Stereochemistry

by Virgil Louis Leighton

1895

Submitted to the Department of Chemistry of the University of Kansas in partial fulfillment of the requirements for the Degree of Master of Arts
Thesis
Leighton, V. 1895
Stereochemistry.
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The existence of two bodies containing the same elements in the same proportions and still having different chemical and physical properties was not considered possible until 1828, when Liebig on comparing his analysis of silver fulminate with that of silver cyanate which Wöhler had made the year before, found that they were the same. To satisfy himself that there had been no mistake he repeated Wöhler's investigation himself. A few years later (1828) Wöhler transformed cyanate of ammonium into urea compounds containing the same elements in the same proportions. Even then chemists hesitated to accept this as a general principle. Berzelius only accepted it on the results of his own investigation. He proved the identity of composition of tartaric acid and racemic acid and proposed the term isomerism for this class of bodies. The idea that Berzelius had was that the atoms of the elementary constituents were grouped differently into compound radicals. This was the theory of structural isomerism and the only theory of isomerism that received definite form for over forty years. The theory of physical or stereoisomerism of the normal outgrowth of that of structural isomerism.
holds that not only the grouping of the atoms—their relation to one another—but also the arrangement of the atoms in space determines the properties of the substance.

The inability to explain certain cases of isomerism by a difference in the structural formula was the immediate cause of the considerations of the special relations of the atoms in the molecule. In 1860 Pasteur working upon the salts of tartaric acid simply as he tells us to become familiar with practical crystallization found that all the salts of the ordinary tartaric acid crystallized in hemihedral forms and hemihedral in the same sense, i.e., the same face were developed on all the crystals. The optical activity of tartaric acid had been discovered by Biot and since hemihedral forms of gypsum crystals and some few other minerals were known to rotate the plane of polarized light, a relationship between hemihedrism and optical activity was suggested. This led to the study of racemic acid with the result that the double salt of sodium and ammonium was found to crystallize in two hemihedral forms, a right and left-handed form, i.e., one corresponding to the mirrored image of the other. By picking out the crystals
the two forms were separated and found to turn the plane of polarized light to the right and left respectively, while a mixture of equal quantities of the two was inactive. It was further found that the right-handed crystals were identical with those obtained from ordinary tartaric acid. This work established the relation between optical activity and crystalline form, the characteristic properties of physical isomers.

In 1863 W. K. Clifford called attention to the fact that there were more isomeric lactic acid than could be accounted for by the existing structural theory. He showed that the optically active zemic lactic acid as well as the ordinary inactive lactic acid must be represented by the same structural formula \(\text{CH}_3\text{C(OH)}\text{COOH}\) and suggested as a possible explanation of this a different arrangement in space of the groups composing the molecule. Even before this time Beale suggested that in the case of phthalic acid which forms an anhydride so easily the carboxyl groups are attached to neighboring carbon atoms, while in the isomeric acids which do not form anhydrides the carboxyl groups are not attached to neighboring carbon atoms. Similar hints and suggestions are found in the works of other authors. But the stereochemical idea received no definite form until the publication of Le Bel's
and Vonit Hoff's work in 1874.

Vonit Hoff's "La Chémie dans l'Espace" appeared in Sept. 1874 an edition revised and much improved was published in 1884 under the title "Dix années dans l'Histoire d'une Théorie." Le Bel published his work in Nov. 1874. It was entirely independent of Vonit Hoff's and contained practically the same ideas. Vonit Hoff was led to the consideration of the special relations of the constituents of the molecules by a comparison of the number of isomers possible in the ordinary plane formula and the formula representing them equally distributed in space. In the plane formula, there would be two isomeric forms of $C\text{H}_2\text{R}_2$, a disubstituted product of methane. Fig. (2) and (3)

![Diagram](image)

If the carbon atom is placed at the center of a tetrahedron and the four monosubstituted constituents placed at the corners, Fig. (4)

![Diagram](image)

a, b, c, and d, all bear the same relation to the carbon atom. If however we change the position of any two of them, as in Fig. (5) and (6) they bear the relation to each other of object and mirror image or right and left-handed models.
Donit Hoff recognised the peculiarity of this isomerism and called the carbon atom united in this way to form different radicals the asymmetric carbon atom. He mentioned that all optically active substances in solution would be found to contain the asymmetric carbon atom and he also pointed out the relation between this arrangement and the crystalline form.

Léonard was led to adopt the dimensional formula by his attempts to account for optical activity. The physical phenomena observed by Pasteur, Koenig and Lavoisier and accounted for theoretically by the mathematician Sonnenschein was the starting point. These accounted for the optical activity of solids by a certain arrangement of their particles. An arrangement characteristic by its lack of symmetry. Léonard reasoned that in the case of bodies optically active when in solution, it must be due to the arrangement of the atoms or the constituents of the molecule. The statement of Léonard's theory is the converse of that of Donit Hoff, that is, "In general if a substance is derived from an asymmetric type MA₄ by substitution of three different atoms or radicals for A, the molecule will be asymmetric and will possess the power of rotation." This if in the formula
formulas of a substance we have carbon united
with three monosubstant radicals differing
from one another and from hydrogen the
substance should be active." Further since
M. may be a radical simple or complex it
is not necessarily a single carbon atom
to which the form unlike groups must
be attached to cause rotation; as will be
seen later in some cases the distinction
is important.

There are in brief the theories with
which Kekulé and Perkin start out. The
form of the regular tetrahedron is used
singly for convenience to represent the
relations that actually exist. A regular tetrahedron
would imply that all the groups were equal
distances from the carbon atom. But since
all the groups are different therefore of
different weights and different forms of
distinction for the carbon atom and for
each other it is hardly natural to suppose
that the form would be that of the
regular tetrahedron but rather an asymmetric
one.

Of course such a theory as the
above is of value only so far as it conforms
to the known facts and fulfills the purpose
for which it was intended in explaining
cases of isomerism otherwise inexplicable.
And we may say here that in all the
field of science there has been few
generalisations so far reaching and comprehensive that they have been so well supported by facts and of so much value as an aid and stimulus to investigation.

The characteristics of "physical isomer" are their crystalline form and power of rotating the plane of polarised light. Substances containing the asymmetric carbon atom are not necessarily active, they may be a mixture of equal quantities of right and left-handed modifications, one neutralising the effect of the other. This has been found to be the case with racemic acid, malic acid, lactic acid and many other compounds. In all such cases the compounds can be resolved into two a right and a left-handed modification. The power of rotation may be nullified by the opposite effect of different parts of the same molecule. Take for example tartaric acid if we represent the ordinary active acid (deuteron)

\[ \text{Formula (1)} \]

\[
\begin{align*}
+\text{H} &- \text{B} - \text{HO} +
+\text{H} &- \text{B} - \text{HO} +
+\text{H} &- \text{B} - \text{HO} +
+\text{H} &- \text{B} - \text{HO} +
\end{align*}
\]

Then (2) would represent the left-handed variety while that represented by the third formula would be in active, and distinguished from racemic acid by the impossibility of resolving it into the two active
 Bodies. The crystalline form was shown by Pasteur to correspond to the power of rotation i.e. the crystals of the dextro-rotary had been the same relation to those of the laevorotary acid that the right hand bears to the left (i.e. by enantiomorphy). This has also been shown to be the case in numerous other compounds. In the crystals of the binolate of ammonium \(\text{(7)}\) and \(\text{(8)}\) the two crystalline forms bear relations exactly analogous to the models as shown in fig. \(\text{(7)}\) and \(\text{(8)}\) according to this.

The existence of an active body would call for the existence (or possibility of existence) of another with an opposite dextro form. This has been observed in a great many cases, as the tartrate, angé alcohol, valeric acid, asparagine, glucon, mauninit, cynthiae acid, conifor, formed, etc.

The study of the structure of active bodies has shown that as far as made out they all contain the asymmetric carbon atom. There have been some observations contrary to this hypothesis but they have all been proved due to errors of one kind or another, for example, fungyl alcohol \(\text{\textit{Bl}}\) etc. has reported an active by Brenchal. This activity was found to be due to the presence of strong alcohol.
The results of trimethylathylamine (C7H13N) used was reported as active by Hirschel. This was shown by Label to be due to an error of observation.

By Henninger, styrone 66 77 61 72 was reported as active by Berthelot. This has also been shown to be due to an impurity (Nostastyrone). The iodide of trimethylbromostyrene (C7H13Br) was reported as active by Friedlander.

This was the iodide to be due to an impurity, possibly contained in the alcohol used in its preparation. 8-B cholines 66 (CH3)8CHCH2N+ was attributed to an error of observation.

Paradise, the series of observations most conclusive in support of the theory is that the activity of compounds diaphragm in those derivatives in which the asymmetric carbon atom becomes symmetric. For example, the inactive methyl amide 64 80 04, furaneic and urea amides 64 80 04 are derived from the active methyl amide 64 80 04. Foraminic acid amide 64 80 04 as derived from active crotonic acid 64 80 04 and pyrene 64 80 04.

For the inactive derived from camphor active, and a number of other similar observations have been made. The derivatives of active amyl alcohol 66 80 04, 64 80 04, NBR 64 80 04, retinam formactive in the ethyl amyl sulfite, chloride, bromide, isothiocyanate, and various acids, amylcyclohexyl, crotonic acid, ethylene, and many others recently examined by Gugg.

These compounds have been found by Label and just to contain the asymmetric carbon.
on the other hand, methylamyl (C₆H₅)₂CH₂CH₃, amylene $C_7H_{15}$ (C₆H₅)₂CH₂ and (C₆H₅)₂CH₂, were found to be inactive.

The action of organisms in fermentation has been found particularly favorable to the production of active compounds. Therefore, when compounds derived in this way are found to be inactive there is reason to believe it is due to a structure incompatible with the power of rotation. Decimic acid obtained by the fermentation of starches (active) $C_7H_{15}COOH$ is inactive, the same is true of that obtained by the fermentation of calcium nitrate and calcium tartrate, compounds containing the asymmetric carbon atom. Produced by the action of organisms almost without exception are active. The reason that these compounds produced artificially are not active has been considered due to a mixture of equal quantities of two isomers with opposite rotatory power. This has been shown to be the case in numerous instances by resolving the inactive compound into two active isomers. Some of the compounds thus resolved are:

- Proglycemic glycid $C_7H_8 \text{CH} \text{CH}_3 \text{COOH}$
- Secondary amyl alcohol $C_7H_{15} \text{CH}_2 \text{OH}$
- Primary $C_7H_{15} \text{CH} \text{CH}_3 \text{COOH}$
- Mollic acid $C_7H_{15} \text{CH} \text{CH}_3 \text{COOH}$
- Butyroylformic acid $C_7H_{15} \text{CH} \text{CH}_3 \text{COOH}$
- Glycemic acid $C_7H_{15} \text{CH} \text{CH}_3 \text{COOH}$

By Bock

By Essener

By Lewkowitsch.
Many attempts have been made to resolve compounds that did not possess the asymmetric carbon atom into two active modifications, but in no case has it been done.

One of the objections that Perkëlott first urged against the theory of von Haff and Le Bel was that some inactive compounds containing the asymmetric carbon atom were not resolvable into two active compounds.

We have mentioned one condition in which one part of the molecule would tend to nullify the effect of the other and produce inactivity, in such a case of course the compound could not be resolved into active components. But this condition could only occur in compounds containing two asymmetric carbon atoms.

Perkëlott cited the case of inactive acetic acid 

\[ \text{CH}_3\text{COOH} \]

containing but one

\[ \text{CH}_3\text{COOH} \]

asymmetric carbon atom and the inactivity could only be accounted for according to the theory by supposing it to consist of equal quantities of right and left-handed modifications. The experiments of Perkëlott, van't Hoff, and J. H. van't Hoff made since that time have shown this to be the case. The inactive acetic acids obtained by different methods were identified with that made by mixing equal quantities of dextro and laevorotary acids. The crystallography of the salts obtained from the different acids was also found to
be the same and corresponded to the right and left-handed helical forms obtained by
Eisenman from racemic acid. The electrical
conductivity of the quinol solution is also
the same as the two active modifications.
From the foregoing it seems clear
that all active bodies as far as known
contain the asymmetric carbon atom, and
from the great diversity of active compounds
it seems that any four different groups
united to a single carbon atom is sufficient
to produce optical activity.
Such in brief is the theory of the
simple asymmetric carbon atom, as advanced
by von Hoff and Lebel, and the tests on
which it is based. Since the publication of
their works there have been numerous
contributions to the literature of stereochemistry
by Wilibaldy, Von Brönig, Bichoff, W. Meyer,
Hantzig and Werner & Fischer, Bunge and others.
Some of these have made some very
important additions to von Hoff's theory.
Much credit is due to Wilibaldy
for his work published in 1886 for explaining
such cases as quinonic and like acids.
Although he added but little to the theory
of von Hoff, yet by the introduction of
one additional hypothesis and the logical
and systematic application of the
hypothesis of von Hoff he was able to
render the theory amendable to the
test of experiment. Van't Hoff had said that two carbon atoms united by a single bond were free to rotate around the axis joining their centers, but for the fact that they are held in position by the affinity of the groups united to one carbon atom for those of the other, the position of equilibrium depending on the nature of the groups, but was left undetermined. Wilsinewas said that by the aid of his hypothesis that the greater the "positivity" or "negativity" the greater the affinity between the two radicals, we could in many cases determine the position of equilibrium.

For example in ethylenechlorid (1)

\[ \text{CH}_2=\text{CHCl} \]

chlorine stands over chlorine and hydrogen over hydrogen, and we may assume that this would be the unstable position. In (2) hydrogen stands over chlorine and chlorine over hydrogen and since the attraction would be between these two the latter would be the stable configuration. But atomic motion due to heat may modify the conditions so that at a sufficiently high temperature all the possible rearrangements might exist at successive intervals of time. But under ordinary circumstances the latter condition would be the most favorable. In the same way sucinnic
acid might be represented by

\[ \ce{H-\text{COO}H} \quad \text{and} \quad \ce{H-\text{COO}H} \]

and as the carboxyl groups have no affinity for each other the first formula would represent the unfavourable configuration and the second the most favourable as the hydrogen and carboxyl groups are in closer relation. The first is the only one that would form an anhydride and the anhydride formed must have the formula \( \ce{\text{C}_4\text{H}_6\text{O}_2} \). As the ring formation fixes the configuration and prevents further rotation.

Another idea of Willardus of considerable importance is that when a triple combination is changed to a double combination by the addition of two monovalent radicals their position can be forecast with considerable probability. Vant Hoff had represented the triple combination with the two tetrahedrons face to face. Willardus showed that on the principle of least disturbance the radicals added would occupy adjacent corners, thus

\[ \begin{array}{c}
\text{3} \\
\text{2} \\
\text{1} \\
\text{4}
\end{array} + c d = \begin{array}{c}
\text{1} \\
\text{3} \\
\text{2} \\
\text{4}
\end{array} \]
In this case no more bonds are broken than absolutely necessary. The same principle was applied to the double bond but in this case there is not the double bond left to prevent rotation. One of the best examples of the double bond condition is that of fumaric acid and malonic acid. They were given the formulae by Hantzsch of:

\[ 
\begin{align*}
\text{H}_2\text{C} &- \text{COOH} + \text{H}_2\text{C} &- \text{COOH} \\
\text{H}_2\text{C} &- \text{COOH} &- \text{COOH} \\
\text{malonic acid} & & \text{fumaric acid}
\end{align*}
\]

According to these formulae malonic acid would be the least stable and would form an enolhydrate which is the case. Also according to the foregoing the acid formed by the addition of \( \text{H}_2\text{C} \) to \( \text{H}_2\text{COOH} \) would have the carbonyl groups on the same side of the molecule, while in fact it is found to be the last stable and forms an enolhydrate. Fumaric acid is formed by the splitting off of the \( \text{H}_2\text{O} \) on heating malonic acid to 150°. Now the favourable configuration for malic is (1)

\[ 
\begin{align*}
\text{H}_2\text{C} &- \text{COOH} \\
\text{H}_2\text{C} &- \text{COOH} \\
\text{H}_2\text{C} &- \text{CO} &- \text{H}_2
\end{align*}
\]

This less favoured would be (2)

\[ 
\begin{align*}
\text{H}_2\text{C} &- \text{COOH} \\
\text{H}_2\text{C} &- \text{CO} &- \text{H}_2
\end{align*}
\]

Fumaric acid. Then again malic enolhydrate which can only form the formula...
produces maleic acid on being heated. Michael and Anschütz have also attempted to show by the theory how by the addition of Ba and the subsequent removal of H₂, fumaric acid could be changed into maleic acid and maleic acid in fumaric acid. This has been objected to by Michael and Anschütz. But no theory more satisfactory has been advanced.

Another case of the extension of Kekulé's theory of great importance is that made by von Baeyer in applying it to the ring formations. He introduced the hypothesis that the four valencies of the carbon atom, not in the direction of the lines connecting the center of a regular tetrahedron with the faces, lines which are at an angle of 109° 28' with one another. The direction of the attraction can undergo a divergence, which, however, is attended by a proportional strain. Thus to compounds like octylene von Baeyer ascribed the negative heat of formation and the explosive nature of its compounds to the valences connecting the two C₆H₅ groups being in a state of stress. In ring formations of four, five, and six carbon atoms there is the least divergence; therefore these are the
most stable. In the five-membered ring there is scarcely any divergence. That this does not show such remarkable stability as the six-membered ring is due to other causes. It is claimed however by König that the pentamethylene ring is more stable than the hexamethylene ring. It is a well known principle that the highly symmetrical compounds are more stable than the unsymmetrical.

The benzene ring expressed by the formula of Kekulé is highly symmetrical. While it is impossible to arrange the five-membered ring in symmetrical form, there must be one 6+ group and four 6++ groups present. With fitalic and hexamethylene it is otherwise. However, the case is different. They are both equally symmetrical, and as has been observed the five-membered ring is the more stable. The tendency to ring formation is shown frequently in compounds containing the requisite number of carbon atoms. Thus succinic acid by the loss of the elements of water
\[ \text{C}_6\text{H}_5\text{COOH} \rightarrow \text{C}_6\text{H}_5\text{CO} + \text{H}_2\text{O} \]
forms an oxide while a five-membered ring. Also phthalic acid in the same way forms a five-membered ring.
and all the oxides with a sufficient number of carbon atoms easily form oxohydrates and these compounds are especially stable.

Von Baeyer's observations have led to the conclusion that in the ring formations the atoms are actually arranged in a plane.

The theories of Von Baeyer have shown themselves capable of the most wonderful development, and has been of the greatest assistance in the study of the ring forming compounds.

Steroschmistry of Nitrogen

Von Baeyer was also the founder of the stereoschmistry of nitrogen. He based his theory upon the fact that if all the substituted ammonia (\( \text{N}_a\text{b}_c\text{c}_d \)) none of them show isomerism.

In regard to nitrogen there are two cases to be considered, one in which nitrogen is trivalent the other in which it is pentavalent. For convenience the three volumes as in \( \text{N}_3 \) are called the ordinary valences, while the other two are called the supplementary valences. In all the research upon the substituted ammonias no isomerism has been observed as in the case of the asymmetrical carbon atom (\( \text{C}_a\text{b}_c\text{d}_d \)). Therefore Von Baeyer thought these three valences must be arranged in a plane, as so.
In this case if simply turning one formula over they become identical. This would not be so were the valences extended in any other direction. If they are not in a plane then the nitrogen atom must be placed at the solid angle of a tetrahedron the edges of which represent the valences, as fig (1) and (2). We see here that there are two forms exactly analogous to that of (a, b, c, d) or that the molecule is asymmetric and should therefore show stereoisomerism, but such isomerism are not known in compounds in which nitrogen occurs. However isomerism have been observed and Prof. Hoff proposed as an explanation of such isomerism that the supplementary valences were not in the same plane as the ordinary valences, and for convenience he represents them at right angles to the plane of the three ordinary valences.

According to this form, like (N A, B, C) and (N A, B, C) should show isomerism. In dimethyl-ethyl ammonium iodide there is said to be no isomerism N(BF)2(NH3)4BF and N(BF)2(NH3)4BF as indicated by the theory. But Prof. Hoff claims that there is not sufficient evidence as to the identity of the two compounds, that the plane of symmetry
would be the same and hence the crystalline form. In a parallel case the triethyl-ethyl-
aminium iodide isomerism has been shown by Tschentscher to exist as N(ethyl)₃H·Br₂
and N(ethyl)₂H·Br·H₂O. Sakel has also obtained by the action of peroxide on methyl-
ethyl-ethyl-propyl-isobutyl ammonium chloride a solution optically active, thus in an exception
to the statement of Voit-Hoff that all substances optically active when in solution will be
found to contain the asymmetric carbon atom and for this reason Sakel's converse
statement seems preferable). He has also discovered two isobutyl trimethyl ammonium
chlorides.

An explanation of the fact that nitrogen which has five valence often shows
only three or given by Burch and Marshall is that the two supplementary valences
are not equally constant and used in binding together
molecules such as the formula for ethylamine
would be $\text{C}_2\text{H}_5\text{N}^+\text{H}_2\text{O}^-\text{N}^+\text{H}_2\text{O}^-$ and if the
$\text{H}_2\text{O}^-\text{N}^+\text{H}_2\text{O}^-$ molecule was
associated by rise or fall of temperature the
inter would give an abnormal expansion or
contraction to the original volume on cooling.
It is also suggested that the impossibility
of separating ethyl, diethyl and triethyl-
amine by fractional distillation is due
to the molecules being connected by
the supplementary valence of nitrogen.

In the course of an investigation
in the benzyl dioxines, Goldschmidt observed
that by treating benzyl with hydroxylamine
two isomeric benzyl dioxines were obtained
and that they both were to be represented
by the formula \( \text{C}_6 \text{H}_5 \text{ON} \cdot \text{ON} \cdot \text{C}_6 \text{H}_5 \)
with the \( 3 \text{C} = \text{N} \text{O} \) is neither an
assignment nor a
double bond.

The theories that have advanced
do not account for such a case as this.
Moreover, Ruzicka and W. Meyer have shown
that there is a third isomer of theazole
formula. To account for the W. Meyer
made use of the rotation theory of Van
Hoff, in which two carbon atoms united
by a single bond was regarded as free
to rotate about the line joining their
centers as an axis unless on account
of some special form of construction this
rotation was prevented. In such a case
there would be a favorable and one in
more less favorable positions. Of the
dioxines above referred to, the \( 3 \) dioxine is
the more stable, the other two being
easily changed to it by heat or the riper
reagents. But the \( 3 \) dioxine cannot be changed
to the others. The \( 7 \) dioxine is changed to
the \( 3 \) by slightly warming. To change the \( 3 \)
It is necessary to heat it to 120° with
alcohol or benzene. Pierce from this that in
the case of the dichlorines there cannot be
free rotation as in the case of succinic
acid, but that certain positions are
maintained until some outside force
is applied. To represent this condition
K. Meyer first proposed the formula

\[
\begin{align*}
\text{n-} & \text{n-} \\
\text{Cl} & \text{Cl}
\end{align*}
\]

in which \text{n-} \text{n} stands for the \text{N-OH} group.
In the first case \text{OH} stands over \text{OH} and
\text{Cl} over \text{Cl}, hence it would be the
most unstable, and most easily form an
ethylene, which are characteristics of the
\text{X} modification. The other two should
show very similar properties. K. Meyer
later represented the dichlorines thus

\[
\begin{align*}
\text{Cl} & \text{Cl} \\
\text{Cl} & \text{Cl}
\end{align*}
\]

Making for theoretically possible dichlorines,
although but three are known to exist.
But the latter representation has the advantage
that it does not require a right and
left-handed structure for the \text{A} and \text{B}
modifications to which they evidently are
were analogous.

Much objection was made to V. Meyer's theory. It was claimed that there was not sufficient evidence that the structure of the three derivatives were identical.

Michael held for a time the formula for one of the oximes but on the discovery of the second monoxide and its conversion into a dioxime he was forced to abandon it. The presence of the two groups $=NO\tilde{H}$ and $=NH\tilde{O}$ was urged by some for a time. In some respects this answer may well for explaining all the monoximes and the dioximes; thus:

\[
\begin{align*}
16. & \quad H_2 - \tilde{N} = NO\tilde{H} \\
26. & \quad H_2 - \tilde{N} = NH\tilde{O}
\end{align*}
\]

\[
\begin{align*}
16. & \quad H_2 - \tilde{N} = NO\tilde{H} \\
26. & \quad H_2 - \tilde{N} = NH\tilde{O}
\end{align*}
\]

This theory gained especial interest when Reckniew announced the discovery of a second monoxide which had the formula $16. H_2 - \tilde{N} = NH\tilde{O}$, the ordinary monoxide being $16. H_2 - \tilde{N} = NO\tilde{H}$. This was the accession for a series of investigations carried out by Bowers and Dittrick under the direction of V. Meyer which showed that the group $=NO\tilde{H}$ was present in the monoxide but not the group $=NH\tilde{O}$. This work
settled the question of the structural identity of the dioximes, and for a time left the theory of V. Mayer in full possession of the field.

Kortyged and Namer proposed a theory for the explanation of the dioximes which has been of great interest especially during the last few years and has suggested many new lines of investigation.

They start with the fundamental hypothesis that the three ordinary molecules of nitrogen are not always in a plane but may occupy the solid angle of a tetrahedron and does do this at least in the oximes. According to this there are three possible classes of isomers as follows.

1. \( \begin{align*} &\text{Z} \quad \text{and} \quad \text{NZ} \quad \text{analogue to} \quad \text{H}_3 \text{Z} \quad \text{and} \quad \text{Z}_6 \text{H} \quad \text{X}_6 \quad \text{Y} \quad \text{X}_6 \quad \text{Y} \end{align*} \)

2. \( \begin{align*} &\text{NX} \quad \text{and} \quad \text{NX} \quad \text{analogue to} \quad \text{H}_3 \text{X} \quad \text{and} \quad \text{H}_3 \text{X} \quad \text{Y} \quad \text{Y} \quad \text{Y} \quad \text{H} \end{align*} \)

3. \( \begin{align*} &\text{NXYZ} \quad \text{and} \quad \text{NXYZ} \quad \text{analogue to} \quad \text{H}_3 \text{XYZ} \quad \text{and} \quad \text{H}_3 \text{XYZ} \quad \text{Y} \quad \text{Y} \quad \text{R} \end{align*} \)

4. \( \begin{align*} &\text{NXYZ} \quad \text{and} \quad \text{NXYZ} \quad \text{analogue to} \quad \text{H}_3 \text{XYZ} \quad \text{and} \quad \text{H}_3 \text{XYZ} \quad \text{Y} \quad \text{Y} \quad \text{R} \end{align*} \)
At examples of the first class we have benzyldioxines \( \text{H}_2\text{C}=\text{C}-\text{H} \) and \( \text{H}-\text{C}=\text{C}-\text{H} \)
\[ \text{H}_2\text{N} \quad \text{H}_2\text{N} \]

benzyllmonoxines \( \text{H}_2\text{C}-\text{C}-\text{H} \) and \( \text{H}_2\text{C}-\text{C}-\text{H} \)
\[ \text{H}_2\text{N} \quad \text{H}_2\text{N} \]

" dioxines
\[ \text{H}_2\text{C}=\text{C}-\text{H} \text{N} \quad \text{H}_2\text{C}=\text{C}-\text{H} \text{N} \]
\[ \text{H}_2\text{N} \quad \text{H}_2\text{N} \]

It is seen that explains the two known monoximes, a third would be impossible. It also explains the existence of the three known dioxines. It will be remembered that according to V. Majes theory these monoximes and four dioxines were possible. Also, according to the theory of Hantzsch and Warners many oximes are indicated that are not known.

On this account the theory meet with considerable opposition. The oximes of the ketones are compounds which should according to this theory show monoximism, as \( \text{X}-\text{C}=\text{C}-\text{Y} \) and \( \text{X}-\text{C}=\text{C}-\text{Y} \)
\[ \text{H}_2\text{N} \quad \text{H}_2\text{N} \]

Immediately after the publication of Hantzsch and Warners work, Awars made a thorough study of the oximes of the ketone
\[ \text{H}_2\text{C}=\text{C}-\text{H} \quad \text{H}_2\text{C}=\text{C}-\text{H} \]
but could to obtain oximes. This work
in a negative way proved the theory of
N. Meyer, for if isomers should be found
among the hormones in which there are not
two carbon atoms united by a single bond
it would of course render his theory
untenable, for it was based upon the
single bond arrangement. The work of
Ewers also illustrates well the fact that
two much reliance must not be
placed upon negative results. We have
many analogous cases where even a well
founded theory indicates the possibility
of isomers and yet the isomers are
not known. Such is the case with
\( {\text{H}}_2\text{H}_2\text{C} \) and \( \text{H}_2\text{H}_2\text{C} \), the theory indicates
two forms as

\[ \text{H}_2\text{H}_2\text{C} \quad \text{H}_2\text{H}_2\text{C} \]

\[ \text{H}_2\text{H}_2\text{C} \quad \text{H}_2\text{H}_2\text{C} \]

Yet only one
\[ \text{H}_2\text{H}_2\text{C} \quad \text{H}_2\text{H}_2\text{C} \]

is known. Of
however the two hydrogen atoms are
substituted by chlorine the two well
known compounds \( \text{H}_2\text{H}_2\text{C} \) and \( \text{H}_2\text{H}_2\text{C} \)
may be obtained.

Another case is that of \( \text{H}_2\text{H}_2\text{N} \) and
\( \text{H}_2\text{N} \) (or \( \text{H}_2\text{N} \)). While experiment has
shown that the silver salt must be represented
by the formula \( \text{AgN} \) and the potassium
salt by \( \text{K} \cdot \text{N} \) yet only one hydrochloric
acid is known. It may or may not
be possible for such isomers to exist
We have no evidence that they can and no proof that they cannot. Such care serve to show the difficulty of proving by deliberate investigation the existence in absence of isomers in any given acid. As a general rule isomer compounds have been discovered by accident. In this case work was not abandoned upon the failure of Armour, and later V. Meyer and Armour obtained isomer oxime of jorachlorbenzophenone.

\[
\begin{align*}
&\text{N} \quad \text{H} - \text{C} - \text{C} \quad \text{H} - \text{N} \\
&\text{N} \quad \text{H} - \text{C} - \text{C} - \text{H} - \text{N}
\end{align*}
\]

Other similar compounds have since been discovered by Kortyska and Wanner. These discoveries while they prove that V. Meyer's theory cannot be correct, afford a strong confirmation to that of Kortyska and Wanner.

Other compounds showing isomerism similar to that of the oxime are the hydroxime of \(\text{X} - \text{H} - \text{Y}\) and \(\text{X} - \text{N} - \text{H} - \text{C} - \text{H} - \text{N}
\]

Isomers of the formula \(\text{N} \times \text{Y}, \text{Z} \), and \(\text{X} \times \text{Y}\) and \(\text{X} \times \text{Z}\) have not been found. Krupsky tried to break of ethylsubtrine \(\text{N} - \text{C} - \text{H} - \text{C} - \text{H} - \text{N}\) but was unable to do so.
He found also that the method employed in the crystallization of the isocyanate in the presence of sodium tartrate was also unsuccessful when tried with an inactive base containing the asymmetric carbon atom so that the experiment shows the difficulty not the impossibility of obtaining isomeric camphor derivatives.

The study also indicates isomeric among the diiso compounds. Bamberg has recently obtained isomers which he says are to be regarded as $\text{C}_6\text{H}_5-\text{N}=-\text{VH}^+$ a true diiso-benzene and $\text{C}_6\text{H}_5\text{N}=-\text{NO nitroamine (iso diiso-benzene)}$ Schraube and Schmidt arrive at the same results with different compounds and are confirmed by von Behnmon and Frosenius. Hantzsch also claims that these compounds are stereoisomers and are to be represented as $\text{C}_6\text{H}_5-\text{N}$ and $\text{C}_6\text{H}_5\text{N}^+$

Hantzsch has shown that there are two compounds of the formula $\text{C}_6\text{H}_5-\text{N}=-\text{NS}_2\text{K}$ one of them unstable and easily transformed into the other. This would seem to be impossible if they were represented by the formular $\text{C}_6\text{H}_5\text{N}=-\text{NS}_2\text{K}$ and $\text{C}_6\text{H}_5\text{NS}_2\text{K}^+$ but Bamberg suggests the formula for one of them $\text{C}_6\text{H}_5\text{N}=-\text{NS}_2\text{K}$ and Hantzsch attempts to show that the main frequently held by him is the more capable. However the question is unsettled as yet.
That such compounds as NXYZ and XNY do not in general show isomerism has been explained by Kortysh on the ground that the three ordinary volumes of nitrogen are in a plane except when directed by some special force and the force is absent in these compounds.

The stereochemistry of nitrogen is at present in a very incomplete state owing to the comparatively few cases of unexplained isomerism and the lack of experimental data. In this direction there is an open field for future investigation. The theory of Kortysh and Werner while it has the preference it doesn't in complete as it does not touch the cantilevered atom whatever cause the stereochemistry of nitrogen may take in the future the work of W. Meyer and Furnes and the one hand and Kortysh and Werner on the other had added greatly to our knowledge of this subject and has proved the existence of isomers which none of the existing theories would account for.

While it is the aim of the science to obtain a knowledge of the physical relations of all the elements as far as possible the facts thus far are insufficient to advance any theories in that direction.

Concerning the stereochemistry of oxygen it is assumed that from a fur
carbon atom unite readily with oxygen to form rings, from which it is inferred that the dimensions of the oxygen atom are not greatly different from those of the carbon atom. Among the dibasic acids only succinic acid \( \text{C}_4\text{H}_6\text{O}_4 \) and glutamic acid \( \text{C}_5\text{H}_8\text{O}_4 \) can form anhydrides. In this respect the acids differ from the glycols and alcohols. Ethylene glycol and trimethylene glycol readily form anhydrides. The great variety of ring formations in which oxygen enters shows without doubt that the release of oxygen is not fixed in position but are capable of some degree of flexibility.

While ethylene oxide itself is well known, the phenylene oxide \( \text{C}_6\text{H}_4\text{O} \) is known only in its double molecule. Kekulé had recognized this as impossible even before the development of stereochemistry. If we take Brauns's model for benzene we will see that the space occupied by an oxygen atom in the position it would have in the oxid in the ortho-position is less than half that occupied by the oxygen atom in styrene oxide. From this it would follow that the dimensions of the oxygen atom in two rings for the position in phenylene oxide. It is of interest in this connection to know that in an isomer of phenylene oxide, we have a carbon atom occupying a position into which it is impossible to place
Of the stereochemistry of the atom chlorine
very little is known. Some observations
concerning the sulfur atom have been
made which indicate that its dimensions
are larger than that of oxygen. For example
ethylene sulfid is unknown although the
acid is a stable compound. In thiophene
the sulfur atom takes the place of two H
groups in benzene. This compound bears a
remarkable resemblance to benzene. While in
thiophene
\[ \text{CH}_2 = \text{CH}_2 \]
the oxygen atom seems to have the
same function as the sulfur
atom in thiophene; yet these
two bodies differ much more
in their properties than do
thiophene and benzene.

In conclusion we must say that
although the new science is still in its
infancy, yet it has already done much
for the science of chemistry. It has given
chemists new ideas of the atom and molecule and
has demonstrated that the forces must be considered
to occupy the three-dimensional space. It has
suggested new lines of research and been a stimulus
to investigation that nothing else could have
been. There is much to admire in the
work that has been done. What will be done in the future of course we cannot tell, but it is safe to say that stereochemistry will occupy most of the attention of the leading thinkers in chemical science for some years to come. It offers a rich field for the investigator and plenty of scope for the theoriser.

The following works have been consulted:

Handbuch der Stereochemie (Eichhoff)

*Über die Asymmetrie bei natürlich vorkommenden Organischen Verbindungen* (J. Pastera)

*Dix Années sur l'Histoire d'une Théorie* (Mayerhoffer)

*Stereochemie* (Eiltsart)

*Über die Raumliche Anordnung der Sterne in Organischen Molekülen und ihre Bestimmung in geometrisch-isomeren, ungesättigten Verbindungen* (Johannes Wilhelm)