Elements of Stereochemistry

THE

Elements of Stereochemistry

BY A. HANTZSCH

Translated from the last French Edition of
Guye and Gautier

BY CHARLES G. L. WOLF

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AUTHOR'S PREFACE.

These elements of stereochemistry are not more extensive than the stereochemistry of van 't Hoff and Meyerhoffer, recently published. There would hence scarcely be any reason for publishing them if they were not distinguished by a different rearrangement of the contents, and particularly in their treatment of developments of the stereochemistry of nitrogen compounds and of inorganic substances.

The first part is devoted to the study of molecular asymmetry and of optical isomerism. These questions have been treated so splendidly by the founders of stereochemistry, that they scarcely need mention, and therefore their treatment in this book has been somewhat condensed. Moreover, the theoretical conceptions which serve as a basis for their explanation are no longer discussed; hence a fuller treatment than has been given in these elements has not been deemed necessary.

The same cannot be said of the second part, which is devoted to geometric isomerism and to the study of facts which can be attributed to relative distances of the atoms in the molecule. In the above-mentioned classic work, these facts are treated in rather a summary way. Because of their increasing importance and of the extension of this new chapter in chemistry, a more complete explanation of these developments seems justifiable. With regard to the stereochemistry of nitrogen there has not been, up to the present, any complete monograph concerning the same. This has been the reason for treating this question in some detail. Moreover, in consequence of the scientific discussions of which it has been the center, it seems somewhat advisable to show that, as a matter of fact, it was not so complicated as it would appear at first sight.

Nevertheless the book which I present to the public still preserves the character of a "precis," as the time is not yet at hand when one may represent a complete work on stereochemistry. In order to preserve this sketchy character all details and all bibliographic references which were not strictly necessary have been left out. I wish to express my thanks to Dr. A. Miolati for the part which he has taken in the editing of a chapter of this book.

ENGLISH TRANSLATOR'S PREFACE.

The translation of the French edition of Prof. Hantzsch's "Grundriss der Stereochemie," from the enlarged French translation of Guye and Gautier, was undertaken in the hope that a small handbook dealing more particularly with the important stereochemistry of the compounds of nitrogen, would be acceptable to English readers. This translation has been made, not only from the French edition, but the original German work has also been freely used, and the translator has had the advantage of the personal advice of Prof. Hantzsch, to whom he wishes to express his sincere thanks.

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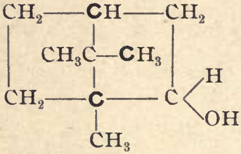
CORRECTIONS.

Page 35, last formula,

for



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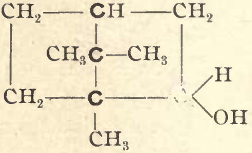
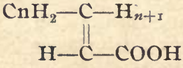


Page 75, line 15, *for* diaceyl *read* diacetyl.

Page 111, last formula,

for



$$\begin{array}{c} CnH_2\text{—}C\text{—}H_{n+1} \\ \| \\ H\text{—}C\text{—}COOH \end{array}$$

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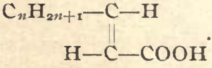

$$\begin{array}{c} C_nH_{2n+1}\text{—}C\text{—}H \\ \| \\ H\text{—}C\text{—}COOH \end{array}$$

Page 171, footnote 2, *for* Paulz *read* Pauly.

INTRODUCTION

Stereochemistry, as the name indicates, is the study of the relations between the chemical phenomena of compounds, and the arrangement in space of the atoms composing them. One terms this arrangement of atoms in space molecular configuration, or more simply, configuration, and one defines as stereoisomers those compounds of the same chemical constitution but with different configuration.

Stereochemistry is based on the fundamental assumption that a molecule has three dimensions, as have all bodies in nature. Nevertheless it has no need whatever of any precise notion of affinity, that is of the working of atoms one on the other, nor of numerical relations which govern the joining of one element to another or the property which is usually designated "valence." It rests in the second place on the following consideration which is a result of isomerism itself; that is, the knowledge that the atoms in a molecule cannot be in a state of chaotic confusion but must within certain limits occupy positions of stable equilibrium.

It is not necessary to take into account intramolecular atomic movements, although their existence cannot be doubted, but, because by reason of their periodicity one can assume that the atoms occupy a certain relatively fixed position to one another.

Under these conditions one ought to assume stereochemically that the molecule consists of a stable system of material points, and dynamics should be taken into consideration only in such special cases as molecular transpositions.

According to le Bel[1] the ground work of stereochemistry ought to be deduced from purely mechanical considerations independent of conceptions regarding valency and structural formulae, simply by using our notions of equilibrium and of symmetry. In any case the developments of this theory are independent of a hypothesis which is apparently not true, and which is in fact contradicted by certain facts which consist in regarding valence as an attractive force regulating the relative positions of atoms to one another.

Nevertheless it is more convenient to found stereochemistry as Van't Hoff has done by using constitutional formulae. This has the advantage in the first place that it lends itself easily to the conception of the student already familiar with the notation currently used in chemistry, and in the second place that stereochemistry is born of constitutional formulae. Let us admit then, for the sake of simplicity and in the absence of negative indications, that the valence of an element represents not only its capacity for uniting with other elements, but is the resultant of forces regulating the spatial position of that element with others; that with elements other than monovalent these forces themselves equal, are orientated in space in definite directions, but can according to circumstance be changed; and lastly in the case of unsaturated compounds these forces or linkings can be double or multiple.

These are the isomeric phenomena which have most contributed to show the necessity of stereochemical conceptions. It was thought in the beginning that consti-

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[1] *Revue Scientifique*, **48**, 609 (1891).

tutional formulae should enable one to take into consideration the number as well as the properties of all isomeric compounds, and the latter should conform to the different modes of intra-atomic linkage. It is necessary to remember that facts had appeared for a long time quite in accordance with this view. Meanwhile some exceptions rare at first, but ever increasing, demonstrated the existence of cases of isomerism quite unexplained by means of constitutional formulae.

These exceptions were classed under the vague term *physical isomers*, of which the characteristics were never precisely defined. Constitutional formulae at first being constructed in a plane, the natural sequence was to explain these exceptional cases of isomerism as due to different arrangement of the atoms in space. This idea was the starting-point of stereochemistry.

THE DEVELOPMENT OF STEREOCHEMISTRY

It was Pasteur[1] who, in 1860 and 1861, founded stereochemistry by showing the remarkable properties which characterize the tartaric acids, and by attributing to molecules certain of the properties of crystals.

Wislicenus[2] in 1873 pronounced constitutional formulae as then known insufficient, notably in the case of the lactic acids, and proposed that one should substitute spatial formulae.

Shortly after, Van't Hoff[3] and le Bel[4] quite independently of one another developed the fundamental theory of the asymmetric carbon atom, and of its application to the explanation of optically active compounds. These

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[1] Pasteur: "Réchèrches sur la désymmétrie moléculaire des produits organique naturels," Conf. Soc. Chim. Paris (1861).

[2] Ann. Chem. (Liebig), **167**, 343.

[3] Chimie dans l' éspace 1873; "Dix années dans l'histoire d. une théorie 1887."

[4] Bull.Soc. Chim. (2) **22**, 337.

two scientists have been the founders of modern stereochemistry. Their conceptions are very nearly the same, the differences being superficial.

Le Bel bases his theories on considerations of chemical mechanics, while Van't Hoff bases his on the consideration of constitutional formulae as ordinarily employed. The opinions of Van't Hoff, spread in Germany by the translation, by Hermann, of Van't Hoff's book (1877), led Baeyer[1] to explain in a stereochemical way certain remarkable properties of cyclic compounds, and one should mention as a product of the evolution of this newer organic chemistry the bringing forward of the prismatic formula for benzene by Ladenburg, the remarks of Graebe on the nature and formula of the phthalic acids, and other observations of different authors.

A publication by Wislicenus[2] constitutes an important advance which opened the way to experimental work of a new kind. Since then the stereochemistry of carbon has been studied by other chemists, notably V. Meyer, Friedel, Bischoff, and particularly by Emil Fischer whose work in the sugar group is well known.

Recently Guye has undertaken the study of these questions from a mathematical point of view, while Werner has formed the basis of a stereochemistry of inorganic compounds.

Van't Hoff and Wunderlich[3] have already endeavored to apply stereochemical methods to other elements, particularly sulphur and nitrogen.

The "stereochemistry of nitrogen" has only received

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[1] Ber. d. chem. Ges., 18, 2277.

[2] Abhadg. d. mathem. phys. Classe der Sächs, Akad. Wissenschaften, V, xiv.

[3] Die Configuration organischer Molekule, 1886.

experimental confirmation since[1] the work of Hantzsch and Werner[2] and of le Bel.[3]

GENERAL CHARACTERISTICS OF STEREOCHEMICAL ISOMERISM

Stereochemical isomers identical in the mode of union of the atoms, one to another, differ only in the geometrical relations of the atoms composing the compound. It is indeed difficult to formulate any characteristic distinctions, but one may say that usually they differ from constitutional isomers, in that they are transformed more easily, one into the other. This should tend to prove that the geometrical positions of atoms in a molecule, can be much more easily changed than the respective linking.

Stereoisomers may be included in two classes:

I. *Substances identical in all their principal properties, but which produce different effects on polarized light, in other words, which are characterized by difference in optical activity. These are called optical isomers or enantiomorphous isomers.*

In these compounds one can regard the atoms as placed at the same absolute distance from one another, but disposed in a different order. For this purpose it will, perhaps, be opportune to style them relative stereoisomers. We shall see that these substances are characterized by asymmetrical atomic groupings.

Isomers of this kind which contain only one asymmetric group are identical in all their properties, except in their action on polarized light. Those, however, which con-

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[1] V. Meyer and Goldschmidt: Ber. d. chem. Ges., **16**, 2177; Auwers and Meyer: *Ibid.*, **21**, 790; Beckmann: *Ibid.*, **22**, 429; etc.

[2] *Ibid.*, **23**, 1, 1243.

[3] Compt. rend., **112**, 724.

tain several asymmetric groups may not only differ in their physical, but also in their chemical properties.

According to the element determining the asymmetry we distinguish :

a. Compounds of carbon optically active, i. e., those in which the grouping is asymmetric with regard to the atoms of carbon.

b. Derivatives of nitrogen optically active, i. e., those in which the grouping is asymmetric with regard to the atoms of nitrogen.

II. *Substances which without action on polarized light, and in spite of the identity of their constitutional (plane) formulae, and the characteristics which result therefrom, present differences in their chemical and physical behavior unexplainable by simple formulae.*

These substances are to be met with in the groups of cyclic compounds, and also in the unsaturated groups, or in those containing double bonds. For lack of a more precise term this class of compounds is called geometrical isomers. In the case of these isomers, stereochemistry assumes that the distance between the atoms is different. In order to distinguish, one might call substances in the first class, absolute stereoisomers. One finds bodies of this class among the derivatives of carbon and of nitrogen. We may subdivide the members of the second class under the following four heads :

α. Compounds characterized by one or more double bonds between two atoms of carbon. These are true geometrical isomers of carbon.

β. Saturated cyclic compounds.

γ. Compounds characterized by one or more double bonds *between an atom of carbon and an atom of nitrogen, or geometrical isomers of carbon and nitrogen.*

δ. Compounds characterized by double bonds between atoms of nitrogen or geometrical isomers of nitrogen.

PART I.—OPTICAL ISOMERISM

THE STEREOCHEMISTRY OF COMPOUNDS PRESENTING MOLECULAR ASYMMETRY

I. THEORY OF MOLECULAR ASYMMETRY OR OF THE ASYMMETRIC CARBON ATOM

Analogy between Crystalline Asymmetry and Molecular Asymmetry

The first cases of isomerism unexplained by ordinary plane formulae, were observed in the class of bodies grouped in Class I. These substances, alike for the most part in their properties, are distinguished by their action on polarized light whether in the liquid state or in solution. From their turning the plain of polarized light to the left, or to the right, they are called dextrorotatory or laevorotatory. These substances can be compared to a class of mineral compounds which have been known for a long time, the crystalline forms of which are active and present themselves in two modifications, left- and right-handed crystals.

But there is a fundamental difference between these two classes, the organic and the mineral isomers, and it is above all concerned with the disappearance or maintenance of these differences under distinct conditions.

The rotatory power of inorganic compounds has only been observed in the crystalline state. It disappears if the substance is converted into the amorphous condition, as in the case of melted silica, and when the substance is brought into solution as in the case of sodium chloride. It depends then on a peculiarity in the structure of the crystal itself since it disappears when the crystalline form is destroyed.

It was in connection with quartz that enantiomorphism was first discovered by Biot and Pasteur. The dextro- or laevorotatory individual crystals are really right- and left-handed ; they present hemi- or tetrahedral faces, non-superposable, the projection of which, on a cylinder, gives rise to a spiral, turning either to the left or to the right. Crystals, otherwise identical in form, are dissimilar, in that the one is the mirror image of the other. The cause of this rotatory power[1] results from the disposition in a helix, of the crystalline elements around the principal axis of the crystal.

The molecules themselves are inactive, but unite at the moment of crystallization to form elements of an asymmetric structure.

We know that if we arrange a number of layers of mica, one above the other, in such a way that each is turned in a definite direction through at an angle of 60° to the member next lower, that we obtain an artificially active system which is laevorotatory when the lamellae are superimposed with a left-handed turn, and vice versa.[2] Optical activity in this case depends on the form in which the material is arranged.

It is quite otherwise with the optically active organic substances, as these still preserve their optical properties in solution, and even in the gaseous state,[3] conditions

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[1] Sohucke : Zeit f. Kryst. und Min., 13, 229 ; Mallard : Ann d. Mines, 19, 256 (1881).

[2] Reusch : Pogg Ann., 138, 628 ; Frésnel's Works, 1, 460 and 505 ; Verdet: Optique Physique, 11, 201.

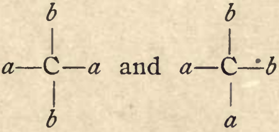
[3] Gernez: Ann. Éc. Normal. Sup. I; Guye and Do Amaral Arch. sc. ph. nat. Géneve, 1895.

under which the molecular aggregation is certainly destroyed.

The cause of this activity then, is not to be sought in the region of molecular physics, but in pure chemistry itself ; it should reside in the peculiar arrangement of the atoms in the molecule, and by analogy with the optically active crystals, it should be attributed to a sort of molecular enantiomorphism, or according to Pasteur, to molecular asymmetry. Van't Hoff and le Bel have since shown that this notion of molecular asymmetry can be reconciled with structural formulae, and that at once one acquires an idea which permits one to foretell, with perfect exactness, the number and the properties of optical isomers as well as other unexpected results which will be developed in the course of this work.[1]

Demonstration based on isomerism (Van't Hoff).—Constitutional formulae, such as one has been in the habit of using, are insufficient for the study of isomerism even in the very simplest cases.

If one considers (according to the principle announced above) that the four valences of carbon are four separate attractive forces acting in a plane, and acting at right angles to one another, then one should expect in the class of substances having the general formula, Ca_2b_2, two isomeric modifications



$$\begin{array}{c} b \\ | \\ a\text{—}C\text{—}a \\ | \\ b \end{array} \quad \text{and} \quad \begin{array}{c} b \\ | \\ a\text{—}C\text{—}b \\ | \\ a \end{array}$$

and should also find two isomers of the formula Ca_2bc and three in the case of $Cabcd$. No known facts correspond to the existence of so great a number of isomers.

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[1] Landolt's "Drehungsvermögen," 1879; Friedel: Rev. gen. des Sci., 4, 825.

All other arrangements of the valences in a plane surface lead to too great a number of modifications. It is not so, however, when one considers these valences as having a position in space.

As a matter of fact, the most simple way in which to dispose of four identical bonds connected with an atom of carbon, consists in arranging them symmetrically on a spherical surface, in which the carbon atom occupies the center of the sphere; in other words the four bonds should be situated at the summits of a regular tetrahedron of which the carbon atom occupies the center.

This fundamental hypothesis can be put forward in the following way:

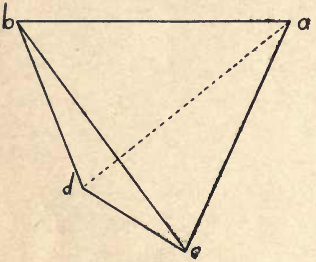

Fig. 1.

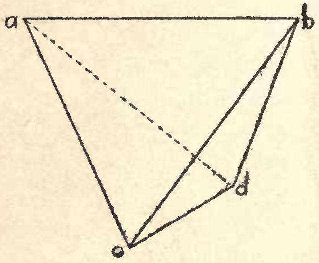

Fig. 2.

The four valences of the atom of carbon are directed towards the summits of a regular tetrahedron.

As a result of this proposition the compounds Ca_2b_2 and Ca_2bc cannot give isomers, but if an atom of carbon is bound to four different groups, one can conceive of two definite stereoisomers represented by figures 1 and 2.

With respect to the group *a*, the three radicals, *b*, *c*, *d*, are orientated in the inverse way in two figures. The molecules so formed, of which the elements are the same, and which only differ in their arrangement in space, are not superposable. They are the reflections, one of the other, in a mirror, and may be compared to the right hand placed opposite the left.

When an atom of carbon is in this way bound to four different groups it is called asymmetric.

NOTE.—It would be more logical to say that an asymmetric carbon atom is an atom of carbon so bound that it no longer contains the elements of symmetry. This is evident in the case of the compound C*abcd* but there are examples of compounds such as inosite $\underline{\text{CHOH. CHOH. CHOH. CHOH. CHOH. CHOH}}$ which though active are not characterized by a carbon atom united to four different radicals. In this case the activity is in relation with the disappearance of the elements of symmetry.—Guye and Gauthier.

The two isomers corresponding to the two formulae given above are called optical isomers or enantiomorphous compounds. In fact, there is a complete analogy between these asymmetric molecules and dissymmetric crystals, for in both cases the dissymmetry is the cause of the rotatory power.

From the point of view of descriptive geometry one can, in the same way as in the case of hemihedral crystals, produce a right- or left-handed helix passing through the four summits, and corresponding to the spiral mentioned in the case of the mica plates, as well as to the crystals which are naturally optically active. They can then represent substances of equivalent rotatory power, but with opposite signs in absolute values.

These substances are besides distinguished when they can be obtained in a crystalline state by true enantiomorphism, but as a result of complete equality of the interatomic distances all their other properties, physical as well as chemical, are absolutely the same.

The particular geometrical form of each tetrahedron has not been taken into account in the preceding development of this theory. It is, however, quite clear that the only molecules which can correspond to a regular tetrahedron with six planes of symmetry are those of the simple formula Ca_4. As the different radicals are bound in different ways to the carbon atom, and as they attract also by reason of their own affinities, it is probable that the form of these tetrahedra is more irregular than the different radicals themselves, so that the molecules of a compound Ca_2bc will be figured as tetrahedra with one plane of symmetry, and consequently, asymmetric molecules of the formulae $Cabcd$ are represented by molecules without a plane of symmetry, or by asymmetric figures of which one can construct two enantiomorphous forms. Finally, the carbon atom itself occupies an asymmetric position, and hence justly, may be called the asymmetric carbon atom. Actually in the present state of stereochemistry we can only consider as yet the question of the mean position of atoms in the molecule, and general notions of symmetry. One can, however, speculate on the relative distances between the atoms and neglect provisionally the precise form of the tetrahedra in each given case.

Demonstration based on molecular asymmetry (Le Bel). —This proof[1] at first sight appears somewhat more abstract than that of Van't Hoff and is developed quite independently of any hypothesis regarding valence.

If one parts with the notions of an atom and of a molecule, notions it is true hypothetical, but generally accepted by reason of the considerable number of facts of which they allow interpretation, one can conceive the molecule as being formed in two distinct ways.

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[1] Conférences Société Chimique, 1889-92, Paris, 1892.

(1) The atoms of which the molecule is composed have relatively, the one to the other, no mean fixed position. We shall designate this state of things as "internally" unstable or chaotic.

(2) The mean centers of gravity of the atoms which form the molecule are fixed relatively the one to the other, a state which in contradistinction we may term 'internal stability.' Different facts allow us to assume that the chemical molecule is in a state of stability. Besides, the study of substitution shows that certain groups or radicals such as benzene and naphthalene, are transported in their entirety from one molecule to another, and at the same time preserve their entity. In the same way in the aliphatic series a certain group, such as the isopropyl, remains different from the propyl, and the same difference is observed in the active and inactive amyl compounds, and in many other analogous cases also. These facts are clearly incompatible with a theory involving a chaotic state.

In the second place, isomerism itself is a proof in favor of a state of internal stability. We recognize numbers of cases of isomeric compounds, such as ethyl formate and methyl acetate which have the same molecular weight in the solid, liquid, and gaseous states; but nevertheless these compounds are quite distinct in their chemical and physical behavior. For a long time this has been attributed to a difference of arrangement of atoms in the molecule and this itself implies a certain internal stability.

(3) We can explain only with difficulty how, in a molecule in which the atoms were in a state of chaos, optical activity could be produced. We know that all active media are necessarily dissymmetric,[1] and that in

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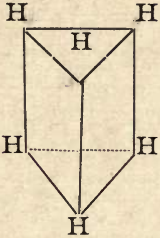
[1] Soret: Traité de Crystallographie, p. 41 (1893).

compounds which display this property in the solid, dissolved, and gaseous states, this activity can only be attributed to asymmetry taking place in the molecule itself. It cannot result from asymmetric aggregations of molecules, since cryoscopic measurements, the study of vapor-densities, and the method of Ramsay and Shields, have shown that aggregations of this sort do not, as a rule, exist in active compounds. Dissymmetry in active molecules cannot be conceived in a chaotic state which presupposes atomic movements which are absolutely irregular.

This necessary relation between rotatory power and asymmetry in the molecule already proposed by Biot, was demonstrated by the classic researches of Pasteur. It is, as with the principle of internal stability, at the basis of stereochemistry of active compounds. The idea of an active compound, on the other hand, is nothing more than a consequence of these two fundamental notions, and of the formulae developed in the course of modern chemistry.

We shall now come back to a characteristic property of these formulae ; *viz.*, mobile union. In the formulae as developed, the linking between two atoms of carbon is mobile.

Let one take as an example, ethane, $CH_3.CH_3$, and admit for an instant that absolute rigidity of the molecule takes place. Then the six atoms of hydrogen form two equilateral triangles parallel to one another, and in arranging in the most simple way, we have a prismatic figure, analogous to Ladenburg's prism formula for benzene :



As a consequence we should find three trichlor derivatives. But experimental evidence leads to two only; *viz.*, ethylene chlorid and ethylidene chlorid. Further, the synthetic reactions and the properties of these compounds show clearly that in the one case the two chlorin atoms are bound each to one carbon atom, while in the other, the two are united to the same carbon atom. As the most simple hypothesis which conceives of molecular rigidity furnishes us with more isomers than experience has shown, we must reject hypotheses which suggest rigid structures in cases which are more complicated.

The results of the consideration of this example, and of the consideration of a large number of analogous cases in which a series of isomers should exist, were there a rigid system, have failed completely to demonstrate that rotation does not take place. We must then conclude that radicals united by a single linking, are not fixed in an unalterable manner, or what comes to the same thing, that if fixed, they are held feebly, and this rigidity is rendered nil by the concussions of successive molecular shocks.

Finally, from the moment that we conclude that this orientation is not permanent, and that it is not able to be the cause of isomeric chemical compounds, we are led to assume that it is insufficient to produce optical isomerism, for this implies molecular asymmetry.

First Law.—Asymmetric Atoms

Let us consider a given molecule with a power of rotation, containing an atom A (carbon or nitrogen), bound to several monovalent atoms or radicals, R, R,′ R″. These radicals being united to A by mobile linking, their orientation can play no part, and they themselves will not be capable of producing asymmetry ; in a word, they act as if all their respective forces were concentrated on a point. Then the asymmetry which necessarily exists in the molecule (for we have assumed it to be active), cannot result from the permanent asymmetric disposition of the radicals, R, R′, R″, around A, or from an asymmetry existing in one of the radicals, R, for example, since this radical can be decomposed into its constituent groups to which we can apply the same reasoning. There must be then in one of these groups a polyvalent atom around which the radicals affect an asymmetric disposition, a condition which can only be fulfilled if they be not in the same plane. This atom will be called in future "asymmetric."

Such is the fundamental law of the asymmetric carbon or nitrogen atom, which is demonstrated by the consideration of mobile union alone (a fact based on purely experimental grounds), and which does not compel us to consider the nature of the forces which maintain equilibrium in the molecule. If we examine this question somewhat more closely, we shall see that the asymmetry due to the arrangement of these four or five radicals can be produced in two ways only :

(1) By their occupying, or not, different positions, these radicals are distinguished by their chemical deportment.

(2) Certain of the radicals are identical, but are distinguished by a peculiarity of orientation.

Facts correspond completely to the first condition, for as yet we know of no simple active compound with two identical radicals united to the atom which is in question, so that we are thus led to the second law.

Second Law.—The rotatory power disappears when two of the radicals united to the polyvalent atom become identical.

We have here an experimental truth to which there is no exception. An active compound becomes, in all cases, inactive when two of the atoms or radicals united to the carbon or nitrogen atom become similar, and cannot be split up by any known means into isomers having dextro- and laevo-rotatory power. We are thus led to specialize the first law. An active compound possesses necessarily, a carbon or nitrogen atom united to atoms or radicals, all different among themselves. As this concerns more particularly the carbon atom we are naturally led to the tetrahedral formula.

In fact, three of the radicals are situated in a plane, the three determining the plane, and the fourth, necessarily outside the plane, forms with the first three, a tetrahedron. This tetrahedron will be more or less changed in form, according to the substitutions which take place in the molecule, but by reason of the internal stability of the molecule the tetrahedral shape will still persist.

It should be here remarked that for compounds of the formula Ca_4 the tetrahedral plan is not necessarily regular if one takes away the notion of valence. In this case the equilibrium of the molecule Ca_4 is the resultant of the attractive or repulsive forces between each of the atoms a and the atom C, and between the atoms a themselves on the other hand. According to the intensity of these attractions or repulsions, we can conceive that the atoms *a* can group themselves in such a way as to form a symmetrical tetrahedron, but different at the same time from a regular tetrahedron. These conditions appear to be realized in the case of certain compounds of the formula $\mathbf{C}a_4$ such as carbon tetraiodid, CI_4, which does not crystallize in the cubic system, which ought to be the case did the molecule possess really a cubical symmetry corresponding to a regular tetrahedron. It must, however, be said that the observed crystalline forms are very near in symmetry to the cube, so that if the tetrahedron be not regular, it differs only in a very slight degree from that form.

II. THE CONSEQUENCES OF THE THEORY OF AN ASYMMETRIC CARBON ATOM, AND THEIR VERIFICATION

This theory is now based on so large a number of facts that it will suffice to mention some of the more striking examples.

a. *All active compounds contain at least one asymmetric carbon atom.*

Example: Lactic acid, $CH_3.\mathbf{CH}(OH).COOH$
Malic acid, $COOH.\mathbf{CHOH}.CH_2.COOH$
Asparagin, $COOH.\mathbf{CH}(NH_2).CH_2NH_2$
Leucin, $C_4H_9.\mathbf{CH}(NH_2).COOH$
Phenylglycollic acid, $C_6H_5.\mathbf{CHOH}.COOH$
Amyl alcohol, $(C_2H_5).CH_3.\mathbf{CH}.CH_2OH$
Ethyl amyl, $CH_3(C_2H_5).\mathbf{CH}.C_3H_7$
Tyrosin, $C_6H_4OH.CH_2.\mathbf{CH}(NH_2).COOH$
Tartaric acid, $COOH.\mathbf{CHOH}.\mathbf{CHOH}.COOH$
Mannite, $CH_2OH.(\mathbf{CHOH})_4.CH_2OH$
Saccharic acid, $COOH.(\mathbf{CHOH})_4.COOH$
Glucose, $CH_2OH(\mathbf{CHOH})_4.CHO$

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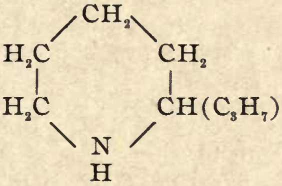
[1] Le Bel: Bull. Soc. Chim. (3), 3, 788.

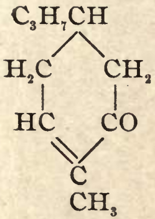
Besides these may be mentioned levulose, dextrin, and the greater number of the carbohydrates, turpentine and its derivatives, camphor, borneol, menthol, conicin, quinin, and many of the alkaloids, the glucosides and the class of albuminoids.

In many compounds the asymmetric carbon atom is to be found in a closed chain; *e. g.*,

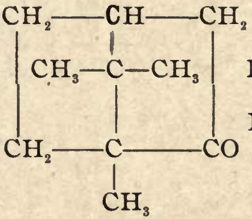


Conicin.[1]

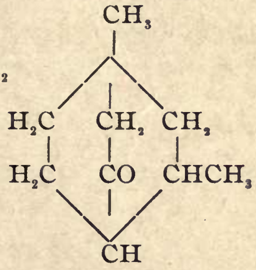
Camphor according to the formula adopted,



Kekulé

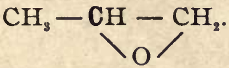


Bredt[2]



Bouveault[3]

and propylene oxid,



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[1] Ladenburg: Ber. d. chem. Ges., **19**, 2578, 2584.

[2] *Ibid.*, **26**, 3047.

[3] Bull. Soc. Chim. (3), **7**, 531.

b. *There are no active compounds without an asymmetric carbon atom.*

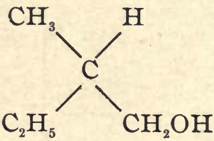
This fact, although at first contested, is now firmly established.

Some substances without an asymmetric carbon atom, such as propyl alcohol, $CH_3.CH_2.CH_2.OH$, styrol, $C_6H_5.CH:CH_2$, β-picolin, etc., were first considered active. It is now placed beyond a doubt that these substances in a state of purity are inactive. The activity was due to traces of active compounds. In the case of propyl alcohol, it was due to an admixture of active amyl alcohol, in the case of styrol to active principles which accompanied it in storax.

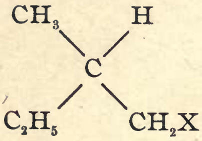
c. *The optical activity disappears when the asymmetric carbon atom becomes symmetrical.*

This is the case when the molecules **Cabcd** are transformed into **Cabc₂**. If the transformation does not destroy the asymmetry, the activity persists.

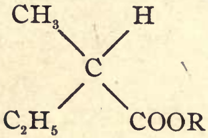
Active amyl alcohol has the formula



We already know more than forty derivatives: esters, halogen substitution products, amins, mercaptans, valeric acid, the aldehyde, etc., having the general formulae



and



All these compounds are active.[1]

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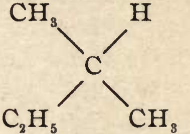
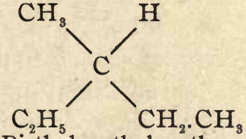
[1] Guye: Ann. chim. phys. (6), **25**, 145.

When the carbon atom remains asymmetric but the optical activity is lost the compound is called *racemic.*

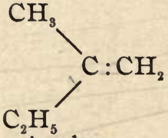
On the other hand all the derivatives which have lost their asymmetric structure are inactive ; *e. g.*,



Dimethyl ethyl methane.



Diethyl methyl methane.



Amylene.

This fact is also confirmed by the optical properties of the products of fermentation, so that, as we shall see further on, the compounds produced under these conditions are generally active when they contain an asymmetric carbon atom and are always inactive when they are of symmetrical structure. An example of the latter is the formation of succinic acid which is inactive from the following active compounds: the lactic, tartaric, malic, and aspartic acids, and starch.

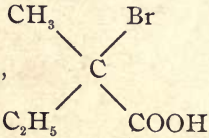
d. *All active compounds exist in two modifications which are identical except in their having opposite rotatory power.*

We have already had occasion to mention this natural sequence of the theory in speaking of optical isomerism.

We may take for examples the *l*- and *d*-tartaric acids, *l*- and *d*-malic acids, *l*- and *d*-asparagins, *l*- and *d*-phenyl glycollic acids, the *l*- and *d*conicins, *l*- and *d*-glyceric acids, and many others.

The only exceptions to this rule are substances with complex formulae of which we know as yet but one modification. The converse of propositions **a** and **b**, *viz.*, that all compounds containing an asymmetric carbon atom must be active, conform neither to the theory or to the facts adduced. On the contrary there exists a large number of compounds containing an asymmetric carbon atom, which are without action on polarized light.

e. *Inactive compounds with one asymmetric carbon atom are mixtures or equimolecular compounds of the laevo- and dextro rotatory isomers.*

As proof of this may be cited the fact that a great number of inactive compounds containing a single asymmetric carbon atom have been split up into their respective isomers by methods which will be given further on, while at the same time these same methods have not allowed us to isolate any active compound which does not contain an asymmetric carbon atom. As a reciprocal of the law formulated under **c**, one might expect that the rotatory power of a compound is transmitted to all its derivatives so long as the carbon remains asymmetric. This rule is not without exception, for although the salts, the esters, and amids of the active lactic, malic, valeric, and phenylglycollic acids are active, the halogen acids derived from them, *i. e.*, the α-brompropionic acid, $CH_3.CHBr.COOH$, dibromsuccinic acid, $COOH.CHBr.CHBr.COOH$, bromovaleric acid, , and phenylbromacetic acid, $C_6H_5.CHBr.COOH$, although dissymmetric are, known only in an inactive modification. One is thus led to ask if the simple difference in the four radicals saturating the valences of the carbon atom suffice to produce the power of rotation, or whether this does not depend also on other factors, *e. g.*, the nature of the radicals themselves.

A short time since, experimental evidence was lacking on this point but to-day numerous examples prove that the smallest difference between the four radicals or even the replacement of a halogen by a hydrogen suffices to bring out again the rotatory power.

Secondary amyl iodid, $CH_3.CHI.C_3H_7$, is active (le Bel) and so is the crystallized hexachlorohexane[1] made from mannite, $CH_2OH.(CHOH)_4.CH_2OH$, monochlorsuccinic acid, $COOH.CHCl.CH_2.COOH$, obtained in an active state by Walden[2] by the action of phosphorus pentachloride on malic acid, while the acid obtained by Kekulé[3] by the action of hydrobromic acid on malic acid is inactive. In this case it is certain that we are dealing with the racemic form. The many chlorhydrins and bromhydrins obtained from propylglycol, and the secondary alcohols, butanol, pentanol, hexanol, and heptanol, and from the ethyl tartrates and lactates are also inactive.[4] Recently Walden has multiplied these examples and has definitely demonstrated that the simple difference between the four radicals united to the carbon atom suffices to produce optical activity.[5] If the active compounds do not always give asymmetric active derivatives it is because certain reactions favor the formation of inactive mixtures (*vide* chapter on Phenomena of Racemization).

[1] Mourques : Compt. rend., **111**, 112.

[2] Ber. d. chem. Ges., **26**, 210.

[3] Ann. Chem. (Liebig), **130**, 21.

[4] Le Bel : Bull. Soc. Chim., (3), **9**, 674.

[5] Ber. d. chem. Ges., 1895.

III. COMPOUNDS WITH MORE THAN ONE ASYMMETRIC CARBON ATOM

The preceding developments of the theory have been concerned, strictly speaking, with compounds characterized by one asymmetric carbon atom, but they can be applied also to compounds containing an unlimited number of asymmetric groups, on condition that one takes into account certain complications which modify the properties of optical isomers, and also their number. It is better at first to meet an objection which strikes one naturally in considering the subject. These compounds consisting of two or more carbon atoms singly linked ought to be represented by two tetrahedra joined by their summits, and thus for ethane we should have the following :

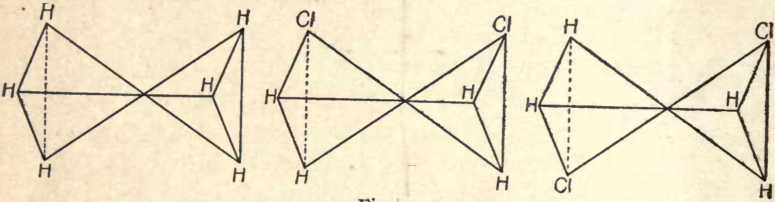


Fig. 3.

Certain derivatives ought, it would seem, to lead to different stereochemical isomers according to the distance separating the respective substituting atoms.

Thus, for ethylene chlorid, $CH_2Cl—CH_2Cl$, one can conceive, at least, of two isomeric forms (Fig. 4) which can be regarded as derived one from the other by a rotation of one of the tetrahedra around the common axis.

It should be the same in the case of compounds containing several asymmetric carbon atoms, such as the compound **Cabc.Cdef.** As cases of this kind have never been observed, we are not able to take them into account in the study of substances containing more than one asymmetric carbon atom, and we shall assume that the rotatory power, and the number of isomers depends exclusively on the number of asymmetric atoms and their + or — character. In this way, one will be able to treat the study of optical isomers independently of the principles involving a mobile union and of a special configuration to which we shall return later.

a. Number and nature of isomers.—Substances containing one asymmetric carbon atom exist, as we have seen in two optically active modifications which can be represented by + A and — A, if one designates by A the rotatory power of the asymmetric group.

Compounds with two asymmetric carbon atoms of the general formula **Cabc.Cdef** are active by reason of an active group A, and also by reason of another, B, both of which can exist in two active modifications. This gives thus four optical isomers :

1. + A	2. + A	3. — A	4. — A
+ B	— B	+ B	— B

1 and 4 have the same rotatory power, but of opposite sign, and this is the same with 2 and 3. They are, in fact, true enantiomorphous isomers. This explains why 1 and 4, and 2 and 3 can give rise to compounds or to equimolecular mixtures which are inactive, while 1 or 4 mixed in the same proportion with 2 or 3 give active mixtures.

Compounds with three asymmetric carbon atoms of the formula **Cabc—Cde—Cfgh** contain three active groups, A, B, and C. There are then $2^3 = 8$ isomers possible.

1. + A	2. + A	3. + A	4. + A
+ B	+ B	— B	— B
+ C	— C	+ C	— C
5. — A	6. — A	7. — A	8. — A
+ B	+ B	— B	— B
+ C	— C	+ C	— C

Among these modifications the compounds, 1 and 8, 2 and 7, 3 and 6, 4 and 5, represent substances with equal rotatory power, but with opposite signs. These will then form four racemic compounds.

Substances containing four asymmetric carbon atoms of the formula **Cabc—Cde—Cfg—Chik** will give as in the preceding cases $2^4 = 16$ isomers. The following table enumerates these isomers. Those placed one above the other differ only by the characteristic signs of the symbols, A, B, C, D.

	1	2	3	4
A	+	+	—	—
B	+	—	+	—
C	+	—	+	—
D	+	+	—	—

11	12	13	14	15	16	
+	+	+	+	+	—	A
+	+	+	—	—	+	B
+	—	—	+	—	—	C
—	+	—	—	—	—	D

5	6	7	8	9	10	
—	+	—	—	—	—	A
+	—	—	+	—	—	B
+	+	+	—	—	+	C
+	+	+	+	+	—	D

To formulate a general law, compounds containing n different asymmetric carbon atoms should exist to the number of 2^n forming $\frac{2^n}{2}$ pairs of bodies of equal rotatory power, but of opposite signs.

Number of optical isomers in the case of compounds with symmetric formulae.

When the structural formula of a substance with several asymmetric carbon atoms is itself symmetrical, the number of optical isomers is less than in the preceding cases. Compounds with two identical asymmetric carbon atoms, **Cabc—Cabc,** are characterized by two groups —**Cabc** with rotatory powers absolutely equal. Then A should equal B, and the configurations 2 and 3, among the four mentioned in speaking of two asymmetric carbon atoms, becoming identical, one should find but three isomers of which the rotatory power can be expressed in the following way:

$$(1).\ \begin{matrix}+A\\+A\end{matrix} = 2A.\quad (2).\ \begin{matrix}+A\\-A\end{matrix} = 0\quad (3).\ \begin{matrix}-A\\-A\end{matrix} = -2A$$

Two of the isomers, 1 and 3, are active enantiomorphous modifications; 2 is inactive in spite of the fact of its having two asymmetric carbon atoms for the optical effect of the $+A$ is compensated by that of $-A$, and in this manner the rotatory power is reduced to zero.

The inactivity of this kind of isomer is such that one is not able to split it into two optically active compounds. It is here that the difference lies between equimolecular mixtures or racemic compounds formed by the union of two molecules, right and left, and the non-racemic inactive compounds which are only found in the case of compounds containing two or more asymmetric carbon atoms. This point cannot be too strongly emphasized, for at one time the existence of an inactive non-racemic malic acid, $COOH.CH_2.CHOH.COOH$, was in doubt, the existence of which would have been in direct opposition to the theory of van 't Hoff and le Bel. This fact has been put beyond question by the researches of Bremer,[1] Anschütz,[2] and J. H. van 't Hoff.[3] The same reasoning can be applied to compounds having two asymmetric carbon atoms indirectly bound; *e.g.*, **Cabc—(Cd^2)$''$—Cabc.**

Compounds with three asymmetric carbon atoms of the type **Cabc—Cde—Cabc**, although apparently symmetrical, are not so by reason of the relation which the central groups holds to the other two, we may use the same figures as those employed on page 26.

	1.	2.	3.	4.
A	+	+	+	+
B	+	+	−	−
C	+	−	+	−

	5.	6.	7.	8.
A	−	−	−	−
B	+	+	−	−
C	+	−	+	−

Now A = C, then 2 and 5 should be identical. Besides 1 = 3 for with these two isomers the central carbon atom becomes symmetrical, two of its valences being saturated by radicals optically identical. (The identity of 1 and 3 is more easily seen by the use of models.) One will have in the same way 6 = 8. Altogether there remain but 4 isomers, which are :

A	+	+	+	−
B	o	−	+	o
C	+	−	−	−

Among these, the first and last are optical antipodes, while the other two, which are two figures non-superposable, and each having one plane of symmetry, are the non-racemic inactive compounds.

For substances with symmetrical structure with four asymmetric carbon atoms, **Cabc—Cde—Cde—Cabc,** the

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[1] Rec. Trav. Pays-Bas, 4, 180.

[2] Ber. d. chem. Ges., 18, 2713.

[3] *Ibid.*, 18, 2170.

asym — equi $a = \alpha$ $r = \alpha$
asym — pseudo — equi $T = 2^n$ $i = 2^{\frac{n}{2}}$

isomers are ten in number, for in making A = D in the formulae given in the table on page 28, the compounds numbered 5–10 become identical with those numbered 11–16, and in this way the 16 modifications are reduced to 10. Among these 10 isomers, 7 and 8 are inactive, through intramolecular compensation, and are not racemic, while the modifications, 1 and 4, 2 and 3, 5 and 9, 6 and 10, represent enantiomorphous compounds, and hence can form four inactive compounds by equimolecular mixture, which compounds are, however, cleavable into their optical constituents.

A careful analysis of cases permits the conclusion that compounds with n asymmetric carbon atoms, of which the structural formula is symmetrical, can give rise to N isomers, N being equal to $2^{\frac{n}{2}-1}\left(2^{\frac{n}{2}}+1\right)$ when n is an even number, and to 2^{n-1} when n is uneven.[1]

b. Representation of optical isomers. Projection formulae.—Different methods of representation have been proposed to bring out clearly the configuration of optical isomers. Models are often made use of among which those described by Friedlaender[2] are the simplest. They consist of small spheres to which are attached four pieces of India rubber tubing pointing in the direction of the four summits of a tetrahedron.

These four tubes represent the valences of a carbon atom, and to them can be attached other spheres of various colors to represent the different groups. These models allow one to grasp mentally the most complex cases of isomerism in an easy manner.

It is more difficult to represent on paper the configu-

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[1] Fischer: Ber. d. chem. Ges., **24**, 1839; **27**, 3208.

[2] *Ibid.*, **24**, 1839; **27**, 3208.

ration of the different isomers, for one must constantly keep in view the relations which the changing of certain groups to the right or to the left involves, as well as the bearing of the anterior or posterior groups on the configuration of the compound, and one unites + A with + A and — A with — A, for one then obtains the following figures :

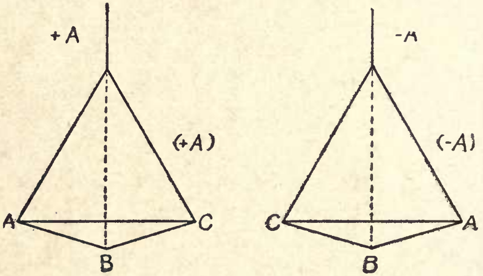


Fig. 4.

These difficulties do not present themselves, it is true, in the case of the compound **Cabc**, but it is necessary at once to take them into account in considering the figures which represent a compound of the type **Cabc—Cabc.**

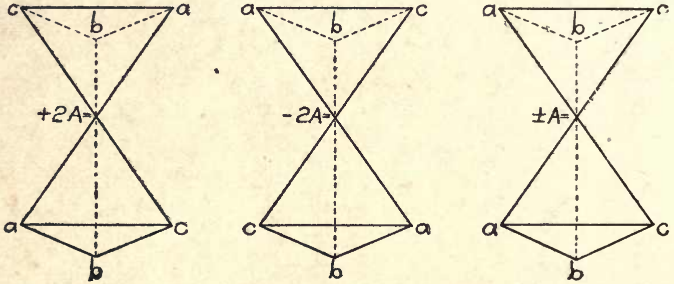


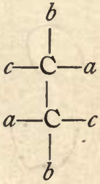
Fig. 5.

The three configurations of a system of this kind are easily comprehended if one observes each half system by itself.

In these figures it seems that the disposition of the groups *abc* and *cba* may have been inverted in passing from the inferior tetrahedron to the superior, in the same way that configuration 3 which represents two tetrahedra, inverted, seems, on the contrary, to be constituted of two identical tetrahedra. In looking at them in the other way one observes that they represent the configuration + A — A.

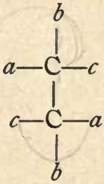
These perspective formulae can be advantageously replaced by projection formulae,[1] by projecting on the plane of paper, groups which are not in this plane.

In this way we obtain the following symbols for the three stereoisomers : **Cabc—Cabc.**



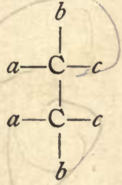
$$\begin{array}{c} b \\ | \\ c{-}\mathrm{C}{-}a \\ | \\ a{-}\mathrm{C}{-}c \\ | \\ b \end{array}$$

+ 2A



$$\begin{array}{c} b \\ | \\ a{-}\mathrm{C}{-}c \\ | \\ c{-}\mathrm{C}{-}a \\ | \\ b \end{array}$$

— 2A



$$\begin{array}{c} b \\ | \\ a{-}\mathrm{C}{-}c \\ | \\ a{-}\mathrm{C}{-}c \\ | \\ b \end{array}$$

± A

One will remark that the isomer ± A possesses also a a plane of symmetry, and this is the fundamental characteristic which marks all inactive non-racemic compounds.

We pass from + 2A to — 2A by rotating each carbon atom with its connected group, so that a certain group passes successively, through the space occupied by two other groups, *a* and *c* for example ; two successive rotations do not change the sign of the asymmetric carbon atom.

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[1] Fischer: Ber. d. chem. Ges., **24**, 2684.

More complicated configurations can in the same way be easily comprehended by using figures of this kind, so that in future these formulae will be exclusively employed in treating these cases of optical isomerism.

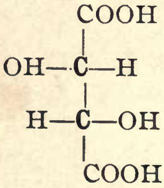
c. Principal examples of isomers with several asymmetric carbon atoms.—In general, it may be said, that the number of isomers that have been observed, is in perfect accord with theory. In the case of complex compounds, the number may be less than that which theory indicates, but it has never been found greater.

The classical example of compounds of symmetric structure and with two asymmetric carbon atoms is that of the tartaric acids.

$$COOH—CH(OH)—CH(OH)—COOH.$$

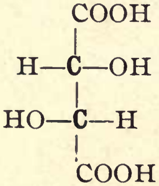
The laevo-, dextro-, and inactive tartaric acids are compounds of single molecular weight ; the racemic form of tartaric acid is double.

The *l*- and *d*-tartaric acids exhibit in their crystalline form a hemihedrism which is non-superposable. The racemic and inactive tartaric acids are without action on polarized light and do not present the above-mentioned crystalline peculiarity. The first is cleavable into two active components, the second is not. The formulae may be expressed as follows :



$$\begin{array}{c} COOH \\ | \\ OH—C—H \\ | \\ H—C—OH \\ | \\ COOH \end{array}$$

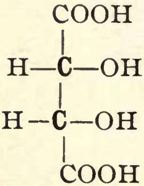
Dextro acid.



$$\begin{array}{c} COOH \\ | \\ H—C—OH \\ | \\ HO—C—H \\ | \\ COOH \end{array}$$

Laevo acid.

Racemic acid.



$$\begin{array}{c} COOH \\ | \\ H—C—OH \\ | \\ H—C—OH \\ | \\ COOH \end{array}$$

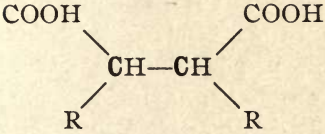
Inactive non-racemic acid.

The two synthetic erythrites obtained by Griner[1] represent a racemic form and an active non-cleavable form.

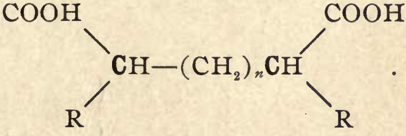
Dimethyl tartaric acid,

$$COOH—C(OH)CH_3—C(OH)CH_3—COOH,$$

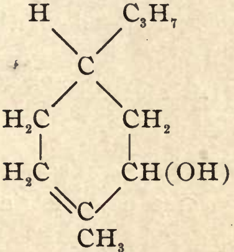
offers the same peculiarities.[2] In this group of compounds it is necessary again to class the numerous symmetrical substitution products, and in particular the dialkyl derivatives of succinic, glutaric, adipic, and pimelinic acids, corresponding to the following structural formulae,



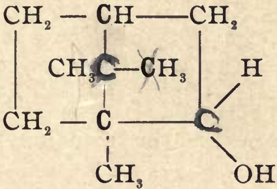
and



The borneols[3] are characterized by two asymmetric atomic groupings differing from one another, if one adopts Kekulé's view. On the other hand Bredt assumes camphor to have three of these groups:



Kekulé.



Bredt.

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[1] Compt. rend., **117**, 553; **119**, 723.

[2] Fittig: Ann. Chem. (Liebig), **249**, 207.

[3] Moutgolfier and Haller: Compt. rend., **105**, 227; **109**, 387; **110**, 149.

From what has been said on page 30, one ought to find at least four active modifications. There have been found two laevo- and dextrorotatory modifications which are stable and two which are unstable. Two of these isomers which are really enantiomorphous, combine racemically to give inactive molecules of double molecular weight, and the same properties are encountered in the bornyl urethanes investigated by Haller. Other examples may be cited which are, however, less complete. Thus among the belladonna alkaloids[1] we find two atropines *l* and *d* and the racemic modification the ordinary inactive alkaloid, but besides these three there is yet hyoscyamin, laevorotatory, having the same structure, but which is optically different from the *l*-atropine. The fourth isomer *d*-hyoscyamin has not as yet been isolated.

The esters and salts resulting from the combination of an active acid (+ or —) with an active base (+ or —) fall also into the same category. One may have them as compounds.

1. + acid + alcohol. 2. + acid — alcohol.
3. — acid + alcohol. 4. — acid — alcohol.

The pentatomic alcohols, aralite,[2] xylite,[3] adonite,[4] having the formula

$$CH_2OH.CHOH.CHOH.CHOH.CH_2OH,$$

and the corresponding trioxyglutaric acids,[5]

$$COOH.(CHOH)_3.COOH,$$

are symmetrical compounds containing three asymmetric

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[1] Ladenburg: Ber. d. chem. Ges., **21**, 3065.

[2] Kiliani: *Ibid.*, **20**, 1234.

[3] Bertrand: Bull. Soc. Chim., [3], **5**, 740.

[4] Fischer :Ber. d. chem. Ges., **26**, 638.

[5] Fischer: *Ibid.*, **24**, 4214.

atoms, and confirm the developments of the theory found on page 30.

The pentoses, alike in structure, arabinose, xylose, and ribose, $CH_2OH.CH(OH).CH(OH).CH(OH).CHO$, have an unsymmetrical formula. These three compounds are active, as are their derivatives, each having a distinct rotatory power, and the existence of their antipodes not being doubted, one conceives six isomers out of eight, which theory demands.

The ketoses,

$$CH_2OH.CHOH.CHOH.CHOH.CO.CH_2OH,$$

of which fructose is the best known example, belong also to this group.

Substances with four asymmetric carbon atoms are particularly interesting, by reason of their close relationship with glucose. Among the derivatives of this class, the hexatomic alcohols, $CH_2OH(CHOH)_4CH_2OH$, and the tetraoxyadipic or saccharic acids,[1]

$$COOH(CHOH)_4COOH,$$

are isomers of symmetrical structure. *L*- and *d*-mannite, *l*- and *d*-sorbite, *d*-talite and inactive non-racemic dulcite are also compounds belonging to this class.[2]

Of the saccharic acids the following have been isolated: *l*- and *d*-saccharic acids, and *l*-mannosaccharic acid,[3] *d*-mannosaccharic acid,[4] the inactive mucic and allomucic acids,[5] *l*- and *d*-isosaccharic acids,[6] *l*- and *d*-talomucic acids.[7]

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[1] Fischer, Piloty: Ber. d. chem. Ges., **24**, 1841, 2684.

[2] Crossley: *Ibid.*, **25**, 2564.

[3] Kiliani: *Ibid.*, **20**, 341.

[4] Fischer: *Ibid.*, **24**, 539; **27**, 384.

[5] Fischer: *Ibid.*, **24**, 2137.

[6] Tiemann: *Ibid.*, **17**, 246.

[7] Fischer: *Ibid.*, **24**, 3626.

In this case we have found by experiment the ten acids indicated by theory.

The aldoses,
$CH_2(OH).CH(OH).CH(OH).CH(OH).CH(OH).CHO$, are optical isomers of dissymmetric structure. Among these glucose, mannose, galose,[1] galactose, and idose are known under both laevo- and dextrorotatory forms. The detailed consideration of these compounds will be made the subject of another chapter.

IV. FORMATION OF ASYMMETRIC ACTIVE COMPOUNDS

a. Synthesis of racemic compounds from symmetric substances.—Compounds with asymmetric carbon atoms are not always optically active, for they present themselves often in the form of equimolecular mixtures of enantiomorphous isomers.

This is the case, without exception, for all the products obtained by synthetic methods. Compounds in an active state are not formed by laboratory reactions, and in order to isolate them, recourse must be often had to the help of living organisms. It was this fact which led one formerly to suppose that rotatory power is the action of a vital force.

Le Bel has shown[2] that the transformation of a symmetrical compound, by substitution, or by addition to an asymmetric compound, must always give rise to equimolecular quantities of laevo- and dextrorotatory isomers, and, if a symmetrical molecule $Cabc_2$ becomes asymmetric by the replacement of one of the groups c by group d (*e.g.*, transformation of propionic acid, $CH_3CH_2.COOH$, into lactic acid, $CH_3.CH(OH).COOH$, the two identical radicals (in the above example, the two hydrogen

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[1] Fischer, Piloty : Ber. d. chem. Ges., **24**, 526 ; Fischer : *Ibid.*, **24**, 532.

[2] Bull. Soc. Chim. (2), **22**, 246.

atoms) being symmetrically placed in the molecule, have an equal chance of being substituted.

If but one molecule participates in the reaction, substitution can be effected with the same probability on one side of the plane which passes between the two groups, *c*, as on the other; but as all chemical reactions take place between considerable numbers of molecules, and if substitution takes place, m times to the right and m' times to the left, the relations, $\frac{m}{m'}$, tend towards unity, for $m + m'$ increase beyond all limits; therefore, equal quantities of laevo and dextro compounds will be formed, and this mixture bears the general name of racemic.

It is the same in phenomena implying addition

$$C_2H_5.CH:CH_2 + HI = C_2H_5.CHI.CH_3.$$

The atoms of iodine which produce asymmetry will, in all probability, fix themselves on both sides of the plane of symmetry in an equal degree, and hence equal quantities of the two enantiomorphous compounds will be formed.

b. Cleavage of inactive mixtures in inactive isomers.—Chemical reagents act in the same way on laevo- or dextrorotatory isomers of which the combination has been termed racemic, and one cannot then hope to destroy one by a chemical reaction. It is for this reason that the methods of splitting are founded on other principles, *viz.*:

α. Action of living organisms, principally microorganisms.

β. Action of compounds already provided with rotatory power.

γ. Spontaneous cleavage with the formation of enantiomorphous crystals.

These three methods discovered by Pasteur have been used with success in the cleavage of a great number of synthetic inactive mixtures, and are to-day well established modes of dealing with these compounds. On the other hand, all efforts at cleavage, based on combination with compounds of symmetrical structure up to the present, have given negative results.

α. **Cleavage of inactive mixtures by means of living organisms.**—This purely physiological method is the oldest of the three above mentioned and was used for so long a time that it was thought that no optically active compound could be formed without the intervention of biological phenomena. It is probable that certain living organisms, asymmetric themselves, or at least containing active asymmetric compounds, have the power of attacking and destroying one of the two isomers in an active mixture. Hence it follows that the products of fermentation when containing an asymmetric carbon atom are nearly always optically active. To Le Bel is due a large number of cleavages based on this method.[1] Other investigators have also made interesting researches in this way.[2]

Examples.—Penicillium glaucum which has given such good results destroys the dextro isomers of racemic acid, synthetic secondary amyl alcohol, $CH_3.\mathbf{C}H(OH).C_3H_7$, propylene glycol, $CH_3.\mathbf{C}H(OH).CH_2OH$, glyceric acid, $COOH.\mathbf{C}H(OH).CH_2OH$, etc., and thus permits the isolation of the laevorotatory isomers. It produces the inverse effect on the following racemic compounds: primary amylic alcohol, $CH_3.C_2H_5.\mathbf{C}H.CH_2OH$, phenyl glycollic acid, $C_6H_5.\mathbf{C}H(OH)COOH$, lactic acid, CH_3.

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[1] Compt. rend., **87**, 213; **89**, 312; **92**, 532; etc.

[2] Lewkowitsch: Ber. d. chem. Ges., **15**, 1505; **16**, 1568, 2721.

CH(OH).COOH, etc., and in these cases it is the left modification which is destroyed and the right which persists. It is not a matter of indifference which micro-organism is employed as all do not act in the same manner on inactive mixtures. According to the ferment used one may obtain the dextro- or laevorotatory isomer. Thus while penicillium glaucum permits the isolation of the dextrogyrous phenylglycollic acid, saccharomyces ellipsoïdlus gives the laevorotatory compound (Lewkowitsch). Laevolactic acid has recently been obtained by the action of a new ferment on cane-sugar.[1] The active compounds found in the vegetable kingdom, the sugars, the starches, the terpenes, alkaloids, and albuminoids are very numerous and we can thus assume that the higher plants also favor cleavage. The animal body seems less prone to produce active compounds, but it does so nevertheless in certain cases in quite the same manner as plants in the sense that it destroys certain active modifications after ingestion of the corresponding racemic compound.[2]

The observations of Chabrie[2] on the degree of toxicity of the different modifications of tartaric acid furnish a new and very interesting confirmation of the varying action of optical isomers on the organism, and Fischer and Thierfelder have shown recently[3] that the phenomena of fermentation are in direct relation with the structure of the compounds investigated.

This method of cleavage is nevertheless restricted in its employment, for a great number of chemical compounds oppose the growth of micro-organisms and even arrest it. This is, of course, the case with antiseptics.

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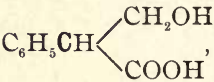
[1] Schardinger, Wiener Monatshefte, **11**, 545.

[2] Baumann: Ber. d. chem. Ges., **15**, 1731.

[3] *Ibid.*, **27**, 2031.

On the other hand does an asymmetric substance lend itself to the culture of a micro-organism, one may be fairly certain to effect splitting into one of its isomers. In very rare instances one has obtained the racemic compound, which is the case with ordinary lactic acid produced in the fermentation of ordinary cane-sugar. This can be explained by assuming that the micro-organisms act as readily on the laevo as on the dextro isomers. It is possible also that the lactic acid is produced from the fructose group only by hydrogenization of the ketone group, in this way producing equal amounts of both isomers.

β. **Splitting of inactive mixtures by means of active compounds.**—This method is based on the fact that inactive acids, combined with active bases, produce salts of which the properties, and in particular the solubilities, are different. These salts can be separated by fractional crystallization and allow thus the formation of the active acids. Active cinchonin, for example, permits the separation of tartaric, racemic, synthetic inactive malic, phenylglycollic, and phenylbromlactic acids. Quinin has been used with tropic acid,  $C_6H_5CH\begin{cases}CH_2OH\\COOH\end{cases}$[1], strychnin with phenyldibrompropionic acid, $C_6H_5.CH\text{-}Br.CHBr.COOH$ as well as with the numerous acids synthesized in the sugar group.

Conversely dextrotartaric acid has been used in the cleavage of synthetic conicin, of the alkyl piperidins, and of tetrahydro-*β*-naphthylamin.

In all these operations it is of advantage to start crystallization by means of a fragment of the dextro or laevo salt.

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[1] Ladenburg and Hundt: Ber. d. chem. Ges., **22**, 2590.

The attempts to produce the cleavage of a racemic alcohol by esterification with an active acid, and on the other hand of the combination of a racemic acid with an active alcohol, have so far yielded negative results.

γ. **Spontaneous separation of inactive mixtures by simple crystallization of the two enantiomorphous isomers.**—This method has only been successful in a small number of cases, as in that by Pasteur of ammonium sodium racemate. The solution of this salt deposits under certain conditions, enantiomorphous hemihedral crystals of the *l*- and *d*-tartrates which one separates by means of the lens and forceps.

Inactive asparagin, $COOH—CH(NH_2).CH_2—CONH_2$, prepared from fumaric and maleic esters always gives, by crystallization, two enantiomorphous modifications.[1] This method is of considerable theoretical importance, for it allows us to pass directly from inactive substances to those having optical properties without the intervention of micro-organisms, as Jungfleisch has proved that dioxysuccinic acid prepared by starting from ethylene and passing by means of the bromid, cyanid, succinic acid, and dibromsuccinic acid is a mixture of racemic acid and inactive tartaric acid.[2]

Curie has indicated recently the interesting observation that a mixture formed in a magnetic field, and an electric field is asymmetric, and could perhaps lend itself to separation, and perhaps to the formation of active substances by purely physico-chemical methods. Experimental verification of this is still wanting.[3]

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[1] Korner and Menozzi : Gaz. chim. ital., 1887, 226.

[2] Bull. Soc. Chim. [2], **19**, 194.

[3] Curie : Société française de physique, 1894, 53.

V. TRANSFORMATION OF ACTIVE INTO INACTIVE COMPOUNDS

a. Without change of configuration. Racemization.—The methods of separation by means of simple crystallization very rarely give good results, for the reason that enantiomorphous molecules have a certain tendency to unite one with another in the same way that active enantiomorphous crystals combine to give symmetrical forms.[1]

It is but natural that an equimolecular mixture of two enantiomorphous substances will be inactive, but up to the present these substances have not been considered as a simple mixture, but rather as a very unstable compound. These compounds have received the generic name racemic derived from the simplest of this class of substances, racemic acid. That it is really a true chemical compound is shown by its lesser solubility than either of its components, and its formation also gives rise to considerable loss of heat (441 calories). The active acids have a melting-point of 170° C., while that of the racemic compound is 204°.

In aqueous solution racemic acid is in great part decomposed into its constituents, and the decomposition increases with increased dilution. Its well-defined character as a true chemical compound has been proved by thermochemical measurements,[2] cryoscopy,[3] variation in specific gravity and electrical[4] properties.[5] The same peculiarities have been observed with salts and esters of

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[1] Gratha: Pogg. Ann., **158**, 214.

[2] Berthelot: Bull. Soc. Chim. (3), **4**, 246.

[3] Raoult: Ztschr. phys. Chem., **1**, 186.

[4] Marchlewsksy: Ber. d. chem. Ges., **15**, 1556.

[5] Ostwald: Ztschr. phys. Chem., **3**, 371.

racemic acid[1] with the fenchons,[2] and it is the same with the inosites from a thermochemical standpoint.[3]

The formation and the existence even in the solid state[4] of a racemic compound is dependent on certain conditions of temperature.[5] The racemic ammonio-sodium tartrate is only formed by the union of the laevo and dextro modifications above 28° ; below this temperature the right and left compounds crystallize out separately.

Racemic compounds deport themselves as substances containing water of crystallization, or as double salts, since the stability of compounds of this class is dependent on certain conditions of temperature.[6]

If certain enantiomorphous compounds, such as the asparagins, the hydrochloride of glutaminic acid and certain lactones of the saccharic acids[7] have not been obtained in a racemic state but always as a mixture of the opposite crystalline forms it is due doubtless to the fact that one does not know the conditions regulating the transformation. The converse has also been found with certain symmetrical modifications of the alkyl succinic acids which are probably racemic in character, but which as yet have not been separated.

b. Formation of inactive compounds starting from active compounds by the influence of heat and with change in configuration.—All active substances can, under certain conditions of temperature, lose their rotatory power, being changed into an inactive mixture

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[1] Anschütz : Ber. d. chem. Ges., **18**, 1397.

[2] Wallach : Ann. Chem. (Liebig), **272**, 108.

[3] Berthelot : Bull. Soc. Chim. (3), **4**, 246.

[4] Van't Hoff and Deventer : Ztschr. phys. Chem., **1**, 172.

[5] Wyrouboff : Ann. chim. phys. (6), **9**, 221.

[6] Van't Hoff and Deventer : Ztschr. phys. Chem., **1**, 65 and 227.

[7] Fischer : Ber. d. chem. Ges., **25**, 1025.

of the two enantiomorphous isomers; for example, in the case of a laevogyrate substance with n molecules there will be $\frac{n}{2}$ molecules transformed to the dextrogyrate variety.

The dextro and laevo modifications of an active compound having exactly the same stability, it is evident that if heat transforms one into the other, equilibrium will be established when the mixture contains the same number of molecules of both isomers; and this has been proved by considerations based strictly on thermodynamic laws.[1]

For example, *d*-tartaric acid heated to 165–175° C. is transformed into racemic acid and inactive tartaric acid; active phenylglycollic and aspartic acids become inactive at 180°; active amyl alcohol loses its activity when heated with sodium, and leucine, and tyrosine when heated with baryta.

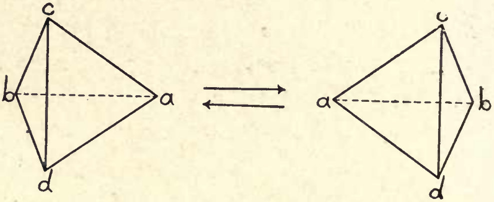

Fig. 6.

Structural formulae, even those with defined spatial relations, are insufficient to give a plausible explanation of these transformations. The passage of one configuration into another can only be conceived if one assumes that two of the groups bound to a carbon atom detach themselves, and change places with each other. It is

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[1] Van 't Hoff: Arch. Néerlandaise, 1886.

here that the difficulty arises if one keeps in mind the idea that one usually has of valence. It can, however, be completely avoided if, according to Werner,[1] one takes away the conception that valences are attractive forces oriented in space. Werner assumes that affinity is an attractive force acting at the surface of the atom which, for simplicity, is supposed to be spherical in shape. The four radicals occupy positions on this sphere corresponding to the summits of a regular tetrahedron because these positions correspond to the positions of greatest stability. Nevertheless, interatomic molecular movements take place, and can be considered as periodic pendulum-like oscillations around four points which are the tetrahedral summits, and the amplitude of these oscillations increases with the temperature.

In the most simple case the oscillation of the atoms *a*, *b*, *c*, *d*, can be considered as taking place in two planes perpendicular to one another as indicated by the arrows in Fig. 7. If the temperature is sufficiently high, the oscillations are sufficiently large to allow of the atoms occupying for an instant the position *abcd* in Fig. 8.

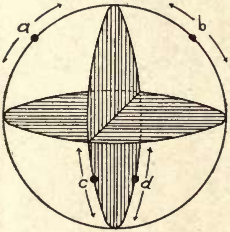

Fig. 7.

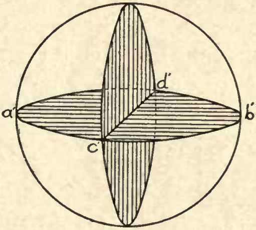

Fig. 8.

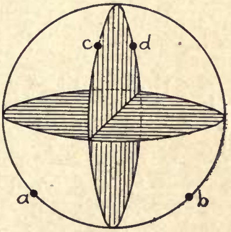

Fig. 9.

In this state the four atoms will be found in a plane of

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[1] Vierteljahrsschrift d. Zürcher Naturf. Ges., **26**, 1.

symmetry and may come back with equal probability to the old position Fig. 8 or to a new one which is the enantiomorph and which is shown in Fig. 9. One easily conceives that the two modifications can be thus formed in equal quantities and one obtains the racemic compound.

Such is, in a few words, Werner's theory of transformation and one can generalize this view in the following way:

The amplitude of atomic oscillations increases when the temperature is raised, the atoms of a simple asymmetric molecule pass through positions of symmetry and come to two positions which characterize a racemic compound.

Mention has been made of a certain number of active compounds giving inactive derivatives. This change should certainly be attributed to a spontaneous transformation of active compounds into their racemic isomers.

Racemization appears to depend on the mode of formation and the constitution of the compounds obtained.

Thus, inactive bromosuccinic acid,

$$COOH.CH_2.CHBrCOOH,$$

obtained from active malic acid,

$$COOH.CH_2.CH(OH).COOH,$$

has not as yet been separated into its isomers. This is a striking case of spontaneous racemization, for if one regenerates malic acid from this compound the product is inactive.

On the other hand active monochlorsuccinic acid has recently been made by starting from active malic acid by treating it, not as was formerly done by hydrochloric acid, but with phosphorus pentachlorid.[1]

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[1] Walden: Ber. d. chem. Ges., **26**, 210.

VI. REVIEW OF COMPOUNDS CONTAINING SEVERAL ASYMMETRIC CARBON ATOMS

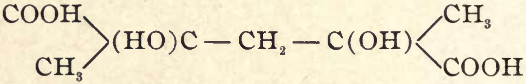
a. General properties of these compounds.—It has been shown that the optical isomers of a compound containing one carbon atom have identical properties with the exception of the sign of their rotatory power. This is not necessarily true in the case of substances containing more than one asymmetric group.

With the tartaric acids, *d* and *l* $(+ 2A)$ and $(l - 2A)$, the isomers are the image, one of the other, but it is different with the inactive compound $(+ A - A)$. This substance differs from the others, not only in that it does not exhibit enantiomorphism, but also because the distances between the atomic groupings are not the same.

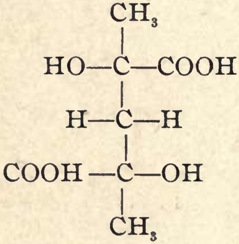
This acid also differs from its isomers, not only in its optical and crystallographic properties, but in its different chemical and physical behavior, especially in its melting-point, its solubility, and its electrical conductivity, and this may be said to hold good also for other non-racemic inactive compounds.

There are always, among the different isomers containing more than one carbon atom, two compounds of inverse rotatory power which can unite to form a third inactive substance. These isomers are designated by the same name, but are distinguished by the letters *d*, *l*, and *i*. The *d*-glucose (ordinary dextrorotatory grape-sugar) has an isomer *l*-glucose, and these combine to form *i*-glucose or racemic grape-sugar. The other isomers which differ in their chemical properties carry other denominations, *e.g.*, the aldoses with six carbon atoms are called *d*- and *l*-glucose, *d*- and *l*-mannose, *d*- and *l*-gulose, etc.

Stereochemical projection formulae permit one to see that certain reactions are dependent on configuration. It is thus that one can explain why in the case of the two dimethyl dioxyglutaric acids with the configurations, 1 and 2 only, that one which corresponds to Formula 2, can give a double lactone.

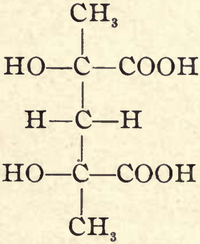


$$\mathrm{\begin{array}{c}COOH\\CH_3\end{array}\!\!>(HO)C-CH_2-C(OH)<\!\!\begin{array}{c}CH_3\\COOH\end{array}}$$



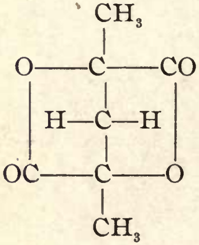
$$\mathrm{\begin{array}{c}CH_3\\|\\HO-C-COOH\\|\\H-C-H\\|\\COOH-C-OH\\|\\CH_3\end{array}}$$

2.



$$\mathrm{\begin{array}{c}CH_3\\|\\HO-C-COOH\\|\\H-C-H\\|\\HO-C-COOH\\|\\CH_3\end{array}}$$

1.



3.

The portion of the groups COOH and OH in Formula 1 gives rise to a single lactone only.

b. Synthesis of compounds containing several carbon atoms.

α. By means of inactive mixtures.—This method of synthesis leads generally to the formation of inactive compounds, but one usually obtains at the same time several substances of like structure, and which are easily separated. These cases of isomerism, which at one time were inexplicable, are in perfect accord with the theory of molecular asymmetry.

If one react on a racemic compound containing one asymmetric carbon atom, and hence of the formula, + A — A, with a second racemic compound of the formula

$+B-B$, then four stereoisomers can be formed, *viz*:

$$\text{with } +A\begin{cases}1.\quad +A+B\\ 2.\quad +A-B\end{cases}$$
$$\text{with } -A\begin{cases}3.\quad -A+B\\ 4.\quad -A-B\end{cases}$$

and of these compounds, 1 and 4, and 3 and 4, can unite to give the racemic compounds

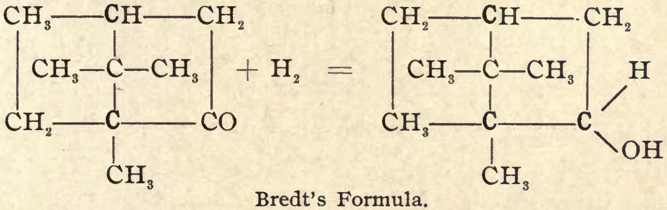
$$\begin{bmatrix}+A+B\\ -A-B\end{bmatrix}$$

and

$$\begin{bmatrix}-A+B\\ +A-B\end{bmatrix}.$$

These two racemic modifications should be different from one another, and hence by reason of their different behavior should be generally separated.

As an example of the above may be cited, the racemic borneols obtained by the reduction of camphor.



Bredt's Formula.

Other examples are: the addition products of the general formula $R.CHBr{-}CHBrCOOH$[1] derived from unsaturated acids, $R.CH:CHCOOH$. The succinic acids substituted by different hydrocarbon radicals, $COOH.CHR'.CHR''.COOH$,[2] the analogous glutaric acids and the glycols of asymmetric structure, $R'CH(OH){-}CH(OH)R''$.[3] All these products have been obtained in two

[1] Wislicenus: Ber. d. chem. Ges., **20**, 1010.

[2] Bischoff: *Ibid.*, **23**, 3422.

[3] Zincke: *Ibid.*, **17**, 708.

modifications which should be racemic, but which, with the exception of the borneols, have not as yet been separated. The general case is simplified when the synthetic compound has two identical asymmetric carbon atoms, **Cabc—Cabc,** and if to a racemic compound, + A — A, one adds the same compound + A — A.

Then starting from + A one obtains :

$$\begin{cases} 1.\ +A+A \\ 2.\ +A-A \end{cases}$$

and from — A

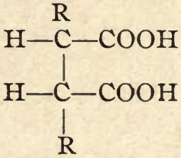
$$\begin{cases} 3.\ -A+A \\ 4.\ -A-A \end{cases}$$

The compounds, 1 and 4 can unite to form a racemic substance, while 2 and 3 represent the same substance which is inactive from intramolecular compensation. One obtains thus, two isomers which are easily separated of which the one is cleavable, while the other is not. The synthesis of the tartaric acids presents an excellent example. This acid obtained by starting from dibromsuccinic acid or glyoxal-cyanhydrin is a mixture of racemic acid and inactive tartaric acid.

The dialkylsuccinic and glutaric acids, the hydrobenzoins viewed as symmetrical diphenyl glycols, $C_6H_5.CH(OH)—CH(OH)C_6H_5$, with their two modifications, are comprised in this group of compounds, although their separation into active substances has not as yet been effected. Of the two isomers which are formed in these reactions, one is inactive from intramolecular causes, the other because of extramolecular compensation, and one can in certain cases decide with some certainty, which is the racemic compound and which is internally compensated.

Thus, the dialkylsuccinic acids may be represented by the following stereochemical formulae :

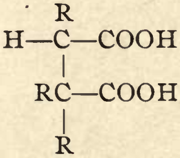
(1)



$$\begin{array}{l}\quad\;\;\text{R} \\ \text{H—C—COOH} \\ \quad\;\;| \\ \text{H—C—COOH} \\ \quad\;\;| \\ \quad\;\;\text{R}\end{array}$$

(*i*)

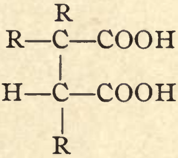
(2)



$$\begin{array}{l}\quad\;\;\text{R} \\ \text{H—C—COOH} \\ \quad\;\;| \\ \;\;\text{RC—COOH} \\ \quad\;\;| \\ \quad\;\;\text{R}\end{array}$$

(*r*)

(3)



$$\begin{array}{l}\quad\;\;\text{R} \\ \text{R—C—COOH} \\ \quad\;\;| \\ \text{H—C—COOH} \\ \quad\;\;| \\ \quad\;\;\text{R}\end{array}$$

(*l*)

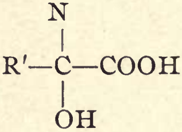
Racemic.

One of the two isomers melts at a temperature somewhat higher than the other, and is also less soluble. It hence is probable that it represents the para, while the other is assumed to be the antipode. One can compare the first to racemic acid, and it thus represents a combination of 2 with 3, while the anti-derivatives corresponds to inactive tartaric acid, and consequently can be represented by Formula 1.

β. Syntheses by means of compounds already active. —One may easily introduce a new asymmetric carbon atom, that is to say, a new element of asymmetry into a substance already active.

The grouping of a rotatory power of + A linked to another asymmetric group ± B can give rise to two isomers (+ A + B) and (+ A — B). There is, therefore, the formation of two optically active isomers without the possibility of racemization taking place. Substances which are produced in this way can be separated, and they differ not only in their rotatory power but in their properties.

Numerous examples can be cited: *e. g.*, *l*- and *d*-camphor each give two active borneols; the nitrosochlorids of *d*- and *l*-limonene furnish also four stereoisomeric nitrolamins[1]. By the addition of hydrocyanic acid and saponification (Winkler's reaction), the same active aldose or ketose gives two acids containing an atom of carbon more and with different optical and physical properties, the grouping R′—CO—H becoming



$$R'-\overset{\overset{\displaystyle N}{|}}{\underset{\underset{\displaystyle OH}{|}}{C}}-COOH$$

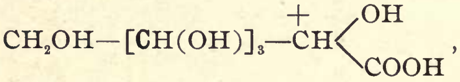
and consequently asymmetric.

Ordinary *l*-arabinose,

$$CH_2(CH).(CH(OH))_3.CHO,$$

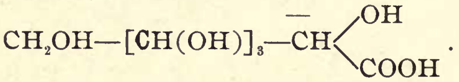
furnishes a mixture of two acids, *viz*:

Mannonic acid,



$$CH_2OH-[CH(OH)]_3-\overset{+}{C}H\left\langle\begin{matrix}OH\\COOH\end{matrix}\right.,$$

and gluconic acid,



$$CH_2OH-[CH(OH)]_3-\overset{-}{C}H\left\langle\begin{matrix}OH\\COOH\end{matrix}\right..$$

In these transformations the two isomers can be formed in unequal quantities, for by reason of the primitive asymmetry of the original compound, one of the two configurations of the new asymmetric group can be more stable than the other.

It is for this reason that in the above reaction, arabinose

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[1] Wallach: Ann. Chem. (Liebig), **252**, 106.

gives an excess of mannonic acid and little gluconic acid,[1] and the same takes place in many other like syntheses in the sugar series.

All these isomers differ not only in their physical properties, but in their chemical behavior, and in their stability. Thus, of the two isomers, mannonic and gluconic acid, the first alone gives a lactone.

c. Molecular transformations of active compounds with several asymmetric carbon atoms.—Isomers having several asymmetric groups have not all the same stability, and this is shown by the readiness with which certain members of a group undergo change.

It seems that each asymmetric atom tends to take up a position of equilibrium, which is characterized by optical inactivity, and which, according to Werner, can be conceived without supposing that the groups have altered their position only in this case by reason of the difference in configuration of the different carbon atoms, each is characterized by a certain velocity of racemization which is peculiar to itself. In other words, given an active compound $(+A-B)$ susceptible of molecular change, and in this compound the group $+B$ is transformed more easily into $-B$ than $+A$ into $-A$, then the compounds $(+A-B)$ will be formed in larger quantity and consequently the rotatory power will be modified.

If $(+A)$ be very stable and $(+B)$ unstable, or if for example, in the conditions of temperature under which the experiment takes place, only one of the two groupings is susceptible to transformation, the reaction can be interrupted at the end of the first phase. Such is the case when *d*-borneol is converted into *l*-borneol under the action of heat, or when *l*-menthol changes to *d*-menthol

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[1] Fischer: Ber. d. chem. Ges., **23**, 2611.

with sulphuric acid.[1] The same takes place with *l*-mannonic acid and *l*-gluconic acids for when heated with quinolin they are partly changed, one into the other, each giving a mixture containing the two acids.[2]

Inactive compounds, containing several asymmetric carbon atoms, react in an analogous manner. Racemic acid, when heated to 165°, yields inactive tartaric acid; the two inactive synthetic dimethyl succinic acids are transformed one into the other, on heating with hydrochloric acid.

The anti-modification of diethyl succinic acid under the same treatment yields the para compound, and this latter heated alone gives the anti-acid.[3] Certain chemical reactions favor these molecular changes, which can be seen in the behavior of the dimethylglutaric acids and of the bromin and hydroxyl derivatives.[4]

VII. DETERMINATION OF THE CONFIGURATION OF OPTICAL ISOMERS

In order to determine the absolute configuration of a given molecule, one must fix the exact position of the atoms therein, and in order to resolve this problem, a fundamental basis is lacking. The denomination as laevo and dextro, and of + and — of the two configurations which characterize the compound C*abcd* are quite arbitrary, and have only a relative significance. One can speak then, for the time being, only of the relative determination of the configuration of a compound, that is to say, to define the relationship which a certain compound with several asymmetric carbon atoms bears to its isomers.

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[1] Beckmann: Ann. Chem. (Liebig), **250**, 322.

[2] Fischer: Ber. d. chem. Ges., **23**, 2616.

[3] Bischoff: Ber. d. chem. Ges., **21**, 2102; **22**, 389; Selinsky: *Ibid.*, **24**, 3997.

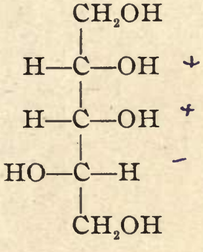
[4] Auwers: *Ibid.*, **25**, 3224.

The rotatory power of a compound allows the deduction of the configuration of compounds with two asymmetric carbon atoms of identical structure, such as the tartaric acids, both the *l*- and *d*-acids, the asymmetric groupings, —CH(OH)—COOH, should be of the same signification, and of opposite sign to the non-racemic inactive tartaric acid.

Among the more complex compounds, mention will be made only of some particularly instructive cases which are in direct relation with the synthesis, and the determination of the constitution of glucose and galactose by Emil Fischer.[1]

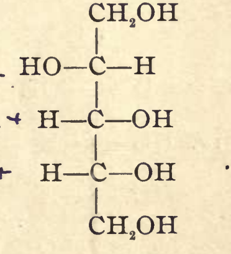
In the case of compounds with three asymmetric carbon atoms the pentites will be first taken up. These substances are symmetrical in constitution and the four modifications (*vide* page 30) can be expressed by the following projection formulae.

1.



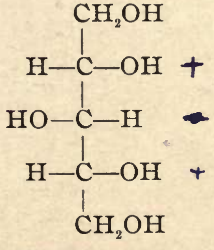
$$\begin{array}{rcll} & CH_2OH & & \\ & | & & \\ H— & C & —OH & + \\ & | & & \\ H— & C & —OH & + \\ & | & & \\ HO— & C & —H & - \\ & | & & \\ & CH_2OH & & \end{array}$$

2.



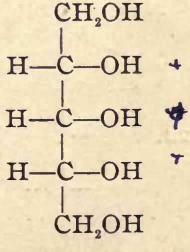
$$\begin{array}{lrcl} & & CH_2OH & \\ & & | & \\ - & HO— & C & —H \\ & & | & \\ + & H— & C & —OH \\ & & | & \\ + & H— & C & —OH \\ & & | & \\ & & CH_2OH & \end{array}$$

3.



$$\begin{array}{rcll} & CH_2OH & & \\ & | & & \\ H— & C & —OH & + \\ & | & & \\ HO— & C & —H & - \\ & | & & \\ H— & C & —OH & + \\ & | & & \\ & CH_2OH & & \end{array}$$

4.



$$\begin{array}{rcll} & CH_2OH & & \\ & | & & \\ H— & C & —OH & + \\ & | & & \\ H— & C & —OH & + \\ & | & & \\ H— & C & —OH & + \\ & | & & \\ & CH_2OH & & \end{array}$$

---

[1] Ber. d. chem. Ges., **23**, 2114 ; **27**, 3189.

Modifications 1 and 2 are active and enantiomorphous, while 3 and 4, having each a plane of symmetry, are inactive. Arabite, produced in the reduction of arabinose, is active. The arabites, *l* and *d*, correspond then to 1 and 2. Xylite, derived from xylose, and adonite, the reduction product of ribose, are inactive. The latter correspond then to formulae 3 and 4. The trioxyglutaric acids are known under the two active forms 1 and 2, and under the two inactive forms 3 and 4.

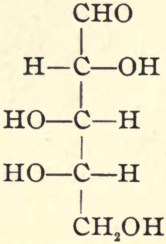
The two parent substances of the pentites, which will be treated of farther on,—*viz.*, arabinose and ribose,—have the asymmetric structure,

$$CH_2(OH)-[CH(OH)]_3-CHO,$$

the central carbon atom possessing this asymmetry. Dextroarabinose has thus one of the configurations 1*a* or 1*b*, derived from the preceding table, and laevo-arabinose 2*a* or 2*b*, derived from formula 2.

Dextroarabinose.

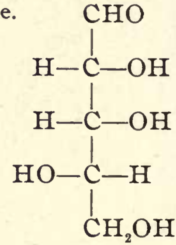
1*a*.



$$\begin{array}{r@{}c@{}l} & \mathrm{CHO} & \\ & | & \\ \mathrm{H-} & \mathrm{C} & \mathrm{-OH} \\ & | & \\ \mathrm{HO-} & \mathrm{C} & \mathrm{-H} \\ & | & \\ \mathrm{HO-} & \mathrm{C} & \mathrm{-H} \\ & | & \\ & \mathrm{CH_2OH} & \end{array}$$

or

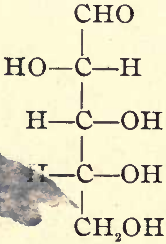
1*b*.



$$\begin{array}{r@{}c@{}l} & \mathrm{CHO} & \\ & | & \\ \mathrm{H-} & \mathrm{C} & \mathrm{-OH} \\ & | & \\ \mathrm{H-} & \mathrm{C} & \mathrm{-OH} \\ & | & \\ \mathrm{HO-} & \mathrm{C} & \mathrm{-H} \\ & | & \\ & \mathrm{CH_2OH} & \end{array}$$

Laevoarabinose.

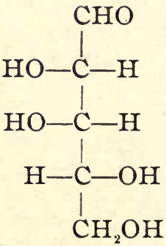
2*a*.



$$\begin{array}{r@{}c@{}l} & \mathrm{CHO} & \\ & | & \\ \mathrm{HO-} & \mathrm{C} & \mathrm{-H} \\ & | & \\ \mathrm{H-} & \mathrm{C} & \mathrm{-OH} \\ & | & \\ \mathrm{H-} & \mathrm{C} & \mathrm{-OH} \\ & | & \\ & \mathrm{CH_2OH} & \end{array}$$

or

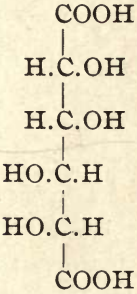
2*b*.



$$\begin{array}{r@{}c@{}l} & \mathrm{CHO} & \\ & | & \\ \mathrm{HO-} & \mathrm{C} & \mathrm{-H} \\ & | & \\ \mathrm{HO-} & \mathrm{C} & \mathrm{-H} \\ & | & \\ \mathrm{H-} & \mathrm{C} & \mathrm{-OH} \\ & | & \\ & \mathrm{CH_2OH} & \end{array}$$

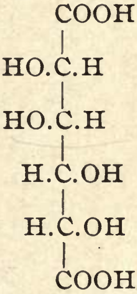
The saccharic or tetraoxyadipic acids are the most important derivatives with four asymmetric carbon atoms and of like structure. The following table represents the ten possible stereoisomers. The enantiomorphous isomers are bracketed together. The numbering is based on the same system as that used in the scheme on page 57.

1.



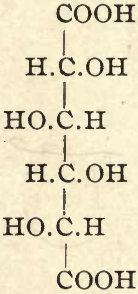
$$\begin{array}{c}\mathrm{COOH}\\ |\\ \mathrm{H.C.OH}\\ |\\ \mathrm{H.C.OH}\\ |\\ \mathrm{HO.C.H}\\ |\\ \mathrm{HO.C.H}\\ |\\ \mathrm{COOH}\end{array}$$

4.



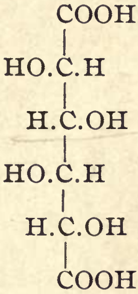
$$\begin{array}{c}\mathrm{COOH}\\ |\\ \mathrm{HO.C.H}\\ |\\ \mathrm{HO.C.H}\\ |\\ \mathrm{H.C.OH}\\ |\\ \mathrm{H.C.OH}\\ |\\ \mathrm{COOH}\end{array}$$

2.



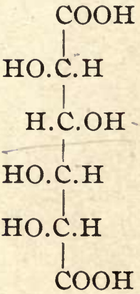
$$\begin{array}{c}\mathrm{COOH}\\ |\\ \mathrm{H.C.OH}\\ |\\ \mathrm{HO.C.H}\\ |\\ \mathrm{H.C.OH}\\ |\\ \mathrm{HO.C.H}\\ |\\ \mathrm{COOH}\end{array}$$

3.



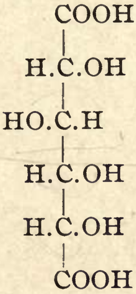
$$\begin{array}{c}\mathrm{COOH}\\ |\\ \mathrm{HO.C.H}\\ |\\ \mathrm{H.C.OH}\\ |\\ \mathrm{HO.C.H}\\ |\\ \mathrm{H.C.OH}\\ |\\ \mathrm{COOH}\end{array}$$

5.



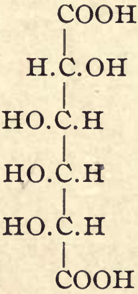
$$\begin{array}{c}\mathrm{COOH}\\ |\\ \mathrm{HO.C.H}\\ |\\ \mathrm{H.C.OH}\\ |\\ \mathrm{HO.C.H}\\ |\\ \mathrm{HO.C.H}\\ |\\ \mathrm{COOH}\end{array}$$

9.



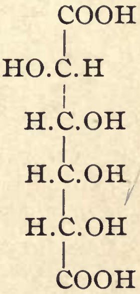
$$\begin{array}{c}\mathrm{COOH}\\ |\\ \mathrm{H.C.OH}\\ |\\ \mathrm{HO.C.H}\\ |\\ \mathrm{H.C.OH}\\ |\\ \mathrm{H.C.OH}\\ |\\ \mathrm{COOH}\end{array}$$

6.



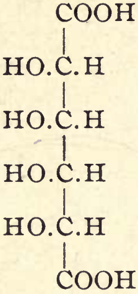
$$\begin{array}{c}\mathrm{COOH}\\ |\\ \mathrm{H.C.OH}\\ |\\ \mathrm{HO.C.H}\\ |\\ \mathrm{HO.C.H}\\ |\\ \mathrm{HO.C.H}\\ |\\ \mathrm{COOH}\end{array}$$

10.



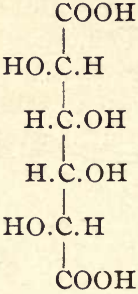
$$\begin{array}{c}\mathrm{COOH}\\ |\\ \mathrm{HO.C.H}\\ |\\ \mathrm{H.C.OH}\\ |\\ \mathrm{H.C.OH}\\ |\\ \mathrm{H.C.OH}\\ |\\ \mathrm{COOH}\end{array}$$

7.



$$\begin{array}{c} COOH \\ | \\ HO.C.H \\ | \\ HO.C.H \\ | \\ HO.C.H \\ | \\ HO.C.H \\ | \\ COOH \end{array}$$

8.



$$\begin{array}{c} COOH \\ | \\ HO.C.H \\ | \\ H.C.OH \\ | \\ H.C.OH \\ | \\ HO.C.H \\ | \\ COOH \end{array}$$

In this table formulae 1 and 4, 2 and 3, 5 and 9, 6 and 10 represent enantiomorphous isomers, while 7 and 8 denote compounds inactive by internal compensation.

As saccharic acid formed by the oxidation of glucose, $CH_2OH—(CH(OH))_4—CHO$, is active and laevo-rotatory it cannot be represented by either formula 7 or 8. It is also obtained, on the other hand, from gulose, a stereoisomer of *d*-glucose, therefore it cannot conform to formulae 1, 2, 3, or 14, as will be seen by consideration of the table on page 30. A single compound of symmetrical formula (*d*-saccharic acid) considered as a derivative of two compounds *d*-gulose and *d*-glucose can only be represented by the formulae 5 to 10. For saccharic acid one has only the choice between 5 and 9 and 6 and 10, which represent respectively enantiomorphous isomers. As one has observed the dextro and laevo modifications of this acid one selects, by the following considerations, formulae 6 and 10 to represent these isomers:

Glucose and mannose are aldoses of identical structure except that they differ by the carbon atom which is next to the aldehyde group and which is in the following formula[1] marked by an asterisk.

$$CH_2(OH)\text{-}CH(OH)\text{-}CH(OH)\text{-}CH(OH)\text{-}CH(OH\overset{*}{)}\text{-}CHO.$$

The derivatives of these two sugars are identical when the group $—CH(OH)^*—$ becomes symmetrical. They both give for example the same osazone. These remarks also apply to the monobasic acids derived from these two aldoses, the gluconic and mannonic acids

$$CH_2(OH)—(CH(OH))_4—COOH$$

and the same also with the dibasic acids, ordinary saccharic acid and mannosaccharic acid,

$$COOH—(CCH(OH))_4—COOH.$$

But, if saccharic acid had the configuration 6, or what is the same 10, mannosaccharic acid should correspond to 7 or 8 and consequently be inactive. Mannosaccharic acid is, however, active and hence it follows that *l*- and *d*-saccharic acids cannot be represented by formulae 6 and 10 but only by formulae 5 and 9.

It is impossible to absolutely decide which of the configurations, 5 or 9, correspond to the laevo or dextro acid. For convenience ordinary *d*-saccharic acid will be designated by 5 and *l*-saccharic acid by 9.

Configuration of glucose, mannose, gulose, and fructose. —Two different asymmetric aldoses correspond to the symmetric *d*-saccharic acid; they are the two aldoses which on oxidation give this acid; *viz.*, *d*-glucose and *d*-gulose, of which the formulae are according to the preceding view.

As has been seen, these two compounds lead to the same derivative when the terminal alcohol and aldehyde groups are oxidized to carboxyl. That *d*-glucose corre-

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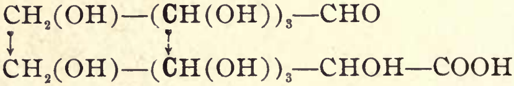
[1] Fischer: Ber. d. chem. Ges., **24**, 1836.

sponds to **a** and *d*-gulose to **b** is shown in the following way:

In being oxidized to saccharic acid glucose gives as a first product *d*-gluconic acid,

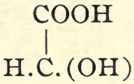
$$CH_2(OH)—(CH(OH))_4—COOH.$$

This identical *d*-gluconic acid is formed at the same time with the stereoisomeric mannonic acid when the nitrile of arabinose is saponified.



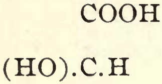
$$\begin{array}{l} CH_2(OH)—(\mathbf{C}H(OH))_3—CHO \\ \downarrow \qquad\qquad\quad \downarrow \\ CH_2(OH)—(\mathbf{C}H(OH))_3—CHOH—COOH \end{array}$$

From a stereochemical point of view this reaction introduces a new asymmetric carbon atom and at the same time forms two stereoisomeric acids. From what has been proved on page 58 regarding the constitution of arabinose, *d*-gluconic acid derived from *d*-arabinose can only be represented by one of the following four formulae according as one replaces the CHO in the two formulae on page 58 by



$$\begin{array}{c} COOH \\ | \\ H.C.(OH) \end{array}$$

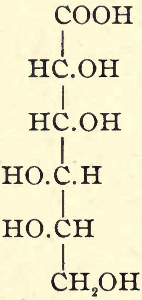
or



$$\begin{array}{c} COOH \\ | \\ (HO).C.H \end{array}$$

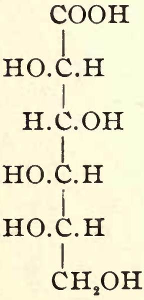
Thus:

1*a*,*α*.



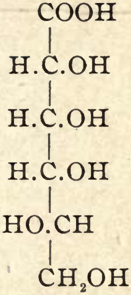
$$\begin{array}{c} COOH \\ | \\ HC.OH \\ | \\ HC.OH \\ | \\ HO.C.H \\ | \\ HO.CH \\ | \\ CH_2OH \end{array}$$

1*a*,*β*.



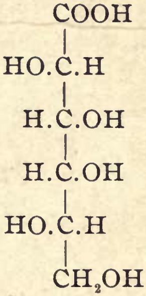
$$\begin{array}{c} COOH \\ | \\ HO.C.H \\ | \\ H.C.OH \\ | \\ HO.C.H \\ | \\ HO.C.H \\ | \\ CH_2OH \end{array}$$

1*b*,α.



$$\begin{array}{c}\mathrm{COOH}\\ |\\ \mathrm{H.C.OH}\\ |\\ \mathrm{H.C.OH}\\ |\\ \mathrm{H.C.OH}\\ |\\ \mathrm{HO.CH}\\ |\\ \mathrm{CH_2OH}\end{array}$$

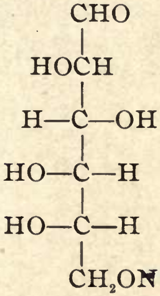
1*b*,β.



$$\begin{array}{c}\mathrm{COOH}\\ |\\ \mathrm{HO.C.H}\\ |\\ \mathrm{H.C.OH}\\ |\\ \mathrm{H.C.OH}\\ |\\ \mathrm{HO.C.H}\\ |\\ \mathrm{CH_2OH}\end{array}$$

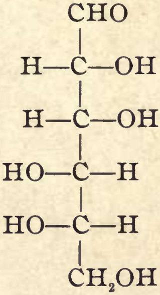
In order to pass from these formulae to that of glucose it is only necessary to replace the carboxyl by an aldehyde group, and one then sees that formula 1*a*,β is the only one agreeing with either of the two formulae deduced for saccharic acid—in this case formula *b*.

Glucose should then be represented by the formula :



$$\begin{array}{c}\mathrm{CHO}\\ |\\ \mathrm{HOCH}\\ |\\ \mathrm{H—C—OH}\\ |\\ \mathrm{HO—C—H}\\ |\\ \mathrm{HO—C—H}\\ |\\ \mathrm{CH_2OH}\end{array}$$

and mannose



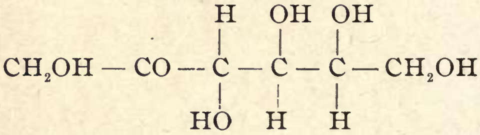
$$\begin{array}{c}\mathrm{CHO}\\ |\\ \mathrm{H—C—OH}\\ |\\ \mathrm{H—C—OH}\\ |\\ \mathrm{HO—C—H}\\ |\\ \mathrm{HO—C—H}\\ |\\ \mathrm{CH_2OH}\end{array}$$

From these results it follows that among the formulae given on page 58 1*a* and 2*a* are those which should be chosen to represent *d*- and *l*-arabinose respectively.

The configuration of the other stereoisomeric aldoses such as mannose and gulose, and of the ketoses, can also be deduced in the same manner.

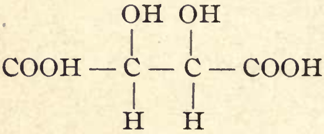
Gulose may then be represented by formula *a;* the formula for mannose differs from that of glucose by a spatial difference in the asymmetric group connected with the aldehyde group.

Mention may be made here of *d*-fructose whose configuration may be represented by the following:



$$\mathrm{CH_2OH-CO-\underset{\underset{HO}{|}}{\overset{\overset{H}{|}}{C}}-\underset{\underset{H}{|}}{\overset{\overset{OH}{|}}{C}}-\underset{\underset{H}{|}}{\overset{\overset{OH}{|}}{C}}-CH_2OH}$$

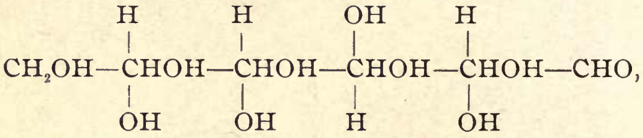
for both *d*-fructose and *d*-glucose give the same osazone, and the ketose on oxidation is transformed into inactive tartaric acid.



$$\mathrm{COOH-\underset{\underset{H}{|}}{\overset{\overset{OH}{|}}{C}}-\underset{\underset{H}{|}}{\overset{\overset{OH}{|}}{C}}-COOH}$$

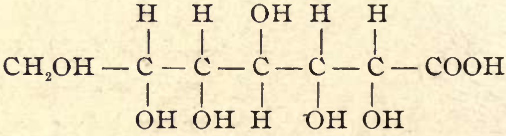
Configuration of the glucoheptoses.—By addition of hydrocyanic acid and saponification, one obtains from glucose, two compounds, the α- and β-glucoheptonic acids.

Glucose having the formula

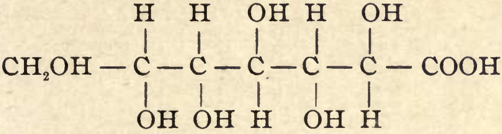


$$\mathrm{CH_2OH-\underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{CHOH}}-\underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{CHOH}}-\underset{\underset{H}{|}}{\overset{\overset{OH}{|}}{CHOH}}-\underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{CHOH}}-CHO,}$$

these two acids can only be represented by the following:

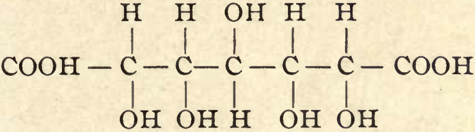
I. 

$$\mathrm{CH_2OH-\underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{C}}-\underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{C}}-\underset{\underset{H}{|}}{\overset{\overset{OH}{|}}{C}}-\underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{C}}-\underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{C}}-COOH}$$

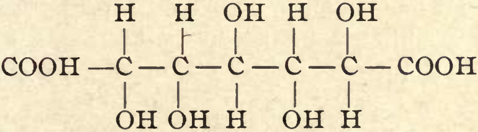
II. 

$$CH_2OH-\underset{OH}{\overset{H}{C}}-\underset{OH}{\overset{H}{C}}-\underset{H}{\overset{OH}{C}}-\underset{OH}{\overset{H}{C}}-\underset{H}{\overset{OH}{C}}-COOH$$

By oxidation, each of these is transformed into a dibasic acid.

I′. 

$$COOH-\underset{OH}{\overset{H}{C}}-\underset{OH}{\overset{H}{C}}-\underset{H}{\overset{OH}{C}}-\underset{OH}{\overset{H}{C}}-\underset{OH}{\overset{H}{C}}-COOH$$

II′. 

$$COOH-\underset{OH}{\overset{H}{C}}-\underset{OH}{\overset{H}{C}}-\underset{H}{\overset{OH}{C}}-\underset{OH}{\overset{H}{C}}-\underset{H}{\overset{OH}{C}}-COOH$$

Of the two pentoxypimelinic acids, one only can be active, for I′ represents a symmetrical compound; that is, an inactive acid which is uncleavable.

According to experiment, α-glucoheptonic acid gives an active pentoxypimelinic acid, while the β-acid gives an inactive compound. Of the two formulae above given, I must then represent the α-acid and II the β-compound. These two acids give, on reduction, two glucoheptites, α and β, of which the constitution was thus determined.[1]

Configuration of the mucic and talomucic acids.[2]—Rhamnose, $CH_3.(CHOH)_4.CHO$, gives an oxidation *l*-trioxyglutaric acid identical with that obtained on the oxidation of arabinose. The configuration of arabinose being known, we have for *l*-trioxyglutaric acid the formula,

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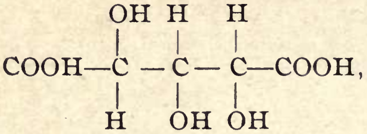
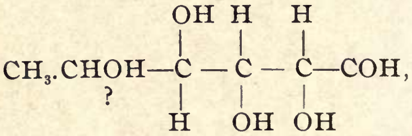
[1] Fischer: Ann. Chem. (Liebig), **270**, 71.

[2] Fischer: Ber. d. chem. Ges., **27**, 384.



$$\mathrm{COOH{-}}\underset{\mathrm{H}}{\overset{\mathrm{OH}}{\mathrm{C}}}\mathrm{{-}}\underset{\mathrm{OH}}{\overset{\mathrm{H}}{\mathrm{C}}}\mathrm{{-}}\underset{\mathrm{OH}}{\overset{\mathrm{H}}{\mathrm{C}}}\mathrm{{-}COOH},$$

and for rhamnose,

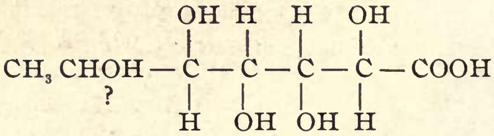


$$\underset{?}{\mathrm{CH_3.CHOH}}\mathrm{{-}}\underset{\mathrm{H}}{\overset{\mathrm{OH}}{\mathrm{C}}}\mathrm{{-}}\underset{\mathrm{OH}}{\overset{\mathrm{H}}{\mathrm{C}}}\mathrm{{-}}\underset{\mathrm{OH}}{\overset{\mathrm{H}}{\mathrm{C}}}\mathrm{{-}COH},$$

the sign ? being placed under the group CHOH to indicate that its configuration is not shown in this relation.

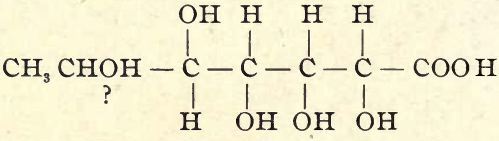
On the other hand, rhamnose adds hydrocyanic acid according to Winkler's reaction and on saponification yields an α-rhamnohexonic acid which is transformed into β-rhamnohexonic acid on heating with pyridin and water to 140°–150°. According to the formula for rhamnose, these two acids can be expressed in the following way:

I.



$$\underset{?}{\mathrm{CH_3\,CHOH}}\mathrm{{-}}\underset{\mathrm{H}}{\overset{\mathrm{OH}}{\mathrm{C}}}\mathrm{{-}}\underset{\mathrm{OH}}{\overset{\mathrm{H}}{\mathrm{C}}}\mathrm{{-}}\underset{\mathrm{OH}}{\overset{\mathrm{H}}{\mathrm{C}}}\mathrm{{-}}\underset{\mathrm{H}}{\overset{\mathrm{OH}}{\mathrm{C}}}\mathrm{{-}COOH}$$

II.



$$\underset{?}{\mathrm{CH_3\,CHOH}}\mathrm{{-}}\underset{\mathrm{H}}{\overset{\mathrm{OH}}{\mathrm{C}}}\mathrm{{-}}\underset{\mathrm{OH}}{\overset{\mathrm{H}}{\mathrm{C}}}\mathrm{{-}}\underset{\mathrm{OH}}{\overset{\mathrm{H}}{\mathrm{C}}}\mathrm{{-}}\underset{\mathrm{OH}}{\overset{\mathrm{H}}{\mathrm{C}}}\mathrm{{-}COOH}$$

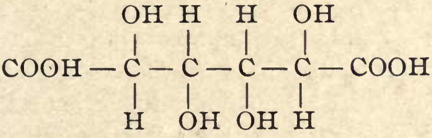
These acids, therefore, differ only in the relation of the CHOH group with the carboxyl.

Finally, if one oxidizes α-rhamnohexonic acid, mucic acid is obtained, known for a long time as an inactive compound, and the *β*-acid gives, in the same way, *l*-talomucic acid. These relations may be expressed as follows:

$$\begin{tikzcd}
\text{Rhamnose} \arrow[r] \arrow[d] & \left\{\begin{array}{l}\alpha\text{-rhamno-}\\ \text{hexonic acid}\end{array}\right. \arrow[r] \arrow[d] & \left\{\begin{array}{l}\beta\text{-rhamno-}\\ \text{hexonic acid}\end{array}\right. \arrow[d] \\
l\text{-trioxyglutaric acid.} & \text{Mucic acid.} & l\text{-talomucic acid.}
\end{tikzcd}$$

It will be shown farther on that in these reactions the methyl group is eliminated. Then the product of oxidation of acid I has the formula:

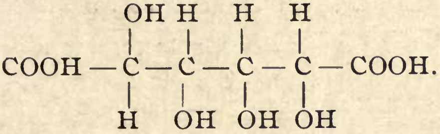
I'.



$$\begin{array}{ccccccccc} & & \text{OH} & & \text{H} & & \text{H} & & \text{OH} \\ & & | & & | & & | & & | \\ \text{COOH} & - & \text{C} & - & \text{C} & - & \text{C} & - & \text{C} & - \text{COOH} \\ & & | & & | & & | & & | \\ & & \text{H} & & \text{OH} & & \text{OH} & & \text{H} \end{array}$$

and that derived from II,

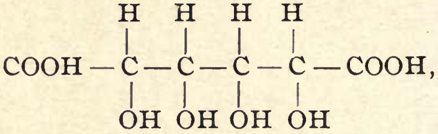
II'



$$\begin{array}{ccccccccc} & & \text{OH} & & \text{H} & & \text{H} & & \text{H} \\ & & | & & | & & | & & | \\ \text{COOH} & - & \text{C} & - & \text{C} & - & \text{C} & - & \text{C} & - \text{COOH.} \\ & & | & & | & & | & & | \\ & & \text{H} & & \text{OH} & & \text{OH} & & \text{OH} \end{array}$$

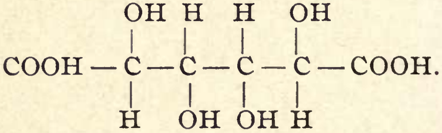
Formula I' is characterized by a plane of symmetry. It represents then an inactive acid, and hence can be none other than mucic acid. On the other hand, II' represents an active compound, and thus corresponds to *l*-talomucic acid. Hence *α*-rhamnohexonic acid is represented by Formula I, and *β*-rhamnohexonic acid by Formula II.

In order to prove that in these reactions the group CH_3 is eliminated, mucic acid will be taken up as an example. Being inactive it can only be represented by a symmetrical formula such as:



$$\begin{array}{ccccccccccc} & & \mathrm{H} & & \mathrm{H} & & \mathrm{H} & & \mathrm{H} & & \\ & & | & & | & & | & & | & & \\ \mathrm{COOH} & - & \mathrm{C} & - & \mathrm{C} & - & \mathrm{C} & - & \mathrm{C} & - & \mathrm{COOH,} \\ & & | & & | & & | & & | & & \\ & & \mathrm{OH} & & \mathrm{OH} & & \mathrm{OH} & & \mathrm{OH} & & \end{array}$$

or equally well by

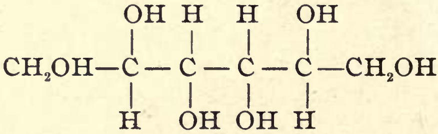


$$\begin{array}{ccccccccccc} & & \mathrm{OH} & & \mathrm{H} & & \mathrm{H} & & \mathrm{OH} & & \\ & & | & & | & & | & & | & & \\ \mathrm{COOH} & - & \mathrm{C} & - & \mathrm{C} & - & \mathrm{C} & - & \mathrm{C} & - & \mathrm{COOH.} \\ & & | & & | & & | & & | & & \\ & & \mathrm{H} & & \mathrm{OH} & & \mathrm{OH} & & \mathrm{H} & & \end{array}$$

One sees at a glance that both these formulae are incompatible with that of rhamnose when the transformation of that compound into mucic acid would result from the replacement of the groups, CH_3 by COOH and the elimination of CHO. In this way have the formulae for mucic and *l*-talomucic acids been definitely established.

Configuration of dulcite, galactose, talose and the galactonic and talonic acids.—Galactose, $CH_2OH—(CHOH)_4—CHO$, gives on oxidation mucic acid and on reduction dulcite, $CH_2OH.(CHOH)_4.CH_2OH$, a compound which for some time was believed to be active but which has since been found to be without action on polarized light.

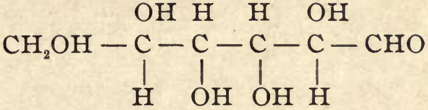
The configuration of mucic acid being established the formula for dulcite will be



$$\begin{array}{ccccccccccc} & & \mathrm{OH} & & \mathrm{H} & & \mathrm{H} & & \mathrm{OH} & & \\ & & | & & | & & | & & | & & \\ \mathrm{CH_2OH} & - & \mathrm{C} & - & \mathrm{C} & - & \mathrm{C} & - & \mathrm{C} & - & \mathrm{CH_2OH} \\ & & | & & | & & | & & | & & \\ & & \mathrm{H} & & \mathrm{OH} & & \mathrm{OH} & & \mathrm{H} & & \end{array}$$

and for galactose

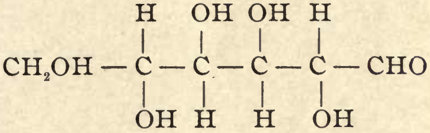
A.



$$CH_2OH - \underset{\underset{H}{|}}{\overset{OH}{C}} - \underset{\underset{OH}{|}}{\overset{H}{C}} - \underset{\underset{OH}{|}}{\overset{H}{C}} - \underset{\underset{H}{|}}{\overset{OH}{C}} - CHO$$

or equally well

B.



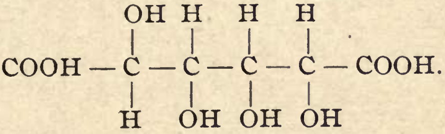
$$CH_2OH - \underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{C}} - \underset{\underset{H}{|}}{\overset{\overset{OH}{|}}{C}} - \underset{\underset{H}{|}}{\overset{\overset{OH}{|}}{C}} - \underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{C}} - CHO$$

according as the group CHO is placed to the right or to the left of the chain of asymmetric carbon atoms.

On the other hand, the first product of the oxidation of galactose is galactonic acid,

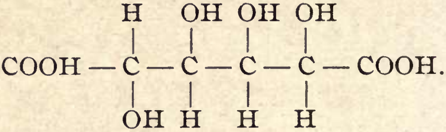
$$CH_2OH.CHOH.CHOH.CHOH.{}^*CHOH.COOH,$$

which heated with pyridin and water to 140°–150° is converted into talonic acid. By analogy with the other compounds so far studied this compound differs from the others only in the arrangement of the group CHOH marked *, and which is nearest the carboxyl group. Further, this talonic acid, when oxidized by nitric acid, gives *d*-talomucic acid the antipode of *l*-talomucic acid, the constitution of which has already been established. This permits us to assign to these different compounds the following configuration starting from *l*-talomucic acid,



$$COOH - \underset{\underset{H}{|}}{\overset{\overset{OH}{|}}{C}} - \underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{C}} - \underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{C}} - \underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{C}} - COOH.$$

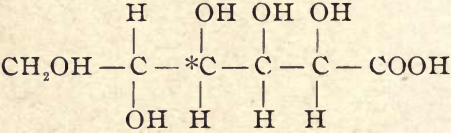
Its isomer, *d*-talomucic acid, will be



$$\begin{array}{ccccccccccc} & & \mathrm{H} & & \mathrm{OH} & & \mathrm{OH} & & \mathrm{OH} & & \\ & & | & & | & & | & & | & & \\ \mathrm{COOH} & - & \mathrm{C} & - & \mathrm{C} & - & \mathrm{C} & - & \mathrm{C} & - & \mathrm{COOH}. \\ & & | & & | & & | & & | & & \\ & & \mathrm{OH} & & \mathrm{H} & & \mathrm{H} & & \mathrm{H} & & \end{array}$$

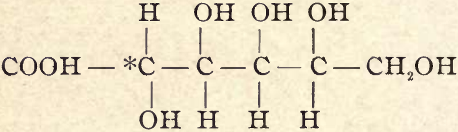
From this formula one may deduce two possible configurations for talonic acid, according as the group CH_2OH derived from COOH is placed to the right or left of the carbon chain.

C.



$$\begin{array}{ccccccccccc} & & \mathrm{H} & & \mathrm{OH} & & \mathrm{OH} & & \mathrm{OH} & & \\ & & | & & | & & | & & | & & \\ \mathrm{CH_2OH} & - & \mathrm{C} & - & {}^*\mathrm{C} & - & \mathrm{C} & - & \mathrm{C} & - & \mathrm{COOH} \\ & & | & & | & & | & & | & & \\ & & \mathrm{OH} & & \mathrm{H} & & \mathrm{H} & & \mathrm{H} & & \end{array}$$

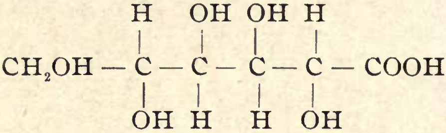
D.



$$\begin{array}{ccccccccccc} & & \mathrm{H} & & \mathrm{OH} & & \mathrm{OH} & & \mathrm{OH} & & \\ & & | & & | & & | & & | & & \\ \mathrm{COOH} & - & {}^*\mathrm{C} & - & \mathrm{C} & - & \mathrm{C} & - & \mathrm{C} & - & \mathrm{CH_2OH} \\ & & | & & | & & | & & | & & \\ & & \mathrm{OH} & & \mathrm{H} & & \mathrm{H} & & \mathrm{H} & & \end{array}$$

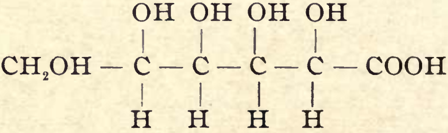
Galactonic acid differs only in the position of the asymmetric carbon atom C*, and can be represented by either of the following two formulae :

E.



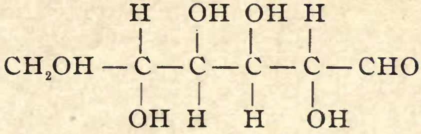
$$\begin{array}{ccccccccccc} & & \mathrm{H} & & \mathrm{OH} & & \mathrm{OH} & & \mathrm{H} & & \\ & & | & & | & & | & & | & & \\ \mathrm{CH_2OH} & - & \mathrm{C} & - & \mathrm{C} & - & \mathrm{C} & - & \mathrm{C} & - & \mathrm{COOH} \\ & & | & & | & & | & & | & & \\ & & \mathrm{OH} & & \mathrm{H} & & \mathrm{H} & & \mathrm{OH} & & \end{array}$$

F.

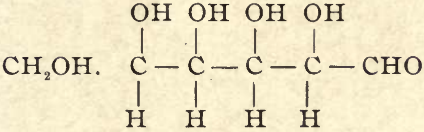


$$\begin{array}{ccccccccccc} & & \mathrm{OH} & & \mathrm{OH} & & \mathrm{OH} & & \mathrm{OH} & & \\ & & | & & | & & | & & | & & \\ \mathrm{CH_2OH} & - & \mathrm{C} & - & \mathrm{C} & - & \mathrm{C} & - & \mathrm{C} & - & \mathrm{COOH} \\ & & | & & | & & | & & | & & \\ & & \mathrm{H} & & \mathrm{H} & & \mathrm{H} & & \mathrm{H} & & \end{array}$$

These then lead to formulae for galactose which can be expressed as follows :

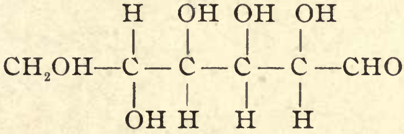
G. 

$$\mathrm{CH_2OH}-\underset{\mathrm{OH}}{\overset{\mathrm{H}}{\mathrm{C}}}-\underset{\mathrm{H}}{\overset{\mathrm{OH}}{\mathrm{C}}}-\underset{\mathrm{H}}{\overset{\mathrm{OH}}{\mathrm{C}}}-\underset{\mathrm{OH}}{\overset{\mathrm{H}}{\mathrm{C}}}-\mathrm{CHO}$$

H. 

$$\mathrm{CH_2OH.}\ \underset{\mathrm{H}}{\overset{\mathrm{OH}}{\mathrm{C}}}-\underset{\mathrm{H}}{\overset{\mathrm{OH}}{\mathrm{C}}}-\underset{\mathrm{H}}{\overset{\mathrm{OH}}{\mathrm{C}}}-\underset{\mathrm{H}}{\overset{\mathrm{OH}}{\mathrm{C}}}-\mathrm{CHO}$$

The formulae G and H on being compared with A and B for which proof has been given above, B is seen to be identical with G. Galactose is hence represented by B or by the identical G. Further, galactonic acid will be E and talonic acid C. Lastly, talose the aldose derived from talonic acid can be expressed as follows :



$$\mathrm{CH_2OH}-\underset{\mathrm{OH}}{\overset{\mathrm{H}}{\mathrm{C}}}-\underset{\mathrm{H}}{\overset{\mathrm{OH}}{\mathrm{C}}}-\underset{\mathrm{H}}{\overset{\mathrm{OH}}{\mathrm{C}}}-\underset{\mathrm{H}}{\overset{\mathrm{OH}}{\mathrm{C}}}-\mathrm{CHO}$$

VIII. RELATION BETWEEN CONSTITUTION AND ROTATORY POWER. MOLECULAR ASYMMETRY

In an asymmetric molecule **Cabcd,** the nature of the four groups bound to carbon ought evidently to exercise a certain influence on the magnitude of the rotatory power. Nevertheless, in an homologous series of active compounds, this constant can vary considerably, even to changing its sign when a compound very nearly allied is examined. Thus, the methyl ester of diacetyl tartaric acid is laevorotatory, while the ethyl ester turns the plane of polarized light to the right.

Biot announced some time since, that the considerable differences observed in the rotatory power of tartaric acid in dilute solutions, was due to the formation of hydrates. Later, Béchamp[1] has demonstrated that the phenomenon of birotation observed by Dubrunfant in sugar solutions is also due to hydration. In the case of sugar one finds that the rotatory power at the end of twenty-four hours is constant and is equal to about half that observed in operating with fresh solutions. This view has been held by Tollens[2] and by Jacobi.[3] It is, however, not the only possible explanation.

In 1890, Crum-Brown,[4] and Guye[5] indicated independently the relation between the rotatory power and the groups bound to the asymmetric carbon atom.

Crum-Brown assigns to each group a function which, among other things, depends on temperature and the nature of the solvent, and which must be experimentally determined. The product of the differences between the respective groups determines the rotatory power.

Guye arrives at an analogous result by the following considerations:

If one designates by d_1, d_2, d_3, d_4, d_5, d_6, the distances from the center of gravity of a tetrahedral scheme with six planes of symmetry corresponding to a regular fundamental tetrahedron, the product of these six distances or the product of the asymmetry should give the size and sign of the rotatory power. The sign depends on the sign of the product, which, in turn, depends on the sign of each factor—positive or negative—according as the distances, d_1, d_2 are to the right or left of the planes of symmetry.

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[1] Compt. rend., **42**, 610, 896; Bull. Soc. Chim. (3), **9**, 511.

[2] Tollens: Ber. d. chem. Ges., **26**, 1799.

[3] Ann. Chem. (Liebig), **272**, 41; vide Lule: Ber. d. chem. Ges., **27**, 594.

[4] Proc. Roy. Soc. Edin., June, 1890.

[5] Compt. rend. (3), **3**, 595; Ann. chim. phys., **6**, 25, 145; Arch. sc. phys. nat., (3), **26**, 97, 201, 333; Rev. Scientifique, **49**, 265.

If one takes into consideration (1) that the different radicals are at different distances from the carbon atom which they saturate (leverage), (2) that the attraction and repulsion exercised by the different groups on one another can displace them from that position which one might call normal, then the algebraic expression of the product of asymmetry assumes a somewhat complex type. It resolves itself into a problem of four masses, four levers, and the twelve angles which determine the orientation in space of the four lever arms. As a matter of fact at present this formula cannot be controlled by experiment.[1]

If, however, one wishes to limit these verifications to a qualitative investigation one may, for a first approximation, suppose that the masses a, b, c, d, which saturate the asymmetric carbon atom, are concentrated at the summits of a regular tetrahedron and this gives the following formula which expresses the product of asymmetry and consequently the rotatory power :

$$P = \frac{(a-b)(a-c)(a-d)(b-c)(b-d)(c-d)}{(a+b+c+d)^6}$$

One can from this formula deduce the following results :

(1) If two groups become identical, that is, if the compound $Cabcd$ is transformed into a symmetrical substance $Cabc_2$ the product P is reduced to zero, and consequently the rotatory power should disappear, a result which conforms with experimental data.

(2) If one passes from dextrorotatory compounds to those that are laevorotatory one will observe that the sign of P depends only on the numerator (the denominator is always positive) and whatever may be the manner in

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[1] Guye: Compt. rend., **116**, 1378.

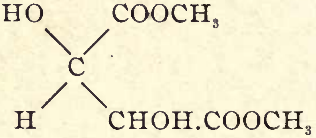
which the groups are formulated, in order to pass from one isomer to the other, the number of factors in the numerator which change sign will always be odd in number. Hence the numerator will change sign in order to keep an absolute value. Experimental evidence in accord with this shows that right and left isomers have the same rotatory power but have opposite signs.

(3) Let a derivative be supposed in which $\mathbf{a} > \mathbf{b} > \mathbf{c} > \mathbf{d}$. If substitutions be effected which change $\mathbf{a}$ into $\mathbf{a}'$ but in such a way that $\mathbf{a} > \mathbf{b} > \mathbf{c} > \mathbf{d}$, the sign of the product, will be unchanged and consequently all these derivatives will be of the same sign as the original compound.

Of the forty derivatives of *d*-amyl chlorid known, which are made by replacing the group, CH_2Cl by groups heavier than $C_2H_5 = 29$, all are dextrorotatory.[1] (The number is actually more than sixty.)

Methyl glycerate, $CH_2OH.CHOH.COOCH_3$, prepared by Frankland and MacGregor,[2] is laevorotatory, and all the other esters in like manner prepared to the octylic ester are also of the same sign.

Methyl tartrate,



,

is dextrorotatory, and the same holds good for the simple esters of tartaric acid according to the researches of Pictet and Freundler.

(4) Given a compound in which $\mathbf{a} > \mathbf{b} > \mathbf{c} > \mathbf{d}$ one can arrange the unequal masses in the following way:

$$\mathbf{a} > \mathbf{b},\ \mathbf{a} > \mathbf{c},\ \mathbf{a} > \mathbf{d},\ \mathbf{b} > \mathbf{c},\ \mathbf{b} > \mathbf{d},\ \mathbf{c} > \mathbf{d}.$$

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[1] Guye: Annales, **6**, 25, 145.

[2] J. Chem. Soc., 1893, 511, 1910.

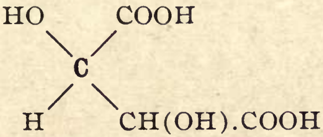
If then $\mathbf{b}$ be replaced by $\mathbf{b}'$ in such a way that the sign of one of the equations only is reversed: *e.g.*, $\mathbf{a} < \mathbf{b}'$, $\mathbf{a} > \mathbf{c}$, $\mathbf{a} > \mathbf{d}$, $\mathbf{b} > \mathbf{c}$, $\mathbf{b} > \mathbf{d}$, $\mathbf{c} > \mathbf{d}$, one of the factors of the numerator will change its sign. Consequently the rotatory power of the substituted compound will be the reverse of that of the original. The same will take place if one substitutes for $\mathbf{a}$ and $\mathbf{b}$, $\mathbf{a}'$ and $\mathbf{b}'$ in the following way:

$$\mathbf{a}' < \mathbf{b}', \mathbf{a}' > \mathbf{c}, \mathbf{a}' > \mathbf{d}, \mathbf{b}' > \mathbf{c}, \mathbf{b}' > \mathbf{d}, \mathbf{c} > \mathbf{d}.$$

This case is found in the transformation of ethyl tartrate into ethyl dibutyryl tartrate, the latter being laevorotatory. These changes of sign which one may foretell have been observed in the tartaric ester series, and have been confirmed by the researches of Freundler.[1]

Esters.	Tartaric.	Diaceyl tartaric.	Dipropionyl tartaric.	Dibutyryl tartaric	Divaleryl tartaric.	Dibenzoyl tartaric.
Methyl	+ 19.87	+ 11.8	+ 11.4	+ 8.6	+ 7.4	42.9
Ethyl	+ 2.11	— 15.5	— 10.7	— 15.1	— 16.1	— 96.6
Propyl	+ 7.66	+ 0.3	+ 0.4	— 0.8	— 2.0	68.4
Isopropyl	+ 12.44	+ 13.4	+ 5.6	+ 5.2	+ 3.3	...
Butyl	+ 14.89	+ 5.9	...	...	..	...
Isobutyl	+ 10.3	+ 8.0	+ 6.9	+ 6.0	+ 4.8	...

It must be noted that in each of these derivatives the two asymmetric carbon atoms are identical. The four groups under consideration may then be expressed as follows:



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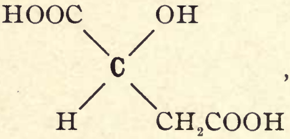
[1] Bull. Soc. Chim. (3), 11, 305–366; Thesis, Paris, 1894; Ann. chim. phys. 1894–1895; Pictet: Arch. sc. phys. nat., Geneva, 1881.

(5) If in the preceding compound **Cabcd**, **C** is replaced by $\mathbf{C'.C' > a}$, one formulates the following:

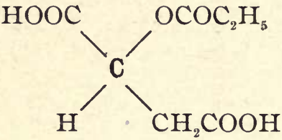
$$\mathbf{a > b,\ a < c',\ a > d,\ b < c',\ b > d,\ c' > d.}$$

The signs of the two unequal groups are reversed; hence in the equation expressing the product of asymmetry two factors will change their sign, which is equivalent to saying that the product P will not change sign. This case is found in the transformation of *l*-malic acid,



,

into propionyl malic acid,



,

or in the transformation of ethyl malate into ethyl benzoyl malate. These derivatives conform to the above, in that they are of the same rotatory sign as their lower homologues.[1]

(6) The cases will now be taken up of an homologous series obtained from an active alcohol or acid by replacement of the heaviest group *a'* in a compound by the groups *a'*, *a''*, *a'''*, which are increasingly heavier.[2] From what has been said under (1) all these derivatives will have the same sign. At first sight it would seem that the rotatory power would constantly increase. This

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[1] Guye: Compt. rend., **116**, 1133; Colson: *Ibid.*, **116**, 818.

[2] Guye: *Ibid.*, **116**, 1451.

cannot be so, for if the three factors $(a-b)(a-c)(a-d)$ increase, this increase will also take place in the denominator, but for great values for a the product P tends toward the limit $\frac{a^3}{a^6}$ const. $= \frac{1}{a^3}$ const. $= 0$. The rotatory power ought then to reach a maximum. Experiment confirms this view. This maximum has been established by Guye and Chavanne in the case of the esters of valeric acid, in those of glyceric acid (Frankland and MacGregor), of lactic acid (Le Bel), secondary amyl alcohol (Le Bel), the mixed oxids of primary amyl alcohol and the fatty esters of the same (Guye and Chavanne), the saturated hydrocarbons containing an active amyl radical (Welt), the esters of active α-oxybutyric acid (Guye and Jordan). The most complete series is the following, comprising the aliphatic esters of primary amyl alcohol:

	$[\alpha]_D$.		$[\alpha]_D$.
Amyl formate	+2.01	Amyl heptylate *n*	+2.21
Amyl acetate	+2.53	Amyl caprylate *n*	+2.10
Amyl propionate	+2.77	Nonylate *n*	+1.95
Amyl butyrate *n*	+2.69	Laurate *n*	+1.56
Amyl valerianate *n*	+2.52	Palmitate *n*	+1.45
Amyl caproate	+2.40	Stearate *n*	+1.45

Among all physical chemical properties so far investigated, none have pointed to the establishment of a maximum; boiling-points, densities, molecular refraction, specific heat, etc., point to a function which is constantly increasing, or is asymptotic. The rotatory power is the first example of a maximal point, and it is interesting to note that this is foreseen by the formula above given.

If the simplified equation for the product of asymmetry holds in a certain number of cases, it is insufficient in many others. For example, if two of the masses become equal, the rotatory power should become zero. Numerous investigations, however, show that this is not the case; one is acquainted, on the other hand, with many isomeric compounds of very like structure which have not the same rotatory power.[1] The researches of LeBel[2] have shown that halogen derivatives are frequent exceptions to the rule given above, and other exceptions of the same kind have since been indicated by Frankland and MacGregor, Guye and Jordan, and by Walden.

The hypothesis according to which the masses are concentrated at the summits of a regular tetrahedron is evidently too simple, and does not correspond to fact. It will be necessary, probably, to take into account the arms of the levers, and the angular deformations produced by the influence of the groups on one another. Unfortunately, experimental data do not furnish us with the means of taking into account these functions.

Compounds with several asymmetric carbon atoms.—The preceding explanations have related to substances characterized by one asymmetric carbon atom, or by several asymmetric carbon atoms which were identical, as in the case of the tartaric acids. The optical effects in the cases now under consideration correspond to the latter.

Researches have been undertaken to formulate a law by which these cumulative effects are controlled, until now only the more simple cases have been studied, and they appear to be governed in the following ways:[3]

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[1] Goldschimdt and Freundt: Ztschr. phys. Chem., **14**, 3; Walden: *Ibid.*, **15**, 638.

[2] Bull. Soc. Chim. (3), **9**, 674.

[3] Guye and Gautier: Compt. rend., **119**, 740 and 954 (1894); Bull. Soc. Chim., (3), **9**, 403; **11**, 1170; **13**, 475.

I. Principle of the Independence of the Optical Effects of Asymmetric Carbon Atoms

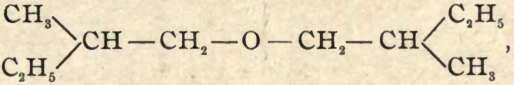
In a molecule containing several asymmetric carbon atoms, each acts as if the rest of the molecule were inactive.

II. Principle of Algebraic Accumulation

The effect of the different asymmetric carbon atoms in a molecule, add themselves algebraically. From these two principles one can deduce the following consequences:

The rotatory power of a compound can be estimated by evaluating the optical effect of each asymmetric carbon atom, and taking the algebraic sum of these different numbers for a result.

Example.—The rotatory power of amyl ether (amyl oxid) with two asymmetric carbon atoms,



should, according to this, be equal to double the rotatory power of amyl oxid obtained by reacting on inactive isoamylate of sodium with active amyl bromid. The experimental results are the following:

	$[\alpha]_D$.
Oxid with two active radicals L = 0.5....	+ 0.49
Oxid with amyl and isoamyl groups......	+ 0.29
Oxid with one active radical............	+ 0.25

For the same reasons diamyl will give a value $[\alpha]_D$ equal to about double that observed with isobutyl-amyl.[1]

	$[\alpha]_D$
Propyl amyl......................	+ 6.23
Isobutyl amyl....................	+ 5.88
Diamyl	+ 12.08–11.95

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[1] Welt: Compt. rend., 1895; Bull. Soc. Chim. (3), 11, 1184.

Amyl valerate derived from *d*-valeric acid and *l*-amyl alcohol will have a rotatory power nearly equal to that of amyl valerate made by starting from active valeric acid, and inactive amyl alcohol increased by the rotatory power of amyl valerate, formed by starting from an active alcohol and an inactive acid:

	$[\alpha]_D$.
Valerate (active) of amyl (inactive).....	+ 4.26
Valerate (inactive) of amyl (active)......	+ 1.08
Sum	+ 5.34
Valerate (active) of amyl (active)........	+ 5.32

Analogous verifications, all confirming the above principle, have been made with amyl glycolate of amyl (Guye and Gautier), oxybutyrate of amyl and valeryl oxybutyrate of amyl (Guye and Jordan), and with many lactic, malic, and tartaric esters (Walden).

Polarimetric observations.—The above are shortly the relations already found to exist between the rotatory power and stereochemical structure.

It is important to add that the conditions under which these relations are observed should be of definite order and it is on this account that many cannot be used for the study of molecular asymmetry. For the most part observations on substances dissolved in water should be excluded, especially those on metallic salts of active acids, or on salts formed by active bases and mineral acids, for one can only estimate the resultant of the derivations, due on the one hand to the decomposed salt, and on the other to that which remains undecomposed, and this decomposition can equally well take place as splitting into acid and base or into ions.[1]

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[1] Ostwald: Lehr. d. allg. Chem., 2d Ed., 1, 497; Van't Hoff: Lager. der Atome im Raume, 1894, p. 100.

Hydrates may also be produced, for it is well known that the salts of tartaric acid, for example, are deposited from their solutions as crystals containing water of crystallization. It may be added also that the relations of the influence of the solvent to the rotatory power have been formulated through a careful study of most of the observations taken by Guye and Rossi.[1]

It was believed that observations, effected in solutions of organic solvents, were outside this cause of error, and Landolt has strongly supported this view, but Freundler has shown that solvents, apparently without influence on the dissolved compound, can alter profoundly the rotatory power of a substance and that this alteration is accompanied by cryoscopic anomalies. Hence Freundler affirms that polarimetric observations of this kind should be controlled by the determination of the freezing- and boiling-points by Raoult's and Beckmann's methods, and more recent researches tend to support his views.

Wyrouboff has in several instances been able to separate molecular compounds of the alkaloids with the alcohols, with chloroform, and with benzene, and it has also been shown that certain active acids do not combine with organic bases in solution in organic solvents.

Cryoscopic or ebullioscopic determinations, although indispensable, do not always indicate the presence of these molecular combinations, but they are of extreme value in cases where polymerization or dissociation takes place.

In order to avoid these sources of error, it is preferable, when possible, to make observations on the substances in a fluid state, and, if this be not possible, to employ the same solvent for the complete series of observations, for Freundler has shown that the same solvent exerts nearly

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[1] Bull. Soc. Chim. (3), 13, 464.

the same influence on all the homologues of a series, and observations thus made will be very nearly comparable. It is also advisable according to Haller to use solutions containing always the same number of gram-molecules per liter.

Observations on the pure substance, even, are not exempt from sources of error, for according to Ramsay and Shields,[1] certain substances in the liquid state are more or less polymerized. It is hence evident that all observations on fluids of this class must be made with regard to this property, and before utilizing them for the study of molecular asymmetry, it will be necessary to decide to what extent this partial polymerization can modify the rotatory power. It is doubtless also that the conditions of temperature and the length of the column of liquid will one day be the object of reserve conditions. For these reasons the study of the relations between the rotatory power and molecular asymmetry can advance but slowly. They also explain why the expression "product of asymmetry" has been the subject of numerous criticisms, notably by Colson, who sees in the many conditions to be observed, difficulties which appear practically unsurmountable.[2]

STEREOCHEMISTRY OF THE ASYMMETRIC COMPOUNDS OF NITROGEN

The stereochemistry of the nitrogen compounds is but begun, as the experimental facts on which it is based are of but very recent date.

It will be shown farther on what the relations are that can be established between the compounds of carbon and

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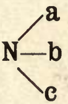
[1] Ztschr. phys. Chem., **12**, 433.

[2] Compt. rend., **115**, 729; **116**, 322, 818.

those of nitrogen where in an asymmetric carbon group **Cabcd** the group $(\mathbf{Cd})'''$ is replaced by $\mathbf{N}'''$. One should then obtain combinations of the formula $(\mathbf{N}'''\mathbf{abc})$; that is, ammonias of asymmetric structure and capable of existing in two enantiomorphous forms.

In order that this may be so it will be necessary to assume that the nitrogen atom occupies the summit of a tetrahedron, and that the other three groups are distributed at the other three apices. Up to the present all attempts made to separate enantiomorphous isomers of the formula  $\mathbf{N}\begin{array}{l} {}^{\diagup \mathbf{a}} \\ -\mathbf{b} \\ {}_{\diagdown \mathbf{c}} \end{array}$ derived from $NH_3.NH_2OH.H_2N—NH_2$, have been unsuccessful[1] and it can be regarded as probable that in this class of compounds the atom of nitrogen and the three other groups are situated in the same plane, a view which corresponds to that of Werner on valence and affinity (vide p. 46).

It is, however, quite the opposite when one comes to deal with ammonium compounds containing a pentavalent nitrogen atom. Here one may well assume the existence of optical isomers for the nitrogen atom is bound to four different groups, but up to the present, substances of this kind have only given inactive non-racemic compounds.[2] The conclusion reached by Le Bel is that the rotatory power is absent in all compounds in which the atom which gives the asymmetry becomes linked to two identical groups, and experiment has shown that in the case of nitrogen the only derivatives of nitrogen which can be obtained in an active state are

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[1] Hantzsch and Kraft: Ber. d. chem. Ges., **23**, 2780; Behrend: Ann. Chem. (Liebig), **257**, 203.

[2] Le Bel: Compt. rend., **112**, 724.

compounds of the following general formula **X—N—abcd.** In these compounds one may compare the group $(\mathbf{X}-\mathbf{N})''''$ to the asymmetric carbon atom $(\mathbf{C})''''$ and conceive therefore an asymmetric nitrogen atom. It is then possible to have two enantiomorphous isomers of equal rotatory power, but with inverse signs and to obtain synthetically racemic compounds by synthetic methods. As an example of the foregoing, Le Bel has, by the growth of bacteria in a solution of methyl ethyl propyl isobutyl ammonium chlorid,

$$Cl-\mathbf{N}(CH_3)(C_2H_5)(C_3H_7)(C_4H_9),$$

been able to isolate a laevorotatory compound from which he has been able to prepare derivatives equally active. Unfortunately these substances are so unstable that the contact of acids diminishes the rotatory power or even causes it to disappear, the active compound being transformed into the racemic derivative.[1] Certain cases of dimorphism, probably related to stereoisomerism have also been observed by Le Bel with trimethyl isobutyl ammonium chlorid,

$$Cl-N-(CH_3)_3.(C_4H_9),$$

and by Schryver and Collie with methyl diethyl amyl ammonium chlorid,

$$Cl-N-(CH_3)(C_2H_5)_2(C_5H_{11}).$$[2]

The platinum salts of these two compounds present themselves in two different modifications which are mutually transformable.[3]

Mention may also be made of the isoconicin of Ladenburg, in which optical isomerism may be attributed to an asymmetric carbon atom. The two modifications are also

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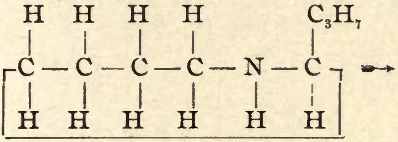
[1] Le Bel: Compt. rend., **112**, 724.

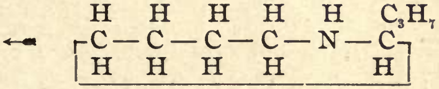
[2] Chem. News, **63**, 147.

[3] Le Bel: Compt. rend., **110**, 141.

distinguished by the different solubility of the double platinum salts in ether and in alcohol. As these two compounds have undoubtedly the same structure, Ladenburg considers them as stereoisomers and assigns to them the following configurations:



and



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[1] Ladenburg: Ber. d. chem. Ges., **26**, 854; Ladenburg and Simon: Bull. Soc. Chim. (3), **9**, 801, 949.

PART II.—GEOMETRICAL ISOMERISM

STEREOCHEMISTRY OF UNSATURATED AND CYCLIC COMPOUNDS, AND THE COMPOUNDS OF NITROGEN

GENERAL THEORY OF SATURATED AND UNSATURATED COMPOUNDS

After having explained shortly what is understood by the configuration of saturated compounds, containing one atom of carbon, we must return with more detail to this question, more particularly to those compounds containing more than one carbon atom. The difference which exists between saturated compounds and those which contain a double or a triple bond should be quite distinct.

According to the tetrahedral theory, the molecule of ethane, the most simple of the compounds containing two carbon atoms, will be represented by two tetrahedra having a common apex, while the other apices will be linked to six hydrogen atoms. If one assume this system to be rigid, the six atoms of hydrogen can be compared to those in the benzene nucleus, which are bound to the solid angles of a triangular prism. Hence, the disubstitution products of ethane should exist in three isomeric forms, analogous to those of benzene (Fig. 12); that is, configuration corresponds to the structure $CH_2—CH_3$, and 2 and 3 represent the two isomers, $CH_2X—CH_2X$, analogous to the ortho and para derivatives of the benzene series.

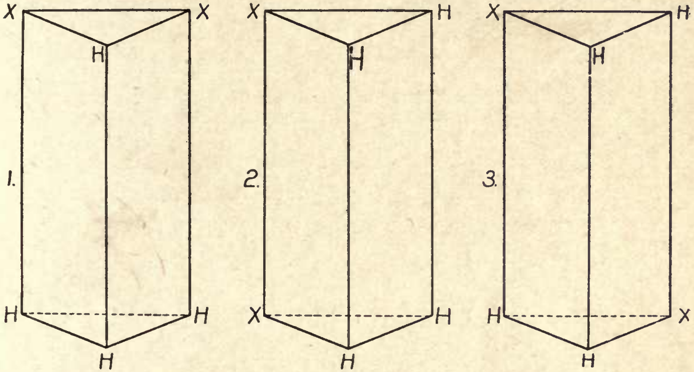


Fig. 10.

But as isomers of this class have never been found, this first assumption must be modified in order to render compounds 2 and 3 identical.

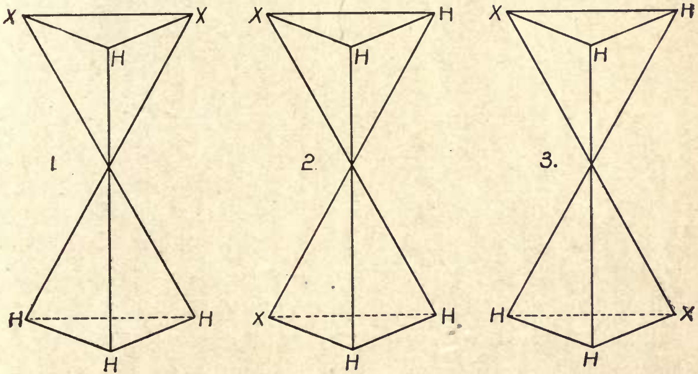
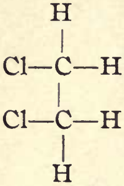


Fig. 11.

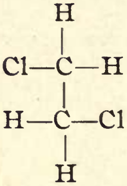
One arrives at this end by assuming that the hydrogen atoms do not occupy an absolutely fixed position in space, or in terms of the valence hypothesis, that the two carbon atoms are mobile about the axis which unites them. Hence, configurations 2 and 3 represent merely two different phases in interatomic motion. The two partial systems, CH_2X, being movable around the connecting bond, configurations 2 and 3 are not clearly defined isomers. This statement does not imply that a like rotation is produced in every case, for chemistry, on the whole, tends to prove that the atoms in the molecule exercise mutual attractive force on one another towards the center of the molecule, and hence by analogy those which are not directly bound, one to another, should also exert a like influence; besides these groups which have the greater attraction for one another should be drawn nearer together, hence, in the ethylene chlorid, configuration 2 should be the more favorable, for it is known that the atoms of chlorin and hydrogen have a reciprocal affinity, one for the other.

1.



$$\begin{array}{c} \text{H} \\ | \\ \text{Cl}-\text{C}-\text{H} \\ | \\ \text{Cl}-\text{C}-\text{H} \\ | \\ \text{H} \end{array}$$

and 2.



$$\begin{array}{c} \text{H} \\ | \\ \text{Cl}-\text{C}-\text{H} \\ | \\ \text{H}-\text{C}-\text{Cl} \\ | \\ \text{H} \end{array}$$

It must, however, always be assumed that modification 2 can be transformed into 1 under the influence of heat, which exerts a repelling force, acting contrariwise to affinity. Experiment has not afforded proof of the actual existence of stereoisomers in compounds of this class. It is, hence, necessary to admit that the groups CH_2X are movable around one another (principle of mobile union), or only one stable position among all those which can be conceived, and that is by reason of the mutual attraction of the atoms forming the groups which make up the molecule (principle of favorable configuration).

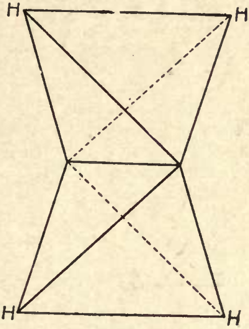
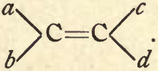


Fig. 12.

This does not hold good in case of unsaturated compounds; that is to say, in compounds containing two atoms of carbon united by a double bond such as the derivatives of ethylene,



$$\begin{matrix}a\\ b\end{matrix}\!\!>C{=}C<\!\!\begin{matrix}c\\ d\end{matrix}.$$

These derivatives should be represented by a scheme in which two tetrahedra are united by two summits each or by an edge.

Such configuration does not allow of the supposition of free rotation, for oscillation in such a case is inconceivable, hence the four atoms or radicals united to the carbon atoms should occupy a fixed position to one another.

The groups *ab* of a compound $abC{=}Ccd$ cannot then, in accordance with the principle of favorable configuration, change places or shift to position **Cc** or **d**, and thus compounds of the general formula **abC=Cab** will give isomers corresponding to the configurations of Fig. 13.

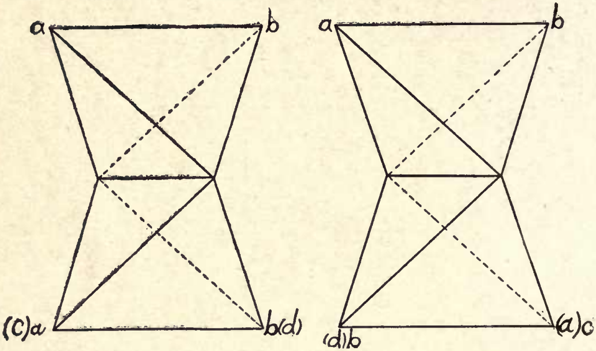
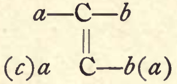


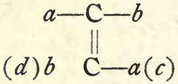
Fig. 13.



$$\begin{array}{ccc} a & \text{—C—} & b \\ & \| & \\ (c)a & \text{C—} & b(a) \end{array}$$

I.

and



$$\begin{array}{ccc} a & \text{—C—} & b \\ & \| & \\ (d)b & \text{C—} & a(c) \end{array}$$

II.

Isomers corresponding to formula I in which identical groups are placed in close relation with one another, have a plane of symmetry perpendicular to the axis of the double bond, and are called plane symmetric or "cis" isomers.

Those corresponding to configuration II have a center, but no plane of symmetry, and are called axial central trans or "cistrans" modifications.[1]

When lastly the carbon atoms are united by a triple bond, as in $a\mathrm{C}\equiv\mathrm{C}b$ as is the case of acetylene and its derivatives, the configuration may be represented by Fig. 14.

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[1] The terms "plane symmetric" and "axial symmetric" are only exact for compounds of the formula $ab\mathrm{C}=\mathrm{C}ba$. They cease to be so, however, when the four H of ethylene are replaced by four different groups—where plainly compounds represented by $ab\mathrm{C}=\mathrm{C}cd$ have no center of symmetry. Hence it is in all cases preferable to designate geometrical isomers by cis and trans.

This mode of union plainly does not admit of isomerism.

Experimental evidence is quite in accord with the foregoing theory regarding isomerism. Geometrical isomerism is found only in the derivatives of ethylene in which group of compounds, numbers of isomeric derivatives have been investigated.

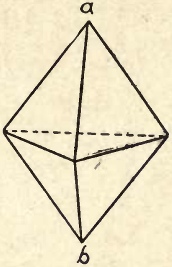


Fig. 14.

I. STEREOCHEMISTRY OF THE UNSATURATED COMPOUNDS OF CARBON. ISOMERISM IN THE ETHYLENE GROUP

a. General Properties

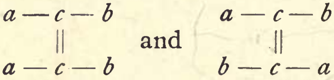
As will be seen, stereochemical isomerism in the group of ethylene compounds is very different from that observed in the derivatives with asymmetric carbon, previously studied. Compounds of the general formula **abC=Cab** are symmetrical in structure, and are hence inactive, and all attempts to split them into optical derivatives have led to negative results.

According to the theory of molecular asymmetry it is not impossible that the compound **abC=Ccd** might exert optical activity, and this view was at first believed to be confirmed by the finding of active modifications of citraconic and mesaconic acids,

$$COOHCH{=}CCH_3COOH,$$

produced by the action of ferments on these acids, but the researches of Le Bel showed that the active compounds so obtained were products of reduction and hence derivatives of malic acid which is characterized by an asymmetric carbon atom.[1]

One clearly defined difference between optical isomers and geometrical isomers is, that with the first, the distance between the groups bound to the carbon atom is equal; with the second there is a difference which will be seen by glancing at the following formulae:



$$\begin{array}{c} a - c - b \\ \| \\ a - c - b \end{array} \quad \text{and} \quad \begin{array}{c} a - c - b \\ \| \\ b - c - a \end{array}$$

Geometrical ethylene isomers differ then fundamentally in their physical properties crystalline form (absence of enantiomorphism), solubility, density, and in their melting- and boiling-points and they have also different chemical properties due to the reciprocal action of the different groups on one another. The difference in their electrical conductivity which serves as an indication of their intramolecular affinity, and certain other intramolecular reactions which will be spoken of further on show, here also, that in this class of compounds, isomers have not the same stability, and this is also confirmed by the results furnished by investigation of the amount of heat evolved on combustion.

Principal groups of geometrical isomers.—Among the X group of ethylene hydrocarbons, stereoisomerism is not as yet known with certainty. It seems first to make its appearance in the halogen and nitro derivatives, *e.g.*;

$$CH_3.CH : CHCl$$
$$CH_3.CBr : CHCH_3$$
$$CH_3.CBr : CBrCH_3$$

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[1] Bull. Soc. Chim. (3), 11, 292.

and particularly in the two dichlorids and dibromids of tolene, $C_6H_5CX : CXC_6H_5$, distinguished by their crystallographic features, and also in the two orthodinitrostilbenes, $C_6H_4.NO_2.CH : CH.C_6H_4.NO_2$.[1]

Griner[2] has indicated that hydrocarbons possessing two double bonds, present geometrical isomerism. Thus,

$$CH_3—CHI—CH_2—CH = CH_2$$

treated with alcoholic potash gives a mixture of two hydrocarbons corresponding to the formula,

$$CH_3—CH=CH—CH_2—CH=CH_2,$$

which are two geometrical isomers giving two distinct tetrabromids. Examples of this are more numerous with the monocarboxylic acids. Thus are known: crotonic and isocrotonic acids, $CH_3.CH:CH.COOH$; angelic and tiglic acids, $CH_3.CH:CCH_3COOH$; oleic and elaidinic acids, $C_{15}H_{31}.CH:CHCOOH$; erucic and brassidic acids, $C_{19}H_{39}.$-$CH:CH:COOH$; the following halogen acids: the two halogen acrylic acids, $CHX : CHCOOH$; two α-chlorocrotonic acids, $CH_3CH : CCl.COOH$; two β-chlorocrotonic acids, $CH_3CBr : CHCOOH$. In the aromatic series may be mentioned, cinnamic and isocinnamic acids, $C_6H_5.CH : CHCOOH$; and the α- and β-bromine acids derived from them, and certain cyclic acids as the cumaric acids, $C_6H_4OHCH : CHCOOH$.

The unsaturated dibasic acids are represented by fumaric and maleic acids, $COOH.CH : CH.COOH$, and their halogen derivatives, and by their homologues citraconic and mesaconic acids, $COOH.C.(CH_3) : CH.COOH$.

Attempts have been made to represent these differences by simple constitutional formulae, but as a result of the

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[1] Bischoff: Ber. d. chem. Ges., **21**, 2073.

[2] Ann. chim. phys., 1893.

most rigid investigation, this method has been found incorrect, and one is led to the view that the one possibility is to represent them as compounds of identical structure. These phenomena were designated by Michael as alloisomerism, and they led van 't Hoff, and later LeBel, to explain them by stereochemical methods.

This interpretation is to-day generally admitted, especially since Johannes Wislicenus further investigated the facts, and found that they admitted of the easy explanation of the transition of one compound into another.

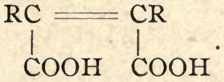
b. Determination of the Configuration of Geometrical Unsaturated Isomers

This determination rests on a fundamental hypothesis, *viz.*, atoms or groups which act on one another in the molecule, should occupy neighboring positions.

This principle is as important for the determination of stereochemical configuration as the principle employed in organic chemistry, to establish structural formulae by methods of substitution, a principle according to which a group entering a molecule takes the place of that leaving it. In the one case as in the other, one assumes that the other groups preserve their relative positions to one another.

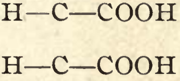
α-Determination of the configuration by relations established between unsaturated and cyclic compounds.— *1. By transformation of ethylene into cyclic compounds.* In intramolecular reactions the groups which unite with one another to form a closed ring must be in close proximity, hence isomers which can be transformed into ring compounds should be plane symmetrical (cis), and not central symmetrical (cistrans). This reaction is special to the oxygen compounds, and really is found only in the case of the internal anhydrids.

Formation of anhydrids from unsaturated dicarboxylic acids of the general formula



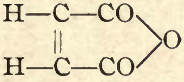
$$\begin{array}{ccc} RC & = & CR \\ | & & | \\ COOH & & COOH \end{array}.$$

The formation of anhydrids is only effected easily by those stereoisomers in which the two carboxyl groups are in close relation. The axially symmetrical compound in which the carboxyl groups are separated does not give an anhydride. This is shown in the case of fumaric and maleic acids, the latter only giving an anhydride.



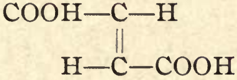
$$\begin{array}{l} H-C-COOH \\ \\ H-C-COOH \end{array}$$

Maleic acid.



$$\begin{array}{l} H-C-CO \\ \quad \| \qquad\quad \rangle O \\ H-C-CO \end{array}$$

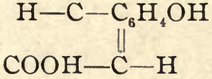
Maleic anhydrid.



$$\begin{array}{rcl} COOH- & C & -H \\ & \| & \\ H- & C & -COOH \end{array}$$

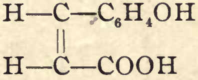
This is also seen with citraconic acid (methyl maleic acid) and mesaconic acid (methyl fumaric acid).

The unsaturated oxy-acids give lactones, thus the cumaric acids, $HO.C_6H_4.CH{:}CHCOOH$, can be represented by the following formulae:



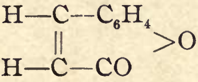
$$\begin{array}{rcl} H- & C & -C_6H_4OH \\ & \| & \\ COOH- & C & -H \end{array}$$

1. Stable modification.



$$\begin{array}{rcl} H- & C & -C_6H_4OH \\ & \| & \\ H- & C & -COOH \end{array}$$

2. Instable modification.



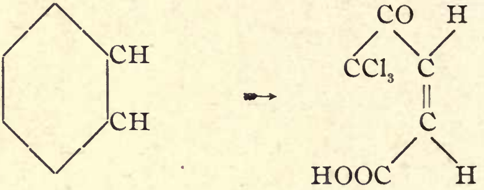
$$\begin{array}{rcl} H- & C & -C_6H_4 \\ & \| & \qquad \rangle O \\ H- & C & -CO \end{array}$$

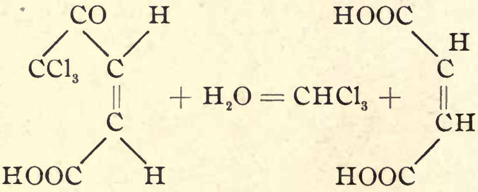
Cumaron.

Configuration II represents the acid which is transformed the more easily into the ring compound by reason of the proximity of the reacting groups.[1]

2. *By transformation of cyclic into ethylene compounds.*—Inversely, as ethylene plane symmetrical compounds alone can give ring compounds, so by the breaking of the ring in a cyclic compound one should obtain a plane symmetrical ethylene compound. Experiment shows that the products of the oxidation of cyclic derivatives are generally acids of the maleinoid form. The following are some examples:

Certain unsaturated acids obtained by the oxidation of aromatic compounds are derivatives of maleic acid; thus benzene yields trichloracetylacrylic acid which splits up into chloroform and maleic acid but gives no fumaric acid.





The oxidation of phenol by potassium permanganate leads to oxalic acid and inactive tartaric acid,[3] and this

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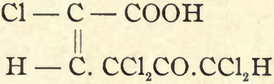
[1] Fittig: Ann. Chem. (Liebig), **226**, 351.

[2] Carius: *Ibid.*), **142**, 131; Kekulé: *Ibid.*, **223**, 179.

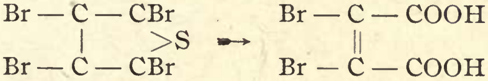
[3] Döbner: Ber. d. chem. Ges., **24**, 1755.

latter must be considered a derivative of maleic acid. (*Vide* page 102). The action of chlorin in alkaline solution on paraamidophenol yields dichlormaleic acid.[1] Resorcin under the same treatment gives a dichloracetyl trichlorcrotonic acid whose configuration is probably expressed by the following formula:[2]



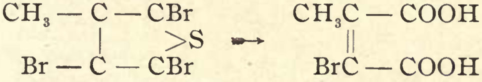
$$\begin{array}{l} Cl-C-COOH \\ \quad\ \ \| \\ H-C.\,CCl_2CO.CCl_2H \end{array}$$

The numerous derivatives of pyrrhol, of furfuran and of thiophene also give derivatives of maleic acid, while their β methyl compounds are transformed into derivatives of citraconic acid;[3] *e.g.*,



$$\begin{array}{l} Br-C-CBr \\ \quad\ \ | \quad\ \ >S \\ Br-C-CBr \end{array} \longrightarrow \begin{array}{l} Br-C-COOH \\ \quad\ \ \| \\ Br-C-COOH \end{array}$$

Thiophene tetrabromid. Dibrommaleic acid.



$$\begin{array}{l} CH_3-C-CBr \\ \qquad\ \ | \quad\ \ >S \\ \ Br-C-CBr \end{array} \longrightarrow \begin{array}{l} CH_3C-COOH \\ \qquad \| \\ \ BrC-COOH \end{array}$$

Thiotoluene tribromid. Bromcitraconic acid.

β. **Determination of the configuration by relations established between ethylene and acetylene derivatives.**—*1. By transformation of acetylene derivatives into ethylene compounds.*—When, as a result of the addition of atoms, members of the acetylene series are transformed into those of the ethylene group, the elements which are added should, according to Wislicenus, attach themselves to the two unsaturated carbon atoms, both on the same side of the

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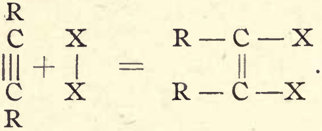
[1] Zincke: Ber. d. chem. Ges., **24**, 912.

[2] Zincke: *Ibid.*, **23**, 3766.

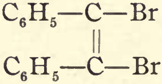
[3] Ciamician: Acad. Lincei, **7**, 22; Ber. d. chem. Ges., **24**, 74 and 1347.

axis of union. In this way one should obtain plane symmetrical compounds,



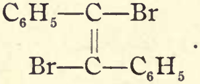
$$\begin{array}{c} R \\ C \\ ||| \\ C \\ R \end{array} + \begin{array}{c} X \\ | \\ X \end{array} = \begin{array}{c} R-C-X \\ \| \\ R-C-X \end{array}.$$

For example, the tolane dibromid which is formed in the greater proportion on treating tolan with bromin, has the following constitution:



$$\begin{array}{c} C_6H_5-C-Br \\ \| \\ C_6H_5-C-Br \end{array}$$

Its isomer has the axial symmetrical formula,

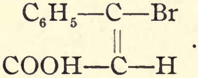


$$\begin{array}{c} C_6H_5-C-Br \\ \| \\ Br-C-C_6H_5 \end{array}.$$

The addition of hydrobromic acid to phenylpropiolic acid,

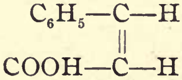
$$C_6H_5C \equiv CCOOH,$$

gives β-bromcinnamic acid represented by the formula,



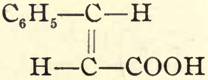
$$\begin{array}{c} C_6H_5-C-Br \\ \| \\ COOH-C-H \end{array}.$$

The product of the reduction of this compound is isocinnamic acid, and not ordinary cinnamic acid. This method of formation[1] and other facts tend to prove that the cinnamic acids have the following configuration:



$$\begin{array}{c} C_6H_5-C-H \\ \| \\ COOH-C-H \end{array}$$

Isocinnamic acid.



$$\begin{array}{c} C_6H_5-C-H \\ \| \\ H-C-COOH \end{array}$$

Cinnamic acid.

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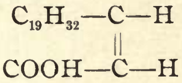
[1] Liebermann: Ber. d. chem. Ges., **25**, 950.

Brassidic acid isomeric with erucic acid,

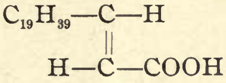
$$C_{19}H_{39}.CH : CHCOOH,$$

should be plane symmetric,[1] for it is produced by the reduction of behenoleic acid, $C_{19}H_{39}.C{\equiv}C.COOH$. The configuration of these two isomers will then be :



$$\begin{array}{rcl} C_{19}H_{32}\text{—} & C & \text{—}H \\ & \| & \\ COOH\text{—} & C & \text{—}H \end{array}$$

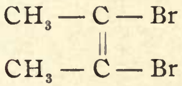
Brassidic acid.



$$\begin{array}{rcl} C_{19}H_{39}\text{—} & C & \text{—}H \\ & \| & \\ H\text{—} & C & \text{—}COOH \end{array}$$

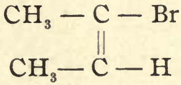
Erucic acid.

Treated with bromin or with hydrobromic acid crotonylene, $CH_3C{\equiv}CCH_3$, gives *p*-brominated derivatives of plane symmetrical dimethyl ethylene,



$$\begin{array}{rcl} CH_3 \text{ — } & C & \text{ — } Br \\ & \| & \\ CH_3 \text{ — } & C & \text{ — } Br \end{array}$$

and



$$\begin{array}{rcl} CH_3 \text{ — } & C & \text{ — } Br \\ & \| & \\ CH_3\text{— } & C & \text{ — } H \end{array}$$

.

These compounds differ from their axial symmetrical isomers obtained by other methods.

2. *By transformation of ethylene into acetylene derivatives.*—Inversely the formation of acetylene derivatives by starting from ethylene compounds should serve to indicate the configuration of the latter.

The general reaction,

$$abC{=}Ccd = ac + bC{\equiv}Cd,$$

is not effected with the same facility in the case of two geometrical isomers.

If the groups *a* and *c* are contiguous, the reaction will naturally take place more readily than when they are axially situated.

Examples.—One of the two β-chlorocrotonic acids, $CH_3CCl : CHCOOH$, heated to 70° with dilute potassium hydroxid solution, is transformed quantitatively into

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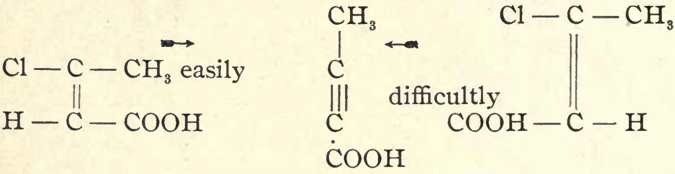
[1] Holt : Ber. d. chem. Ges., **25**, 961.

tetrolic acid,[1] $CH_3C{\equiv}C.COOH$. The isomer is transformed only at 100° and at that temperature even, the change is but partial. These reactions are expressed by the following scheme:

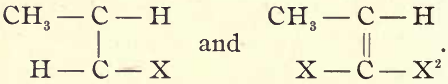


$$\begin{array}{c}\mathrm{Cl-C-CH_3}\\ \Vert\\ \mathrm{H-C-COOH}\end{array}\xrightarrow{\text{easily}}\begin{array}{c}\mathrm{CH_3}\\ |\\ \mathrm{C}\\ |||\\ \mathrm{C}\\ \cdot\\ \mathrm{COOH}\end{array}\xleftarrow{\text{difficultly}}\begin{array}{c}\mathrm{Cl-C-CH_3}\\ \Vert\\ \mathrm{COOH-C-H}\end{array}$$

The two stereoisomeric monohalogen propylenes, $CH_3CH = CHX$, present the same peculiarity. They are prepared by starting from the dihalogen butyric acids (formed by the addition of bromin or chlorin to the stereoisomeric crotonic acids) according to the following equation:

$$CH_3.CHX.CHX.COONA = NaX + CO_2 + CH_3.CH.CHX.$$

By elimination of hydrochloric acid one of the isomers gives allylene, $CH_3C \equiv CH$, easily, the other with difficulty,



$$\begin{array}{c}\mathrm{CH_3-C-H}\\ |\\ \mathrm{H-C-X}\end{array}\quad\text{and}\quad\begin{array}{c}\mathrm{CH_3-C-H}\\ \Vert\\ \mathrm{X-C-X}\end{array}.$$[2]

γ. **Determination of configuration by relations established between saturated and unsaturated compounds.** *1. By transformation of ethylene derivatives into saturated compounds.*—When an unsaturated compound is transformed by addition into a saturated compound of symmetrical structure, and with two asymmetric carbon atoms,

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[1] Friedrich: Ann. Chem. (Liebig), **219**, 361.

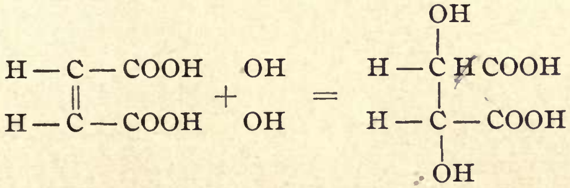
[2] Wislicenus: *Ibid.*, **248**, 279.

$$abC{=}Cab + cc = abcC{-}Cabc,$$

the product obtained is either by extra- or intramolecular compensation always inactive. The following particularly important example shows that a plane symmetrical ethylene derivative produces a non-racemic compound, while an axial compound gives a derivative which cannot be separated into optical isomers.[1] It was known for some time that maleic acid[2] on oxidation with potassium permanganate is transformed into a non-cleavable tartaric acid, while fumaric acid[3] under the same conditions, yields racemic acid,

$$\mathrm{COOHCH : CHCOOH + H_2O + O = COOH.CH(OH).CH(OH).COOH.}$$

It would be impossible by ordinary methods to say which inactive tartaric acid is produced, according as fumaric or maleic acid is used. By considering the phenomenon from a stereochemical standpoint, the reactions must necessarily take place in the way that actual experimental results have shown.



$$\begin{array}{lcr} \mathrm{H-C-COOH} & \mathrm{OH} & & \mathrm{OH} \\ \| & + & = & | \\ \mathrm{H-C-COOH} & \mathrm{OH} & & \mathrm{H-C\,\cancel{H}\,COOH} \\ & & & | \\ & & & \mathrm{H-C-COOH} \\ & & & | \\ & & & \mathrm{OH} \end{array}$$

Maleic acid. Inactive tartaric acid.

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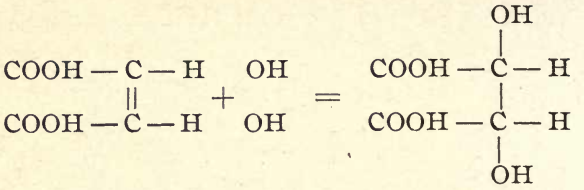
[1] Le Bel: Bull Soc. Chim. (2), **27**, 300; Wislicenus, Konigl. Sächs Gesell. d. Wissenschaft, 14.

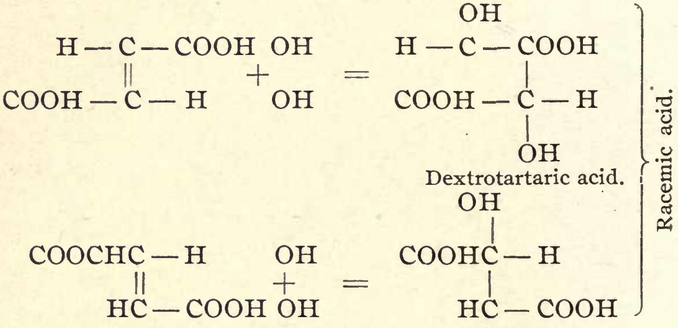
[2] Kekulé and Anschütz: Ber. d. chem. Ges., **14**, 713.

[3] Kekulé and Anschütz: *Ibid.*, **13**, 2150.



Maleic acid. Inactive tartaric acid.

$$\begin{array}{rcl} \mathrm{COOH}- & \mathrm{C} & -\mathrm{H} \\ & \| & \\ \mathrm{COOH}- & \mathrm{C} & -\mathrm{H} \end{array} \begin{array}{c} \mathrm{OH} \\ + \\ \mathrm{OH} \end{array} = \begin{array}{rcl} & \mathrm{OH} & \\ & | & \\ \mathrm{COOH}- & \mathrm{C} & -\mathrm{H} \\ & | & \\ \mathrm{COOH}- & \mathrm{C} & -\mathrm{H} \\ & | & \\ & \mathrm{OH} & \end{array}$$



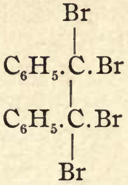
Dextrotartaric acid.

Laevotartaric.

$$\begin{array}{rcl} \mathrm{H}- & \mathrm{C} & -\mathrm{COOH} \\ & \| & \\ \mathrm{COOH}- & \mathrm{C} & -\mathrm{H} \end{array} \begin{array}{c} \mathrm{OH} \\ + \\ \mathrm{OH} \end{array} = \begin{array}{rcl} & \mathrm{OH} & \\ \mathrm{H}- & \mathrm{C} & -\mathrm{COOH} \\ & | & \\ \mathrm{COOH}- & \mathrm{C} & -\mathrm{H} \\ & | & \\ & \mathrm{OH} & \end{array}$$

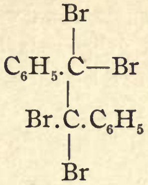
$$\begin{array}{rl} \mathrm{COOCHC} & -\mathrm{H} \\ \| & \\ \mathrm{HC} & -\mathrm{COOH} \end{array} \begin{array}{c} \mathrm{OH} \\ + \\ \mathrm{OH} \end{array} = \begin{array}{rl} \mathrm{OH} & \\ | & \\ \mathrm{COOHC} & -\mathrm{H} \\ | & \\ \mathrm{HC} & -\mathrm{COOH} \end{array}$$

2. *By relations between saturated compounds and substances belonging to the ethylene group.*—If it be assumed, as was done by Wislicenus, that saturated compounds are characterized by a certain configuration, more or less advantageous, one may easily account, for example, for the formation of the dibromid of tolane by simple elimination of bromin from the tetrabromid, and in the same way may be explained the formation of fumaric acid by the dehydration of malic acid. The different configurations, and at the same time the intramolecular attractive forces of the component groups of tolane tetrabromid, and of malic acid, are expressed by the following formulae :



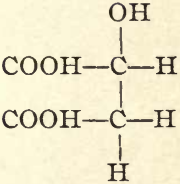
$$\begin{array}{c} \mathrm{Br} \\ | \\ \mathrm{C_6H_5.C.Br} \\ | \\ \mathrm{C_6H_5.C.Br} \\ | \\ \mathrm{Br} \end{array}$$

Disadvantageous.



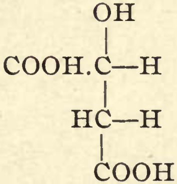
$$\begin{array}{c} \mathrm{Br} \\ | \\ \mathrm{C_6H_5.C{-}Br} \\ | \\ \mathrm{Br.C.C_6H_5} \\ | \\ \mathrm{Br} \end{array}$$

Advantageous.



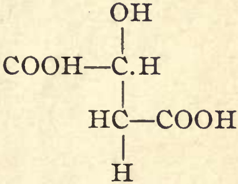
$$\begin{array}{c} \mathrm{OH} \\ | \\ \mathrm{COOH{-}C{-}H} \\ | \\ \mathrm{COOH{-}C{-}H} \\ | \\ \mathrm{H} \end{array}$$

Disadvantageous.



$$\begin{array}{c} \mathrm{OH} \\ | \\ \mathrm{COOH.C{-}H} \\ | \\ \mathrm{HC{-}H} \\ | \\ \mathrm{COOH} \end{array}$$

More advantageous.



$$\begin{array}{c} \mathrm{OH} \\ | \\ \mathrm{COOH{-}C.H} \\ | \\ \mathrm{HC{-}COOH} \\ | \\ \mathrm{H} \end{array}$$

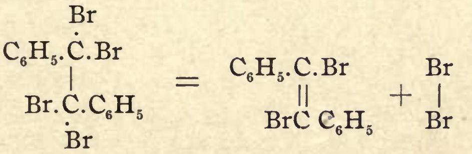
Most advantageous.

The reactions which are expressed by the equations,

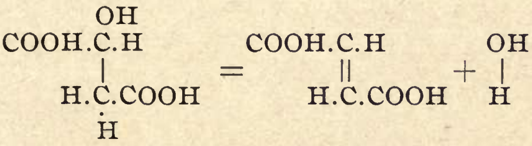
$$C_6H_5.CBr_2.CBr_2C_6H_5 = C_6H_5.CBr : CBr.C_6H_5 + Br_2,$$

$$COOH.CH(OH).CH_2COOH = COOH\ CH : CHCOOH + H_2O,$$

are to be explained principally, or even exclusively, by assuming certain advantageous configurations. It is then necessary to assume that there is a predominant formation of axial symmetrical tolane dibromid, and of fumaric acid.



$$\begin{array}{c} \mathrm{Br} \\ \cdot \\ \mathrm{C_6H_5.C.Br} \\ | \\ \mathrm{Br.C.C_6H_5} \\ \cdot \\ \mathrm{Br} \end{array} = \begin{array}{c} \mathrm{C_6H_5.C.Br} \\ \| \\ \mathrm{BrC\ C_6H_5} \end{array} + \begin{array}{c} \mathrm{Br} \\ | \\ \mathrm{Br} \end{array}$$



$$\begin{array}{c} \mathrm{OH} \\ \mathrm{COOH.C.H} \\ | \\ \mathrm{H.C.COOH} \\ \cdot \\ \mathrm{H} \end{array} = \begin{array}{c} \mathrm{COOH.C.H} \\ \| \\ \mathrm{H.C.COOH} \end{array} + \begin{array}{c} \mathrm{OH} \\ | \\ \mathrm{H} \end{array}$$

In some cases the configurations of the saturated compound and of the unsaturated, which is derived from it, are determined by the fact that the elements eliminated, in order to pass from one to the other, must necessarily occupy neighboring positions. It is thus that dibromsuccinic acid, a substance analogous to inactive tartaric acid, can lose a molecule of HBr only when an atom of hydrogen is placed in contiguity with an atom of bromin. It must follow then, that the acid so yielded is bromfumaric acid and not brommaleic acid.

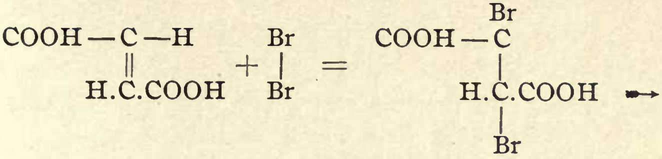
δ. Determination of the configuration by relations established between ethylene derivatives.—Considerations analogous to the preceding, permit a much easier explanation of the passage from axial symmetrical to axial symmetrical isomers. It suffices to admit the formation of an intermediate saturated derivative, and to take into account an advantageous configuration which it will assume during the reaction.

As examples, will be taken the reciprocal transformations of unsaturated dibasic acids. These reactions take place in the presence of a small quantity of bromin, or of hydrobromic acid, thus :

$$C_2H_2(COOH)_2 + Br_2 = C_2H_2Br_2(COOH)_2.$$
$$C_2H_2Br(COOH)_2 = C_2HBr(COOH)_2 + HBr.$$

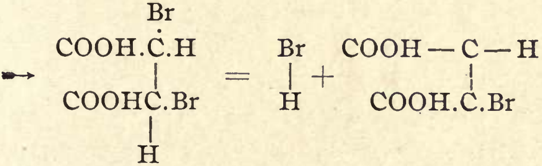
In this case fumaric acid gives brommaleic acid and maleic acid bromfumaric acid.

If one gives to maleic acid a plane symmetrical formula and an axial symmetrical formula to fumaric acid, these transformations may be expressed in the following manner :



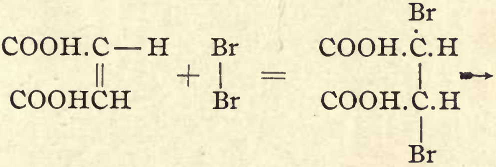
$$\begin{array}{c}\text{COOH}-\text{C}-\text{H}\\ \|\\ \text{H.C.COOH}\end{array} + \begin{array}{c}\text{Br}\\ |\\ \text{Br}\end{array} = \begin{array}{c}\text{Br}\\ \text{COOH}-\text{C}\\ |\\ \text{H.C.COOH}\\ |\\ \text{Br}\end{array} \rightarrow$$

Fumaric acid.
Rotation.
Disadvantageous position of dibromsuccinic acid.



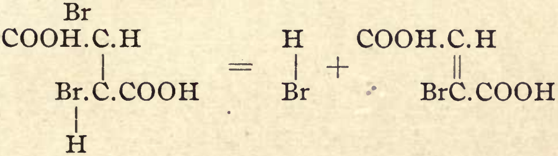
$$\rightarrow \begin{array}{c}\text{Br}\\ \text{COOH.}\dot{\text{C}}\text{.H}\\ |\\ \text{COOHC.Br}\\ |\\ \text{H}\end{array} = \begin{array}{c}\text{Br}\\ |\\ \text{H}\end{array} + \begin{array}{c}\text{COOH}-\text{C}-\text{H}\\ |\\ \text{COOH.C.Br}\end{array}$$

Advantageous configuration of dibromsuccinic acid.
Maleic acid.



$$\begin{array}{c}\text{COOH.C}-\text{H}\\ \|\\ \text{COOHCH}\end{array} + \begin{array}{c}\text{Br}\\ |\\ \text{Br}\end{array} = \begin{array}{c}\text{Br}\\ \text{COOH.}\dot{\text{C}}\text{.H}\\ |\\ \text{COOH.C.H}\\ |\\ \text{Br}\end{array} \rightarrow$$

Maleic acid.
Rotation.
Disadvantageous configuration.

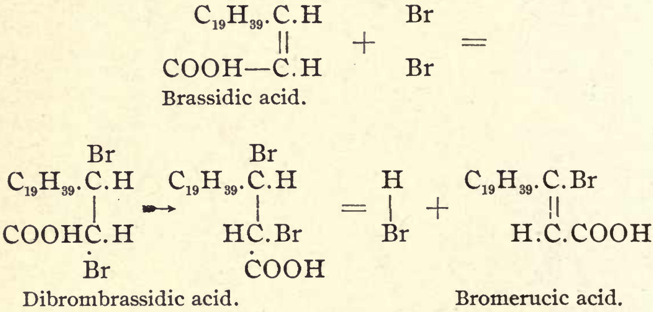


$$\begin{array}{c}\text{Br}\\ \text{COOH.C.H}\\ |\\ \text{Br.C.COOH}\\ |\\ \text{H}\end{array} = \begin{array}{c}\text{H}\\ |\\ \text{Br}\end{array} + \begin{array}{c}\text{COOH.C.H}\\ \|\\ \text{BrC.COOH}\end{array}$$

Bromfumaric acid.

These phenomena are to be found in some stereoisomeric monobasic acids also, *viz.*, the isomeric brassidic and erucic acids, $C_{19}H_{39}.CH{=}CH.COOH$.

The stereochemical formulae given on page 99 alone permit the explanation of the decomposition of dibrombrassidic acid into hydrobromic acid and monobromerucic acid, and the similar transformation of dibromerucic acid into monobrombrassidic acid.[1]



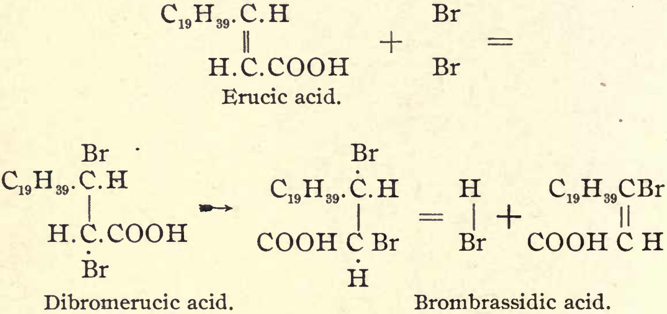
Brassidic acid.

Dibrombrassidic acid.

Bromerucic acid.

$$\begin{array}{c} C_{19}H_{39}.C.H \\ \| \\ COOH—C.H \end{array} + \begin{array}{c} Br \\ \\ Br \end{array} =$$

$$\begin{array}{c} Br \\ C_{19}H_{39}.C.H \\ | \\ COOH\dot{C}.H \\ Br \end{array} \longrightarrow \begin{array}{c} Br \\ C_{19}H_{39}.C.H \\ | \\ H\dot{C}.Br \\ COOH \end{array} = \begin{array}{c} H \\ | \\ Br \end{array} + \begin{array}{c} C_{19}H_{39}.C.Br \\ \| \\ H.C.COOH \end{array}$$



Erucic acid.

Dibromerucic acid.

Brombrassidic acid.

$$\begin{array}{c} C_{19}H_{39}.C.H \\ \| \\ H.C.COOH \end{array} + \begin{array}{c} Br \\ \\ Br \end{array} =$$

$$\begin{array}{c} Br \\ C_{19}H_{39}.C.H \\ | \\ H.\dot{C}.COOH \\ Br \end{array} \longrightarrow \begin{array}{c} Br \\ C_{19}H_{39}.\dot{C}.H \\ | \\ COOH\ \dot{C}\ Br \\ H \end{array} = \begin{array}{c} H \\ | \\ Br \end{array} + \begin{array}{c} C_{19}H_{39}CBr \\ \| \\ COOH\ C\ H \end{array}$$

By replacement of the bromin by hydrogen, one absolutely proves the reciprocal transformation of the two acids. The above formulae also tend to show that brombrassidic acid should be transformed more easily than its isomer, an assumption which is supported by experiment.

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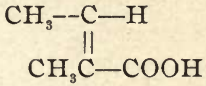
[1] Holt: Ber. d. chem. Ges., **24**, 4120.

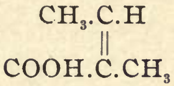
Angelic and tiglic acids, the 1.2 dimethyl acrylic acids, $CH_3.CH.CCH_3.COOH$, should be represented by the following formulae:



$$\begin{array}{l} CH_3\text{--}C\text{—}H \\ \quad\;\; \| \\ CH_3C\text{—}COOH \end{array}$$

Angelic acid.

and



$$\begin{array}{r} CH_3.C.H \\ \| \\ COOH.C.CH_3 \end{array}$$

Tiglic acid.

for their dibrom derivatives, $CH_3.CHBr.C(CH_3)Br$-$COOH$, heated with sodium carbonate give two different monobrompseudobutylenes,

$$CH_3CHBrC(CH_3)BrCOONa = NaBr + CO_2 + CH_3.CH : C(CH_3)Br.$$[1]

The monobrompseudobutylene derived from tiglic acid is the substance described as crotonolyene hydrobromide, as it is more easily transformed into crotonylene than the isomer derived from angelic acid.

It is necessary to assume that sodium salts of the dihalogen acids react with evolution of carbon dioxid and that in consequence the groups Br and COONa were originally in neighboring advantageous positions.

Uncertainty in the determination of configuration.—The different methods employed to determine configurations although giving in most instances good results, always, present an element of uncertainty. The principle of advantageous configuration of the intermediate derivatives, as the name itself indicates, is a somewhat vague conception which is difficult to bring into a more precise view by reason of the insufficiency of our knowledge regarding affinity.

As a matter of fact the affinities which are brought into play in the molecule itself should be influenced, and often modified either by external conditions, such as

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[1] Wislicenus: Ann. Chem. (Liebig), **250**, 224.

temperature, or by such chemical reagents as the solvents in which the reaction takes place, or certain substances in solution which start the reaction. As an example of the last mentioned may be taken the varying influence of different dehydrating agents. Frequently also, secondary reactions take place of such a kind that often the reaction cannot be assumed to be as simple as the ordinary equation indicates.[1] Finally, all these methods presuppose that the groups which take part in the reaction are not otherwise modified by these transformations. This method of reasoning is, then, not applicable in those cases where intramolecular transpositions take place, and these reactions are much more frequent in stereoisomeric reactions, particularly in those in which geometrical isomers take part. It is then necessary to strictly define the conditions which are necessary to the explanation of these cases.

c. Changes in Configuration of Geometrical Isomers of the Ethylene Group

α. **With change of constitution.**—The transformation of geometrical isomers, one into the other, can be regarded as a change in configuration following an intramolecular decomposition, a phenomenon which, as a rule, is favored by an elevation of temperature.

Hence it is that the atomic grouping which is the more stable under the conditions of experiment shows a tendency to re-formation. Thus, the same maleic anhydrid is always formed, whether one distils the maleic acid or fumaric acid.

β. **Direct transformation without change of constitution.**—These reactions are characteristic of geometrical isomers.

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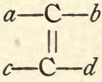
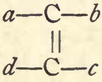
[1] Wislicenus: Ann. Chem. (Liebig), **246**, 53; **248**, 353.

In contradistinction to optical isomers, C*abcd*, two geometrical isomers, $ab\text{C}{=}\text{C}cd$, cannot have the same stability. The stability here depends on many factors, and if, for example, the affinity of *a* for *c*, and *b* for *d* on the one hand, are stronger than those of *a* for *d*, and *b* for *c* on the other, the stable and unstable configurations will be represented by the following formulae :



$$\begin{array}{c} a\text{—C—}b \\ \| \\ c\text{—C—}d \end{array}$$

Stable.



$$\begin{array}{c} a\text{—C—}b \\ \| \\ d\text{—C—}c \end{array}$$

Unstable.

The different stabilities of geometrical isomers correspond also to the different heats of combustion which are thermochemical measures of the stability of these compounds. Thus stable fumaric acid develops 319 calories on combustion, whereas the unstable maleic acid gives 326.3 calories.[1] The transformation of maleic acid into fumaric acid is an exothermic phenomenon which can therefore be effected without the intervention of any extraneous energy. Consequently geometrical isomers have a tendency to the formation of the more stable compound, and not, as in the case of optical isomers, to the formation of a mixture of the two substances in equimolecular proportions.

This explains why in the case of the two butylene, for example, one has not been able to isolate the two isomers. It is, perhaps, well to point out that all the considerations given above are quite independent of any conception regarding intramolecular movement.

Transformation of geometrical isomers of the ethylene series under the influence of heat.—This kind of transformation is quite general and in most cases non-

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[1] Stohmann : J. prakt. Chem., **41**, 575.

reversible. As examples may be cited: maleic acid unstable as such, but stable in the form of an anhydrid heated to 150° is transformed nearly quantitatively into fumaric acid; and the transformation of isocinnamic acid into ordinary cinnamic acid, etc. This does not occur when the two isomers have nearly the same stability. In these cases the reaction may be reversible, and although one may submit the compounds to the action of heat a mixture of the two substances is obtained which is, however, seldom equimolecular. Thus it is that on heating the dibromids or dichlorids of tolane, a mixture of the two compounds

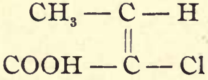
$$\begin{array}{c} C_6H_5\text{—C—Cl(Br)} \\ C_6H_5\text{—C—Cl(Br)} \end{array} \qquad \begin{array}{c} C_6H_5\text{—C—Cl(Br)} \\ \text{(Br(Cl—C—}C_6H_5 \end{array}$$

Unstable. Stable.

is obtained in which the stable modification exists in a larger proportion. As might be expected this state of equilibrium is reached more easily by starting from the unstable plane symmetrical compound than by using the more stable axial symmetrical isomer.

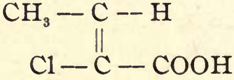
Transformations of this kind can even be utilized to determine the relative stability of two geometrical isomers by investigating the composition of the resulting mixture, and the rapidity with which the reversible reaction takes place. In this way the constitution of the α- and β-chlorocrotonic acids has been established.

α-Chlorocrotonic acids.



$$\begin{array}{c} CH_3\text{ — C — H} \\ \| \\ \text{COOH — C — Cl} \end{array}$$

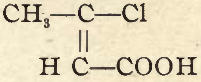
More stable.



$$\begin{array}{c} CH_3\text{ — C — H} \\ \| \\ \text{Cl — C — COOH} \end{array}$$

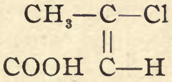
Less stable.

β-Chlorocrotonic acids.



$$\begin{array}{c}\mathrm{CH_3-C-Cl}\\ \|\\ \mathrm{H\ C-COOH}\end{array}$$

More stable.



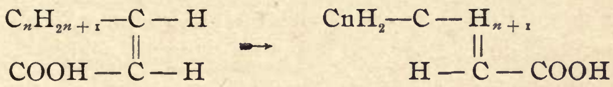
$$\begin{array}{c}\mathrm{CH_3-C-Cl}\\ \|\\ \mathrm{COOH\ C-H}\end{array}$$

Less stable.

Spontaneous transformation of isomeric ethylene derivatives in the presence of certain substances.—Elevation of temperature, as has been seen, has a tendency to produce molecular transformation. An interesting phenomenon, and one which is much more difficult of explanation, is the same reaction produced by the simple presence of certain substances.

In these cases it is observed that unstable modifications suffer transition into their more stable isomers in the presence of substances which apparently take no part in the reaction.

Bromin and certain mineral acids[1] convert maleic acid into fumaric acid ; this reaction is more or less rapid and complete according to the reagent employed, and the temperature at which the experiment is made. The same reaction takes place with the salts of maleic acid, and in this case it appears to depend on the character of the metallic base.[2] Mere traces of iodin suffice to convert the maleic esters into the fumaroid form ;[3] traces of nitrous acid induce the transformation of oleic, hytogeic, and erucic acids into their stereoisomers, elaidic, gaidic, and brassidic acids as the following scheme indicates :



$$\begin{array}{c}\mathrm{C_nH_{2n+1}-C-H}\\ \|\\ \mathrm{COOH-C-H}\end{array} \longrightarrow \begin{array}{c}\mathrm{CnH_2-C-H_{n+1}}\\ \|\\ \mathrm{H-C-COOH}\end{array}$$

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[1] Petrie : Ann. Chem. (Liebig), **195**, 59 ; Kekulé : Ann. spl. **1**, 134 ; *Ibid.* **2**, 93 and 6.

[2] Skraup : Wiener Monatshefte, **12**, 107.

[3] Anschütz : Ber. d. chem. Ges., **12**, 2282.

Amidomaleic acid[1] and anilidomaleic acid when heated with alkalies give fumaric acid, and the citraconic acid derivatives give mesaconic acid. The latter reaction although incomplete is not reversible; equilibrium is reached when the mixture contains 70 per cent. of the mesaconic acid derivative, and 30 per cent. of the citraconic derivative. It is here seen that the salts of the acids are more apt to produce these molecular changes; the presence of a methyl group seems to be more favorable to this end than others.[2]

Difficulties in the determination of configuration in the case of spontaneous molecular transformations.—These changes due to the presence of an apparently indifferent body, and which can be compared to catalytic reactions complicate an exact determination of configuration, and, explain why one is led in some cases to contradictory results.

It has been seen that by means of addition, one should obtain from acetylene derivatives, plane symmetrical ethylene compounds, but there is always yielded a certain amount of the cistrans compound, the presence of which can easily lead to an error in the determination of the configuration.

Acetylene dicarboxylic acid, $COOH—C \equiv C—COOH$, treated with bromin, gives but 30 per cent. dibrommaleic acid and 70 per cent. dibromfumaric acid.[3] Phenylpropiolic acid, submitted to the same treatment, yields a mixture of two dibromcinnamic acids.[4] The analogous dichlorcinnamic acid leads by reduction not to isocinnamic acid, but to ordinary cinnamic acid.[5]

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[1] Anschütz : Ann. Chem. (Liebig), **259**, 138.

[2] Delisle: *Ibid.*, **269**, 95.

[3] Michael : J. prakt. chem., **46**, 209.

[4] Roser : Ann. Chem. (Liebig), **247**, 139.

[5] Niessen : Ber. d. chem. Ges., **25**, 2666.

In all these cases phenomena of addition are accompanied or even hidden by molecular transposition, in which the substance which should normally be produced is converted, more or less, into its more stable isomer, the reaction tending finally to a state of equilibrium. One can easily conceive that these transformations can be favored by the presence of extraneous substances or by the disengagement of heat produced in the reaction.

The number of these abnormal cases will certainly decrease when the conditions under which the different isomers can exist unaltered is known.

Wislicenus has proved that angelic and tiglic acids give their respective dibromo compounds quantitatively only, when one allows the reaction to proceed in the presence of a large excess of bromin at a low temperature, and in the absence of light. If one operates under other conditions, a certain amount of the stereoisomers is always formed. It must be noted that it is not the dibromo compounds which submit to the transformation, but the acids themselves, during the progress of the bromination. Finally, as one might expect, the unstable angelic acid gives a much larger quantity of dibromtiglic acid than does tiglic acid, dibromangelic acid.[1]

Attempts to interpret the phenomena of molecular transposition.—Wislicenus was the first to attempt to give an explanation of the spontaneous transformation of the geometric isomers of ethylene produced by contact action; he applied himself for the most part to the cases detailed on page 93, which are accomplished with changes of constitution, and on the other hand to the transformation of certain structural isomers, such as the passage of primary propyl derivatives to those of the secondary structure.

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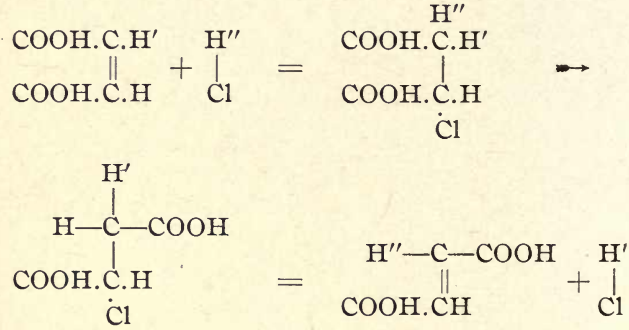
[1] Wislicenus: Ann. Chem. (Liebig), **272**, 1.

According to Wislicenus the body acting purely catalytically should give an addition product with the ethylene compound; this product should follow the more favorable configuration, and under this form the subsequent separation of the elements added would take place with the formation of an unsaturated compound of the same constitution but with a different configuration; or in other words a stereoisomer of the original body.

In this way the substance which acted apparently catalytically would be continuously regenerated to enter anew into the reaction.

Thus the transformation of maleic acid to fumaric acid should take place with the intermediate formation of chlorsuccinic acid according to the following configurations:



$$\begin{array}{c}\mathrm{COOH.C.H'}\\ \|\\ \mathrm{COOH.C.H}\end{array} + \begin{array}{c}\mathrm{H''}\\ |\\ \mathrm{Cl}\end{array} = \begin{array}{c}\mathrm{H''}\\ \mathrm{COOH.C.H'}\\ |\\ \mathrm{COOH.C.H}\\ \mathrm{Cl}\end{array} \longrightarrow$$

$$\begin{array}{c}\mathrm{H'}\\ |\\ \mathrm{H{-}C{-}COOH}\\ |\\ \mathrm{COOH.C.H}\\ \mathrm{Cl}\end{array} = \begin{array}{c}\mathrm{H''{-}C{-}COOH}\\ \|\\ \mathrm{COOH.CH}\end{array} + \begin{array}{c}\mathrm{H'}\\ |\\ \mathrm{Cl}\end{array}$$

This explanation must be taken with certain reservations, for in most cases it is not possible to isolate the intermediate substance which one is compelled to assume, even in traces; and when one performs the reaction in another way the transformation does not take place as the explanation of Wislicenus would indicate. As an example of this, one may cite the case of chlorsuccinic acid which does not give fumaric acid under the condition that one starts from maleic acid in the presence of hydrochloric acid. Moreover, it is difficult to understand how molecular transpositions are effected by the agency of heat alone without the intervention of an indifferent substance and the consequent formation of an unstable addition product.

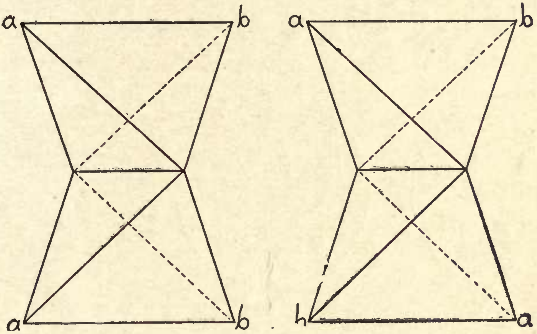


Fig. 15.

According to the notion which one usually has of valence, it is necessary to admit that the two groups *a* and *b* corresponding to the letters in Fig. 15, change place, which is altogether improbable, especially where one of the linkages of the double bond is broken momentarily, and these then revolve through an arc of 180° in order to reunite. All these difficulties which are analogous to those encountered in the consideration of the relation of an active substance to its optical isomer disappear if one will partly abandon the idea of valence as Werner has done.[1] According to him there are no single, double, or triple linkages between the atoms. A system such as *ab*C C*ab* is stable only on condition that

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[1] Beiträge zur Theorie der Affinität und Valenz, p. 16.

the change of affinities (as has already been defined on page 87) is at a maximum. A system of this kind will present two forms satisfying this condition (Fig 16, rings 1 and 2).

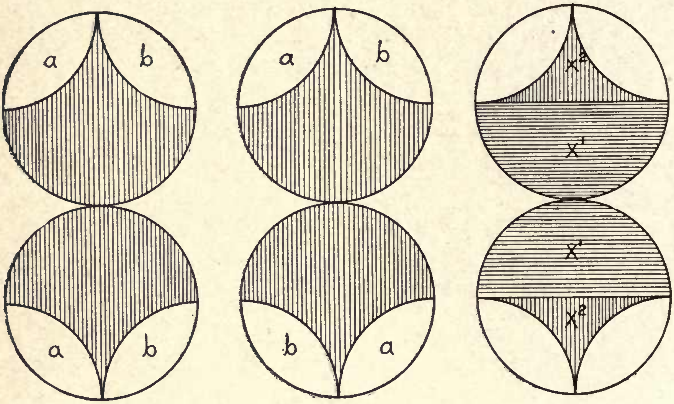


Fig. 16.

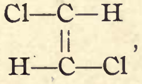
In these figures the zones not covered by shading are those in which the affinities or attractions are saturated by the four groups, *a*, *a*, *b*, *b*; the shaded parts are those in which the affinities serve to link together the two atoms of carbon.

So that in these last mentioned cases the parts X^1 (ring 3), are saturated under all circumstances, as completely in compounds having a single linkage, as in those with a double bond, whilst the parts X^2 which react one on another and belong to the system *ab*C *ca*B have the effect of preventing the free rotation of two atoms of carbon round a common axis. It is this which renders two stable configurations possible. Or stated more simply, if one body passes easily from one to another of these configurations, it is because the affinities changed between the zones X^2, which are certainly feeble, can be rendered still more feeble, either by molecular concussions which are exercised on these zones in certain substances, which is particularly the case in dealing with free ions. When one has a case of this kind, the two atoms of carbon take up again their oscillatory power round their axis of union, and the unstable molecule returns directly to a stable type without the necessity of supposing the formation of an intermediary compound.

Configuration of ethylene compound of which the two geometric isomers are not known.—We have already seen (page 109) that even in certain very simple cases the two geometric isomers have not as yet been isolated. For example, one only knows of but one dihalogen or dialkyl derivative of ethylene and the same is true for stilbene.

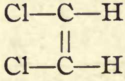
Among the unsaturated dicarboxylic acids one knows, on the one hand, the fumaric and maleic acids, and on the other hand, the mesaconic and citraconic acids, but the dicarboxylic acid, and particularly the diphenyl acids have not yet been isolated in the two isomeric formations despite the numerous efforts that have been made in this direction.

The configuration of the dihalogen derivatives of ethylene should be centro-symmetric by reason of the great affinity of chlorin for hydrogen,



$$\begin{array}{c} Cl-C-H \\ \| \\ H-C-Cl \end{array},$$

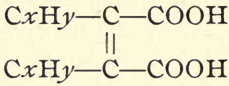
whilst the plane symmetric isomer



$$\begin{array}{c} Cl-C-H \\ \| \\ Cl-C-H \end{array}$$

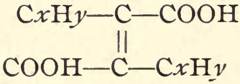
is probably too unstable to be isolated.

There can be no doubt regarding the configuration of the dissociated dicarboxylic acids, for they correspond in their properties very closely to maleic acid, particularly in the ease with which they give an anhydrid from which the name maleinoid has been given to them in contradistinction to the less stable fumaroid type which corresponds to fumaric acid; thus, the acid



$$\begin{array}{rcl} C_xH_y— & C & —COOH \\ & \| & \\ C_xH_y— & C & —COOH \end{array}$$

is well known, while the isomer

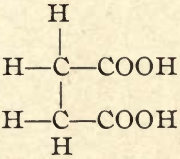


$$\begin{array}{rcl} C_xH_y— & C & —COOH \\ & \| & \\ COOH— & C & —C_xH_y \end{array}$$

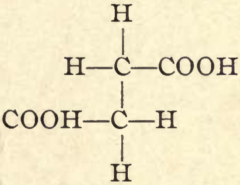
has not been obtained. For reasons which are still unknown, the presence of hydrocarbon radicals favors the plane symmetric configuration. This affords a striking example of the influence of constitution on configurations. Moreover, although it is not always possible to isolate the two geometric isomers, their existence may be established by indirect proof. For example, pyrocinchonic (dimethyl maleic) acid gives, on reduction in alkaline media, not only non-racemic dimethylsuccinic acid, which should be formed according to the equation, but also the racemic dimethylsuccinic acid (page 53). It is necessary on this account to admit, as in the case of the partial transformation of citraconic acid into mesaconic acid, that there is formed by intramolecular transposition a salt of dimethylfumaric acid, which alone can produce the second racemic dimethyl fumaric acid.

II. STEREOCHEMISTRY OF SATURATED COMPOUNDS

It may have already been remarked that the stereochemistry of the derivatives of methane is not strictly comparable in all points with that of the ethylene compounds. By reason of the law of mobile union, the different configurations should be viewed as forms which are more or less stable corresponding to different phases of intramolecular movements. The fact that two unsaturated geometric isomers lead in certain cases to one and the same saturated compound, in particular the fact that the reduction of fumaric and maleic acids performed with the greatest care lead always to the same succinic acid, forces one to conclude that in the two configurations, the maleinoid configuration is transformed probably spontaneously by rotation into the more advantageous fumaroid configuration. Thus it would not be contrary to theory to say that in certain cases these different phases of intratomic movement represent positions of relatively stable equilibrium, but it is evident that they are transformed exceedingly easily one into the other, and would correspond closely to the idea that one has in the term "modification" more than to a true isomer. It is possible that the two characteristic forms of dibrompropionic acids, of monochloracetic acid, and the three modifications of phenylhydrocinnamic acid may be looked upon as belonging to this category.



$$\begin{array}{rcl} & H & \\ & | & \\ H- & C & -COOH \\ & | & \\ H- & C & -COOH \\ & H & \end{array}$$



$$\begin{array}{rcl} & H & \\ & | & \\ H- & C & -COOH \\ & | & \\ COOH- & C & -H \\ & | & \\ & H & \end{array}$$

a. Determination of the position of advantage or of unstable position.—This determination which is of great importance in the stereochemistry of saturated compounds has been studied in detail in the case of dibasic acid by Auwers, V. Meyer, and others, particularly by Bischoff. Succinic acid which yields an anhydrid with difficulty, that is, it has a weak affinity constant[1] ($k = 0.0068$), corresponds in its properties to fumaric acid. In its stable configuration the two carboxyl groups should be opposed to one another or could even be in an intermediary position between the two hydrogen atoms of the other CH_2 group. It is thus necessary to assign to it symbol 1 in Fig. 17. Succinic anhydrid, on the other hand, which corresponds to the maleinoid type should be represented by symbol 2 in Fig. 17, these two types being viewed in the direction of the axis which joins the two carbons $CH_2—CH_2$.

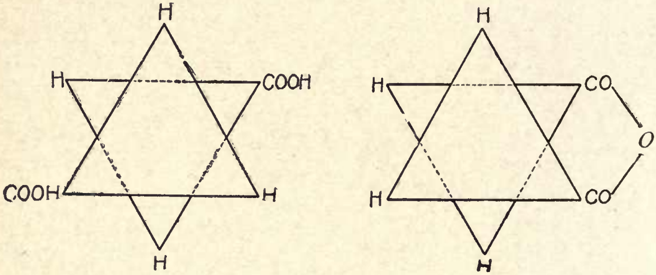


Fig. 17.

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[1] According to Arrhenius all electrolytes in aqueous solution are more or less dissociated into their ions. The electrical conductivity which depends on dissociation increases with increasing dilutions and tends to become constant and reaches a maximum with very weak solution. It denotes the molecular conductivity with weak solutions and in the same constant for a solution containing 1 gram molecule in V liters, the relation $\alpha = \frac{\mu v}{\mu \infty}$ represents the degree of dissociation. This quantity varies with the dilution. So that one may express it by the following formula given by Ostwald:

$$k = \frac{\alpha^2}{V(1-\alpha)}.$$

k is a constant which for the same acid and particularly for monobasic acids preserves the same value in all dilutions. This constant varies with

In the same way that the unsaturated acid is only known in the maleinoid form and gives spontaneously an anhydrid, so in the alkylsuccinic acids the fumaroid character disappears little by little to be replaced by a maleinoid property according as the number of alkyl radicals increase; in other words the acids tend to become stronger[2] and have a greater tendency besides to give an anhydrid. It is thus necessary to conclude that the carboxyl groups are coming closer together. The maleinoid type is stable only in tri- and tetramethyl ethylene (Fig. 18), which are however transformed almost spontaneously into an anhydrid.

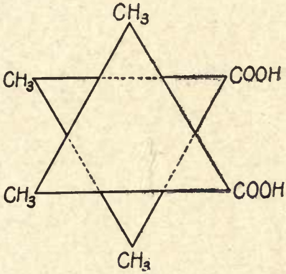


Fig. 18.

Relations of the same kind exist between the glutaric, adipic, and pimelinic acids and their alkyl derivatives. For example, may be cited levulinic acid, $CH_3.CO.$

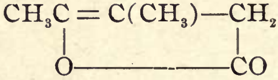
different acids and appears to be directly dependent on the constitution; thus one finds for the chlorbenzoic acids

Parachlorbenzoic acid,	$k = 0.132$
Metachlorbenzoic acid,	$k = 0.0155$
Parachlorbenzoic acid,	$k = 0.0093$
Laevo-tartaric acid,	$k = 0.097$
Dextro-tartaric acid,	$k = 0.097$
Racemic acid,	$k = 0.097$
Inactive non-racemic acid,	$k = 0.060$
Fumaric acid,	$k = 0.093$
Maleic acid,	$k = 1.17$

This constant k is in direct relation with the coefficient of acidity of acids which was calculated by Thomsen. This leads to the name 'affinity constant' which has often been given.

[2] Bischoff: Ber. d. chem. Ges., **24**, 1048; Zelinsky: *Ibid.*, **24**, 3997.

CH_2CH_2COOH, and its monoalkyl derivatives, $CH_3COCH.(CH_3)CH_2COOH$, which form anhydrids, or, more strictly speaking, unsaturated lactones.



$$\begin{array}{l} CH_3C = C(CH_3)—CH_2 \\ \;\;\;\;\;\;\;\;\;\; | \qquad\qquad\qquad\;\; | \\ \;\;\;\;\;\;\;\;\;\; O—————CO \end{array}$$

The alcoholic radicals exert, without doubt, a decided action on the formation of cyclic compounds. According to the dynamic hypothesis of Bischoff,[1] these facts would be in relation with the collision of atomic groups or radicals in the interior of the molecule.

b. Configuration of cyclic compounds of carbon.—The properties of some saturated compounds allow the conception of relative distance between the groups which compose them, and of defining the configuration of the molecule. The hydrocarbons themselves furnish the most simple example. The structural formula of a paraffin, $CH_3 1.CH_2 2.CH_2 3.CH_2 4.CH_2 5.—CH_{3n}$, does not give an exact idea of the relative distance between the groups, for C1 appears nearer to C2 than to C3. But if one represent hydrocarbons such as butane and pentane by solid figures, one obtains the following pictures :

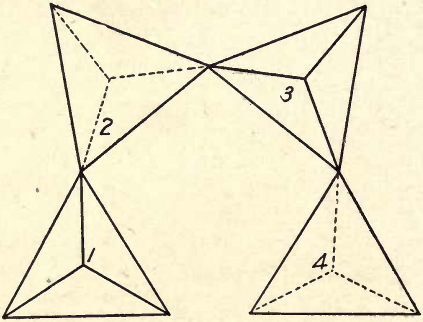


Fig. 19.

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[1] Ber. d. chem. Ges., **23**, 265.

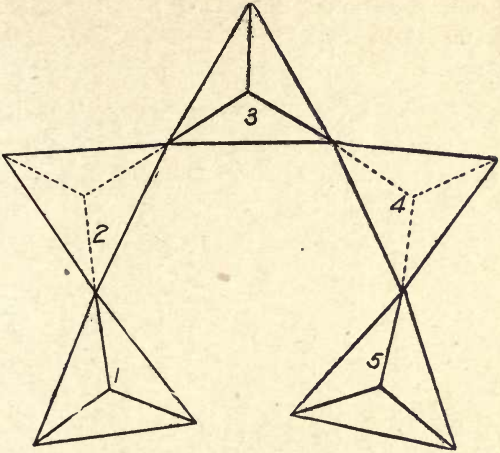
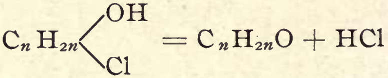


Fig. 20.

which one can conceive as a simple phase of intramolecular movement. As a consequence of the dimensions of the tetrahedra which are assumed in this case to be regular, the distance of the first tetrahedron from the four others, measured from the center, will then have the relation

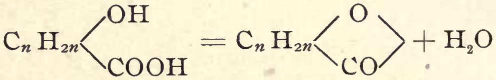
1 : 1.02 : 0.67 : 0.07.

These relations represent approximately the relative distances of the groups united to the carbon atoms at the moment of maximum approach. In conformity with this it follows that the majority of intramolecular reactions which take place in saturated compounds are effected with greater difficulty between neighboring groups, that is to say in the α-position, with more difficulty than between the groups 1 and 3 or β-position, but very easily, much more frequently, and even spontaneously between the groups 1 and 4 and 1 and 5, or in the γ- and δ-positions. Thus it is, that the chlorhydrins[1] lead to the ethylene oxids,



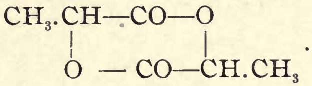
$$C_n H_{2n}\left\langle\begin{matrix}OH\\Cl\end{matrix}\right. = C_nH_{2n}O + HCl$$

while the oxy-acids give lactones,



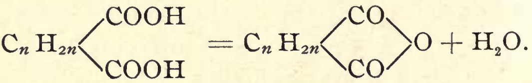
$$C_n H_{2n}\left\langle\begin{matrix}OH\\COOH\end{matrix}\right. = C_n H_{2n}\left\langle\begin{matrix}O\\CO\end{matrix}\right\rangle + H_2O$$

which are formed exceedingly easily by starting from the γ- and δ-derivatives, and exceptionally by using the β-derivatives, but never in the case of α-derivatives.[2] Starting from the derivatives such as the lactic acid two molecules enter into the reaction and thus form a chain consisting of these atoms; *e.g.*, the lactid,



$$\begin{array}{l}CH_3.CH—CO—O\\ \quad\;\;|\qquad\qquad\;\;|\\ \quad\;\;O\;—\;CO—CH.CH_3\end{array}$$

The α- and β-amido acids are not decomposed in the same way as the γ- and δ-amido acids into water and lactams (pyrrolidones and piperidones); one does not know of an anhydrid of oxalic and malonic acids, but succinic and glutaric acids whose carboxyl groups are in the γ- and δ-position to one another yield anhydrids without difficulty.



$$C_n H_{2n}\left\langle\begin{matrix}COOH\\COOH\end{matrix}\right. = C_n H_{2n}\left\langle\begin{matrix}CO\\CO\end{matrix}\right\rangle O + H_2O.$$

It should be noticed that changes of constitution may modify the preceding reactions; for example, the pres-

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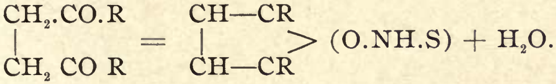
[1] Evans: Ztschr. phys. Chem., 7, 337.

[2] Wislicenus: "Anordung der Atome," p. 67.

ence of certain groups, such as alcohol radicals favor the transformation of dibasic acids into anhydrids and of oxy-acids into lactones. In the same way the formation of the lactocarboxylic acid derivatives of the dicarboxy-oxy-acids appear to be facilitated by the presence of the two carboxyl groups. This is also in agreement with the results obtained from the investigation of the molecular conductivity of these acids. Wislicenus has explained in the same way the characteristic decomposition which the β-halogen acids undergo when treated with sodium carbonate,

$$COONa.CH_2CHBrR = CO_2 + NaBr + CH_2{:}CHBr.$$

The α-halogen acids are, on the other hand, much more stable, as the sodium atom of the group COONa is nearer to the halogen atom in the first case than in the second. This will be easily seen by using solid models. There only remains to be mentioned the transformation of γ-diketones and compounds of this kind into cyclic derivatives of furfuran, pyrrol, and thiophen.



$$\begin{array}{l} CH_2.CO.R \\ | \\ CH_2\ CO\ R \end{array} = \begin{array}{l} CH—CR \\ | \\ CH—CR \end{array} > (O.NH.S) + H_2O.$$

III. STEREOCHEMISTRY OF CYCLIC COMPOUNDS.

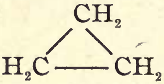
a. General.—The tetrahedral theory is the basis of the new and very striking development which concerns the formation and configuration of cyclic compounds. It suffices to allow that the four valences of a carbon atom considered as isolated forces acting normally in the direction of the four summits of a regular tetrahedron, can be diverted from their original direction. Thus this diversion will naturally produce an increasing tension in the interior of the molecule.[1] (Baeyer's tension theory.) This idea takes into account the properties of ethylene derivatives which are regarded as compounds of dimethylene, but it is principally of use in the study of polymethylene compounds.

The configuration of polymethylene derivatives.—One must admit, in compounds characterized by double or triple linkages, that the valences act as forces parallel to one another; in consequence they act as a result of being deviated from their original direction, and this also holds good with cyclic compounds. The size of the deviation angle serves to measure approximately the forces or tension which tend to the return of the valence to its normal position. One can conceive, therefore, that these forces and consequently the angle on which it depends, are in inverse ratio to the stability of closed chains. In the tetrahedral scheme which represents methane, two of the valences form an angle of 109° 28′.

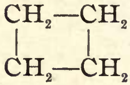
In supposing the centers of the different atoms of carbon to be situated in the same plane, this angle would have the following values in polymethylene compounds.

$\mathrm{CH_2}{=}\mathrm{CH_2}$

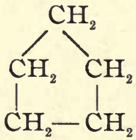
Dimethylene
+ 54° 44′.



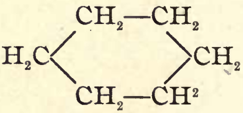
Trimethylene
+ 24° 44′.



Tetramethylene
9° 34′.



Pentamethylene
+ 0° 44′.



Hexamethylene
— 5° 16′.

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[1] Baeyer: Ber. d. chem. Ges., 18, 2279.

The deviation is then at its maximum in the ethylene compounds ; this corresponds to the maximum of tension, and explains why these chains are easily broken, for, as is well known, the mere presence of iodin is sufficient to produce this change. The trimethylene ring is more stable, although it also breaks when treated with hydrobromic acid ; finally closed chains with four and five atoms of carbon are only broken with difficulty in reactions involving addition. These characteristics are shown in the figures on pages 122 and 123. The closed chain with two carbon atoms is the form obtained with the greater expenditure of energy, than a chain containing five carbon atoms. The calorimetric results of Stohmann[1] confirm this view, as the heat consumed in forming a chain containing two or three carbon atoms is practically the same as that used in a tetramethylene synthesis, while the formation of penta- and hexamethylene compounds, consumes a quantity of heat which is much smaller.

The configuration of the polymethylene compound is not without its analogy to that of ethylene. All the atoms of carbon are in the same plane, which one may term as the annular plane, and the atoms of hydrogen united to the carbon are in two parallel planes, situated on each side of the primitive plane. The tension theory applied to the tri, tetra, and penta derivatives of methylene is in favor of this view, for it is under these conditions that one gets the minimum tension of the valences of carbon. One can bring experimental facts as proof also ; for example, one obtains cases of isomerism analogous to those which have been found in the ethylene series and which may be mentioned further on. But in the case of hexamethylene compounds the con-

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[1] Stohmann : J. prakt. Chem., **45**, 475.

ditions are such as to require special consideration. Here, regular tetrahedra have been united to one another by their summits to form a closed chain without compelling one to assume a deviation of the valences from their original direction. This may be done in two ways. Suppose that the carbon atoms are not all in the same plane; then one may get first, an immovable symmetrical configuration with a regular distribution of the two atoms of carbon in two parallel planes, and an orientation of the twelve atoms of hydrogen in three parallel planes, and second, a mobile unsymmetrical constitution without any fixed position for the atoms of carbon and hydrogen. According to this hypothesis which is due to Sachse, the symmetrical configuration would indicate two monosubstituted stereoisomers, and as a matter of fact, two hexahydrobenzoic acids are known, one obtained by the reduction of benzoic acid, the other being the hexanaphthalenecarboxylic acid.

Configuration of the Cyclic Compounds, $(CH)_n$

Benzene derivatives.—In acetylene, $HC\equiv CH$, three of the valences of carbon are deviated 70° 32′ which correspond to strong tension and consequently unstability. One can consider the acetylene molecule as plane; that is to say, that the atoms of carbon and hydrogen of which it is composed are situated in the same plane. It is probable that other bodies of this kind (benzene, naphthalene, phenanthrene) have an analogous configuration, or in other words, in these compounds the carbon atoms are arranged in an annular plane. One can only bring certain negative proofs to bear on this view, particularly the fact that up to the present, one has not found stereoisomers among the substitution derivatives of these hydrocarbons, and that all the efforts made in the direction of separating them into two components have remained fruitless.[1]

Among the views brought forward in this connection the work of Wunderlich[2] should be mentioned, who asserted that atoms had a definite solid form (the tetrahedral form for carbon), of Werner on affinity and valence, and of Hermann, who dispenses with all hypotheses regarding the nature of the carbon atoms and who uses strictly geometrical figures.

Lastly Friedel[3] observes that if one considers the Kekulé formula in the light of his tetrahedral scheme, the only objection which has been made against this formula disappears. This objection was raised in considering the possibility of two ortho derivatives of benzene. With a very small normal tension of the valences (3°, 46′) one may construct a hexagonal scheme in which the distances of the atoms of hydrogen in benzene are equal; consequently the reciprocal action between these atoms will also be equal and the possibility of the existence of two ortho derivatives is dispensed with.

b. The geometrical isomerism of the polymethylene derivatives.—Geometrical isomerism exists in the polymethylene derivatives as it does in those of ethylene, for the formation of a cyclic compound arrests the mobility of the atoms of carbon as it does the double bond. It has been seen in the geometrical isomers of ethylene, that they are represented by schemes in which the atoms are oriented differently in relation to the plane of the double bond. In the same way the stereoisomeric poly-

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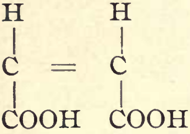
[1] Le Bel: Bull. Soc. Chim., **38**, 398; Lewkowitsch: Ber. d. chem. Ges., **16**, 1578.

[2] "Organische Moleküle," 1886.

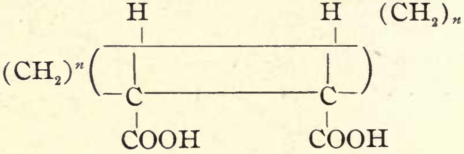
[3] Friedel: Bull. Soc. Chim. (3), **5**, 130.

methylene compound will be represented by figures in which the atoms are placed differently with respect to the annular plane. These compounds, therefore, give two stereoisomeric disubstitution products according as the two atoms of hydrogen are both on the same side of the plane, or are separated by it. The most important polymethylene stereoisomers belong to the hexamethylene series. Among the hydrocarbons of this series may be mentioned the two dihydroterpenes (methylisopropylhexamethylenes); among the halogen derivatives two hexachlorids of benzene, $C_6H_6Cl_6$;[1] among the hydroxyl compounds two paradioxyhexamethylenes, $C_6H_{10}(OH)_2$ (quinites), obtained synthetically;[2] then several hexoxyhexamethylenes; *viz.*, two inosites, $C_6H_6(OH)_6$,[3] two pinites, $C_6H_6(OH)_5.OCH_3$, and lastly numerous stereoisomeric polymethylene acids. These acids are comparable to fumaric and maleic acids, from which one gets the following scheme:

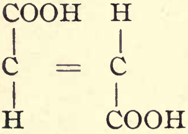


$$\begin{array}{ccc} H & & H \\ | & & | \\ C & = & C \\ | & & | \\ COOH & & COOH \end{array}$$

Maleic acid.

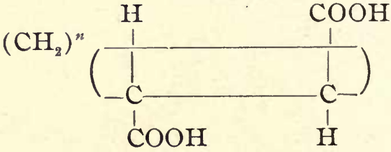


Maleic acid or cis form.



$$\begin{array}{ccc} COOH & & H \\ | & & | \\ C & = & C \\ | & & | \\ H & & COOH \end{array}$$

Fumaric acid.



Fumaroid or cistrans form.

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[1] Friedel: Bull. Soc. Chim. (3), **5**, 130.

[2] V. Baeyer: Ber. d. chem. Ges., **25**, 1037 and 1804.

[3] Maquenne: Ann. chim. phys. (6), **22**, 264.

Experimentally there have been found several acids corresponding to the maleinoid type. These are characterized by their solubility, their low melting-points and their pronounced acid reaction, and, on the other hand, other acids, less soluble and melting less readily which correspond to fumaric acid. These latter are formed by direct molecular transposition, by means of hydrochloric acid, which indicates their relative stability, while the less stable modifications can be looked upon as the direct product of the reduction of polymethylene acids. These properties are met with in the dicarboxyl, and tricarboxyl derivatives of trimethylene, which are found in two modifications;[1] in the numerous hexamethylene dicarboxylic acids, and in particular in the hexahydrogen derivatives of phthalic[2] and terephthalic[3] acids, and in the hexahydromellitic[4] acids. These acids are distinguished somewhat from fumaric and maleic acids in the way in which they give an anhydrid, which forces one to assume relative remoteness of the two carboxyl groups. The cisdicarboxylic acids in which the two carboxyl groups are close together, *e.g.*, the cishexahydrophthalic acid are transformed easily into anhydrids corresponding in this particular to maleic acid; but the cisdicarboxylic acid in which the carboxyl groups are separated by several atoms of carbon does not do so. For example, the hexahydroterephthalic acid does not give an anhydrid.

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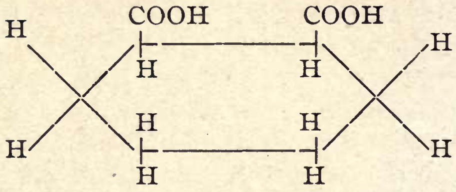
[1] Buchner: Ber. d. chem. Ges., **27**, 702; Conrad and Gutzheit: *Ibid.*, **17**, 1186.

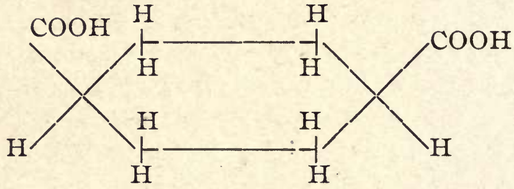
[2] v. Baeyer: Ann. Chem. (Liebig), **258**, 145.

[3] v. Baeyer: *Ibid.*, **245**, 103; **251**, 257; **256**, 1; **258**, 1 and 145; **266**, 169; **269**, 145.

[4] v. Baeyer: Ber. d. chem. Ges., **1**, 118.

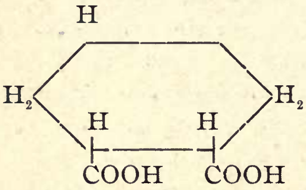


Cishexahydrophthalic acid, yielding an anhydrid.

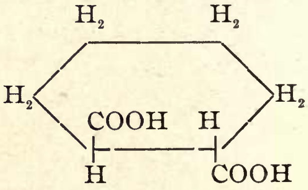


Cishexahydrophthalic acid, not yielding an anhydrid.

Conversely and worthy of note is the fact that certain transdicarboxylic acids of the fumaroid type give anhydrids which are different from those yielded by the cis acids, and can be transformed into the latter. Thus, the formation of anhydrids is only possible when the two carboxyl groups are united to neighboring carbon atoms, and depends besides on other conditions. Thus, starting with the two hexahydrophthalic acids, cis and trans,

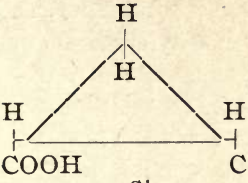


Cis.

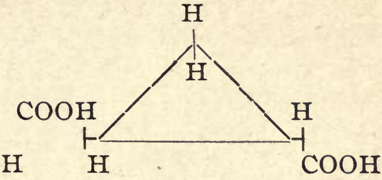


Cistrans.

one may prepare two stereoisomeric anhydrids while with the trimethylene dicarboxylic acids,



Cis.



Cistrans.

the trans modification does not give anhydrids any more easily than fumaric acid itself. One may explain these facts in the following way. The valences united to the carboxyl groups form between them an angle of 180° which may be shown readily on the solid model, while in the fumaroid hexahydrophthalic acid the replacing of the double bond (*e. g.*, the chain C_2) by the ring C_6 reduces this angle to something less than 109° ; this angle then becomes nearly equal to the angle of the valence in the original tetrahedron. With the corresponding acids of tri-, tetra-, and pentamethylenes the angle is intermediate between the two extreme values of 180° and 109°. As a result, in cyclic compounds, as the number of carbon atoms increases the angle in question diminishes, and consequently the distance between the two carboxyl groups. This explains why the transdimethylene dicarboxylic acid and the transtrimethylene dicarboxylic acid do not give anhydrids, while one has been able to isolate an anhydrid of the transhexahydrophthalic acid.

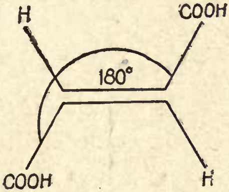
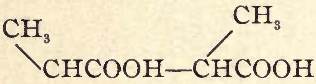
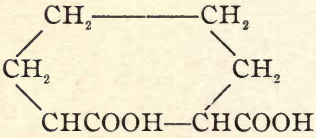


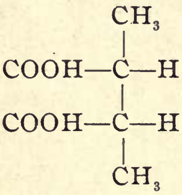
Fig. 21.

The optical and geometrical isomerism of polymethylene compounds.—The geometric isomers of ethylene without a symmetric carbon atom do not present molecular dissymmetry; but this dissymmetry may be met with in the geometrical isomers of polymethylene acids. The presence of two asymmetric carbon atoms renders them analogous to the derivatives of tartaric acid, or more closely to the dialkyl succinic acids. The structural analogy which exists for instance between dimethyl succinic acid and hexahydrophthalic acid is shown in the following formula:

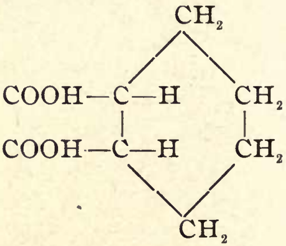

Dimethyl succinic acid.


Hexahydrophthalic acid.

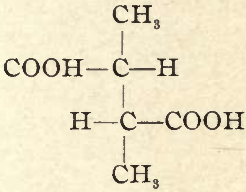
The hexahydrogenated cis acid is thus, from a stereochemical point of view, comparable to non-racemic inactive dimethyl succinic acid (corresponding to inactive tartaric acid).



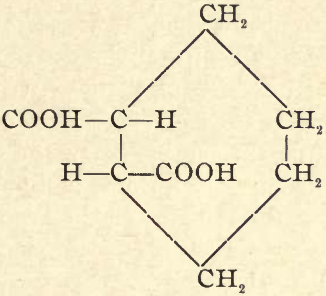
$$\begin{array}{c} CH_3 \\ | \\ COOH—C—H \\ | \\ COOH—C—H \\ | \\ CH_3 \end{array}$$

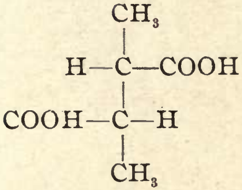


The trans acid, on the other hand, may be compared to racemic dimethyl succinic acid (corresponding to racemic acid, although it has not yet been decomposed into its two isomers). It should thus exist in two enantiomorphous modifications :

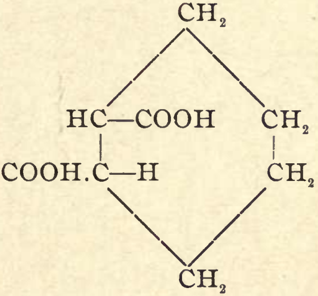


$$\begin{array}{ccc} & CH_3 & \\ & | & \\ COOH- & C & -H \\ & | & \\ H- & C & -COOH \\ & | & \\ & CH_3 & \end{array}$$



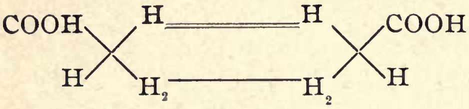


$$\begin{array}{ccc} & CH_3 & \\ & | & \\ H- & C & -COOH \\ & | & \\ COOH- & C & -H \\ & | & \\ & CH_3 & \end{array}$$

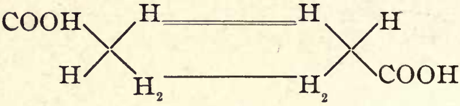


Cis acids or those corresponding to the maleinoid type are hence inactive by intramolecular compensation. The trans or fumaroid acids, on the contrary, are rendered inactive by intramolecular compensation. The first are incapable of decomposition in a stereochemical sense; the latter should be, although experimentally this has not yet been realized. The existence of a laevo- and dextroinosite, $CH(OH)_6$, shows besides, that optical inactivity can exist in cyclic compounds and especially in substances containing the hydroxyl group.

c. The geometrical isomerism of cyclic compounds with double bonds.—The isomerism here is of the same kind as that which has already been described and has only been observed in that group of compounds which are the result of the plane reduction of benzene and naphthalene. Among these the many compounds belonging to the di- and tetrahydrogen derivatives of the dicarboxylic acids of benzene are the result of the work of v. Baeyer; they form stereoisomers analogous to those of the hexahydrogen acids; thus one has:



Cis non-racemic.



Cis trans racemic.

The racemic dihydrophthalic acid, which has been split up into two isomers by Proost,[1] furnishes an example of substances belonging to this class.

The trans dihydrophthalic and tetrahydrophthalic acids also give anhydrids which may be transformed into anhydrids of cis acids. The atomic arrangements which characterize mixed cyclic compounds have not yet been fixed; it is therefore probable that conversely to that which has been observed in the polymethylene compounds, and in the derivatives of the type $(CH)_n$, the atoms of carbon in the benzene nucleus are not in the

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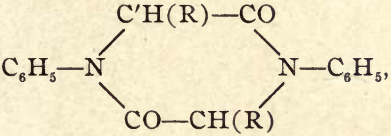
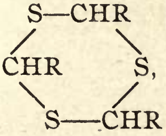
[1] Proost: Ber. d. chem. Ges., **27**, 3185.

same plane ; hence, one would not here have to deal with an annular plane. As a result of this, the stereoisomerism of these compounds would become still more complex, and the terpene series, and the group of derivatives of camphor furnish an example of this statement.

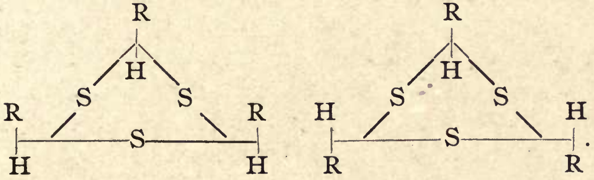
d. The geometrical isomerism of compounds analogous to polymethylene derivatives.—Among the saturated cyclic compounds, the piperazones[1] with two asymmetric carbon atoms of the formula,



exist in two isomeric modifications, corresponding to the dialkyl succinic acids ; the trithioaldehydes, $(RCHS)_3$, regarded as derivatives of trithiomethylene,[2]



, also give two isomers corresponding to the configurations,



These configurations are borne out by the fact that the unstable cis derivatives when heated slightly above their

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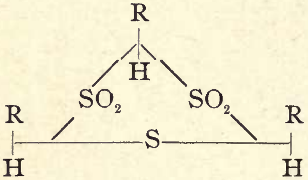
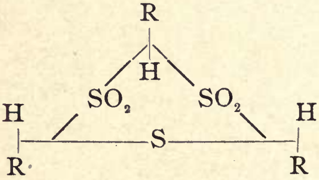
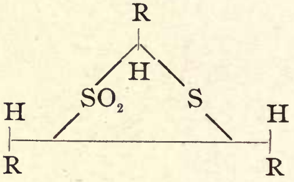
[1] Bischoff : Ber. d. chem. Ges., **25**, 2999.

[2] Baumann : *Ibid.*, **24**, 1425.

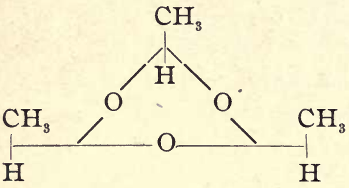
melting-point give, by partial oxidation, a disulfone sulfid; on the other hand the stable and higher melting trans derivatives give two stereoisomeric sulfids of disulfone.



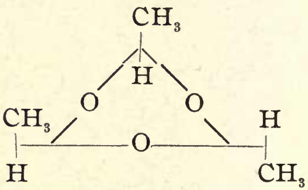




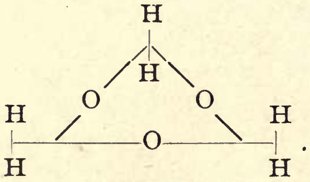
One may explain in the same manner the isomerism of metaldehyde and paraldehyde which may be represented by the figures



Cis paraldehyde (?).



Cistrans metaldehyde (?).



Paraformaldehyde.

[1] Friedel: Bull. Soc. Chim. (3), **9**, 384.

In agreement with this explanation one has the experimental evidence that formic aldehyde gives but one polymer.

IV. THE GEOMETRICAL ISOMERISM OF NITROGEN

Theoretical.—It has been seen in the foregoing that the absence of optical isomers among the ammonium bases of the type NRR′R″ tends to prove that the three valences of nitrogen are situated in the same plane. However this element does not always behave in this way, even when it acts in a trivalent sense; consequently it can give rise to cases of isomerism which correspond very closely with the geometrical isomerism of ethylene compounds.[1]

The following are some considerations on which is based the conception of geometrical isomerism in nitrogen compounds. In assuming that the trivalent nitrogen N‴ is equivalent to the group (CH)‴, one can replace in any derivatives containing (CH) one or more of these groups by nitrogen atoms. Thus, hydrocyanic acid, $HC{\equiv}N$, corresponds to acetylene, $CH{\equiv}CH$, pyridin, $(CH)_5N$, and the diazins, $(C_6H)_4N_2$, to benzene, $(CH)_6$, and as three valences of carbon directed towards the summit of a tetrahedron can be replaced by nitrogen, it is necessary to conclude that in these bodies the three valences of nitrogen are also directed towards the angles of a tetrahedron (which cannot be a regular one), of which the nitrogen atom occupies the fourth summit.

Hence, compounds analogous to acetylene, *i.e.*, the nitriles, do not present the phenomena of isomerism. On the other hand, just as the ethylene derivatives give two isomers, the compounds with a double linkage between an atom of carbon and an atom of nitrogen, and the com-

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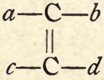
[1] Hantzsch and Werner: Ber. d. chem. Ges., **23**, 1 and 1243.

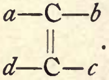
pounds with a double linkage between two atoms of nitrogen will occur in two modifications.

Experimentally these different cases of isomerism have been observed, and it will be necessary to make a similar classification to that which was followed out in the study of geometric isomers of the preceding compounds.

1. Derivatives of geometrical isomeric carbon of the general formula, $ab\mathrm{C}:\mathrm{C}cd$, corresponding to two configurations,

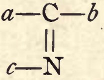


$$\begin{array}{c} a\text{—C—}b \\ \| \\ c\text{—C—}d \end{array}$$

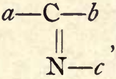


$$\begin{array}{c} a\text{—C—}b \\ \| \\ d\text{—C—}c \end{array}.$$

2. Geometrical isomers of carbon and nitrogen of the general formula, $ab\mathrm{C}:\mathrm{N}c$, corresponding to the two configurations,



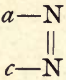
$$\begin{array}{rcl} a\text{—} & \mathrm{C} & \text{—}b \\ & \| & \\ c\text{—} & \mathrm{N} & \end{array}$$



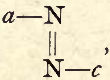
$$\begin{array}{rcl} a\text{—} & \mathrm{C} & \text{—}b \\ & \| & \\ & \mathrm{N} & \text{—}c \end{array},$$

of which the best known examples are the oximes, the hydrazones, and the imido compounds.

3. Derivatives of double linked nitrogen of the general formula, $a\mathrm{N}:\mathrm{N}c$, corresponding to the two configurations,



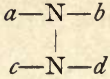
$$\begin{array}{rc} a\text{—} & \mathrm{N} \\ & \| \\ c\text{—} & \mathrm{N} \end{array}$$



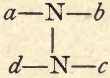
$$\begin{array}{rcl} a\text{—} & \mathrm{N} & \\ & \| & \\ & \mathrm{N} & \text{—}c \end{array},$$

of which the most important representatives are found among the diazo and azo compounds.

It is still possible that compounds containing a single linkage, nitrogen (for example, the derivatives of hydrazin, $ab\mathrm{N}.\mathrm{N}cd$), exist in two modifications, indicated by the following:



$$\begin{array}{c} a\text{—N—}b \\ | \\ c\text{—N—}d \end{array}$$



$$\begin{array}{c} a\text{—N—}b \\ | \\ d\text{—N—}c \end{array}$$

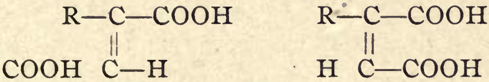
The two modifications of picrylhydrazin,[1] $C_6H_5NH.NHC_6H_2(NO_2)_3$, correspond perhaps to these two modifications.

The general properties of the geometric isomers of nitrogen.—The characteristics which differentiate the geometric isomers of nitrogen are comparable to those distinguishing the carbon compounds. They are met with in all the physical and chemical properties which depend on intramolecular reactions, and the distance between the atoms. Spatial formulae explain the chemical characteristics of the nitrogen isomers, as well as those of the corresponding ethylene compounds. According to this view, it is necessary to assume that the geometric isomers of nitrogen have the characteristic property of passing very easily from one configuration to another, and similarly the affinity constants are different for compounds, such as

$$\begin{array}{r} \text{R—C—COOH} \\ \| \quad\quad\;\; \\ \text{HO—N} \quad\quad\;\; \end{array} \qquad \begin{array}{l} \text{R—C—COOH} \\ \quad\; \| \\ \quad\; \text{N—OH} \end{array}$$

Geometric isomeric oximido carboxylic acids.

as for



$$\begin{array}{r} \text{R—C—COOH} \\ \| \quad\quad\;\; \\ \text{COOH C—H} \quad\quad\;\; \end{array} \qquad \begin{array}{l} \text{R—C—COOH} \\ \quad\; \| \\ \text{H C—COOH} \end{array}$$

Geometric isomeric ethylene carboxylic acids.

In both cases the constants vary between the same limits. These facts are explained clearly if one assumes,

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[1] Willgerodt: J. prakt. Chem., **41**, 297.

as with the ethylene derivatives, that the nitrogen compounds are true stereoisomers.[1]

The explanation of the geometrical isomerism of nitrogen compounds has been sought for as was formerly done in the case of the ethylene compounds by using constitutional formulae. The following explanation gives the reasons why this interpretation has been abandoned. In the first place, the number of known isomers does not coincide with the number of the different constitutional formulae, which can be conceived for these compounds; besides, one cannot explain why compounds of the symmetric structure $aa\mathrm{C} : \mathrm{N}d$ give but one modification, while those of asymmetric structure give two. Hence, one would be forced to represent these two types by different structural formulae, which would be to a greater or less extent problematical, for one knows that the oximes of the aromatic series and of the aliphatic series do not behave in the same way. In this case, the mutual transformation of these isomers would be no longer attributable to the same causes. Lastly, structural formulae would not explain intramolecular transpositions, nor the evident analogy of isomers derived from nitrogen with those of the stereoisomeric ethylene derivatives.

V. THE GEOMETRICAL ISOMERS OF CARBON AND NITROGEN

a. The historical proofs of identical constitution.—The two benzildioximes corresponding to formula

$$C_6H_5NOH.CNOH.C_6H_5$$

were first isolated by Goldschmidt,[2] and v. Meyer and

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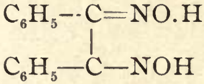
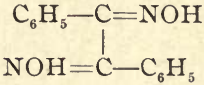
[1] Hantzsch and Miolati : Ztschr. phys. Chem., **10**, 1.

[2] Ber. d. chem. Ges., **16**, 2176.

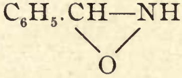
Auwers[1] proved that these two compounds had the same constant, and discovered a third isomer;[2] they thought to explain the cause of this isomerism by assuming that the simple bond between the two atoms of carbon had ceased to be completely mobile.

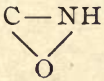


$$\begin{array}{l} C_6H_5-C=NO.H \\ \qquad\;\, | \\ C_6H_5-C-NOH \end{array}$$



$$\begin{array}{l} \qquad C_6H_5-C=NOH \\ \qquad\qquad\quad\;\, | \\ NOH=C-C_6H_5 \end{array}$$

Beckmann,[3] a short time after this, prepared an isomer of ordinary benzaldoxime, $C_6H_5CH:NOH$. He also considered it as a structural isomer,[4] and gave to it the formula  , although Goldschmidt[5] had proved the structural identity of the two benzaldoximes. These facts which do not coincide with the interpretation of the benzildioximes which had been given by v. Meyer and Auwers induced Hantzsch and Werner to the explanation which is given in this book, and which led to the discovery of different stereoisomeric aldoximes, ketoximes, dioximes, oximido acids, etc. At first these facts appeared difficult of explanation, for about the same time it was proved that the oximes gave rise to tautomeric phenomena. The group (CNOH) could in reality react not only as a normal group, CNOH, but also as an iso group,



Now the general formula of oximes,

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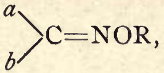
[1] Ber. d. chem. Ges., **21**, 784 and 3510.

[2] *Ibid.*, **22**, 705.

[3] *Ibid.*, **20**, 2766; *Ibid.*, **22**, 432.

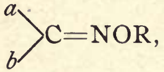
[4] *Ibid.*, **22**, 429, 514, 1531, 1588.

[5] *Ibid.*, **22**, 3113.



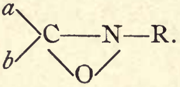
$$\left.\begin{matrix}a\\b\end{matrix}\right\rangle C=NOR,$$

is confirmed by reactions which they undergo without difficulty, and which are completed under conditions which exclude the intervention of the least traces of moisture. One thus obtains in all cases, derivatives of the formula

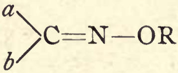


$$\left.\begin{matrix}a\\b\end{matrix}\right\rangle C=NOR,$$

and not of the formula

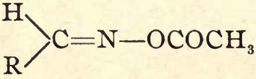


Isomerism in oximes is also found among other substituted products; two isomeric compounds corresponding to the formula

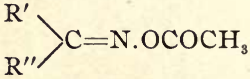


$$\left.\begin{matrix}a\\b\end{matrix}\right\rangle C=N-OR$$

are known. These two bodies, like the oximes themselves, are mutually transformed one into the other in a similar manner to the geometric isomers of ethylene. Thus, for example, two isomers of each of the alkyl and acetyl esters are known:

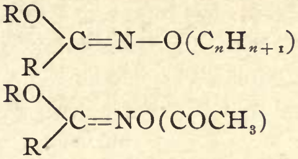


$$\left.\begin{matrix}H\\R\end{matrix}\right\rangle C=N-OCOCH_3$$

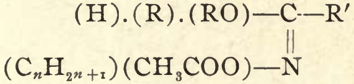


$$\left.\begin{matrix}R'\\R''\end{matrix}\right\rangle C=N.OCOCH_3$$

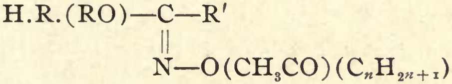
The same is true with the alkyl and acetyl esters of the hydroxamic acids:



This can only be expressed by configuration formulae :

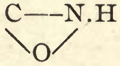


$$\begin{array}{rl}(H).(R).(RO)\text{—} & C\text{—}R' \\ & \| \\ (C_nH_{2n+1})(CH_3COO)\text{—} & N\end{array}$$

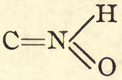


$$\begin{array}{rl}H.R.(RO)\text{—} & C\text{—}R' \\ & \| \\ & N\text{—}O(CH_3CO)(C_nH_{2n+1})\end{array}$$

Explanations based on the difference in the structure of the group (CNOH), such as are indicated by the formulae



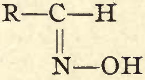
or



must thus be absolutely abandoned.

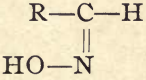
b. The different classes of stereoisomeric oximes. Determination of their configuration.

Aldoximes and aldoximecarboxylic acids.—Among this class of compounds one defines the synaldoximes in which the oximic hydroxyl and the aldehyde hydrogen are in neighboring positions, and the antialdoximes in which the two groups are in opposite positions.



$$\begin{array}{c}R\text{—}C\text{—}H \\ \| \\ N\text{—}OH\end{array}$$

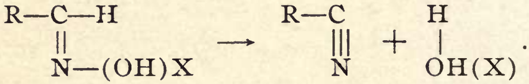
Synaldoxime.



$$\begin{array}{c}R\text{—}C\text{—}H \\ \| \\ HO\text{—}N\end{array}$$

Antialdoxime.

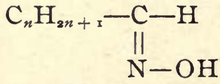
The synaldoximes are decomposed as the formula would indicate into water and nitriles. This reaction is effected more or less easily, according to the nature of the radical R. It is produced sometimes with the oximes themselves, as in trimethyl benzaldoxime, but more often with their acetates or their phenyl carbamic esters,



$$\begin{array}{l}\mathrm{R-C-H}\\ \quad\;\| \\ \quad\mathrm{N-(OH)X}\end{array} \longrightarrow \begin{array}{c}\mathrm{R-C}\\ \quad ||| \\ \quad\mathrm{N}\end{array} + \begin{array}{c}\mathrm{H}\\ | \\ \mathrm{OH(X)}\end{array}.$$

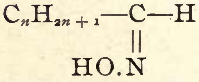
Under the same conditions the antialdoximes do not undergo any change, and the same holds good for their derivatives, from which it is always possible to reproduce unaltered, the original oxime.

This kind of stereoisomerism is very general among the aromatic compounds. It is found in the oximes of thiophene and of furfuran. Sometimes however, the differences between the two isomers are only brought out in their acetyl derivatives. This is the case with benzoyl formoxime, $C_6H_5-CO-CNOH-H$, and aldoxime acetic acid (β-oximidopropionic acid), $COOH-CH_2-CNOH-H$. The aldoximes properly speaking, such as the acetaldoxime and oenanthaldoxime, furnish examples of this class. The nature of the radical R exerts a great influence on the relative stability of the two configurations. In the aliphatic series where $R = C_nH_{2n+1}$ the synaldoximes are more stable, but in the aromatic series the antialdoximes undergo change the less readily. Thus one will have:



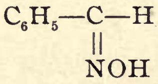
$$\begin{array}{r}\mathrm{C_nH_{2n+1}-C-H}\\ \| \qquad\;\; \\ \mathrm{N-OH}\end{array}$$

Stable alkyl synaldoxime.



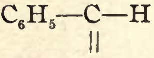
$$\begin{array}{r}\mathrm{C_nH_{2n+1}-C-H}\\ \| \qquad \\ \mathrm{HO.N}\quad\;\end{array}$$

Unstable alkyl antialdoxime.



$$\begin{array}{r}\mathrm{C_6H_5-C-H}\\ \| \qquad \\ \mathrm{NOH}\quad\end{array}$$

Unstable phenyl synaldoxime.

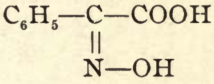


$$\begin{array}{r}\mathrm{C_6H_5-C-H}\\ \| \qquad \\ \mathrm{HO-N}\quad\;\end{array}$$

Stable phenyl antialdoxime.

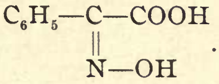
The aldoxime or α-ketoxime carboxylic acids, R—CNOH—COOH, resemble the aldoximes in their general properties, but they differ with regard to their stability.

Thus, one has the oximes of phenylglyoxylic acid, $C_6H_5—CNOH—COOH$.



$$\begin{array}{c} C_6H_5—C—COOH \\ \| \\ N—OH \end{array}$$

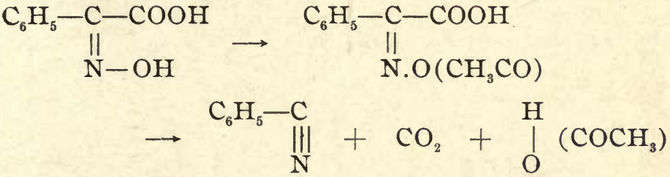
Stable synphenylketoxime carboxylic acid.



$$\begin{array}{c} C_6H_5—C—COOH \\ \| \\ N—OH \end{array}$$

Unstable antiphenylketoxime carboxylic acid.

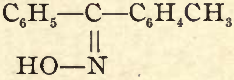
The first of these two acids which contains the two groups (OH) and (COOH) in neighboring positions, is the only one which gives (as in the synaldoximes) an acetate with acetic anhydrid.



$$\begin{array}{c} C_6H_5—C—COOH \\ \| \\ N—OH \end{array} \longrightarrow \begin{array}{c} C_6H_5—C—COOH \\ \| \\ N.O(CH_3CO) \end{array}$$

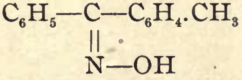
$$\longrightarrow \begin{array}{r} C_6H_5—C \\ ||| \\ N \end{array} + CO_2 + \begin{array}{c} H \\ | \\ O \end{array}(COCH_3)$$

β-Ketoximes.—The structural unsymmetrical ketoximes are also designated by the prefixes syn- and anti-; *e.g.:*



$$\begin{array}{c} C_6H_5—C—C_6H_4CH_3 \\ \| \\ HO—N \end{array}$$

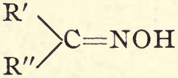
Synphenyltolylketoxime.



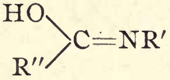
$$\begin{array}{c} C_6H_5—C—C_6H_4.CH_3 \\ \| \\ N—OH \end{array}$$

Antiphenyltolylketoxime.

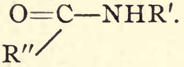
These configuration formulae allow one to see that the differences between two isomeric ketoximes should be much less sharply marked than those of the aldoximes, for the two groups, R and R′ which determine the dissymmetry, have much more in common than the H and R of aldehydes. According to Hantzsch, the determination of the configuration is based on the transformation of oximes into the isomeric amids (Beckmann's reaction). If one assume that the intermediate products vary according to the reagent employed (H_2SO_4, HCl, PCl_5 and H_2O), one may consider this reaction as leading to a change of position between the hydroxyl united to nitrogen, and one of the radicals united to carbon in the molecule



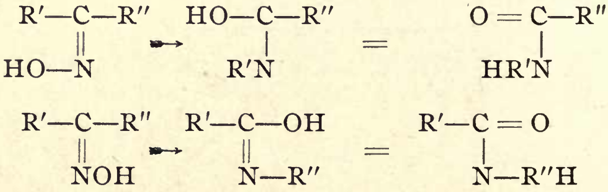
It thus forms an unstable amido modification, for example,



by tautomeric transposition; and this passes into the stable form, the true amid



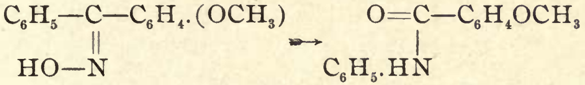
The stereoisomeric ketoximes will then give two isomeric substituted amids, according as the radical R′ or R″ takes the place of the hydroxyl. But, as the determination of the configuration by the study of intramolecular reactions supposes that the two groups which entering into the reaction occupy neighboring positions (syn), the radical which takes the place of the hydroxyl should be in a contiguous position to it.



$$\begin{array}{c}R'-C-R''\\ \|\\ HO-N\end{array} \rightarrow \begin{array}{c}HO-C-R''\\ |\\ R'N\end{array} = \begin{array}{c}O=C-R''\\ |\\ HR'N\end{array}$$

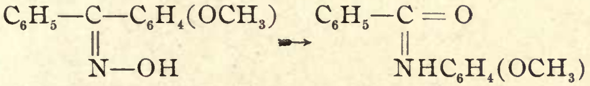
$$\begin{array}{c}R'-C-R''\\ \|\\ NOH\end{array} \rightarrow \begin{array}{c}R'-C-OH\\ \|\\ N-R''\end{array} = \begin{array}{c}R'-C=O\\ |\\ N-R''H\end{array}$$

Thus, the constitution of the amid which has been formed allows a determination of the configuration of the oxime; for the radical which has passed from carbon to nitrogen is the one which in the oxime was in the vicinity of the hydroxyl, and vice versa. Examples:



$$\begin{array}{l}C_6H_5-C-C_6H_4.(OCH_3)\\ \qquad\quad \| \\ \; HO-N\end{array} \longrightarrow \begin{array}{l}O=C-C_6H_4OCH_3\\ \qquad | \\ C_6H_5.HN\end{array}$$

Synphenyl anisyl ketoxime. Anisic anilid.



$$\begin{array}{l}C_6H_5-C-C_6H_4(OCH_3)\\ \qquad\quad \| \\ \qquad\;\; N-OH\end{array} \longrightarrow \begin{array}{l}C_6H_5-C=O\\ \qquad\quad \| \\ \qquad\;\; NHC_6H_4(OCH_3)\end{array}$$

Antiphenyl anisyl ketoxime. Benzoic anisid.

There are actually known among the stereoisomeric ketoximes numerous substitution products of the oximes of benzophenone, $C_6H_5—CNOH—C_6H_4X$, such as the oximes of phenyltolyl ketone, and of phenylxylyl ketone of parachlor-, brom-, iodo-, oxy- and amidobenzophenones, and some ortho and meta derivatives; besides these are two monoximes of benzil, $C_6H_5CNOH—CO—C_6H_5$, and of hydrobenzoin, $C_6H_5CNOH—CHOHC_6H_5$. If the fluid ketoximes of the fatty series,

$$C_nH_{2n+1}CNOH—C_{n'}H_{2n'+1},$$

are transformed into amids, they behave as a mixture of two isomers, but as a rule, it has been impossible to isolate the two modifications.

On the other hand, the oximes of benzoylpropionic, or of phenylketoximepropionic acids,

$$C_6H_5CNOH.CH_2CH_2COOH,$$

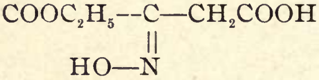
of which two stereoisomers are known, contain both an aromatic and aliphatic radical, and the stereoisomeric oximes of oximidosuccinic,

$$\mathrm{COOH—CNOHCH_2COOH},$$

and oximidoethylsuccinic acid,

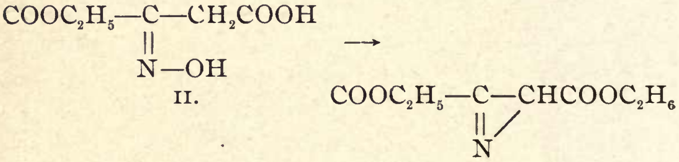
$$\mathrm{COOC_2H_5—CNOHCH_2COOH}$$

contain two radicals belonging to the fatty series. Numerous methods of determining the configuration of these compounds have been used. The most striking relies on the transformation of derivatives (2) into nitrile succinic ester,



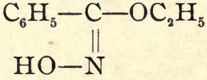
$$\begin{array}{l} \mathrm{COOC_2H_5\text{--}C\text{—}CH_2COOH} \\ \qquad\qquad\;\; \| \\ \qquad\quad \mathrm{HO\text{—}N} \end{array}$$

I.



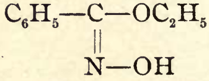
II. III.

Stereoisomeric derivatives of hydroxamic (hydroximic) acids.—It has been placed beyond doubt that many of the curious physical isomers discovered by Lossen belong to the stereoisomers of nitrogen. This is the case with the α-and β- ethylbenzhydroxamic or ethylbenzhydroximic acids, $\mathrm{C_6H_5—CNOH—OC_2H_5}$. The configuration of these compounds corresponds to the following formulae :



$$\begin{array}{l} \mathrm{C_6H_5\text{—}C\text{—}OC_2H_5} \\ \qquad\quad \| \\ \;\; \mathrm{HO\text{—}N} \end{array}$$

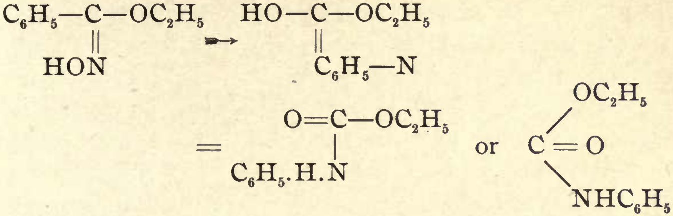
Syn acid.



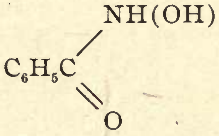
$$\begin{array}{l} \mathrm{C_6H_5\text{—}C\text{—}OC_2H_5} \\ \qquad\quad \| \\ \qquad\quad \mathrm{N\text{—}OH} \end{array}$$

Anti acid.

For the first alone gives phenylurethane (according to Beckmann's reaction)



while the second leads to completely different derivatives, on account of the immobility of the group OC_2H_5. The nonsubstituted hydroximic acids are not yet known in stereoisomeric forms, probably because the passage from one configuration to another is effected so easily by the intermediate tautomeric form



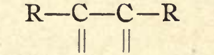
which is the same whatever be the original configuration.

Stereoisomeric dioximes or glyoximes.—These substances can exist in three modifications with a symmetrical formula

$$R—CNOH—CNOH—R\,;$$

these three modifications are designated respectively by the prefixes anti-, amphi- and syn-, corresponding to the formulae

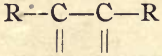
1



$$\begin{array}{ccc} R— & C—C & —R \\ & \| \quad \| & \\ HO—N & & N—OH \end{array}$$

Antiglyoxime.

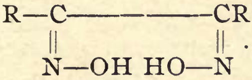
2



$$\begin{array}{cc} R—C & C—R \\ \| & \| \\ NOH & NOH \end{array}$$

Amphiglyoxime.

3



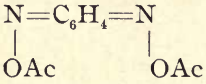
$$\begin{array}{cc} R—C & —CR \\ \| & \| \\ N—OH & HO—N \end{array}$$

Synglyoxime.

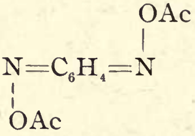
The three dioximes of benzil (diphenylglyoximes), $C_6H_5\text{—}CNOH.C.NOHC_6H_5$, correspond to these three configurations, while the dioximidosuccinic or glyoxime dicarboxylic acids, $COOH.CNOH.CNOHCOOH$, of which only two isomers are known, will be represented by formulae (1) and (3).

The unsymmetrical glyoximes which should give four modifications are only known as yet in three different forms. To this group of compounds belong the three monophenyl glyoximes, $C_6H_5.CNOH.CNOH.N$, the chlordioximes, and the glyoxime monocarboxylic acids, $Cl.CNOH.CNOH.H$, of which two isomeric modifications are known, and lastly, the methyl- and phenylglyoxime carboxylic acids, $COOH.CNOH.CNOH.H$, and methyl and phenyl glyoxime carboxylic acids, of which two isomers only have been isolated in the form of esters, acetates, and salts.

Stereoisomeric quinonoximes have recently been obtained; *e. g.*, two more oximes of orthochlorquinone, each giving a benzoyl derivative, and two[1] acetates of quinone dioxime. This last corresponds to the two formulae:



$$\underset{\text{OAc}}{\underset{|}{N}}=C_6H_4=\underset{\text{OAc}}{\underset{|}{N}}$$



$$\underset{\text{OAc}}{\underset{|}{N}}=C_6H_4=\overset{\text{OAc}}{\overset{|}{N}}$$

Determination of configuration.—The configuration of these compounds may be established either by means of the preceding methods or by reactions which hold good for each particular case. Thus the more stable of the three dioximes of benzil can be transformed into oxani-

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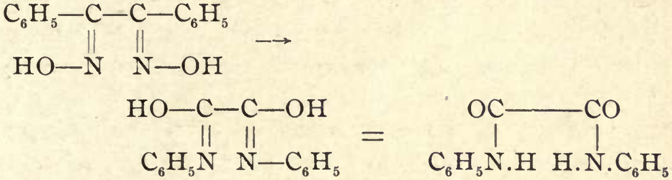
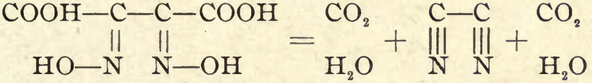
[1] Behrmann: Ber. d. chem. Ges., **27**, 217; **28**, 341.

lid in the same way that the simple quinoximes gave amids. Hence this oxime is antidiphenylglyoxime.



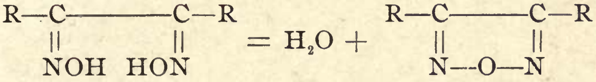
$$\begin{array}{c}C_6H_5-C-C-C_6H_5\\ \parallel \qquad \parallel\\ HO-N \quad N-OH\end{array} \longrightarrow \begin{array}{c}HO-C-C-OH\\ \parallel \qquad \parallel\\ C_6H_5N \quad N-C_6H_5\end{array} = \begin{array}{c}OC-\!\!-\!\!-CO\\ | \qquad\qquad |\\ C_6H_5N.H \quad H.N.C_6H_5\end{array}$$

Antiglyoxime dicarboxylic acid is decomposed by means of acetic anhydrid into carbon dioxid, and cyanogen as are the aldoxime carboxylic acids with an analogous configuration,



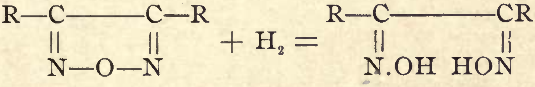
$$\begin{array}{c}COOH-C-C-COOH\\ \parallel \qquad \parallel\\ HO-N \quad N-OH\end{array} = \begin{array}{c}CO_2\\ \\ H_2O\end{array} + \begin{array}{c}C-C\\ ||| \quad |||\\ N \quad N\end{array} + \begin{array}{c}CO_2\\ \\ H_2O\end{array}$$

the syn-glyoximes in which the two hydroxyl groups are in apposition, have the property of giving anhydrids, azoxazols or furazans, respectively,



$$\begin{array}{c}R-C-\!\!-\!\!-C-R\\ \parallel \qquad \parallel\\ NOH \quad HON\end{array} = H_2O + \begin{array}{c}R-C-\!\!-\!\!-C-R\\ \parallel \qquad \parallel\\ N-O-N\end{array}$$

the synglyoximes are also produced by the reduction of the glyoxime peroxids,[1]



$$\begin{array}{c}R-C-\!\!-\!\!-C-R\\ \parallel \qquad \parallel\\ N-O-N\end{array} + H_2 = \begin{array}{c}R-C-\!\!-\!\!-CR\\ \parallel \qquad \parallel\\ N.OH \quad HON\end{array}$$

c. Transformation of stereoisomers into one another.—According to their configuration the isomeric oximes possess a stability which is different in each case. It may be imagined that the radicals united to carbon, exercise a greater or less attraction on the oximic

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[1] Angeli: Gazz. chim. ital., **22**, 450.

hydroxyl, which should depend on their electropositive or electronegative character, and on their relative spatial position. Hence, the changes in the configuration of an oxime, are dependent on the same cause as that met with in the ethylene derivatives, but with this difference, that they change much more readily. This explains why the isolation of the two stereoisomers is not always possible.

Transformations taking place under the influence of heat.—The action of heat always induces the transformation of the unstable modification of the oxime into the stable form, and even in certain cases this change takes place more or less rapidly at ordinary temperature, leading to a complete transformation, or to a state of equilibrium between the two oximes, *e. g.*,

$$\begin{array}{c} C_6H_5—C—C_6H_4OH \\ \| \\ N—OH \end{array} \longrightarrow \begin{array}{c} C_6H_5—C—C_6H_4OH \\ \| \\ HO—N \end{array}$$

By heating.

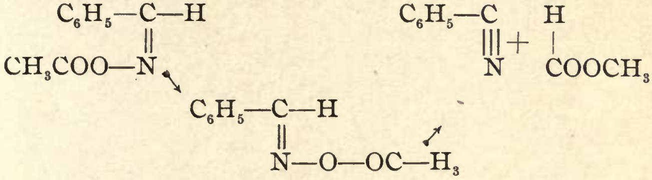
Synparabenzophenonoxime. Antiparaoxybenzophenoneoxime.

$$\begin{array}{c} C_6H_5—C—COOH \\ \| \\ HO—N \end{array} \longrightarrow \begin{array}{c} C_6H_5—C—COOH \\ \| \\ N—OH \end{array}$$

Gradually. Spontaneously.

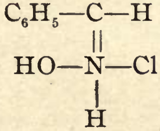
Antiphenylketoxime carboxylic acid. Synphenylketoxime carboxylic acid.

If the temperature be raised, and if it produce an intramolecular change, one obtains the same substances, no matter which of the oximes be employed. This takes place in quite the same way as in the case of maleic anhydrid, which is obtained equally as well in starting from fumaric acid as from maleic acid. The modification which is not directly decomposed is transformed probably first of all into its isomer. In this way one may account for the formation of benzonitril by the distillation of the antibenzaldoxime acetate,

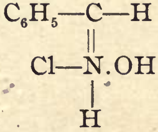


$$\begin{array}{l} C_6H_5—C—H \\ \qquad\quad \| \\ CH_3COO—N \end{array} \searrow \begin{array}{l} C_6H_5—C—H \\ \qquad\quad \| \\ \qquad\; N—O—OC—H_3 \end{array} \nearrow \begin{array}{l} C_6H_5—C \quad H \\ \qquad\quad \||| + \; | \\ \qquad\quad N \quad COOCH_3 \end{array}$$

Transformation taking place with the aid of chemical reagents.—These transformations are very numerous, and are accomplished sometimes by simply contact action, but more frequently with the formation of intermediate products, which as in the oximes, the metallic compounds, compounds with acids, or in some cases with dibromids, the nitrogen atom behaves as pentavalent. These results evidently depend on different conditions of molecular stability, but it must not be forgotten that the terms stable and unstable refer only to the oximes in a free state, and that they are more or less relative. Thus, the syn- and antialdoximes of the aromatic series can give, when treated with dry hydrochloric acid, the corresponding hydrochlorids,

(1) 

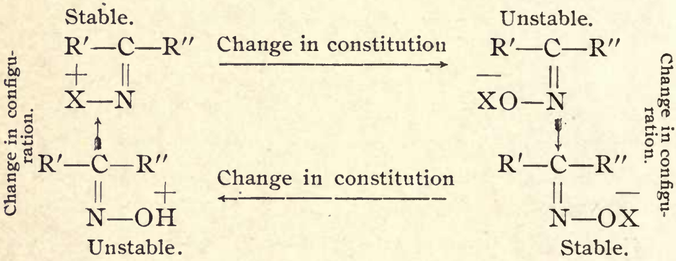
$$\begin{array}{c} C_6H_5—C—H \\ \| \\ HO—N—Cl \\ | \\ H \end{array}$$

(2) 

$$\begin{array}{c} C_6H_5—C—H \\ \| \\ Cl—N.OH \\ | \\ H \end{array}$$

Conversely however, with the free oximes, the antihydrochlorid is unstable, while the syn derivative is stable. This will explain why by the molecular transposition, induced by hydrochloric acid gas, one may pass from the anti series to a derivative of the syn series.

The transformations of the stereoisomeric oximes under the influence of chemical reagents conform to certain general rules. A change in the constitution can hence modify the configuration and the stability of the isomers. The following scheme will give a general résumé of these different transformations. The symbol X denotes for example, Na, and the symbol R the groups ($CH_3.CO$) :

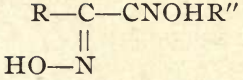


It will be seen according to this figure, that it is more or less easy to obtain oximes of a given configuration, for there is for each oxime a stable configuration in an alkaline medium, which will correspond, for instance, to that of the sodium derivatives, and also a stable configuration in acid media which correspond to an hydrochlorid, or to an acetyl derivative. Hence, one of these isomers will be formed in the greater quantity or even completely, according as the hydroxylamin reacts in an acid or an alkaline medium. Thus, for example, for the different stereoisomeric glyoximes,

$$R'—C.NOH—CNOH—R''$$

(oximes of benzil, phenylglyoxal, chlorglyoximes, glyoxime carboxylic acids), one will obtain the following relations :

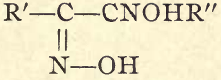
(1)



$$\begin{array}{l}\mathrm{R{-}C{-}CNOHR''} \\ \qquad \| \\ \mathrm{HO{-}N}\end{array}$$

Stable modification in acid solutions.

(2)

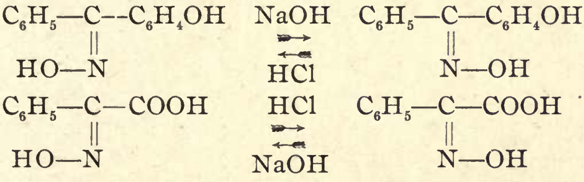


$$\begin{array}{l}\mathrm{R'{-}C{-}CNOHR''} \\ \qquad \| \\ \qquad \mathrm{N{-}OH}\end{array}$$

Stable modification in alkaline solutions.

The glyoximes corresponding to formula 2 will always be formed when hydroxylamin reacts in a markedly alkaline solution; these glyoximes treated with acids are transformed into oximes corresponding to formula 1. This last reaction is effected more or less easily. Sometimes a strong acid such as hydrochloric acid is necessary, at other times the transformation takes place so easily that in order to isolate the oxime which has been formed in an alkaline medium, it is necessary to set it free with carbon dioxide.

Similar relations exist between the isomeric oximes of paraoxybenzophenone and phenylglyoxalic acid. These may be represented by the following figures:

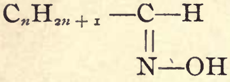


$$\begin{array}{lcl}\mathrm{C_6H_5{-}C{-}C_6H_4OH} & \mathrm{NaOH} & \mathrm{C_6H_5{-}C{-}C_6H_4OH} \\ \qquad\ \| & \rightleftarrows & \qquad\ \| \\ \mathrm{HO{-}N} & \mathrm{HCl} & \qquad\ \mathrm{N{-}OH} \\ \mathrm{C_6H_5{-}C{-}COOH} & \mathrm{HCl} & \mathrm{C_6H_5{-}C{-}COOH} \\ \qquad\ \| & \rightleftarrows & \qquad\ \| \\ \mathrm{HO{-}N} & \mathrm{NaOH} & \qquad\ \mathrm{N{-}OH}\end{array}$$

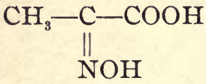
In agreement with this, the oximes which are unstable in the free state are still more so in the form of acetyl derivatives, and accordingly the introduction of an acetyl group by means of acetic anhydrid is performed usually without a change in configuration, while if one use acetyl chlorid, the hydrochloric acid disengaged induces a speedy molecular rearrangement.

d. Configuration of oximes of which two stereoisomers have not been isolated.—The unsymmetrical oximes which have up to the present been discovered only in a single isomeric modification should always be represented by one of the two possible configurations. This has already been mentioned in speaking of the ethylene compounds (see p. 89). When it is impossible to isolate the two modifications it must be assumed that one of the configurations is particularly unstable, and if one compare this single oxime with stereoisomers having an analogous constitution and whose configuration is known, one may find that by these chemical and physical properties it conforms closely to one of the isomers, and differs completely from the other.

But one oxime of pyruvic acid and of thienylglyoxylic acid have been isolated; the aldehyds of the fatty series gives but one oxime; all these compounds must hence be synaldoximes and synaldoximecarboxylic acids, because they bear a strong resemblance to the benzalsynaldoxime and to the synbenzaldoximecarboxylic acids, and are decomposed into water or CO_2 and a nitril.

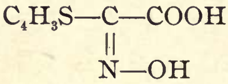


$$C_nH_{2n+1}—\underset{\underset{\displaystyle N—OH}{\|}}{C}—H$$



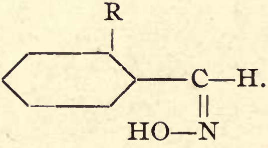
$$CH_3—\underset{\underset{\displaystyle NOH}{\|}}{C}—COOH$$

and

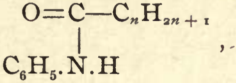


$$C_4H_3S—\underset{\underset{\displaystyle N—OH}{\|}}{C}—COOH$$

The oximes of the ortho-substituted aromatic aldehydes, of which but one modification has yet been isolated, have properties analogous to those of antibenzaldoxime, and hence one assigns to them the same configuration as antialdoxime,

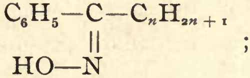


The oximes of mixed ketones which are easily decomposed into anilids of fatty acids,



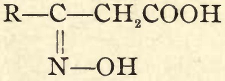
$$\begin{array}{c} O{=}C{-}C_nH_{2n+1} \\ | \\ C_6H_5.N.H \end{array},$$

have the configuration,

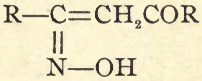


$$\begin{array}{c} C_6H_5{-}C{-}C_nH_{2n+1} \\ \| \\ HO{-}N \end{array};$$

the β-ketoximic acids, $RCNOH.CH_2.COOH$ (oximes of acetoacetic and benzoyl acetoacetic acids), and the β-oximido ketones, $R{-}CNOH.CH_2COR$, are only known in a single modification,

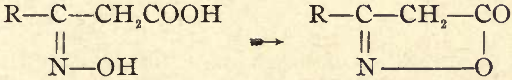


$$\begin{array}{l} R{-}C{-}CH_2COOH \\ \quad\| \\ \quad N{-}OH \end{array}$$

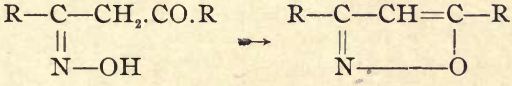


$$\begin{array}{l} R{-}C{=}CH_2COR \\ \quad\| \\ \quad N{-}OH \end{array},$$

These two configurations take into account the formation of internal anhydrids derived from synoxazol.

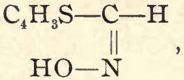


Synketoximeacetic acid. Synoxazolone.



Synoximidoketone. Synoxazol.

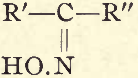
Although but one isomer of these different compounds has as yet been prepared, it must not be thought impossible to isolate the second modification, despite its instability. For example, recently, the derivatives of thiophene antialdoxime,

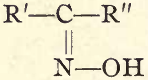


$$\begin{array}{r} C_4H_3S-C-H \\ \| \quad \\ HO-N \quad \end{array},$$

have been obtained, although the parent compound is not stable in the free state; in the same way the existence of antioenanthaldoxime which is still less stable appears to be beyond doubt, from the way in which certain of its derivatives behave. Finally Franchimont[1] has been able to prepare two isomeric acetaldoximes.

Influence of constitution on configuration.—The influence[2] of configuration on constitution has been less studied in the case of the oximes than in the case of the ethylene derivatives. The existence and intramolecular reactions of two derivatives,





$$\begin{array}{c} R'-C-R'' \\ \| \\ HO.N \end{array} \quad \text{and} \quad \begin{array}{c} R'-C-R'' \\ \| \\ N-OH \end{array},$$

depend to such an extent on the two radicals R′ and R″, and occur in such a regular way, that one is able to systematically classify these radicals according to their affinity for the oximidohydroxyl and to predict beforehand the properties of an oxime of a given constitution, if one knows the nature of the two groups R′ and R″. This can be classified in the following way:

1. $COOH.CH_2-$, 2. $COOH-$, 3. C_6H_5-, 4. C_6H_4H-, 5. C_4H_3S-, 6. $C_nH_{2n+1},-$, 7. CH_3-.

The methyl carboxyl group which has the greatest affinity for the oxime hydrogen, stands at the head of the list. The group with the lowest affinity for the hydrogen, is the hydrocarbon radical methyl. Among all the alkyl radicals it is this last which has the weakest

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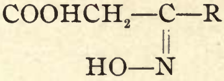
[1] Franchimont: Rec. trav. Pays Bas., **10**, 236.

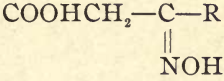
[2] Hantzsch: Ber. d. chem. Ges., **15**, 2164.

affinity for the oximidohydroxyl. According as the hydroxyl will be more or less remote from the latter, one may deduce the stability of the following compounds :



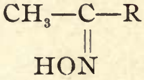
$$\mathrm{COOHCH_2{-}\underset{\substack{\| \\ HO{-}N}}{C}{-}R}$$

Very stable.



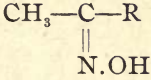
$$\mathrm{COOHCH_2{-}\underset{\substack{\| \\ NOH}}{C}{-}R}$$

Very unstable, not isolated.



$$\mathrm{CH_3{-}\underset{\substack{\| \\ HON}}{C}{-}R}$$

Very stable.



$$\mathrm{CH_3{-}\underset{\substack{\| \\ N.OH}}{C}{-}R}$$

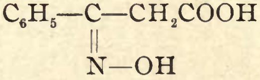
Very unstable, not isolated.

The stability of these two compounds is then more or less modified by the nature and position of the radical R. Gradual transformations which go to substantiate this stability are particularly well marked in the group of oximes of the general formula, $C_6H_5{-}CNOH{-}R$, R, representing respectively the above-mentioned radicals.

Oximes, $C_6H_5{-}CNOH{-}R$.

1. $R{=}CH_2COOH$ $C_6H_5{-}CNOH{-}CH_2COOH$
Synphenylketoxime acetic acid.
(Oximes of benzoyl acetic acid).

a.



$$\mathrm{C_6H_5{-}\underset{\substack{\| \\ N{-}OH}}{C}{-}CH_2COOH}$$

Synphenylketoxime acetic acid.
Known, very stable.

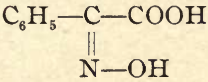
b.

$$\mathrm{C_6H_5{-}\underset{\substack{\| \\ HO.N}}{C}{-}CH_2COOH}$$

Antiphenylketoxime acetic acid.
Unknown

2. $R{=}COOH$ $C_6H_5{-}CNOH{-}COOH$
Phenylketoxime carboxylic acid.
(Oxime of phenylglyoxylic acid.)

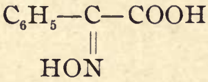
a.



$$\mathrm{C_6H_5{-}\underset{\substack{\| \\ N{-}OH}}{C}{-}COOH}$$

Synphenylketoxime carboxylic acid. Stable.

b.

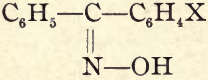


$$\mathrm{C_6H_5{-}\underset{\substack{\| \\ HON}}{C}{-}COOH}$$

Antiphenylketoxime carboxylic acid. Unstable.

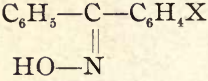
3. $\mathrm{R{=}C_6H_4X}$ $\mathrm{C_6H_5{-}C{-}C_6H_4X}$

Oximes of substituted benzophenones.



$$\mathrm{C_6H_5{-}\underset{\underset{\displaystyle N{-}OH}{\|}}{C}{-}C_6H_4X}$$

Usually unstable.

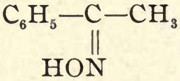


$$\mathrm{C_6H_5{-}\underset{\underset{\displaystyle HO{-}N}{\|}}{C}{-}C_6H_4X}$$

Usually stable.

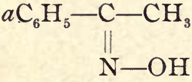
A greater or less stability of these oximes depends besides on the nature of the substituent X, as is shown in the above-mentioned table, as well as the place which it occupies in the benzene nucleus, or in other words on its relative remoteness from the oximido hydrogen. The substituent thus exerts a more energetic action in the ortho position than in the para.[1]

$\mathrm{R{=}CH_3}$

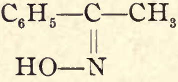


$$\mathrm{C_6H_5{-}\underset{\underset{\displaystyle HON}{\|}}{C}{-}CH_3}$$

Phenyl methyl ketoximes.
Oximes of acetophenone.

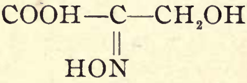


$$a\mathrm{C_6H_5{-}\underset{\underset{\displaystyle N{-}OH}{\|}}{C}{-}CH_3}$$



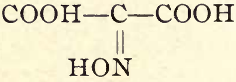
$$\mathrm{C_6H_5{-}\underset{\underset{\displaystyle HO{-}N}{\|}}{C}{-}CH_3}$$

The influence of two radicals on the stability of oximes is also very well marked in the case of their compounds, as for example, in the oximido acids, $\mathrm{COOH{-}CNOH{-}R}$. If one replaces R in the latter by some one of the above mentioned radicals, one has a series in the following order :



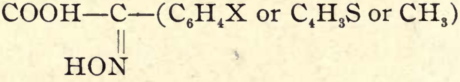
$$\mathrm{COOH{-}\underset{\underset{\displaystyle HON}{\|}}{C}{-}CH_2OH}$$

Unstable.



$$\mathrm{COOH{-}\underset{\underset{\displaystyle HON}{\|}}{C}{-}COOH}$$

Stable.



$$\mathrm{COOH{-}\underset{\underset{\displaystyle HON}{\|}}{C}{-}(C_6H_4X\ or\ C_4H_3S\ or\ CH_3)}$$

Very stable.

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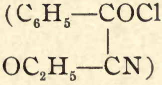
[1] Smith : Ber. d. chem. Ges., **24**, 4057.

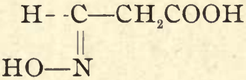
In the anti series one will have the stability occurring in reverse order.

These relations have to a very large extent a general character, and the way in which their radicals behave, *e.g.*,



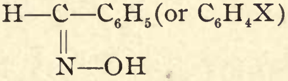
$$\left(\begin{array}{l} C_6H_5\text{—}COCl \\ \qquad\quad | \\ OC_2H_5\text{—}CN \end{array}\right),$$

allows one to place them in the table on p. 160, although with more or less uncertainty. Hydrogen occupies an independent position in this table as will be seen when one has indicated the properties of the aldoximes clearly. According to the configuration of aldoxime acetic acid,



$$\begin{array}{l} \quad\; H\text{- -}C\text{—}CH_2COOH \\ \qquad\quad \| \\ HO\text{—}N \end{array},$$

hydrogen should be placed at the head of the list of radicals, but as the aromatic aldoximes, especially those of the ortho series, are stable in the inverse configuration,

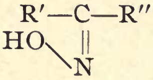


$$\begin{array}{l} H\text{—}C\text{—}C_6H_5(\text{or } C_6H_4X) \\ \qquad \| \\ \qquad N\text{—}OH \end{array},$$

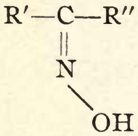
it is necessary on the contrary, to place hydrogen after the aromatic radicals. This peculiar influence of the hydrogen atom on the configuration depends perhaps on its small size, and its relatively great mobility. These properties have already been ascribed to it in the study of the tautomerism of hydrogen compounds. It is thus seen that the two radicals R′ and R″ determine not only the stability of the configuration but also the chemical characteristics, and allow the prediction of the intramolecular reactions which depend solely on the relative distance of the atoms making up the complex. It suffices thus to allow that in molecules, such as

R′—CNOH—R″,

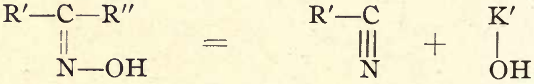
the absolute distance of the oximido hydroxyl from the two radicals depends on their reciprocal affinities and their more or less electropositive or electronegative character, as will be seen by referring to the table on p. 160. If, for example, R′ represent a group having a strong affinity for hydroxyl and R″ a group possessing a feeble attraction or even a repulsion, the two configurations may be perhaps represented in the following manner:



and



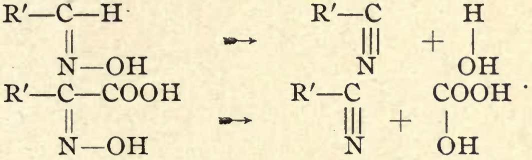
If then in the case of oximes that the analogous constitution radical R, which is situated near the hydroxyl, reacts in the following manner:



$$\begin{array}{c}R'-C-R''\\ \| \\ N-OH\end{array} = \begin{array}{c}R'-C\\ ||| \\ N\end{array} + \begin{array}{c}K'\\ | \\ OH\end{array}$$

and if without changing R″, one replace R′ successively by the different groups in the table on page 160, the mechanism of this intramolecular action will be greatly modified in the following manner: If the varying radical R′ is one of the latter terms of the series, the attractive action which it exercises on hydroxyl will be weak, and consequently the radical R″ will attract the group, OH, with greater force, and decomposition will take place more readily. If, on the contrary, the group R represents one of the first members of the series, it will tend to attract this hydroxyl from the sphere of influence of the group R″, and the reaction mentioned above will not take place, or if it does, will take place to a limited extent only.

The transformation of the synaldoximes and their acids into nitriles, examples of these :

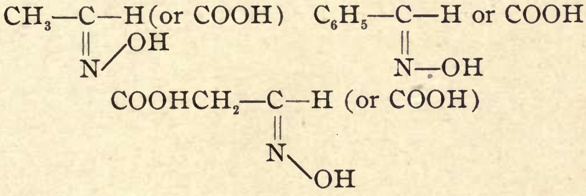


$$\begin{array}{c} R'{-}\underset{\substack{\| \\ N{-}OH}}{C}{-}H \longrightarrow \underset{\substack{||| \\ N}}{R'{-}C} + \underset{\substack{| \\ OH}}{H} \\ R'{-}\underset{\substack{\| \\ N{-}OH}}{C}{-}COOH \longrightarrow \underset{\substack{||| \\ N}}{R'{-}C} + \underset{\substack{| \\ OH}}{COOH} \end{array}$$

This reaction proceeds easily if $R' = CH_3$ and C_nH_{2n+1}; hence the acetates of acetaldoxime and its homologues and the oxime of pyruvic acid are decomposed sometimes spontaneously at ordinary temperature. When

$$R' = C_4H_3S$$

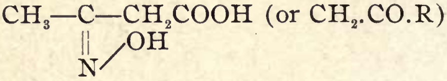
(thiophenealdoxime and the oxime of thienylglyoxylic acid), if $R' = C_6H_5$ (synbenzaldoxime and the oxime of phenylglyoxylic acid), the acetates are still more stable; lastly if $R' = CH_2COOH$ (aldoxime acetic acid and oximido succinic acid or synketoxime acetyl carboxylic acid), the acetates no longer react the same, in spite of their identical configuration. The capability of reacting differently in these compounds is shown by the following symbolic formulae which are given concretely as a result of the study of the thiophene compounds,



$$CH_3{-}\underset{\substack{\| \\ N\diagup OH}}{C}{-}H\,(\text{or } COOH) \qquad C_6H_5{-}\underset{\substack{\| \\ N{-}OH}}{C}{-}H \text{ or } COOH$$

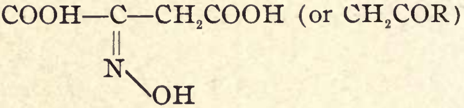
$$COOHCH_2{-}\underset{\substack{\| \\ N\diagdown OH}}{C}{-}H\ (\text{or } COOH)$$

This is the same for the most part in intramolecular reactions; for example, in the formation of anhydrids (derivatives of oxazol), starting from β-ketoxime acids and oximido ketones which may be represented by the following formulae:



$$\mathrm{CH_3{-}\underset{\underset{\displaystyle N\diagup OH}{\|}}{C}{-}CH_2COOH\ (or\ CH_2.CO.R)}$$

and



$$\mathrm{COOH{-}\underset{\underset{\displaystyle N\diagdown OH}{\|}}{C}{-}CH_2COOH\ (or\ CH_2COR)}$$

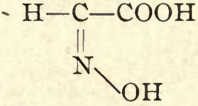
If one replace the radical R in the group R—CNOH, by the group CH_3, the anhydrids are formed easily, and on the other hand, with much difficulty, or even not at all, if the radical R be replaced by $COOC_2H_5$.

The groups which are not participating in the reaction always act in the same way at the moment of intramolecular decomposition, and the absolute configuration is modified according to previous relations deduced from the table on page 160. In all these cases, the alcoholic radicals exercise the same influence as that which was observed in the group of ethylene compounds, and as a general rule, favor intramolecular decomposition. Their constitution ought thus to be taken into consideration, if one wishes to form some idea of their relative influence on intramolecular decomposition. It would appear that this is in close connection with their molecular conductivity, and K, their constant of affinity. This constant which was studied in the homologous series of the α-ketoxime carboxylic acids,

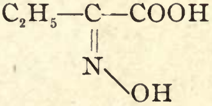
$$C_nH_{2n+1}\text{—CNOH—COOH},$$

does not decrease when n augments, but conversely to that which is found in the melting-points of certain classes of acids which increase and decrease alternately;

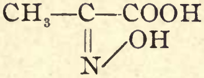
the differences become less and less great. This would tend to show that the carboxyl group always exerts the greatest attraction for the oximido hydrogen. This attraction is strongly compensated by hydrogen, much less by methyl; ethyl acts somewhat more markedly than methyl, and propyl less than ethyl. This is shown in the following figures :



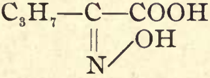
$K = 0.0995$



$K = 0.0830$

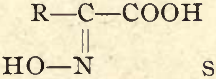


$K = 0.0514$



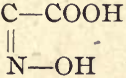
$K = 0.0685$

The affinity constant, of the stereoisomeric oximido acids vary between the same limits as in the ethylene carboxylic acids, but they also present differences varying with the distance which separates the two groups NOH and COOH.



$$\begin{array}{l}\mathrm{R{-}C{-}COOH}\\ \qquad \|\\ \mathrm{HO{-}N}\end{array}$$

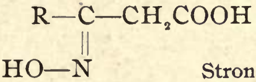
Stronger.



$$\begin{array}{l}\mathrm{R{-}C{-}COOH}\\ \qquad \|\\ \qquad \mathrm{N{-}OH}\end{array}$$

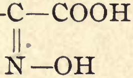
Weaker.

Stereoisomeric and ketoximic acids.



$$\begin{array}{l}\mathrm{R{-}C{-}CH_2COOH}\\ \qquad \|\\ \mathrm{HO{-}N}\end{array}$$

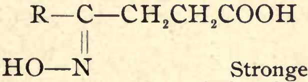
Stronger.



$$\begin{array}{l}\mathrm{R{-}C{-}COOH}\\ \qquad \|\\ \qquad \mathrm{N{-}OH}\end{array}$$

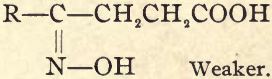
Weaker.

Stereoisomeric β-ketoximic acids.



$$\begin{array}{l}\mathrm{R{-}C{-}CH_2CH_2COOH}\\ \qquad \|\\ \mathrm{HO{-}N}\end{array}$$

Stronger.



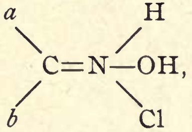
$$\begin{array}{l}\mathrm{R{-}C{-}CH_2CH_2COOH}\\ \qquad \|\\ \qquad \mathrm{N{-}OH}\end{array}$$

Weaker.

Stereoisomeric γ-ketoximic acids.

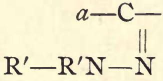
The affinity constant analogous to the ketoxime acids increases or diminishes for each addition of a CH_2 group. This is a formulation of the statement given on page 122; *viz.*, that the structural formula of compounds consisting of long chains of carbon atoms, does not express the real distance between the atoms.

The isomerism of oximes is found in their derivatives and sometimes in the salts formed with hydrochloric acid of the formula



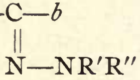
in which nitrogen is pentavalent,[1] but these two isomeric compounds are much more easily transformed one into the other than in the case of free oximes.

Stereoisomeric hydrazones.—



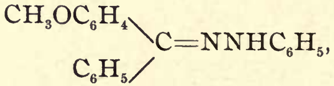
$$\begin{array}{r} a\text{—C—}b \\ \| \\ R'\text{—}R'N\text{—}N \end{array}$$

and



$$\begin{array}{l} a\text{—C—}b \\ \| \\ N\text{—}NR'R'' \end{array}$$

Cases of isomerism of this kind were observed first in the phenylhydrazone of orthonitrophenylglyoxylic acid[2] which exists in two modifications, and independently with hydrazones obtain in a single modification, starting from the ketones a—CO—b. These hydrazones are obtained by treating ketonechlorids, $a—CCl_2—b$, with hydrazins;[3] thus,[4] in this group of compounds there are two monophenylhydrazones of anisylphenylketone,



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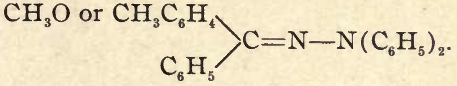
[1] Proc. Chem. Soc., 1893, 253.

[2] Fehrlin and Krause: Ber. d. chem. Ges., **23**, 1574 and 3617.

[3] Hantzsch and Kraft: *Ibid.*, **24**, 3511.

[4] Hantzsch and Overton: *Ibid.*, **26**, 9 and 18.

and two diphenyldihydrazones of anisylphenylketone, and of tolylphenylketone,

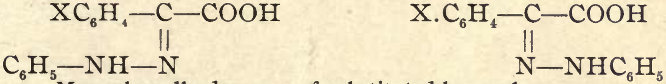


$$\begin{array}{l}CH_3O \text{ or } CH_3C_6H_4 \\ \qquad\qquad\quad C_6H_5\end{array}\!\!>\!C{=}N{-}N(C_6H_5)_2.$$

These latter compounds are particularly interesting because they exclude all structural differences in the hydrazone group, and show very markedly the cause of stereoisomerism as strictly due to nitrogen. The following are configuration formulae for these compounds:

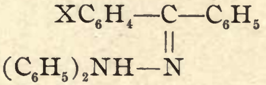
$$\begin{array}{r} NO_2.C_6H_4{-}C{-}COOH \\ \| \quad\qquad\qquad \\ C_6H_5{-}NH{-}N \qquad\qquad\qquad \end{array} \qquad \begin{array}{l} NO_2.C_6H_4{-}C{-}COOH \\ \qquad\qquad\quad \| \\ \qquad\qquad\quad NC_6H.C_6H_5 \end{array}$$

Hydrazones of orthonitrophenylglyoxylic acid.

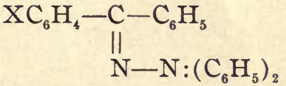


$$\begin{array}{r} XC_6H_4{-}C{-}COOH \\ \| \quad\qquad\qquad \\ C_6H_5{-}NH{-}N \qquad\qquad\qquad \end{array} \qquad \begin{array}{l} X.C_6H_4{-}C{-}COOH \\ \qquad\qquad \| \\ \qquad\qquad N{-}NHC_6H_5 \end{array}$$

Monophenylhydrazones of substituted benzophenones.



$$\begin{array}{r} XC_6H_4{-}C{-}C_6H_5 \\ \| \quad\qquad \\ (C_6H_5)_2NH{-}N \qquad\quad \end{array}$$



$$\begin{array}{l} XC_6H_4{-}C{-}C_6H_5 \\ \qquad\qquad \| \\ \qquad\qquad N{-}N{:}(C_6H_5)_2 \end{array}$$

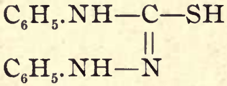
These formulae present some analogy with those of the stereoisomeric oximes, which is still more striking when the reciprocal transformations are studied. Thus, by the action of an alkaline solution, the isomer of the hydrazone of orthonitrophenylglyoxylic acid is obtained. This recalls the properties of the oximes of phenylglyoxylic acid. There is, thus, a stable modification which is the antipode of that observed with acids in speaking of the oximes, and a stable modification, which is the reverse of that seen in the case of alkalies acting on these last-mentioned substances. The two modifications of the hydrazones of asymmetric ketones are not equally stable. This is comparable to what has been observed in the case of the asymmetric oximes,

$$XC_6H_4\text{—}CNOH\text{—}C_6H_5.$$

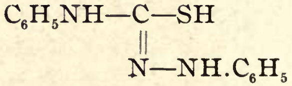
The unstable modifications of monophenylated hydrazones melt at a low temperature, are soluble, and are transformed into less soluble modifications which melt at a higher temperature, and this takes place more easily than with the unstable oximes. This reaction takes place at room temperature when an alcoholic solution of hydrochloric acid is used, or even when such reagents as acetyl chlorid or anhydrid are allowed to act. The stable hydrazones may be transformed into their unstable modifications by treating the addition products formed with acetyl chlorid with dry ammonia gas. This reaction has not been effected in the case of diphenylated hydrazones.

The methods mentioned to determine the configuration of oximes cannot be applied to the determination of the configuration of hydrazones, and hence, the problem still awaits a solution.

The two modifications of diphenylsemicarbazid and its two ethers which are characterized by the group $(SCH_3)C_6H_5NH\text{—}C(NNHC_6H_5)\text{—}SHCH_3$ should be classified among the stereoisomerism of hydrazones. These compounds form condensation products with carbonyl chlorid according to the following :

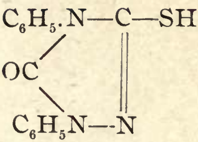


$$\begin{array}{rl} C_6H_5.NH\text{—} & C\text{—}SH \\ & \| \\ C_6H_5.NH\text{—} & N \end{array}$$

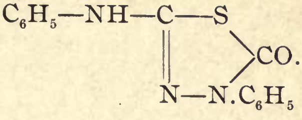


$$\begin{array}{rl} C_6H_5NH\text{—} & C\text{—}SH \\ & \| \\ & N\text{—}NH.C_6H_5 \end{array}$$

and subsequently form cyclic compounds of different structure,



and



This reaction is not effected completely with the second of the two isomers ; as with the first, two condensation products are obtained, the one representing a stable modification, the other an unstable.

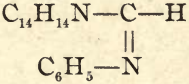
The stereoisomeric hydrazones of[1] salicylic aldehyde have recently been isolated ; dioxysuccinic esters and phenylhydrazine react on one another to give different oxazones, according to the formula,

$$COOR—C(NH_2C_6H_5)—C(NH_2C_6H_5)—COOR,$$

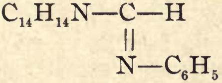
which behave like the symmetrical dioximes and correspond to the three : Syn, amphi,[2] and anti configurations. Lastly the two modifications of dimolecular ethylidene anilins[3] of the formula,

$$2C_6H_5CH:NC_6H_5 = C_6H_5CH:NHC_6H_5CH_2CHNC_6H_5,$$

must be considered as geometric isomers corresponding to the following configurations :



$$\begin{array}{r} C_{14}H_{14}N—C—H \\ \| \\ C_6H_5—N \end{array}$$



$$\begin{array}{l} C_{14}H_{14}N—C—H \\ \qquad\quad\ \| \\ \qquad\quad\ N—C_6H_5 \end{array}.$$

This is indicated by their different behavior, and in particular by the possibility of transforming the more fusible modification into the higher melting compound.

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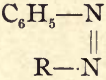
[1] Bitz : Ber. d. chem. Ges., **27**, 2288.

[2] Anschütz and Paulz : *Ibid.*, **28**, 64.

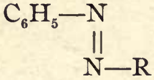
[3] Miller and Plöchl : *Ibid.*, **27**, 1297.

IV. NITROGEN COMPOUNDS EXHIBITING GEOMETRICAL ISOMERISM

1. Stereoisomeric diazo compounds,



$$\begin{array}{r} C_6H_5—N \\ \| \\ R—N \end{array}$$



$$\begin{array}{l} C_6H_5—N \\ \quad\quad\;\| \\ \quad\quad\;N—R \end{array}.$$

a. Historical. The identity of the structural formulae.—These compounds are interesting not only from a chemical point of view, but as an example of historical development. Like the "iso-oximes," the isodiazo hydrates were considered at first as isomers, which were represented by different constitutional formulae. Schraube and Schmidt[1] who discovered the potassium salt of isodiazobenzene, as well as the hydrate of nitroisodiazobenzene, regarded these compounds as primary nitrosamins, $C_6H_5—NKNO$ and $NO_2C_6H_4NHNO$. Their alkaline salts treated with alkyl iodids are transformed into secondary nitrosamins, $C_6H_5N.CH_3.NO$, and $NO_2C_6H_4NCH_3NO$. Shortly after this, Bamberger[2] described isodiazonaphthalin as a naphthylnitrosamin. In opposition to this view, Hantzsch,[3] in bringing forward the analogy which exists between the geometric isomers of nitrogen and carbon (oximes), and the compounds characterized by two atoms of nitrogen, doubly linked (diazo compounds), showed that the introduction of an alkyl radical into a diazohydrate does not furnish any indication of its constitution as was already shown in the case of the isooximes. Hence, this reaction might only be considered as an argument in favor of tautomerism, for the same isodiazo hydrates, transformed

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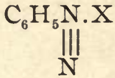
[1] Ber. d. chem. Ges., **27**, 514.

[2] *Ibid.*, **27**, 679.

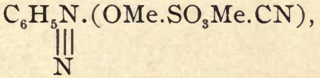
[3] *Ibid.*, **27**, 701.

into their silver salts, give true oxy esters ;[1] *e. g.*, $NO_2C_6H_5{-}N{=}N{-}OCH_3$. Moreover, isomeric salts corresponding to the formulae $C_6H_5{-}N = N.OMe$ and $C_6H_5.NMe.NO$, would constitute an absolutely unique case of this kind. At the same time, Hantzsch[2] brought forward the first experimental basis for the stereochemistry of diazo bodies by isolating the salts of the diazosulfonic acids, $R.N_2.SO_3Me$, and shortly after the diazocyanid compounds,[3] $R.N_2.CN$—compounds which no longer contain the carboxyl group of diazohydrates, but in which the two isomeric forms present the same analogies. On the other hand, the synthesis of isodiazobenzene hydrate, starting from nitrosobenzene and hydroxylamin,[4] showed that the isodiazo hydrates are true hydroxyl compounds.

Nevertheless, an attempt has been made to explain these, by means of constitutional formulae. The salts of diazo benzene with mineral acids, the normal metallic salts of the sulfonic acids, and the cyanid of diazobenzene should, in accordance with an interpretation given by Blomstrand and Erlenmeyer, be represented by formulae conforming to the ammonium type,

I. 

$$\begin{array}{l} C_6H_5N.X \\ \quad\ \ ||| \\ \quad\ \ N \end{array}$$

II. 

$$\begin{array}{l} C_6H_5N.(OMe.SO_3Me.CN), \\ \quad\ \ ||| \\ \quad\ \ N \end{array}$$

while the isodiazo salts should correspond to a true diazo formula,

$$C_6H_5N : N(OMeSO_3MeCN).$$

The following objection has been raised to this interpretation: The compounds which have been considered

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[1] Pechmann : Ber. d. chem. Ges., **27**, 672.

[2] Hantzsch : *Ibid.*, **27**, 1276, 2099.

[3] Hantzsch and Schultze : *Ibid.*, **28**, 266.

[4] Bamberger : *Ibid.*, **28**, 1218.

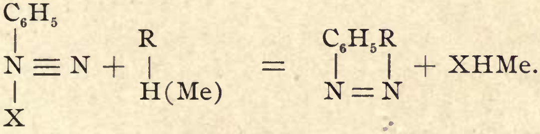
as derivatives of the true diazo group, form, as a matter of fact, two distinct series of compounds which differ with the constitution of the diazo radical, and which have not been confused up to the present, although they are changed very readily, one into the other. The following is a résumé of the Hantzsch theory regarding these compounds :

First, the salts formed by diazo benzene with acids should be represented by Formula 1. By reason of their analogy with ammonium type, one may assign to them the name diazonium. Their aqueous solutions have a neutral reaction, and are as completely dissociated as the salts of potassium and ammonium. Diazo carbonates are also known, which are soluble in water; also double salts which are less soluble and are colorless, which properties are also characteristic of potassium and ammonium. "Diazonium" appears then to behave like a compound radical, having metallic characteristics.

Second, salts like the cyanid and the sulfonate of normal diazobenzene do not correspond to Formula 2, but to the usual formula, $C_6H_5N : NR$, only, in this group, we find isomers of identical structure; *viz.*, the isodiazo compounds which must be distinguished from the normal diazo compound. Hence, since diazonium should be regarded as a compound alkali, this radical cannot give at the same time alkaline salts and salts of silver. One can no longer explain why the colorless sulfonic compounds with the group $N.SO_3Me$, are transformed into cyanids, absolutely different from all cyanids known, corresponding to the ammonium type. The diazonium cyanid should be colorless, soluble in water dissociating into its ions, as do the different cyanids of ammonium, or of tetramethyl ammonium ; but as is well known, diazonium cyanid is colorless, is insoluble in water, and is a bad electrolyte. Lastly, the normal and isodiazo compounds present strong analogies to those properties which exist in the geometric isomers of the ethylene group and of the oximes. It would hence be impossible to attribute to one, an ammonium structure, and to the other, a structure like that of the azo compounds. As is even the case with stereoisomers, they are characterized by special intramolecular reactions; *i. e.*, by their capability of reciprocal transformation. These two series of compounds corresponding to the single formula $C_6H_5N{=}NX$, can then be designated by the names, syndiazo and antidiazo.

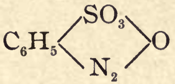
In spite of the very marked differences between the derivatives of diazonium and the syndiazonium compounds there are very close relations between these two groups of compounds. To sum up what has been mentioned in these two paragraphs:

Third, the diazonium salts are transformed easily into normal diazo compounds. It will be seen further on that the latter correspond to the syn configuration. This reaction can then be expressed by the following:



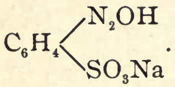
$$\begin{array}{c} C_6H_5 \\ | \\ N \equiv N \\ | \\ X \end{array} + \begin{array}{c} R \\ | \\ H(Me) \end{array} = \begin{array}{cc} C_6H_5 & R \\ | & | \\ N & = N \end{array} + XHMe.$$

A striking example of a transformation of this kind is furnished by diazosulfonic acid. The free acid,



,

has all the properties of a salt. Its reaction is neutral and like the compound betain, which is an internal salt of ammonium, this acid is an internal salt of diazonium. If a molecule of alkali be added, the solution which is strongly alkaline at the beginning, becomes gradually neutral. It thus contains the salt,



$$C_6H_4\begin{cases}N_2OH\\SO_3Na\end{cases}.$$

But the salt of diazonium is transformed into the syn-diazo complex, otherwise one could not understand how a solution of an acid which was originally neutral, could regain its neutral reaction after the addition of an alkali.

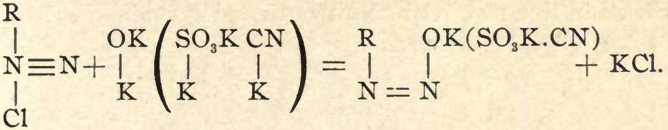
b. The properties and methods of formation of the stereoisomeric diazo compounds.—In the group of stereoisomers corresponding to the formula, R.N:N.X, there are at present known:

First, the metallic salts of diazobenzene, among these the alkaline and silver salts. These two series of isomers are colorless; in aqueous solution the alkaline salts are electrolytically dissociated; the salts of silver, however, undergo hydrolysis. From this point of view they behave like the stereoisomeric salts of the benzaldioximes.

Second, the diazosulfonic salts, RN_2SO_3Me. The two series of salts give strongly colored solutions.

Third, the diazo cyanids, $R—N_2CN$. The two series of salts dissolve only in organic media. In both groups the substances are colorless, which is in conformity with what one would expect from their constitution.

The normal diazo salts are formed by starting from the diazonium salts by the interaction of alkalies, silver oxid, and sulfite or cyanid of potassium.



$$\begin{matrix}R\\|\\N\equiv N\\|\\Cl\end{matrix} + \begin{matrix}OK\\|\\K\end{matrix}\left(\begin{matrix}SO_3K & CN\\ | & |\\ K & K\end{matrix}\right) = \begin{matrix}R & OK(SO_3K.CN)\\ | & |\\ N = & N\end{matrix} + KCl.$$

The isodiazo salts are formed by the molecular rearrangement of the syn compounds. The less stable syn compounds pass into the more stable antiderivatives,

$$\begin{matrix} & R-N\\ & \|\\ (CN.SO_3K.OK)- & N\end{matrix} \rightarrow \begin{matrix}R-N & \\ \| & \\ N- & (OKSO_3KCN)\end{matrix}$$

The less stable syn isomers are more soluble than the more stable anti isomers. This is in agreement with what was found in the case of the cis and trans compounds of ethylene.

c. Determination of configuration.—*1. By means of intramolecular reactions.*—According to the principle which governs intramolecular actions, the syn compounds alone can be decomposed with the disengagement of diazo nitrogen.

$$\begin{matrix}C_6H_5N\\ \|\\ R-N\end{matrix} \rightarrow \begin{matrix}C_6H_5\\ |\\ R\end{matrix} + \begin{matrix}N\\ |||\\ N\end{matrix}$$

The normal diazo compounds thus conform to the syn configuration.

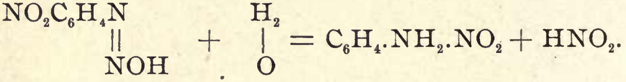
Examples: The diazo salt of sulfanilic acid, $KOSO_2.C_6H_4N_2.OH$, is transformed at ordinary temperature into nitrogen and potassium phenolsulfonate,

$$\begin{matrix}KOSO_2-C_6H_4-N\\ \|\\ HON\end{matrix} \rightarrow \begin{matrix}KOSO_2.C_6H_4\\ |\\ OH\end{matrix} + \begin{matrix}N\\ |||\\ N\end{matrix}.$$

The syndiazo cyanids, or normal diazo cyanids are converted in like manner into nitrogen and cyanids by means of finely divided copper.

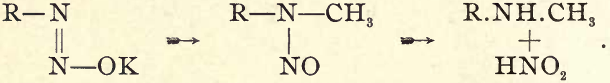
$$\begin{array}{r}\mathrm{Cl.C_6H_4N}\\ \Vert\\ \mathrm{NC{-}N}\end{array} \longrightarrow \begin{array}{c}\mathrm{ClC_6H_4}\\ |\\ \mathrm{CN}\end{array} + \begin{array}{c}\mathrm{N}\\ |||\\ \mathrm{N}\end{array}$$

The isodiazo or antidiazo compounds are not decomposed directly with the formation of nitrogen. They return to the syn type. In direct decompositions, they do not give a compound free from nitrogen, (RX), and substances containing two atoms of this element, but rather two derivatives, each containing an atom of nitrogen. Examples: The hydrate of nitroantidiazobenzene is transformed on boiling with water into nitranilin and nitrous acid,



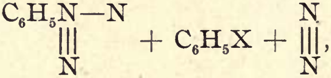
$$\begin{array}{r}\mathrm{NO_2C_6H_4N}\\ \Vert\\ \mathrm{NOH}\end{array} + \begin{array}{c}\mathrm{H_2}\\ |\\ \mathrm{O}\end{array} = \mathrm{C_6H_4.NH_2.NO_2} + \mathrm{HNO_2}.$$

The decomposition of secondary nitrosamins may be explained by regarding them as alkyl derivatives of antidiazo hydrates,



$$\begin{array}{l}\mathrm{R{-}N}\\ \;\;\;\Vert\\ \;\;\;\mathrm{N{-}OK}\end{array} \longrightarrow \begin{array}{c}\mathrm{R{-}N{-}CH_3}\\ |\\ \mathrm{NO}\end{array} \longrightarrow \begin{array}{c}\mathrm{R.NH.CH_3}\\ +\\ \mathrm{HNO_2}\end{array}.$$

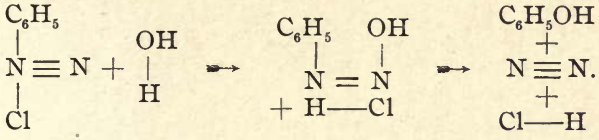
It will be noticed that the diazonium derivatives often react, apparently at least, as true diazo derivatives. The transformations, therefore, are not direct as the following equation would indicate,



$$\begin{array}{l}\mathrm{C_6H_5N{-}N}\\ \qquad\;\; |||\\ \qquad\;\; \mathrm{N}\end{array} + \mathrm{C_6H_5X} + \begin{array}{c}\mathrm{N}\\ |||\\ \mathrm{N}\end{array},$$

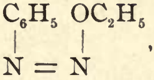
but are indirect, in the sense that they form a syndiazo compound, which is frequently exceedingly unstable.

This is what should be understood when phenol is formed by boiling benzene diazonium chlorid with water,



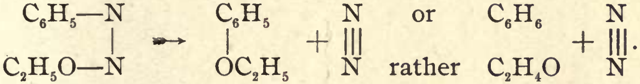
$$\begin{array}{c}C_6H_5\\|\\N\equiv N\\|\\Cl\end{array}+\begin{array}{c}OH\\|\\H\end{array}\longrightarrow\begin{array}{cc}C_6H_5&OH\\|&|\\N&=N\\+\,H&{-}Cl\end{array}\longrightarrow\begin{array}{c}C_6H_5OH\\+\\N\equiv N.\\+\\Cl{-}H\end{array}$$

Similarly in the formation of benzene and the ethyl ester of phenol by boiling the same chlorid with alcohol, the syndiazo ester,



$$\begin{array}{cc}C_6H_5&OC_2H_5\\|&|\\N&=N\end{array},$$

produced as an intermediate product in the reaction, can in reality be decomposed in two ways:



$$\begin{array}{r}C_6H_5{-}N\\|\\C_2H_5O{-}N\end{array}\longrightarrow\begin{array}{c}C_6H_5\\|\\OC_2H_5\end{array}+\begin{array}{c}N\\|||\\N\end{array}\quad\begin{array}{c}\text{or}\\ \\ \text{rather}\end{array}\quad\begin{array}{c}C_6H_6\\ \\C_2H_4O\end{array}+\begin{array}{c}N\\|||\\N\end{array}.$$

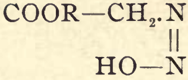
Hence the solution of diazonium carbonate,

$$(C_6H_5N_2)_2CO_3,$$

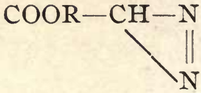
cannot give phenol as one would expect, if its diazonium salt undergoes a direct decomposition analogous to that found in the case of ammonium carbonate.

2. *By the formation of internal anhydrids.*—The syndiazo compounds (like the maleinoid hydrocarbon derivatives), are alone capable of giving in certain cases internal anhydrids, which are substances of cyclic structure, formed with the elimination of water. These anhydrids are often so stable that the substances from which they are derived are not known.

Diazophenol.



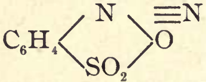
$$\begin{array}{r} \mathrm{COOR{-}CH_2.N} \\ \| \\ \mathrm{HO{-}N} \end{array}$$



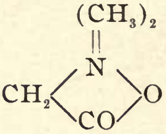
Diazoacetic ester.

Besides the characteristic reactions of diazo compounds, these substances possess the properties to cyclic compounds, to which they are closely related.

Diazonium derivatives are also capable of giving, in certain cases, internal salts of the diazonium type. Thus, diazo sulfanilic and diazo anthranilic acids are, in in this respect, closely related to betain.



Diazonium sulfanilate.



Betain.

3. By relations with the azo coloring-matters.—It is an experimental fact, that of the two stereoisomeric compounds, the syn compound always reacts much more easily (even exclusively), with phenols to form dyes. This reaction which is so often used for technical purposes in the manufacture of coloring-matters is exceedingly important from a stereochemical point of view, since it furnishes a means of determining the configuration of diazo compounds.

The diazonium salts appear at first to be capable of acting directly with phenols. Here again, it is probable that this reaction is preceded by the transformation of the salt into a syndiazo hydrate.

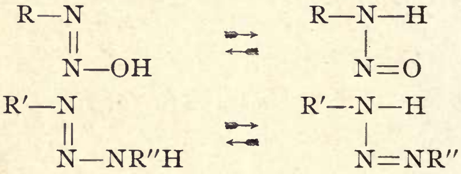
It is found lastly that the syn isomer is decomposed much more easily than the anti derivative. Thus, the syndiazo sulfonates are often decomposed with explosive violence; the antidiazo isomers are completely stable.

d. Reciprocal transformation of stereoisomeric diazo compounds.—Substances which exhibit geometrical isomerism possess the characteristic property of being transformed easily into one another. This behavior which has been frequently observed in the case of ethylene derivatives, and particularly well marked also in the case of oximes, is also exhibited to a marked degree in the stereoisomeric diazo compounds, with this difference, that the transformation of a syndiazo compound into the antidiazo up till now, alone, has appeared possible. The alkaline salts of the syn series pass more or less easily into the anti type. With the syndiazosulfonates this transformation is effected in aqueous solution; with the syndiazocyanids in alcoholic solution. In the latter case it has often been observed to take place without the use of the solvent.

e. Configuration of diazo compounds of which there are no stereoisomers.—It has been found, in the series of oximes, that two geometrical isomers are not always to be isolated, and this happens more frequently in the study of diazo compounds. Up till the present, one of these isomers is lacking in the following groups: The diazo esters, $R.N:N.OCH_3$; the thiodiazo esters; diazoamido compounds, $RN:N.NHR$; and diazo sulfones, $R.N:N.SO_2C_6H_5$. The compounds isolated in these groups should all belong to the stable anti type. The syn compounds are decomposed spontaneously, as is the case when one tries to introduce a hydrocarbon group by treating the silver salt of normal diazobenzene with an alkyl halogen derivative, or are transformed spontaneously into their isomers, as has been proved in preparing the diazosulfones of diazonium chlorid, or of benzenesulfonic acid. In the case of the diazoamido compounds, the tautomeric phenomena,

$$R'.N{:}N.N.HR'' \rightleftarrows R.NH.N{:}NR'',$$

exhibit a different behavior to that which is observed in the anti series. They correspond precisely to the tautomeric character of the antidiazo hydrates and the nitrosamins,



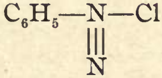
$$\begin{array}{l} R-N \\ \quad \| \\ \quad N-OH \end{array} \rightleftarrows \begin{array}{l} R-N-H \\ \quad | \\ \quad N=O \end{array}$$

$$\begin{array}{l} R'-N \\ \quad \| \\ \quad N-NR''H \end{array} \rightleftarrows \begin{array}{l} R'-N-H \\ \quad | \\ \quad N=NR'' \end{array}$$

f. Influence of constitution on configuration.—The influence of constitution on the configuration of the diazo compounds has never been doubted, but it has not been so well studied as has been the case in the series of oximes. The alkaline salts of syndiazo benzene appear to be more easily transformed into antidiazo compounds, when the negative substituents are more numerous than the benzene rest. The potassium salt of syndiazo benzene undergoes this transformation below 100°; the parabrom derivative at ordinary temperature and the paranitro derivative almost spontaneously. Conversely the presence of halogen atoms retard the transformation of syn sulfonates into anti sulfonates.

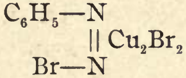
The manner in which the haloid salts of diazo compounds, $C_6H_5N_2(Cl.Br.I)$, behave is particularly characteristic. They do not, strictly speaking, exist in two isomeric formations, but they give two series of double salts which are perfectly distinct. The first are colorless, even when the salt entering into their composition is colorless; *e. g.*, the double salt of diazonium and mercury, $C_6H_5N_2ClHgCl$. The others possess intense color as do azo compounds; they are less stable and are decomposed easily into halogen derivatives of benzene, in the same manner as the syndiazo cyanid of benzene, which is colored, is transformed into benzonitrile. As typical examples may be mentioned the compounds formed with cuprous chlorid or bromid, $C_6H_5N_2Br.Cu_2Br_2$. It is very probable that the halogen diazonium compound can exist in two isomeric forms (not stereoisomeric); *viz.*, chlorid of diazonium and syndiazo chlorid and bromid,

Mercuric diazonium chlorid,



$$\begin{array}{rl} C_6H_5-N & -Cl \\ ||| & \\ N & \end{array}$$

Syndiazo cuprous bromid,



$$\begin{array}{rl} C_6H_5-N & \\ \| & Cu_2Br_2 \\ Br-N & \end{array}$$

It is likely that the more simple diazo halogen compounds, $R.N_2(Cl.Br.I)$, belong to the syndiazo or diazonium type, according to the nature of the hydrocarbon radical, and of the halogen.

2. Stereoisomeric Azo Compounds.

There are no stereoisomeric compounds of the azobenzene or azo color series known. For the present, the diazocyanids which are characterized by the group, $C+N=N-C$, can be considered as stereoisomeric azo derivatives. All their members, for example, the substances, $C_6H_5.N=NCONH_2$, belong to the anti series. One may, hence, conclude that the azo compounds as actually known, belong to the same series.

THE STEREOCHEMICAL ISOMERISM OF INORGANIC COMPOUNDS

BY A. WERNER

In order to facilitate the study of stereochemical isomerism which is exhibited in certain cases of inorganic compounds, it will be necessary to give a short résumé of the constitution of compounds which are to be mentioned in the following note. The substances which will be studied are molecular compounds, of which the constitution can only be expressed with difficulty by using the idea of valence, unless one has recourse to several secondary hypotheses, each being used for a special case, and hence being limited to a small number of compounds.

The constitution of molecular compounds can be established by making use of the relations between molecular compounds known under the name of metallic ammonium compounds, and double salts, such as the chlorids, fluorids, and double nitriles. In reality, the two extreme groups can be closely connected by a certain number of intermediate substances of mixed character, thus establishing a continuous series in which the molecular compounds of the first class are gradually transformed into double salts.

This curious transformation will be taken up in one of the more simple cases. In the study of the compounds in question, the fact that certain electronegative radicals form part of the molecule, and behave in a special and anomalous manner, is of great importance. In order to explain this apparent anomaly, a special case will be taken.

There are two ammoniacal compounds of cobalt known. The first corresponds to the formula, $CO(NH_3)_6Cl_3$, the second to $Co(NH_3)_5Cl_3$. These two compound differs only by a single molecule of ammonia, while their chemical properties are different and are characterized by the following reactions: If a solution of silver nitrate act upon the first salt, three atoms of chlorin are precipitated as silver chlorid, and a nitrate, $Co(NH_3)_6(NO_3)_3$, is formed. In treating the second salt in the same way, silver nitrate precipitates but two atoms of chlorin; the third differs evidently in its chemical behavior from the other two. There is thus formed a chlornitrate of the following composition: $Co(NH_3)_5\begin{matrix}Cl\\(NO_3)_2\end{matrix}$. This difference is also observed in using other reagents; thus, by using concentrated sulfuric acid, the first salt gives up three atoms of chlorin to form hydrochloric acid, while the second, under the same conditions, loses but two molecules of hydrochloric acid.

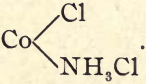
The three atoms of chlorin in the second compound of salts have hence different chemical properties. The one of them behaves in a special manner as does chlorin in certain organic compounds. Arrhenius' hypothesis of the electrolytic dissociation of salts takes this anomaly into account. The two atoms of chlorin which have the same properties as chlorin in ordinary chlorids, behave as ions, while the third is deprived of this character.

It is well known that one of the factors which enter into the molecular conductivity of a saline solution is the number of ions which it contains. Hence the properties of the two salts, $Co\begin{matrix}/(NH_3)_6\\ \backslash Cl_3\end{matrix}$ and $Co\begin{matrix}/(NH_3)_5\\ \backslash Cl_3\end{matrix}$, should allow one to predict a characteristic difference in the molecular conductivity of solution of these compounds. Experimental evidence has confirmed this statement, for in a dilution of 1000 liters the molecular conductivity of the first salt is equal to 432.6 and in the second to 261.3.

There can hence be no doubt that the first salt contains three atoms of chlorin with identical properties, all of which behave as ions, while the second salt contains but two having this property.

The principal question which is of interest, is to know what is the constitutional difference which will explain the different properties of negative groups taking part in molecular complexes such as those we have mentioned.

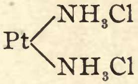
All chemists are occupied with this question. Whatever may be the theory adduced as to the composition of ammoniacal metallic compounds, they regard this difference as a consequence of the different union of the negative group to the metallic atom and believe that this union may be direct or indirect. If the union be a direct one, that is to say, if the negative group be directly connected with the metallic group, it does not behave as an ion; if on the other hand there be indirect union, that is to say, if the negative group is united indirectly to the metallic atom with the intervention of molecules of ammonia, the group comports itself as an ion. The difference between these two methods of union is indicated by the following formula:



$$\mathrm{Co}\begin{matrix}\diagup\mathrm{Cl}\\ \diagdown\mathrm{NH_3Cl}\end{matrix}.$$

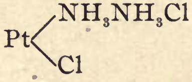
Although this method of regarding the constitution of this compound does not coincide very well with the idea which one usually has of the state of salts in solution, it is so well confirmed by the experimental facts observed in the class of ammonio-metallic compounds, that there is scarcely room to doubt it is correct, and it will be adopted in the development of the subject. One of the more simple series of compounds related to the ammonio-metallic salts with double ions is that of the derivatives of a divalent platinum atom Pt with four molecules of ammonia to form a compound of the formula, $Pt(NH_3)_4X$, the letter X representing a monovalent acid radical. The reactions of these salts and their molecular conductivity prove that the two acid groups behave as ions. They represent the acid radical of a salt of which the positive part is the radical, $Pt(NH_3)_4$.

The second member of the series is a compound, $Pt(NH_3)_3X_2$. The constitutional formula, $Pt\left\langle\begin{matrix}NH_3NH_3X\\NH_3X\end{matrix}\right.$, previously given does not correspond with the observed molecular conductivity, according to which one, and one only of the chlorin atoms behaves as an ion. The constitutional formula should then be represented by the symbol, $\left(Pt\begin{matrix}(NH_3)_3\\X\end{matrix}\right)X$. The third member of the series, $Pt(NH_3)_2X$, is found in two isomeric forms; *viz.*, the salts of platosamin and the salts of platosemidiamin. The formulae given by Cleve and Jörgensen to these salts are the following:

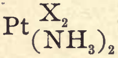
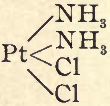


$$Pt\left\langle\begin{matrix}NH_3Cl\\NH_3Cl\end{matrix}\right.$$

and

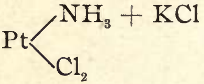
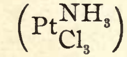


$$Pt\left\langle\begin{matrix}NH_3NH_3Cl\\Cl\end{matrix}\right.$$

Neither of these formulae takes into account the chemical properties and the conductivity in solution of the salts. In reality these substances do not behave any longer as salts of strong bases, but rather as salts in which the chlorin $\left(e.g.\text{ in the salts } Pt\begin{matrix}(NH_3)_2\\Cl_2\end{matrix}\right)$ would have analogous properties with those of this element in the organic chlorin compounds; they tend to become non-electrolytes, and chemical reactions are very difficult of production. All this would indicate a formula such as  $Pt^{X_2}_{(NH_3)_2}$ in which the two negative radicals should be in direct combination with platinum. In this case the molecules of ammonia should also be united in a corresponding way, and the structural formula would then be  $Pt\begin{matrix}NH_3\\NH_3\\Cl\\Cl\end{matrix}$, the negative groups being united by means of valence as the term is habitually employed and the molecules of ammonia by means of secondary force. This difference may be indicated by saying that the molecules of ammonia are coordinated, that is to say, that they should be directly linked to the metallic platinum atom, although their union could not be due to that which is usually expressed as valence.

The next term of the series is a compound,

$$PtNH_3Cl_2ClR,$$

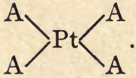
where R figures as a monovalent positive group. This is a double salt in the ordinary sense of the word. When R represents an atom of potassium, one obtains a general formula of the following kind:  $Pt\begin{matrix}NH_3 + KCl\\Cl_2\end{matrix}$. These bodies do not behave in any way as this formula would indicate; their molecular conductivity shows on the contrary that they contain a complex radical  $\left(Pt^{NH_3}_{Cl_3}\right)$ which behaves as a negative ion, the potassium being the ion with the electropositive character. The compound in question is a salt of a special kind, of which the acid radical is the group $\left(\mathrm{Pt}\genfrac{}{}{0pt}{}{\mathrm{NH_3}}{\mathrm{Cl_3}}\right)$ and potassium takes the place of the basic radical.

The last member of the series is the compound, $\mathrm{PtCl_2 + 2KCl}$, the addition product which is formed with platinum chlorid and potassium chlorid. This compound has not the properties which the formula indicates ; the conductivity shows in a striking manner that one is dealing with a salt in which the acid radical is formed by the group, $\mathrm{PtCl_4}$, the basic radical being the two atoms of potassium. The negative is $\mathrm{PtCl_4}$, and the positive ions are $\mathrm{K_2}$. Hence, the rational formula of this compound is the following : $\mathrm{(PtCl_4)K_2}$. To sum up, these compounds form the following series :

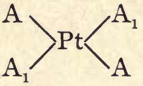
$$\mathrm{Pt(NH_3)_4Cl_2};\ \left[\mathrm{Pt}\genfrac{}{}{0pt}{}{\mathrm{(NH_3)_3}}{\mathrm{Cl}}\right]\mathrm{Cl};\ \left[\mathrm{Pt}\genfrac{}{}{0pt}{}{\mathrm{(NH_3)_2}}{\mathrm{Cl_2}}\right];$$

$$\left[\mathrm{Pt}\genfrac{}{}{0pt}{}{\mathrm{NH_3}}{\mathrm{Cl_3}}\right]\mathrm{K};\ \mathrm{PtCl_4K_2}.$$

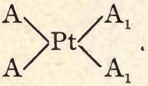
In this series it is clear that all compounds contain a special radical, $\mathrm{PtA_4}$, of which the character varies with the nature of the group A. In the first members, the radical has basic properties ; in the center members it behaves as neutral, and in the last members it is of distinctly acid character. The constitution of the radical, $\mathrm{PtA_4}$, is a matter of considerable interest. All the facts known tend to show, as has been seen, that the four groups A are directly united to the platinum atom. If the four radicals are distributed in the same plane as the atom of platinum, the constitutional formula of these radicals will be represented by



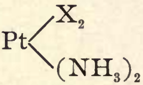
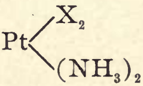
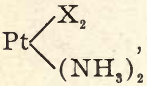
In assuming a plane arrangement of the groups, we obtain in the case where two of the radicals A are different from the other two, two geometrical isomers, expressed by the formulae,

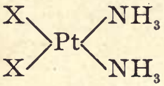


and

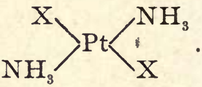


It is to these theoretical formulae that certain of the cases of isomerism which have been observed in the compounds of platinum are related.

One of the most characteristic examples is the isomerism of the salts of platosemidiamin,  $\mathrm{Pt}\genfrac{}{}{0pt}{}{X_2}{(NH_3)_2}$, with the salts of platosamin,  $\mathrm{Pt}\genfrac{}{}{0pt}{}{X_2}{(NH_3)_2}$; the two series of compounds correspond to the same formula,  $\mathrm{Pt}\genfrac{}{}{0pt}{}{X_2}{(NH_3)_2}$, and one cannot explain their isomerism in any way than by means of stereochemical formulae,

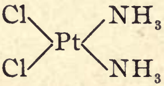


and

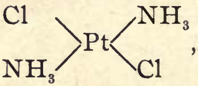


One can even determine the figures representing the two series of compounds.

If it be assumed, for example, that the first formula corresponds to the compounds of platosemidiamin, and the second formula to the platosamin derivatives,

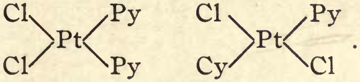


Platosemidiamin chlorid.

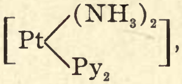


Platosamin chlorid.

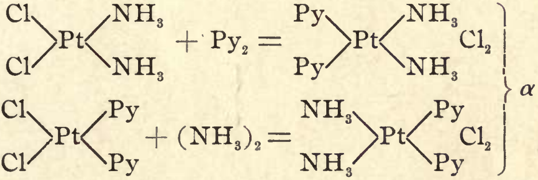
the corresponding compounds which are formed from platinum chlorid with pyridin would have the formulae:

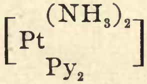


When chlorid of platosemidiamin is treated with pyridin and the chlorid of platosemidipyridin is treated with ammonia, the same compound,

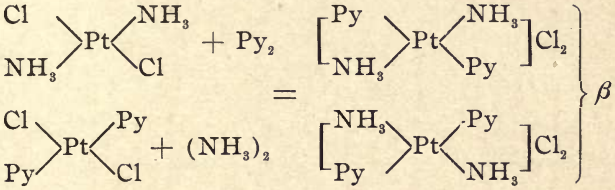


is obtained. This compound will be designated as the α compound and is formed in the following way:

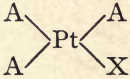


Similarly by treating platosamin chlorid with pyridin and platopyridin chlorid with ammonia, a compound,  $\left[\mathrm{Pt}\begin{matrix}(NH_3)_2\\ Py_2\end{matrix}\right]$ Cl_2, is obtained differing from α, and which will be called the β compound. This latter is the stereochemical isomer of the first.

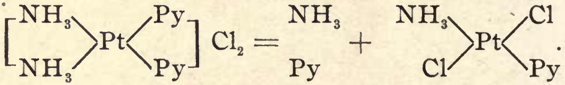
It is formed in the following way:



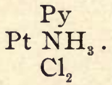
On heating the α- and β-compounds, they are transformed with a loss of ammonia and of pyridin into substances belonging to the platosamin series, that is to say, into substances corresponding to the general formula,



In considering the formulae of the α- and β- compounds, it will be easily understood how such a transformation is effected, for the α-compounds by loss of a molecule of ammonia, and of a molecule of pyridin, according to the equation,

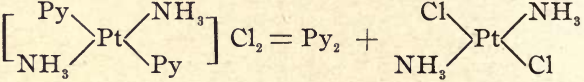


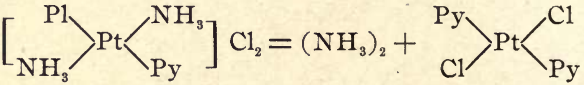
The compound should hence furnish a substance of the formula,

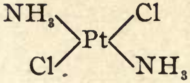
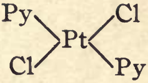


$$\mathrm{Pt}\begin{matrix}\mathrm{Py}\\ \mathrm{NH_3}\\ \mathrm{Cl_2}\end{matrix}.$$

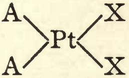
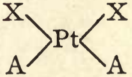
The β-compound, on the other hand, should undergo a rearrangement into salts of the platosamin series in two different ways, either by the loss of two molecules of ammonia or of two molecules of pyridin, as follows:

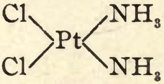
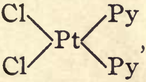
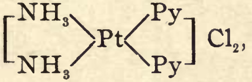


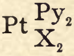
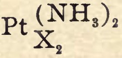
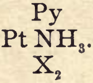


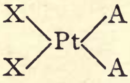
On heating the β-compound, a mixture of two substances should be obtained, one corresponding to the formula,  , and second to  .

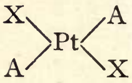
These reactions which are the result of the examination of stereochemical formulae of the platosamin and platosemidiamin compounds, have in reality been observed in heating these two compounds, thus furnishing a proof of the constitution of these substances.

It can be shown by the following consideration that one would obtain theoretical deductions, which would not be any more with experimental evidence if the formulae,  , should be given to the salts of platosamin, and that of  to the salts of platosemidiamin.

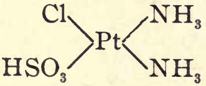
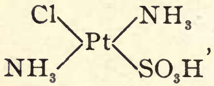
Experimentally on adding to the salts of platosamin,  and  , to the first, two molecules of pyridin, and to the second, two molecules of ammonia, one should obtain a compound,  but the latter would be transformed in three different ways into salts of the platosamin series. First, by loss of two molecules of ammonia, second, by loss of two molecules of pyridin, and third, by loss of a molecule of ammonia, and a molecule of pyridin.

Hence one should obtain a mixture of the following three substances :  $\mathrm{Pt}\begin{matrix}\mathrm{Py}_2\\ \mathrm{X}_2\end{matrix}$;  $\mathrm{Pt}\begin{matrix}(\mathrm{NH}_3)_2\\ \mathrm{X}_2\end{matrix}$; and  $\mathrm{Pt}\begin{matrix}\mathrm{Py}\\ \mathrm{NH}_3\\ \mathrm{X}_2\end{matrix}$. This has, however, not been observed even when the amin radicals of the composition $\mathrm{Pt}\begin{matrix}a_2\\ b_2\\ X_2\end{matrix}$ are closely related to one another, *e.g.*, ethylamin and propylamin. The two isomeric series should then correspond to the following formulae:

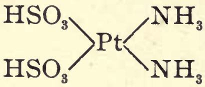
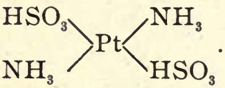

Salts of platosemidiamin.


Salts of platosamin.

The number of stereoisomeric derivatives of divalent platinum is already considerable. Special interest is attached to the compounds with sulfurous acid which have the formulae,


and


and also to the compounds,


and


The compounds so far investigated have contained a complex radical MA_4. There exists, however, a large number of inorganic compounds, in which the molecule is characterized by the presence of a complex radical, MA_6, and which may be brought together in a series having analogies with those which we have found above in the divalent platinum series.

In order to give some idea of this series the following are formulae of compounds derived from tetravalent platinum and divalent cobalt.

$\mathrm{Pt(NH_3)_6Cl_4}$; $\left[\mathrm{Pt}^{\mathrm{Cl}}_{\mathrm{(NH_3)_5}}\right]\mathrm{Cl_3}$; $\left[\mathrm{Pt}^{\mathrm{Cl_2}}_{\mathrm{(NH_3)_4}}\right]\mathrm{Cl_2}$;

$\left[Pt^{Cl_3}_{(NH_3)_3}\right]Cl$; $Pt^{Cl_4}_{(NH_3)_2}$; $\left[Pt^{Cl_5}_{NH_3}\right]K$; $(PtCl_6)K_2$;

$[Co(NH_3)_6]Cl_3$; $\left[Co^{NO_2}_{(NH_3)_5}\right]Cl_2$; $\left[Co^{(NO_2)_2}_{(NH_5)_4}\right]Cl$;

$\left[Co^{(NO_2)_3}_{(NH_3)_3}\right]$; $\left[Co^{(NO_2)_4}_{(NH_3)_2}\right]K$; $\left[Co^{(NO_2)_5}_{NH_3}\right]K_2$;

$[Co(NO_2)_6]K_3$.

Similarly to that which was found with the radicals MA_4 in which the four groups are directly united to the metallic atom; in these compounds with the complex radical, MA_6, these groups are in direct union with the metal. Proof of this is given by the quantitative examination of the molecular conductivity of these substances in solution. It is now necessary to obtain some idea of the configuration of the group, MA_6. The most simple hypothesis which can be formed assumes an octahedral arrangement, the metallic atom occupying the center of an octahedron, and the six groups A would be arranged at the summits of the figure. Hence, in a molecular arrangement of this sort, one should obtain certain cases of stereoisomerism, of which but one can be considered at present, and this one is supported by experimental evidence. Suppose in the first place, a radical, MA_6, in which the four groups A are alike, and the two others different. One should then have an arrangement, $\left[M^{A_4}_{A'_2}\right]$. In this case, the two radicals A could occupy different positions. They could be arranged on the two summits of the octahedron which are bound by an axis, or on two united by an edge as the following figures will show:

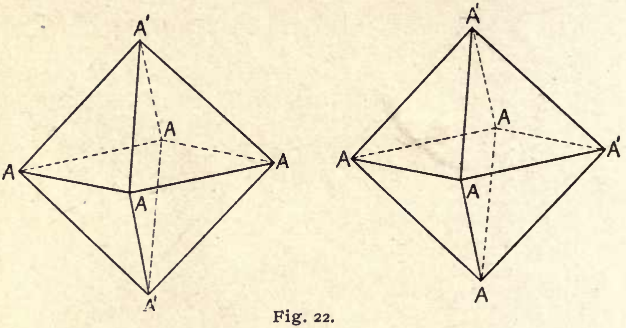


Fig. 22.

That is to say, the compounds containing a radical $\left[\mathrm{M}\genfrac{}{}{0pt}{}{A_4}{A'_2}\right]$ should be obtained in two isomeric forms.

The radical $\left[\mathrm{M}\genfrac{}{}{0pt}{}{A_4}{A'_2}\right]$ is found in certain ammoniacal derivatives of cobalt; *viz.*, in the salts of praseocobaltamin corresponding to the general formula,

$$\left[\mathrm{Co}\genfrac{}{}{0pt}{}{X_2}{(NH_3)_4}\right]X.$$

If the theoretical considerations are well founded, these salts should be obtained under special isomeric forms. As a matter of fact this has been experimentally realized. The beautiful work of Jörgensen has shown that there exist two series of salts of the formula,

$$\left[\mathrm{Co}\genfrac{}{}{0pt}{}{X_2}{A_4}\right]X.$$

The two series scarcely differ in a chemical point of view. Of the three acid radicals one alone behaves as an ion, but the two series of salts are markedly distinguished by the characteristic property; *viz.*, that while the salts of the praseocobalt series are green, the isomeric purpureocobaltamin salts are violet as their name would indicate.

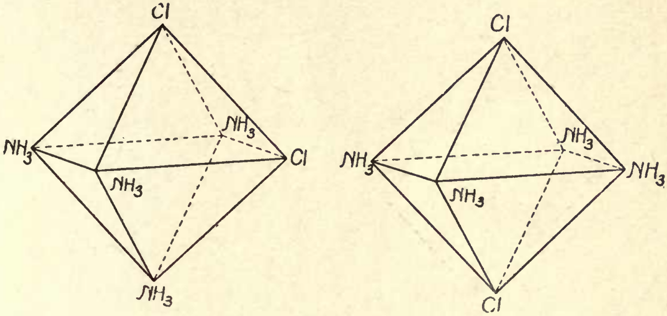


Fig. 23.

This interesting case of isomerism is the first proof in favor of stereochemical isomerism of the radicals, $\left[\mathrm{M}{\mathrm{X}_2 \atop \mathrm{A}_4}\right]$. In another series, also, cobalt presents a special isomerism. It has been known for some time that there exists a group of cobaltamin salts known as the derivatives of the croceocobaltamin of the formula, $\left[\mathrm{Co}{(\mathrm{NO}_2)_2 \atop (\mathrm{NH}_3)_4}\right]\mathrm{X}$, and hence containing a radical of the type $\left[\mathrm{M}{\mathrm{X}_2 \atop \mathrm{A}_4}\right]$. Recently Jörgensen has discovered a new series of compounds having the same formula, $\left[\mathrm{Co}{(\mathrm{NO}_2)_2 \atop (\mathrm{NH}_3)_4}\right]$, and only differing from the former in its physical properties. The name flaveocobaltamin has been given to this series of salts, and there is scarcely any doubt that the isomerism of these two series is due to the presence of two isomeric radicals corresponding to the formula $\left[\mathrm{Co}{(\mathrm{NO}_2)_2 \atop (\mathrm{NH}_3)_4}\right]$. According to the position occupied by the two groups, NO_2, one may have the following formulae:

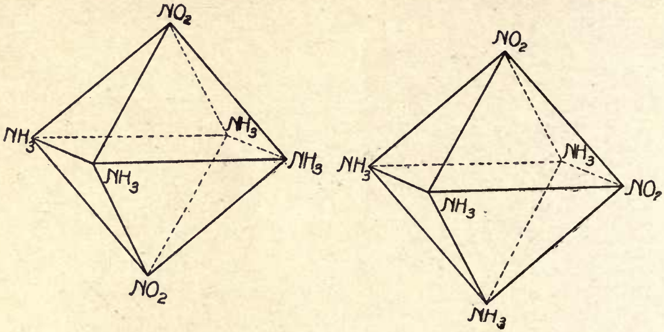


Fig. 24.

Among the ammoniacal derivatives of tetravalent platinum, there is found a case of isomerism perfectly analogous to those observed in the compounds of cobalt. There are two series of compounds known, corresponding to the general formula, $Pt\begin{smallmatrix}(NH_3)_2\\X_2\end{smallmatrix}$. These are the salts of platinosemidiamin, and the salts of platinamin; here also the radical $\left[M\begin{smallmatrix}A_4\\A'_2\end{smallmatrix}\right]$ is present. It cannot be doubted that this again is a case of isomerism due to the same cause as that of the cobalt compounds, as the following formulae represent:

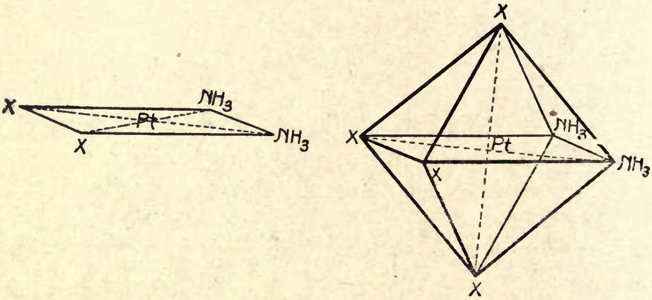


Fig. 25.

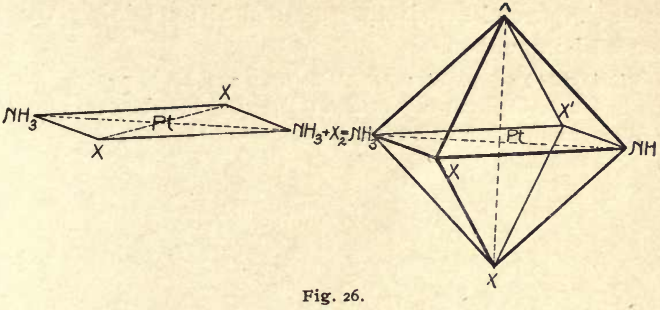


Fig. 26.

One can even determine with a certain amount of probability the spatial formulae corresponding to the one, and to the other of the two series. The compounds of the platinosemidiamin series and of the platinamin series are formed by the addition of two negative groups to salts of platosemidiamin and platosamin, the divalent platinum being transformed into tetravalent platinum.

In the case of the divalent platinum compounds, plane formulae have been used and for salts of tetravalent octahedral formulae. The most simple hypothesis which can be used with this connection consists in assuming that the negative groups are added to the salts of divalent platinum in such a way as to occupy two summits, united by an axis determined by the four radicals which complete the molecule.

This transformation is explained by the above formulae which give at the same time stereochemical formulae for the two isomeric series.

In the short sketch which has been given above of the stereoisomerism of certain classes of inorganic compounds, some of the principal points of the new theory have been explained. This theory seems to afford the most simple and satisfactory method of explaining these cases of isomerism.

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