

Stereochemistry

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Thesis

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Stereochemistry.

Stereochemistry

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 1823, 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 stereo-isomerism is the natural outgrowth of that of structural isomerism. It

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 spatial 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 crystallography, 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 quartz 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.

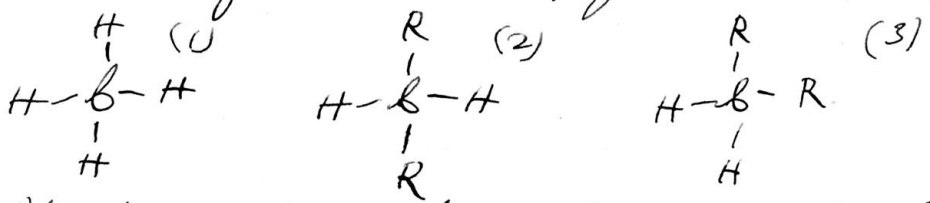
In 1863 Wislicenus called attention to the fact that there were more isomeric lactic acid than could be accounted for by the existing structural theory. He showed that the optically active sarcosolactic acid as well as the ordinary inactive lactic acid must be represented by the same structural formula, viz. $\text{C}_2\text{H}_5\text{C}(\text{H})-\overset{\text{OH}}{\text{C}}\text{OOH}$ and suggested as a possible explanation of this a different arrangement in space of the groups composing the molecule.

Even before this time Lieber 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.

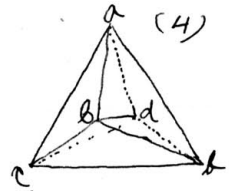
Similar hints and suggestions are found in the works of other authors. But the stereochemical idea received no definite form until the publication of Le Bel's

and Van't Hoff's work in 1874.

Van't Hoff's "Le Chimie dans l'Espace" appeared in Sept. 1874, an edition revised and much improved was published in 1885 under the title "Dix années dans l'histoire d'une Théorie" Le Bel published his work in Nov. 1874. it was entirely independent of Van't Hoff's and contained practically the same ideas. Van't Hoff was led to the consideration of the special relations of the constituents of the molecule 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 $C H_2 R_2$, a disubstitution product of methane, fig. (2) and (3)

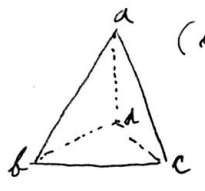
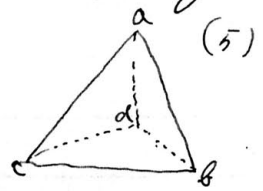


If the carbon atom is placed at the center of a tetrahedron and the four monosubstituted constituents placed at the corners. fig. (4)



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



other of object and mirrored image as

right and left-handed models.

Voit Hoff recognised the peculiarity of this isomerism and called the carbon atom united in this way to four different or radicals, the asymmetric carbon atom. He maintained 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.

LeBel was led to adopt the dimensional formula by his attempts to account for optical activity. The physical phenomena observed by Pasteur, Kammerberg and Rauch and accounted for theoretically by the mathematician Sorou was his 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. LeBel 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 LeBel's theory is the converse of that of Voit Hoff, that is, "In general if a substance is derived from an primitive type MA_4 by substitution of three different atoms or radicals for A_3 , the molecule will be asymmetric and will possess the power of rotation." Thus if in the formula

formula of a substance we have carbon united with three monovalent 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 four unlike groups must be attached to cause rotation." As will be seen later in some cases the distinction is important.

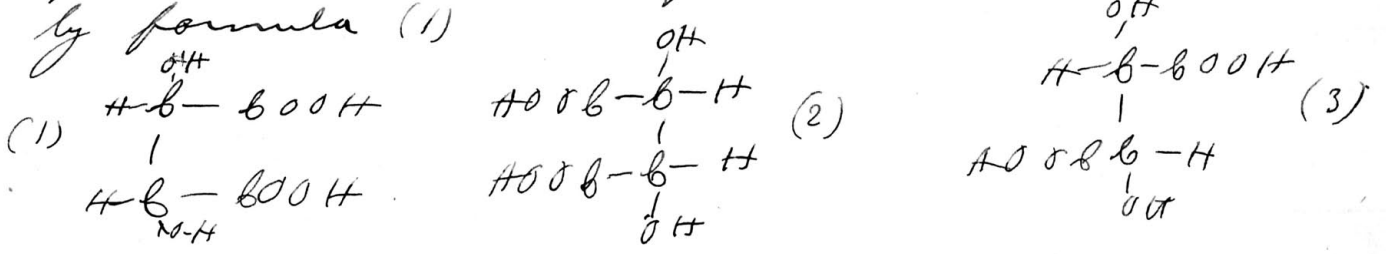
These are in brief the theories with which Van't Hoff and Le Bel start out. The form of the regular tetrahedron is used simply for convenience to represent the relations that actually exist. A regular tetrahedron would imply that all the groups were equal distances from the carbon atom, but since all the groups are different therefore of different weights and different powers of attraction 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 have been so well supported by facts, and of so much value as an aid and stimulus to investigation.

The characteristics of "physical isomers" are their crystalline form and power of rotating the plane of polarized 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 neutralizing 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.

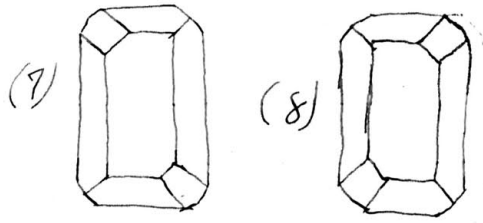
Take for example tartaric acid if we represent the ordinary active acid (dextro rotatory)



then (2) would represent the left-handed variety, while that represented by the third formula would be inactive, 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} acid bear the same relation to those of the laevorotary acid that the right hand bears to the left. (i.e. they are enantiomorphs)

This has also been shown to be the case in numerous other compounds. In the crystals of the bitartrate of ammonium fig (7) and (8) the two crystalline forms bear



relations exactly analogous to the models as shown in fig. (5) and (6)

According to this

the existence of an active body would call for the existence (or possibility of existence) of another with an opposite rotatory power. This has been observed in a great many cases, as the tartarates, amygdalcohol, malic acid, asparagine, glucose, mannite, sulphonic acid camphor, borneol, 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 has been some observations contrary to this hypothesis but they have all been proved due to errors of one kind or another, for example, propyl alcohol $\text{C}_3\text{H}_7\text{OH}$ was reported as active by Brouncell. This activity was found to be due to the presence of amygdalcohol

by Heringer. Styrene $C_6H_5CH=CH_2$ was reported as active by Berthelot, this has also been shown to be due to an impurity, (Metastyrene) The iodide of trimethylethylstibine $(C_6H_5)_3(C_2H_5)SbI_4$ was reported as active by Friedländer. This was shown by Lebel to be due to an impurity probably contained in the alcohol used in its preparation. β Picoline $C_5H_7N(C_6H_5)$ reported active by Kessiel has been attributed to an error of observation.

Perhaps the series of observations most conclusive in support of the theory is that the activity of compounds disappear in those derivatives in which the asymmetric carbon atom become symmetric. For example, the inactive malonic acid $C_3H_4O_4$, fumaric and maleic acids $C_4H_4O_4$ are derived from the active malic acid $C_4H_6O_5$. Tartaric acid inactive $C_4H_4O_6$ derived from active tartaric acid $C_4H_6O_7$ and glycere $C_3H_8O_3$.

$C_6H_5CH_2-CH_2-CH_2$ inactive derived from camphor active, and a number of other similar observations have been made. The derivatives of active amyl alcohol $C_5H_{11}OH$ retain their activity in the ethers amylsulfates, chloride, bromide, iodide, amylamine, aldehyde and valeric acid, amylcyanid, caproic acid, ethylamyl, diamyl and many others recently examined by Guze.

These compounds have been found by Lebel and just to contain the asymmetric carbon

atom. On the other hand methylamyl $(C_2H_5)_2CH-CH_2$; amyrene $C_6H_5(C_2H_5)CH=CH_2$ and $(C_2H_5)_2CH-CH_2$ were found to be inactive

The action of organisms on 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. Succinic acid obtained by the fermentation of asparagine (active) $C_4H_7NO_4$ is inactive, the same is true of that obtained by the fermentation of calcium malate and calcium tartrate. Compounds containing the asymmetric carbon atom, produced by the action of organisms almost without exception are active. The reason that those compounds produced artificially are not active has been considered due to a mixture of equal quantities of two isomers with opposite rotary power. This has been shown to be the case in numerous instances by resolving the inactive compound into two active isomers. Some

- | | | |
|------------------------|------------------------------|------------------|
| propylenic glycol | $C_3H_8O_2$ | } By Le Bel |
| secondary amyl alcohol | $C_5H_{12}O$ | |
| primary " " | $(C_2H_5)(CH_3)CH_2CH_2CH_3$ | |
| malic acid | $C_4H_6O_5$ | } By Pasteur |
| benzoylformic acid | $C_9H_8O_3$ | |
| glyceric acid | $C_3H_8O_6$ | } By Leukowitsch |
| lactic acid | $C_3H_6O_3$ | |

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 Berthelot first urged against the theory of Van't Hoff 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, Berthelot cited the case of inactive malic acid $\text{H}(\text{OH})\text{COOH}$ containing but one asymmetric carbon atom and the inactivity could only be accounted for according to the theory by supposing it to consist of a mixture of equal quantities of right and left-handed modifications. The experiments of Preuner, Kraschütz and J. H. Van't Hoff. made since that time have showed this to be the case. The inactive malic acids obtained by different methods were identical with that made by mixing equal quantities of dextro and laevulo-rotary 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 hemihedral forms obtained by Pasteur from racemic acid, the electrical conductivity of the aqueous solution is also the same as the two active modifications.

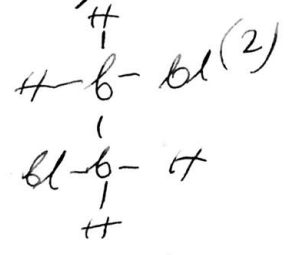
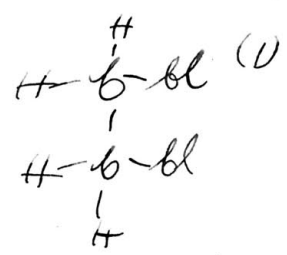
From the foregoing it seems clear that all active bodies as far as known contain the asymmetric carbon atom, and from the great diversity of active compounds it seems that any four different groups united to a single carbon atom is sufficient to produce optical activity.

Such in brief is the theory of the simple asymmetric carbon atom as advanced by Vout Hoff and Zebel, and the facts on which it is based. Since the publication of their works there have been numerous contributions to the literature of stereochemistry by Wislicenus, Von Beyer, Richoff, N. Meyer, Aurtysch and Werner, E. Fisher, Guze and others. Some of these have made some very important additions to Vout Hoff's theory.

Much credit is due to Wislicenus for his work published in 1886 for expounding such cases as fumaric and maleic acids, although he added but little to the theory of Vout Hoff, yet by the introduction of one additional hypothesis and the logical and systematic application of the hypothesis of Vout Hoff, he was able to render the theory amenable 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.

Wulffius said that by the aid of the 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.

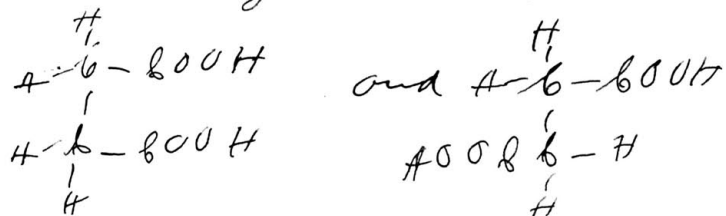


For example, in ethylene chloride (1) chlorine stands over chlorine and hydrogen over hydrogen, and we may assume that this would be the unstable position. In (2)

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 arrangements might exist at successive intervals of time.

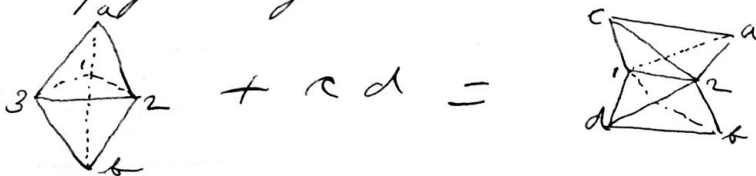
But under ordinary circumstances the latter condition would be the most favorable. In the same way succinic

acid might be represented by



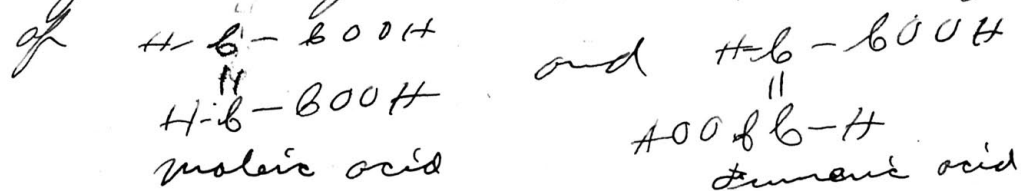
And as the carboxyl groups have no affinity for each other the first formula would represent the unfavorable configuration and the second the most favorable as the hydrogen and carboxyl groups are in closer relation. The first is the only one that would form an anhydride, and the anhydride formed must have the formula $\begin{array}{c} \text{H} \\ | \\ \text{H}-\text{C}-\text{CO} \\ | \\ \text{H} \end{array}$ as the ring formation fixes the configuration and prevents further rotation.

Another idea of Wislicenus 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 foretold with considerable probability. Vant Hoff had represented the triple combination with the two tetrahedrons face to face. Wislicenus showed that on the principle of least disturbance the radicals added would occupy adjacent corners, thus

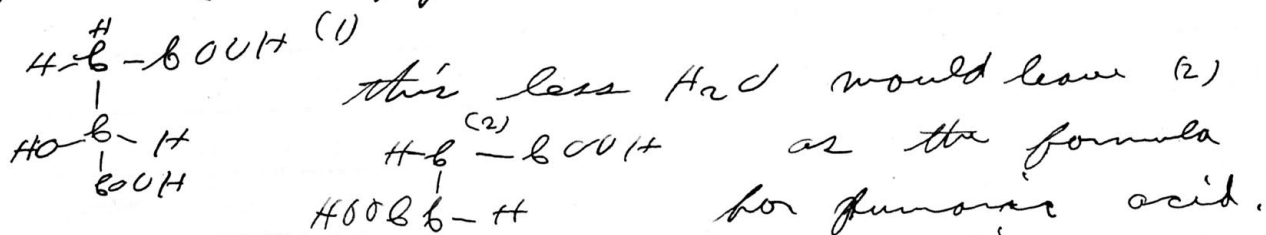


In this case no more bonds are broken than absolutely necessary. The same principle was applied to the double bond but in this case there is not the double bond left to prevent rotation. One of the best examples of the double bond condition is that of fumaric and maleic acid.

They were given the formulae by Vout Hoff

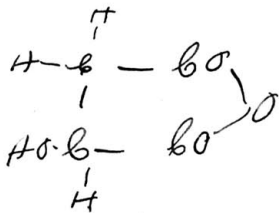


According to these formulae maleic acid would be the least stable and would form an anhydride which is the case. Also according to the foregoing the acid formed by the addition of Br_2 to $\text{C}_6\text{H}_5\text{COOH}$ would have the carboxyl groups $\text{C}_6\text{H}_5\text{COOH}$ on the same side of the molecule, this in fact is found to be the less stable and forms an anhydride. Fumaric acid is formed by the splitting off of H_2O on heating maleic acid to 150° . Now the favorable configuration for maleic is (1)



Then again maleic anhydride which can only have the formula

over

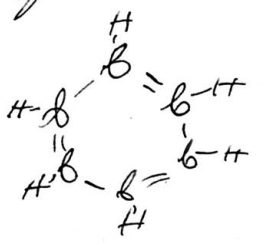


produces maleic acid on being heated. Wislicenus has also attempted to show by the theory how by the addition of Br₂ and the subsequent removal of HBr fumaric acid could be changed into bromo-maleic acid and maleic acid in bromo-fumaric acid. This has been objected to by Michael and Anshütz. But no theory more satisfactory has been advanced.

Another case of the extension of Van't Hoff'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 valences of the carbon atom act in the direction of the lines connecting the center of a regular tetrahedron with the apices, 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 acetylene Von Baeyer ascribed the negative heat of formation and the explosive nature of its compounds to the valences connecting the two C-H 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

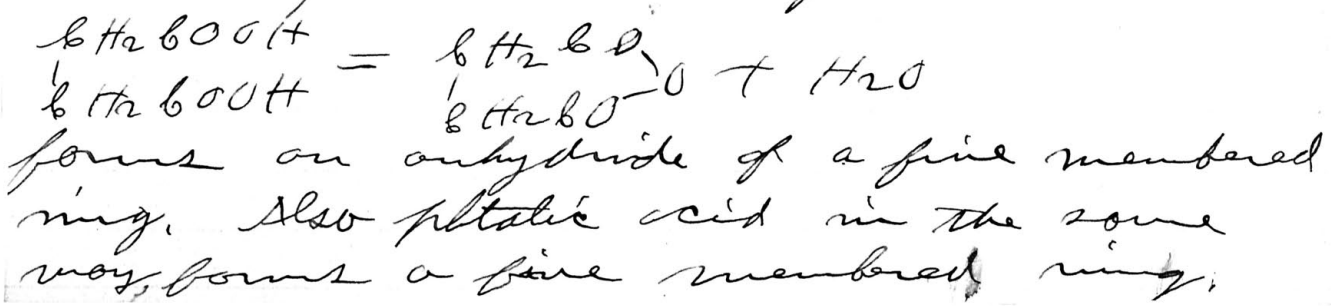
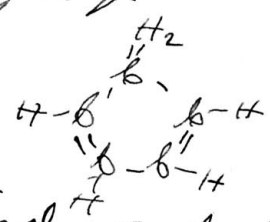
most stable. In the five membered ring there is scarcely any divergence. That this does not show such remarkable stability as the six membered ring is due to other causes. It is claimed however by König that the pentamethylene ring is more stable than the hexamethylene ring. It is a well known principle that the highly symmetrical compounds are more stable than the unsymmetrical.

The benzene ring represented 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 C_2H_2 group and four C_2H groups present.

With penta and hexamethylene 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



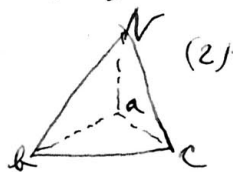
$\text{C}_6\text{H}_4\text{COOH} = \text{C}_6\text{H}_4\text{CO} + \text{H}_2\text{O}$
 and all the acids with a sufficient number of carbon atoms easily form anhydrides and these compounds are especially stable. Von Baeyer's observations have led to the conclusion that in the ring formations the atoms 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.

Stereochemistry of Nitrogen

Van't Hoff was also the founder of the stereochemistry of nitrogen. He based his theory upon the fact that of all the substituted ammonias (N a, b, c,) 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 valences as in NH_3 are called the ordinary valences, while the other two are called the supplementary valences. In all the research upon the substituted ammonias no isomers have been observed as in the case of the asymmetric carbon atom (C a, b, c, d) Therefore Van't Hoff these three valences must be arranged in a plane, as 



In this case by 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 $(C a, b, c, d)$ or that the molecule is asymmetric, and should therefore show stereoisomerism. But such isomers are not known, in compounds in which nitrogen appears as pentavalent however isomers have been observed and Vant 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 forms like $(N A_3, B, B)$ and $(N A_2, B_2, B)$ should show isomerism. In dimethyl-ethyl ammonium iodid there is said to be no isomerism $N(BH_3)(EtH_3)_2$ and $N(BH_3)_3(EtH_3)$ as indicated by the theory. But Vant Hoff claims that there is not sufficient evidence as to the identity of the two compounds, that the planes of symmetry

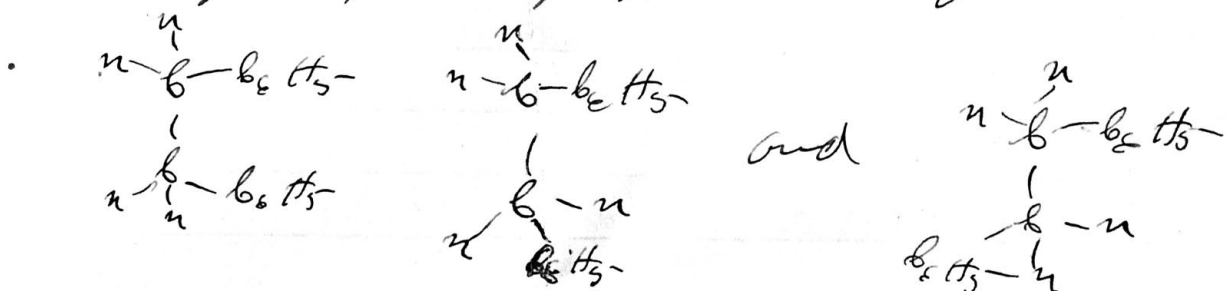
would be the same and hence the crystalline form. In a parallel case the triethyl-benzyl ammonium iodid isomerism has been shown by Todenburg to exist as $N(b_{2t}t_3)_3 - b_6t_3 - b_{2t}t_3$ and $N(b_{2t}t_3)_2 - b_6t_3 - b_{2t}t_3$, De Bel has also obtained by the action of ferments on methyl-ethyl, propyl-isobutyl ammonium chlorid a solution optically active, this is an exception to the statement of Van't Hoff that all substances optically active when in solution will be found to contain the asymmetric carbon atom, and for this reason De Bel's converse statement seems preferable). He has also discovered two isobutyl trimethyl ammonium chlorids.

An explanation of the fact that nitrogen which has five valences often shows only three, as given by Burch and Moosh is that the two supplementary valences apparently latent are used in binding together molecules, thus the formula for ethyl-amine would be $C_2H_5 - N_{\frac{1}{2}}H_{\frac{1}{2}} - N_{\frac{1}{2}}H_{\frac{1}{2}} - b_{2t}t_3$ and if the molecule was dissociated by rise of temperature the vapor would give an abnormal expansion on the rise of temperature. Experiment shows a rise of 5-6% above the normal with 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

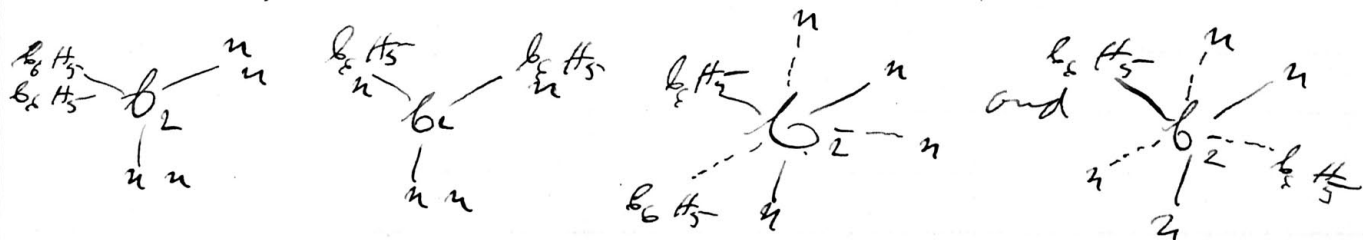
to the molecules being connected by the supplementary valences of nitrogen.

In the course of an investigation on the benzyl-dioximes, Goldschmidt observed that by treating benzyl with hydroxylamine two isomeric benzyl dioximes were obtained and that they both were to be represented by the formula C_6H_5 a formula as we see in which there is neither an asymmetric carbon atom nor a double bond between any two carbon atoms. The theories that have advanced do not account for such a case as this. Moreover Kummer and V. Meyer have shown that there is a third isomer of the same formula. To account for this V. Meyer made use of the rotation theory of Voit Hoff, in which two carbon atoms united by a single bond was regarded as free to rotate about the line joining their center or 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 or more less favorable positions. In the dioximes above referred to the β dioxime is the more stable, the other two being easily changed to it by heat, or the proper reagents. But the β dioxime cannot be changed to the others. The γ dioxime is changed to the β by slight warming. To change the α

it is necessary to heat it to 170° with alcohol or benzene. We see from this that in the case of the dioximes there cannot be free rotation or in the case of succinic acid, but that certain positions are maintained until some outside force is applied. To represent this condition V. Meyer first proposed the formulae



in which, n, n stands for the NOH group. In the first case OH stands over OH and C₂H₅ over C₂H₅ hence it would be the most unstable, and most easily forms an anhydride, which are characteristic of the γ modification. The other two should show very similar properties. V. Meyer later represented the dioximes, thus

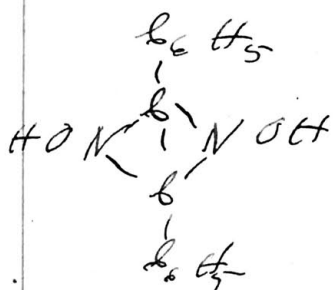


Making four theoretically possible dioximes, although but three are known to exist. But the later representation has the advantage that it does not require a right and left handed structure for the α and β modifications, to which they evidently are

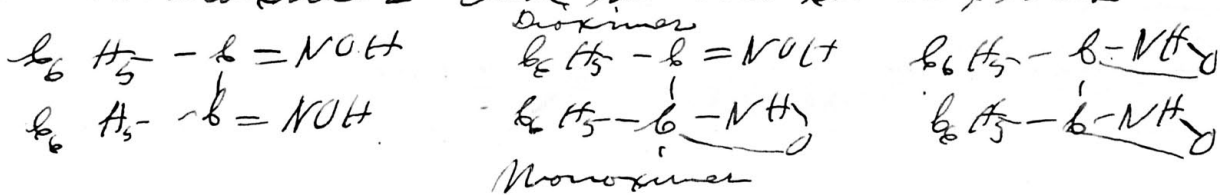
are not analogous.

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

Micholl held for a time the formula for one of the oximes, but on the discovery of the second monoxime and its conversion into a dioxime he was forced to abandon it. The presence of



the two groups = NOH and -NH₂ was urged by some for a time. In some respects this answers very well for explaining all the monoximes and the dioximes, thus -

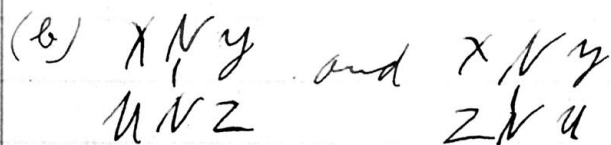
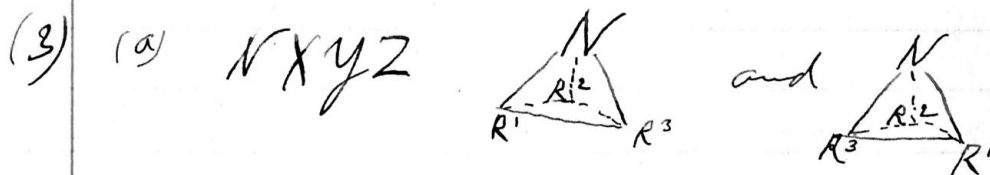
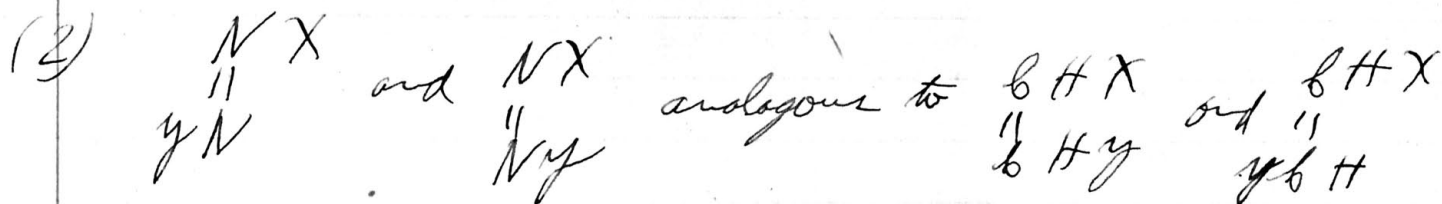
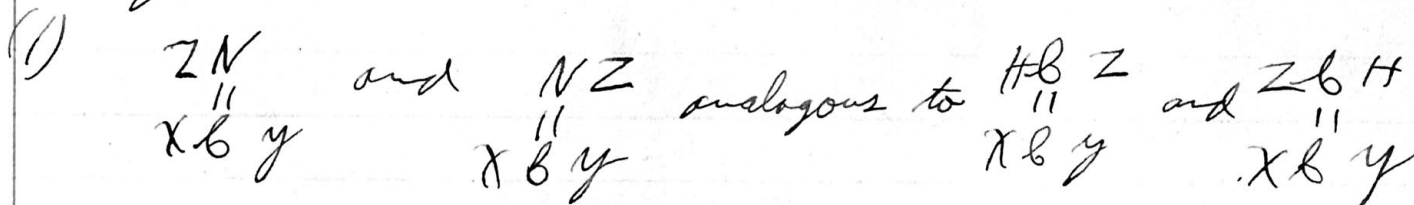


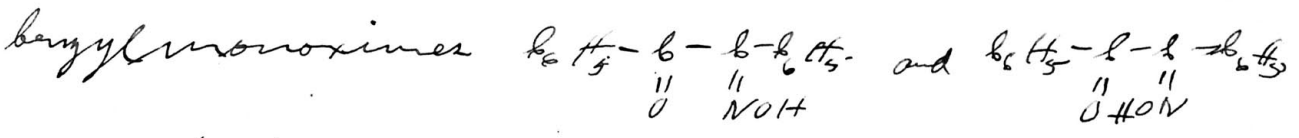
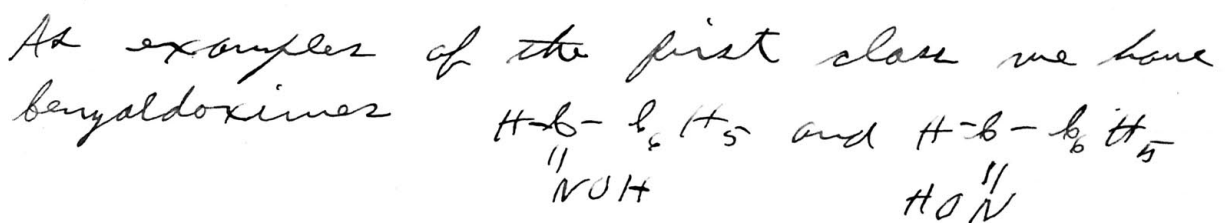
This theory gained especial interest when Bechmann announced the discovery of a second benzaldoxime which had the formula $\text{C}_6\text{H}_5 - \text{C} \text{H} - \text{NH}_2$ the ordinary benzaldoxime being $\text{C}_6\text{H}_5 - \text{C} \text{H} = \text{NOH}$. This was the occasion for a series of investigations carried out by Suwers and Dietrich under the direction of V. Meyer which showed that the group = NOH was present in the benzaldioxime but not the group -NH₂. This work

settled the question of the structural identity of the dioximes, and for a time left the theory of V Meyer in full possession of the field.

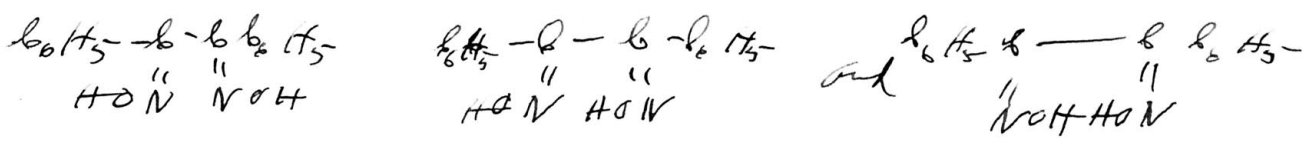
Hantzsch and Werner proposed a theory for the explanation of the dioximes which has been of great interest especially during the last few years, and has suggested many new lines of investigation.

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





" dioximes



As is seen this explains the two known monoximes, a third would be impossible, it also explains the existence of the three known dioximes. It will be remembered that according to V. Meyer's theory three monoximes and four dioximes were possible, also according to the theory of Hantzsch and Werner many isomers 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 isomerism, as $\text{X}-\text{C}-\text{Y}$ and $\text{X}-\text{C}-\text{Y}$

$$\begin{array}{c} \parallel \\ \text{NOH} \end{array} \quad \text{and} \quad \begin{array}{c} \parallel \\ \text{HON} \end{array}$$

Immediately after the publication of Hantzsch and Werner's work, Auwers made a thorough study of the oximes of the ketone $\text{C}_6\text{H}_5-\text{C}-\text{C}_6\text{H}_4-\text{C}_6\text{H}_5$ but failed to obtain isomers. This work

in a negative way favored the theory of V. Meyer, for if isomers should be found among the ketones 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 Kewenaw also illustrates well the fact that too much dependence must not be placed upon negative results. We have many analogous cases where even a well founded theory indicates the possibility of isomerism and yet the isomers are not known. Such is the case with $\text{C}_2\text{H}_2\text{Cl}_2$ and $\text{C}_2\text{H}_2\text{Cl}_2$ the theory indicates two forms as $\text{H}-\text{C}-\text{C}-\text{Cl}_2$ and $\text{H}-\text{C}-\text{C}-\text{Cl}_2$ yet only one is known. If however the two hydrogen atoms are substituted by chlorine the two well known compounds $\text{Cl}-\text{C}-\text{C}-\text{Cl}_2$ and $\text{Cl}-\text{C}-\text{C}-\text{Cl}_2$ may be obtained.

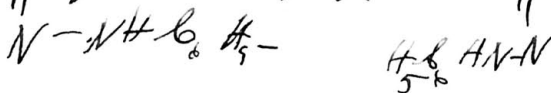
Another case is that of $\text{H}-\text{C}\equiv\text{N}$ and $\text{H}-\text{N}=\text{C}$ (or $\text{H}-\text{N}=\text{C}$). While experiment has shown that the silver salt must be represented by the formula $\text{Ag}-\text{N}=\text{C}$ and the potassium salt by $\text{K}-\text{C}\equiv\text{N}$ yet only one hydrocyanic 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 case serve to show the difficulty of proving by deliberate investigation the existence or absence of isomers in any given case. As a general rule isomeric compounds have been discovered by accident. In this case work was not abandoned upon the failure of Aumer, and later V. Meyer and Aumer obtained isomeric oximes of perchlorbenzophenone



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

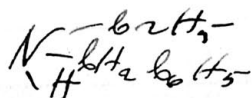
Other compounds showing isomerism similar to that of the oximes are the hydroxones as $\text{X} - \overset{\parallel}{\text{N}} - \text{Y}$ and $\text{X} - \overset{\parallel}{\text{N}} - \text{Y}$



Isomers of the formula $\text{N} \cdot \text{X} \cdot \text{Y} \cdot \text{Z}$, and



have not been found. Kropfer tried to break up ethyl tetraidine



into two optically active isomers but was unable to do so.

He found also that the method employed - the crystallization of the tartrate in the presence of conine 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 ammonia derivatives.

The theory also indicates isomerism among the diazo compounds. Bomberger has recently obtained isomers which he says are to be regarded as $C_6H_5-N=N-OH$ a true diazo-benzene and $C_6H_5-NH-NO$ nitrosamine (iso-diazo-benzene) Schraube and Schmidt arrive at the same results with different compounds and are confirmed by Von Beckmann and Frobenius, but Hantzsch claims that these compounds are stereoisomeric and are to be represented as C_6H_5-N and C_6H_5-N " NOH

$\begin{matrix} HON \\ || \\ N \end{matrix}$ Hantzsch has shown that there are two compounds of the formula $C_6H_5-N=N-NSO_3K$, one of them unstable and easily transformed into the other. This would seem to be impossible if they were represented by the formulae $C_6H_5-N=N-NSO_3K$ and $C_6H_5-N-NSO_2KNa$. But Bomberger suggests as the formula for one of them $C_6H_5-N=NO-SO_3K$ and Hantzsch attempts to show that the view previously held by him is the more probable. However the question is unsettled as yet.

That such compounds as NX_2YZ and XNY_2 do not in general show isomerism $4N_2$ has been explained by Hantzsch on the ground that the three ordinary valences of nitrogen are in a plane except when diverted 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 Hantzsch and Werner while it has the preference at present is incomplete as it does not touch the pentavalent atom. Whatever course the stereochemistry of nitrogen may take in the future the work of V. Meyer and Werner on the one hand and Hantzsch 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.

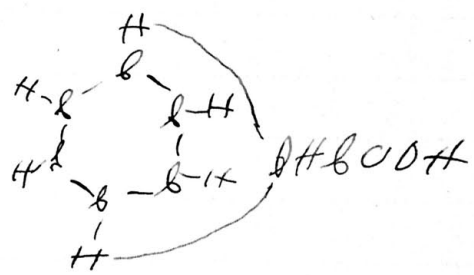
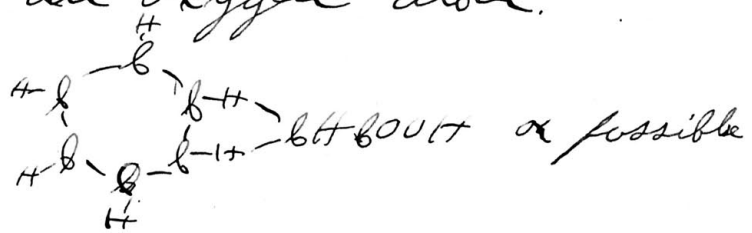
While it is the aim of the science to obtain a knowledge of the special relations of all the elements as far as possible, the facts thus far are insufficient to advance any theories in that direction.

Concerning the stereochemistry of oxygen it is observed that four or five

carbon atoms 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 glutaric acid $\text{C}_5\text{H}_8\text{O}_4$ can form anhydrides. In this respect the acids differ from the glycols & alcohols. Ethylene glycol and trimethylene glycol readily form anhydrides. The great variety of ring formations in which oxygen enters shows without doubt that the valence of oxygen are not fixed in position but are capable of some degree of flexibility.

While ethylene oxide $\text{C}_2\text{H}_4\text{O}$ 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 ~~Bayes's~~ model for bayene we will see that the space occupied by an oxygen atom in the position it would have in the oxide in the ortho position is less than half that occupied by the oxygen atom in ethylene oxide. From this it would appear that the dimensions of the oxygen atom are two large for that position in phenylene oxide. It is of interest in this connection to know that in an isomer of phenylacetic acid, we have a carbon atom occupying a position into which it is impossible to force

an oxygen atom.



Of the stereochemistry of the latter element 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 CH groups in benzene. This compound bears a remarkable resemblance to benzene. While in thiophene 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 former must be considered to occupy tridimensional 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 theorist.

The following works have been consulted.

Handbuch der Stereochemie (Bichhoff)

Über die Asymmetrie bei natürlich vorkommenden organischen Verbindungen. (L. Pasteur)

Dix Années dans l'histoire d'une théorie (Meyerhoff)

Stereochemie (Eilhart)

Über die räumliche Anordnung der Atome in organischen Molekülen, und ihre Bestimmung in geometrisch-isomeren, ungesättigten Verbindungen (Johannes Wislicenus)

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