if the two valences of carbon bound to nitrogen in diazopropionic ester,  were equivalent, both *d*- and *l*-alanine must give on treatment with nitrous acid or nitrosyl halide respectively equal amounts of the *d*- and *l*-derivatives, *i. e.*, racemates or at any rate the same products—which is however not the case; consequently the two diazopropionic esters which are the intermediate products[1] in the various reactions are not identical but isomers of space—in other words the two valences of carbon joined to nitrogen in these compounds are *not* equivalent.

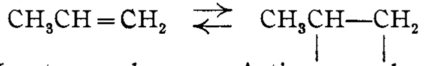
Have we any other evidence which throws doubt on the equivalence of the four valences of carbon? Yes. I refer to asymmetric addition, which shows us in a most simple manner why we have such a vast array of optically active substances in the vegetable and animal kingdom. You are all familiar with the properties of the unsaturated hydrocarbons called the olefines; they absorb with great ease, by addition, such substances as hydrogen, halogens, sulphuric acid and haloid acids. Now propylene absorbs the two last-named reagents to give almost exclusively the isopropyl derivatives,



$$\underset{\substack{| \\ \mathrm{HOSO_2{-}O}}}{\mathrm{CH_3CH}}{-}\underset{\substack{| \\ \mathrm{H}}}{\mathrm{CH_2}} \quad \text{and} \quad \underset{\substack{| \\ \mathrm{X}}}{\mathrm{CH_3CH}}{-}\underset{\substack{| \\ \mathrm{H}}}{\mathrm{CH_2}}.$$

Why is this ?

The absorption reaction takes place first because we have in propylene a certain very definite but small number of molecules in an active molecular condition, thus,

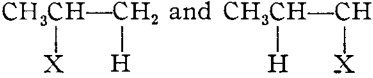


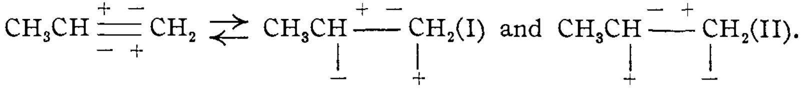
$$\mathrm{CH_3CH{=}CH_2} \rightleftarrows \underset{|}{\mathrm{CH_3CH}}{-}\underset{|}{\mathrm{CH_2}}$$

Inert propylene. Active propylene.

Furthermore the concentrated sulphuric acid or the dry haloid acid is also partially dissociated into the active masses, H— and —OSO_2OH or —X respectively. Hence a simple union takes place between these active substances to give the addition products named above.

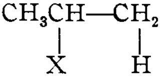
Now if we assume the equivalence of the four valences of carbon it is very difficult to understand why the addition of the dissociated H and X particles does not take place equally on both active carbon atoms of propylene giving like amounts of the propyl and isopropyl derivatives, $\underset{\substack{| \\ \mathrm{X}}}{\mathrm{CH_3CH}}{-}\underset{\substack{| \\ \mathrm{H}}}{\mathrm{CH_2}}$ and $\underset{\substack{| \\ \mathrm{H}}}{\mathrm{CH_3CH}}{-}\underset{\substack{| \\ \mathrm{X}}}{\mathrm{CH_2}}$, respectively. This is self-evident when we realize that the two active valences of active propylene are not equivalent but must be represented thus:





$$\mathrm{CH_3CH}\overset{+\ \ -}{\underset{-\ \ +}{=\!=}}\mathrm{CH_2} \rightleftarrows \underset{\substack{| \\ -}}{\mathrm{CH_3CH}}\overset{+\ \ -}{—\!—}\underset{\substack{| \\ +}}{\mathrm{CH_2}}\mathrm{(I)} \text{ and } \underset{\substack{| \\ +}}{\mathrm{CH_3CH}}\overset{-\ \ +}{—\!—}\underset{\substack{| \\ -}}{\mathrm{CH_2}}\mathrm{(II)}.$$

We have now only to make the further assumption that active propylene contains at ordinary temperatures relatively more active (II) than active (I) molecules; the addition of the dissociated reagent, $\underset{+\ \ -}{\mathrm{H{-}X}}$, must then obviously give $\underset{\substack{| \\ \mathrm{X}}}{\mathrm{CH_3CH}}{-}\underset{\substack{| \\ \mathrm{H}}}{\mathrm{CH_2}}$ as the chief product.



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[1] In view of the importance of ascertaining this with certainty, I am at present working on the problem of isolating these two isomers of space. It is obvious, as Dr. A. F. McLeod suggested to me in reading this paper, that the long known space isomerism existing among the oximes of ketones and aldehydes, as well as among the diazo and azo compounds, may likewise be due to the non-equivalence of the valences of the carbon and nitrogen atoms respectively.

Emil Fischer's work in the sugar group shows that prussic acid when added to various aldoses often gives a decided preponderance of one of the two isomers theoretically possible. Similarly the benzilic acid rearrangement, which also depends upon an addition of active carbon monoxide to various aldoses,[1] often proceeds asymmetrically.

We are thus able to understand, in a strikingly simple way, why various enzymes can convert the sugars into optically active destruction products such as *d*- or *l*-lactic acid, etc., etc. Finally we may ask ourselves whether the two unlike valences of carbon are positively and negatively charged. It is impossible to answer this question with certainty at the present time; it is my conviction, however, that the peculiar ease with which carbon forms chains of great complexity and stability, as well as the fact that the vast majority of the carbon compounds are non-ionizable substances whose reactions proceed mainly in the manner indicated above,[2] must be attributed to the non-equivalence of the four valences of the carbon atom; furthermore the existence of various compounds containing bivalent carbon can also be readily understood on this basis.

NEW BOOKS.

Immunochemistry. The Application of the Principles of Physical Chemistry to the Study of the Biological Antibodies. By SVANTE ARRHENIUS. The Macmillan Company. Price, $1.60.

The preface of this book states that the contents contain a summary of six lectures on the immunity reactions, delivered at the University of California during the summer of 1904, amplified by the addition of new matter covering the subject to the date of publication. No information is given as to whether this is a translation of the German edition, or conversely; but as the German edition preceded the American by several months the latter is presumably a translation, which assumption is supported by the occasional occurrence of characteristic German forms of construction.

Under the title of "Immuno-chemistry" (a useful term which this book will probably cause to be adopted into the vocabulary of the "immunologist") Arrhenius gathers much of the literature bearing upon the studies that have so far been made of the chemical nature of the reactions of immunity, but most of the space is devoted to discussion and interpretation of the results so far obtained by the application of the methods of physical chemistry to the problems of immunity. As by far the greater part of this work has been done by, or under the direction of the author or his colleague, Dr. Madsen, the "Immuno-chemistry" partakes largely of the nature of a monograph upon the physical chemistry of immunity reactions; consequently a review of the book almost necessarily resolves itself into a criticism of the value of the in-

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[1] Cf. *Ann.*, 357, 231-3.

[2] See THIS JOURNAL, 26, 1577.