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J.H. van't Hoff, Nobel (Chemistry), 1901

Stereochemistry

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The origins of stereochemistry: the contributions of J. H. van't Hoff and J. A. Le Bel

The solution to the questions posed by Pasteur and Wislicenus was provided in two papers published independently in 1874 by the Dutch chemist, Jacobus Henricus van't Hoff (1852–1911) and the French chemist, Joseph Achille Le Bel (1847–1930). Although both Van't Hoff and Le Bel had worked together in Wurtz's laboratory in Paris earlier in 1874, they apparently had not discussed the ideas that appeared in the papers. Le Bel's paper, published in the *Bulletin of the Chemical Society of Paris* in November 1874, was entitled 'On the Relations Which Exist Between the Atomic Formulas of Organic Compounds and the Rotatory Power of their Solutions'. Van't Hoff's ideas appeared in a 12-page booklet in Dutch in September 1874 which was entitled 'A Suggestion Looking to the Extension into Space of the Structural Formulas at Present Used in Chemistry – and a Note upon the Relation between the Optical Activity and the Chemical Constitution of Organic Compounds'. Although a French translation of this booklet appeared shortly afterwards, Van't Hoff's ideas were more widely disseminated after the publication of an expanded (44 pages) version in 1875, the title of which was *La Chimie dans l'Espace*. A German translation was published in 1877.

Although Van't Hoff (Plate 9) had worked in Kekulé's laboratory at Bonn for about a year in 1872–73, he does not mention Kekulé's tetrahedral carbon models. In 1894, Van't Hoff stated:

> On the whole, Le Bel's paper and mine are in accord; still, the conceptions are not quite the same. Historically the difference lies in this, that Le Bel's starting point was the researches of Pasteur, mine those of Kekulé. My conception is a continuation of Kekulé's law of the quadrivalency of carbon, with the added hypothesis that the four valences are directed toward the corners of a tetrahedron, at the center of which is the carbon atom.

> . . . all of the compounds of carbon which in solution rotate the plane of polarized light possess an asymmetric carbon atom.

The observation of optical inactivity indicated either the absence of such asymmetric carbons or that the substance existed as a 50:50 mixture of the enantiomers (a racemic mixture). In the 1874 booklet, Van't Hoff does not discuss the optical inactivity of compounds (such as the 'inactive' tartaric acid) containing more than one asymmetric carbon atom. Marcellin Berthelot (1827–1907) in fact criticized Van't Hoff (and Le Bel) for not accounting for the optical inactivity of the 'indivisible inactive type' of compounds, such as the inactive forms of tartaric acid and malic acid reported by Pasteur. Van't Hoff responded to this criticism in a booklet published in 1875. The maximum number of stereoisomers possible was shown by Van't Hoff to equal 2^n, where n = the number of asymmetric carbon atoms. In the case of compounds containing two asymmetric carbon atoms, each of which had the same substituents, two of the mirror-image isomers would be identical, and therefore that particular compound would be optically inactive. This is illustrated by the general formula, $C(R_1R_2R_3)C(R_1R_2R_3)$, which in the case of tartaric

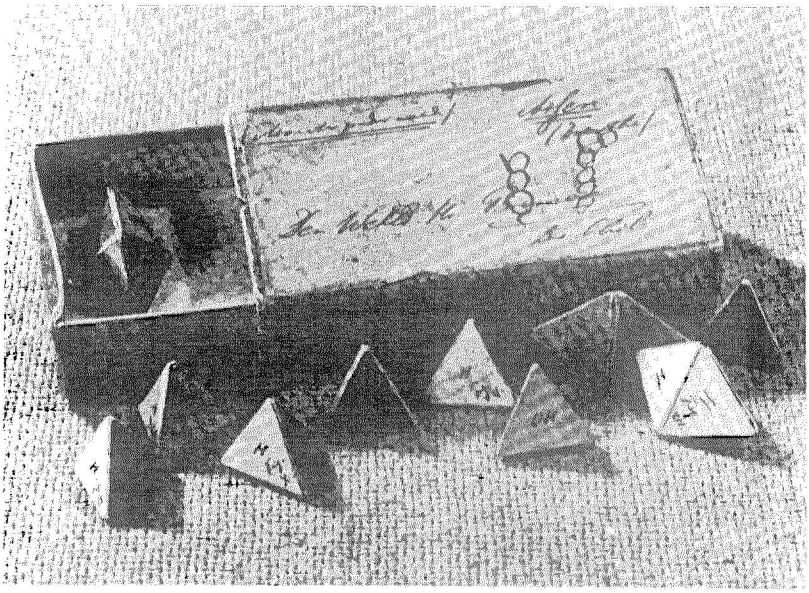


Figure 19. Cardboard tetrahedral models prepared by J. H. van't Hoff in 1874–75 (History of Science Museum, Leiden).

acid, the three substituents (R_1, R_2 and R_3) correspond to H, OH and COOH.

Van't Hoff realized that the relationships between the various stereoisomers were not always easily visualized – even in the perspective drawings included in the publication. He therefore prepared a number of cardboard models (Fig. 19) which he sent along with a copy of the 1875 booklet to a number of well-known chemists: A. von Baeyer (Strasbourg), A. Butlerov (St Petersburg), L. Henry (Louvain), A. Hofmann (Berlin), A. Kekulé (Bonn), E. Frankland (London), J. Wislicenus (Würzburg), A. Wurtz and M. Berthelot (Paris).

Six of the models shown here consist of single tetrahedra (about 2 cm on edge) that illustrate the enantiomers of malic acid and tartaric acid (with respect to only one of the two asymmetric carbon atoms). One model illustrates the symmetry found in malonic acid, $HOOCCH_2CH_2COOH$, with respect to one of the methylene carbons. The remaining three models consist of two tetrahedra joined at their faces and illustrate (+)- and (–)-tartaric acid and *meso*-tartaric acid. In these models the carbon valencies pass through the *faces* of the tetrahedra rather than the apexes as is more common (see, for example, Fig. 18). Normally two tetrahedra that share a face represent the carbon–carbon triple bond (see the discussion below). The collection of the Van't Hoff models preserved in the Deutsches Museum in Munich contains a variety of models that were used by Van't Hoff to illustrate his solution to a number of stereochemical problems.

The models in Fig. 19 constructed by joining two tetrahedra faces represent particular 'conformations' of the tartaric acid stereoisomers. The term 'conformation' was not used by Van't Hoff – instead he talks about the various possible 'phases' of the molecule, which should not be considered in the same sense as 'isomers'. It was only in a later edition of his book (1891) that he considered whether there might be preferred 'phases':

> To avoid the prediction of an isomerism [for a substance such as $C(R)_3C(R_1)_3$] which at first sight appears endless, it is not necessary to introduce any additional hypothesis; the difficulty disappears at once if we take into account the mutual action which must take place between the groups R_3 and the groups R_1, united to each of the two atoms of linked carbon. In fact, if this action depends, as in the case with every known force besides, on the distance and nature of the groups in question, there will be among the possible positions only one which corresponds to the state of stability.

Later (1898) Van't Hoff suggested that there must be a 'free rotation' about the carbon–carbon single bonds since not to assume that would allow for an excess of isomers. Nevertheless, he thought that the interactions of the substituents should lead to a 'favored configuration'.

The second half of Van't Hoff's 1874 booklet was entitled 'The Influence of the New Hypothesis upon Compounds Containing Doubly Linked Carbon Atoms'. The theoretical implications of the proposals contained in this section had an importance perhaps equal to that of the tetrahedral carbon atom. The proposal provided a solution to the observation of several puzzling cases of isomerism – that found, for example, between maleic acid and fumaric acid. Although it was not clear to many chemists, such as Kekulé, that these compounds were not structural isomers, Van't Hoff felt the evidence indicated that these compounds were 'geometrical isomers' (a term used by Wislicenus somewhat earlier). Van't Hoff's discussion below refers to the two illustrations shown in Fig. 20:

> Double linking is represented by two tetrahedrons with one edge in common in which A and B represent the union of the two carbon atoms, and $R_1 R_2 R_3 R_4$ represent the univalent groups which saturate the remaining free affinities of the carbon atoms. If $R_1 R_2 R_3 R_4$ all represent the same group, then but one form is conceivable, and the same is true if R_1 and R_2 or R_3 and R_4 are identical, but if R_1 differs from R_2 and at the same time R_3 differs from R_4, which does not preclude R_1 and R_3, R_2 and R_3 from being equal, then two figures become possible, which differ from one another in regard to the positions of R_1 and R_2 with respect to R_3 and R_4. The dissimilarity of these figures, which are limited to two, indicates a case of

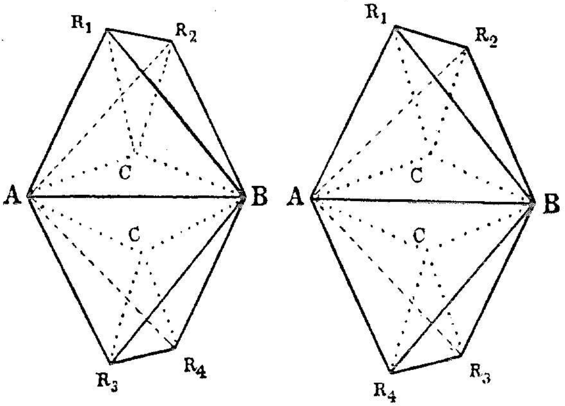


Figure 20. Van't Hoff's illustration of geometrical isomers (1874).

> isomerism not shown by the ordinary formulas. [To illustrate the maleic acid/fumaric acid isomerism: R_1, R_3 = H and R_2, R_4 = COOH.]

Since the double bond involved the sharing of the edges of two tetrahedra, it was a natural extension for Van't Hoff to consider that the triple bond involved the sharing of the faces of two tetrahedra (Fig. 21). There was, however, no experimental evidence available that could be used to support this suggestion.

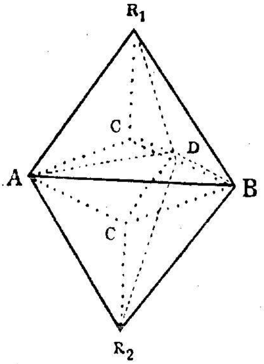


Figure 21. Van't Hoff's illustration of the structure of an alkyne, $R_1C\equiv CR_2$.

The style and scope of the paper published by Le Bel in 1874 differs significantly from Van't Hoff's. Although the names of both of these men are associated with the origins of stereochemistry, an historical analysis would suggest that Van't Hoff's proposals had the greater impact on the subsequent development of stereochemistry. Le Bel (Plate 10) was more concerned with understanding the relationship between molecular symmetry and the observation of optical activity:

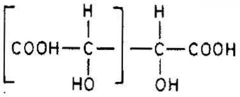
> The labors of Pasteur and others have completely established the correlation which exists between molecular asymmetry and rotatory power. If the asymmetry exists only in the crystalline form the crystal alone will be active; if, on the contrary, it belongs to the chemical molecule the solution will show rotatory power, and often the crystal also if the structure of the crystal allows us to perceive it, as in the case of the sulphate of strychnine and the alum of amylamine.

In contrast to Van't Hoff, the concept of the tetrahedral carbon atom is considered only once by Le Bel, and then only in the context of a general discussion of molecular geometry:

Plate 10. Joseph Achille Le Bel (1847–1930) (Edgar Fahs Smith Collection).

> Let us consider a molecule of a chemical compound having the formula MA_4; M being a single or complex radical combined with four univalent atoms A, capable of being replaced by substitution. Let us replace three of them by simple or complex univalent radicals differing from one another and from M; the body obtained will be asymmetric. Indeed, the group of radicals R, R′, R″, A when considered as material points differing among themselves form a structure which is enantiomorphous with its reflected image, and the residue M cannot re-establish the symmetry.
>
> Again, if it happens not only that a single substitution furnishes but one derivative, but also that two and even three substitutions give only one and the same chemical isomer [that is, other than optical isomers], we are obliged to admit that the four atoms A occupy the angles of a regular tetrahedron, whose planes of symmetry are identical with those of the whole molecule MA_4; in this case also no bisubstitution product can have rotatory power.

Unlike Van't Hoff, Le Bel does not use perspective drawings or models to illustrate his ideas.



$$\left[COOH-\overset{H}{\underset{HO}{C}}- \right] -\overset{H}{\underset{OH}{C}}-COOH$$

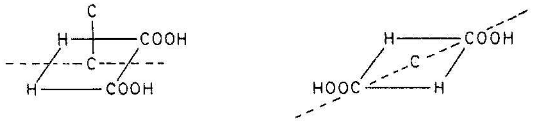
The cause of the isomerism in tartaric acid was discussed in terms of a formula (shown above) which can be derived by replacing three of the hydrogens in methane by HO, COOH and COOH–CH(OH):

> Moreover, an examination of the formula shows that the last of the substituted groups is identical with the grouping of the entire remainder of the compound; we have to deal therefore, with the second class of exceptions to the first general principle . . . if the two groups combined with one another are identical and superposable their effect upon polarized light will be added – this is what takes place with the active acid; if, on the contrary, the combined groups have an inverse symmetry they will exactly neutralize one another and we will have the inactive tartaric acid.

That the tetrahedral carbon atom did not play a central role in Le Bel's concept of the geometry of molecules can be seen from his treatment of unsaturated compounds. Since Van't Hoff's structure of substituted alkenes (Fig. 20) is symmetrical, optical activity for this class of compounds is impossible. Le Bel, on the other hand, felt that the four substituents on the carbons of the carbon–carbon double bond were not coplanar:

> . . . To explain the isomerism of the ethylene derivatives, we must suppose the hydrogen atoms to be at the angles of a hemihedral quadratic pyramid superposable upon its image . . . and we should obtain by two substitutions two isomers, one of which would be symmetrical, and the other asymmetrical. These isomers will both be symmetrical if the two substituted radicals are the same, as happens in the case of maleic and fumaric acids. Hence it is sufficient for the optical study of two disubstitution derivatives, such as the amylene of active amyl alcohol, $CH{=}C\genfrac{}{}{0pt}{}{CH_3}{C_2H_5}$, and its isomer $CH_3CH{=}CH{-}C_2H_5$, to decide whether the four hydrogen atoms are in the same plane or not.

Several things need to be clarified in this passage. First of all, Le Bel apparently assumed that the formulas for maleic acid and fumaric acid



Maleic acid, $HOOCCH{=}CHCOOH$ Fumaric acid, $CH_2{=}C(COOH)_2$

β-Amylene, $CH_3CH{=}CHCH_2CH_3$ Isoamylene, $CH_2{=}C(CH_3)CH_2CH_3$

Figure 22. Probable structures of ethylene derivatives according to Le Bel.

were $HOOCCH = CHCOOCH$ and $CH_2 = C(COOH)_2$, a view not shared by Van't Hoff. Even when Le Bel later corrected this view, he still had not abandoned the geometrical structure he had proposed for substituted ethylenes. Although Le Bel does not include any drawings to illustrate what was meant by a 'hemihedral quadratic pyramid', the best guess is that he was talking about a square pyramid (Fig. 22).

If these in fact correspond to the structures envisioned by Le Bel, it can be seen that neither maleic acid nor fumaric acid can be expected to exist in optically active form, since both contain a plane of symmetry. (The dotted line indicates where the plane would bisect the base of the square pyramid.) Isoamylene can also be expected to be inactive. On the other hand, the mirror image of β-amylene is non-superimposable on itself and could therefore be obtained in an optically active form. Even though Le Bel's attempts to confirm his theory experimentally were without success, he was reluctant to abandon his ideas even 15 years later. Nor did Le Bel wish to have his name associated with the concept of the tetrahedral carbon atom, as can be seen from statements he made repeatedly in the early 1890s:

> I use the greatest efforts in all my explanations to abstain from basing my ideas on the preliminary hypothesis that compounds of carbon of the formula CR_4 have the shape of a regular tetrahedron.

Le Bel considered that the particular geometry would be determined by the 'zones of repulsions' surrounding each atom in the molecule. It was possible then for a methane derivative, CR_4, to have a tetragonal pyramidal structure (similar to the square pyramid, but without the second carbon atom in the base). Although Le Bel was unsuccessful in his search for the observation of optical activity in a number of unsaturated compounds, his studies of quaternary ammonium compounds initiated the development of inorganic stereochemistry (Chapter 10).

Van't Hoff's demonstration in 1874 that all of the known optically active compounds contained an 'asymmetric' carbon atom provided organic chemists with a convenient means by which they could decide whether optical isomerism was possible for a new compound. The concept did not take an immediate foothold, however, because of reports of the isolation of optically active compounds which did not contain any asymmetric carbon atom. Among some of the compounds initially reported were: styrene, 1-propanol, α-picoline, papaverine, chlorofumaric acid and chloromaleic acid. Within a decade or so, it was demonstrated that the optical activity associated with these compounds was due to the presence of optically active impurities. Any reservations chemists had about Van't Hoff's proposal were removed by the reports of increasing numbers of optically active substances, all of which were found to contain asymmetric carbon atoms. In the late 1880s a few chemists, such as A. C. Brown and P. A. Guyé, undertook experimental and theoretical studies designed to elucidate the relationship between the sign (and magnitude) of the optical rotation and the nature of the groups bound to the asymmetric carbon atom. It was not always clear, however, whether optical activity would be observed in molecules having a small number of carbon atoms – since some felt that the stability of the asymmetric group was controlled by the bulk of the attached groups. Le Bel, for example, thought that the tetrahedral arrangement would be preferred only when the four groups were of sufficient size to exert repulsive forces that would favor that geometry over a square pyramid. Another chemist, Arnold Eiloart, proposed in 1898 that optically active compounds should contain at least three carbon atoms, since smaller compounds could undergo 'intramolecular transformations favored by the mobility of the small radicals attached to the asymmetric carbon'. The experimental refutation of this idea, however, was not provided until 1914 by W. J. Pope and J. Read who reported the chemical resolution of a compound containing only one carbon atom: chloroiodomethanesulfonic acid, $ClIHCSO_3H$.

When Van't Hoff's and Le Bel's papers were published in 1874, few chemists considered that speculations about the arrangement of atoms in space would be of any practical value for organic chemical research. From most of the chemists who were sent reprints of the 1875 pamphlet and the cardboard models, Van't Hoff received only a polite response. Adolph von Baeyer, however, was enthusiastic and showed the book and the models to his students in his laboratory with the remark: 'Here we have again a really new good thought in our science, which will bear ripe fruit.'

Wislicenus, as can be imagined after working so many years on the lactic acid problem, was quite receptive to Van't Hoff's proposals and was instrumental in seeing to the publication of an expanded German

Plate 11. Hermann Kolbe (1818–1884).

edition of Van't Hoff's book. The translation, published in 1877, contained a preface in which Wislicenus urged chemists to consider the ideas of Van't Hoff seriously, in spite of what he recognized was the scepticism of most chemists of that time:

> It is no long time since strong protests were frequently made by champions of the most advanced views in theoretical chemistry, against the idea that chemistry would ever reach such a point as to bring forward the conception of the position of the atoms in space in order to explain the properties of a compound.

One of the more influential chemists of the period, and one who was highly suspicious of the theoretical speculations of many chemists, was Adolf Wilhelm Hermann Kolbe (1818–1884) (Plate 11). In his position as editor of the *Journal für Praktische Chemie*, he often took it upon himself to comment on the deficiencies of chemical research. Kolbe attributed the decay in chemical research in Germany to the introduction of an increasing amount of 'speculative philosophy' which indicated a 'lack of general and at the same time thorough chemical training' in chemical research:

> If anyone supposes that I exaggerate this evil, I recommend him to read, if he has the patience, the recent fanciful publications of Messrs Van't Hoff and Hermann on *Die Lagerung der Atome*

> *in Raume*. This paper like many others, I should have been content to ignore had not a distinguished chemist taken it under his protection and warmly recommended it as a performance of merit.
>
> A Dr J. H. van't Hoff, of the Veterinary College, Utrecht, appears to have no taste for exact chemical research. He finds it a less arduous task to mount his Pegasus (evidently borrowed from the Veterinary College) and to soar to his Chemical Parnassus, there to reveal in his *La Chimie dans l'Espace* how he finds the atoms situated in the world's space.
>
> It is not possible, even cursorily, to criticize this paper, since its fanciful nonsense carefully avoids any basis of fact, and is quite unintelligible, to the calm investigator . . . It is one of the signs of the times that modern chemists hold themselves bound and consider themselves in a position to give an explanation for everything, and when their knowledge fails them to make use of supernatural explanations. Such a treatment of scientific subjects, not many degrees removed from a belief in witches and from spirit-rapping, even Wislicenus considers permissible.

As Van't Hoff commented ten years later:

> Such was the debut of this theory. Only fourteen years have passed, Kolbe is now dead, and, as if by the irony of fate his place at the University of Leipzig has been taken by Wislicenus.

If anything, Kolbe's intemperate attack probably did more than anything Van't Hoff or Wislicenus could have done to publicize the proposals. Kolbe probably represents an extreme view of the scepticism that many chemists had for theoretical speculations. It should be remembered that the atomic theory itself was considered only a useful hypothesis a decade earlier, as can be seen, for example, in Kekulé's comments in 1867:

> . . . The question whether atoms exist or not has but little significance in a chemical point of view, its discussion belongs rather to metaphysics. In chemistry we have only to decide whether the assumption of atoms is an hypothesis adapted to the explanation of chemical phenomena.

It should come as no surprise then to learn that Kekulé was only mildly receptive to Van't Hoff's ideas and referred to the tetrahedral carbon atom as a 'usable hypothesis'.

There were, however, more legitimate sources of criticism of Van't Hoff's ideas, mainly from the physical chemists who had difficulty in accepting Van't Hoff's proposal of spatially directed valence forces. As A. Claus noted in 1881:

> . . . to suppose that the chemical attraction inherent in its atom is divided into parts each of which acts independently of each other is as unnatural as it is unfounded.

Claus argued that the total, unified affinity of carbon only separated into parts when it combines with other atoms. Most organic chemists, however, were not affected by this kind of criticism since they found the idea of the tetrahedral carbon atom useful to explain the existence of stereoisomers. That it violated the physics of the period did not concern them to any great degree. The 1880s was a period in which a number of physical and organic chemists engaged in polemics directed toward deciding on the 'shape' of the carbon atom. To summarize the major points of the discussion: Should the carbon atom be regarded as a sphere with the four valencies oriented towards the corners of a tetrahedron, or did the atom itself have a tetrahedral shape with the valency forces concentrated on either the corners or faces? As Demut and Meyer stated in 1881:

> We cannot assume that valences come across in the empty space free of atoms, it is only possible on paper or in a model where these are lines or wires but not forces.

While Van't Hoff himself rather generally supposed that the number and direction of the valences should be related to the shape of the atoms, Wislicenus thought it possible that the carbon atom might be tetrahedral in shape with the maximum attraction concentrated at the apexes of the tetrahedron. Other chemists (Wunderlich, Knoevenagel, Knorr, Vaubel and Auwers) proposed various models in which the atom was considered to have several points of attraction whose number and location were dependent upon the shape of the atom. H. Sachse (Chapter 13) even used the tetrahedral shape of the carbon atoms as the basis for his calculations of what he thought would be the relative carbon–carbon single, double and triple bond lengths.

In 1891 Alfred Werner discussed the stereochemistry of carbon compounds in terms of his new theory of valency (see Kauffman's book, *Inorganic Chemical Complexes*, in this series). Although the attractive power of an atom is distributed evenly over its surface, in the case of carbon, the number of atoms it can attract is limited to four and these will be distributed over the surface so as to produce the greatest possible neutralization of the reciprocal affinities between the carbon atom and the groups. If the four groups were identical, this would presumably produce a tetrahedral geometry. Not all of the affinity of the carbon atom is completely neutralized, however, and can therefore be used to form molecular complexes which could be either relatively stable or transitory – as would be illustrated in the Walden inversion (Chapter 7). The utilization of the residual affinity of a centrally binding atom had its greatest success in explaining the existence and stereochemistry of inorganic complexes (Chapter 7).

In unsaturated compounds, Werner thought that some of the 'excess' of free affinity not utilized in the formation of the carbon–carbon 'double' bond, was oriented in such a way as to restrict rotation about the bond. The tendency of the atoms in cyclic compounds to return to positions which produced the greatest possible neutralization of affinities provided a qualitatively appealing explanation of Baeyer's 'tension' theory (Chapter 13). Werner's theory contrasted with that of Le Bel (1890) who argued that the zone of repulsion about the atoms determined the molecular geometry.

Most of the theories would be consistent with the existence of irregular tetrahedral geometries in compounds in which the four groups joined to a carbon atom were not identical. This was first suggested by Van't Hoff himself in 1877 and his book includes diagrams illustrating the construction of irregular tetrahedra from cardboard. It was, of course, difficult to experimentally establish whether in fact the valences were 'equivalent' or not, but a few attempts were made to answer this question. In 1887, L. Henry could find no differences between the two 'isomeric' (α- and β-) acetonitriles produced in a series of substitution reactions:

$$\mathrm{CH_3I + KCN} \longrightarrow \underset{(\alpha\ -)}{\mathrm{CH_3{-}CN}} \longrightarrow \mathrm{CH_3COOH} \longrightarrow \mathrm{ClCH_2COOH} \longrightarrow \underset{(\beta\ -)}{\mathrm{NC{-}CH_3}}$$

He concluded, therefore, that the valency forces themselves were equivalent. That this work was not without ambiguity can be found in the observation of the abstractor of the paper:

> The whole argument is, of course, based on the principle of substitution and the stability of complex molecular structure throughout the course of a chemical reaction.

This synthesis was done some ten years before Walden's observations (Chapter 7) called into question the assumptions that had previously been made regarding the stereochemistry of substitution reactions, which reopened the debate. For example, in 1914 Emil Fischer re-examined some

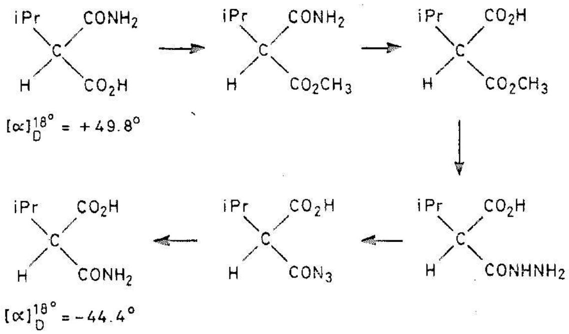


Figure 23. E. Fischer's experimental demonstration of the interconversion of enantiomers produced by the interchange of two groups attached to an asymmetric carbon.

of his assumptions regarding the geometry and stability of the asymmetric carbon atom, even though this had been assumed in his earlier work in establishing the configurations of the carbohydrates. Would the interchange of two groups (not involving the bonds to the asymmetric carbon) on an asymmetric carbon atom produce the enantiomer? The series of reactions (Fig. 23) studied by Fischer provided him with an affirmative answer to the question.

Ten years later, however, K. Weissenberg and H. Mark called into question the primacy of the tetrahedral carbon atom with their interpretation of the X-ray crystallographic study of pentaerythritol, $(HOCH_2)_4C$. They proposed that the central carbon atom was to be found at the apex of a square pyramid. Suffice it to say, this proposal generated considerable interest and controversy for several years until it was determined that the original data were found to be in error.

Although there continued to be other isolated reports (for example by A. N. Campbell in the 1930s relating to the non-identity of enantiomers) that questioned the concept of the tetrahedral carbon, the rapid rise of stereochemical investigations in the latter part of the 19th century attests to the general acceptance of the main assumptions of the theory. Where difficulties were found, they arose in areas in which the theory had been extended in order to explain the stereochemistry of compounds not containing asymmetric carbons or the stereochemistry of substitution, addition or elimination reactions.

It was not until the 1930s that a satisfactory theory was available that explained directed 'valences'. This was provided by Linus Pauling in 1931 based on a quantum-mechanical interpretation of the chemical bond. Pauling calculated the eigenfunctions for an sp^3-hybridized atom and concluded:

> We have thus derived the result that an atom in which only *s* and *p* eigenfunctions contributes to bond formation and in which quantization in polar coordinates is broken can form one, two, three, or four equivalent bonds, which are directed toward the corners of a regular tetrahedron. This calculation provides the quantum mechanical justification of the chemist's tetrahedral carbon atom.

This represented a considerable theoretical advance over the ideas proposed by G. N. Lewis some ten years earlier (see Chapter 10). More recently, a number of chemists have revived and extended the Lewis–Langmuir theory with considerable success in predicting the geometry of molecules. The 'valence shell electron pair repulsion' theory that now enjoys considerable popularity was largely the result of the proposals of Ronald Nyholm and Ronald J. Gillespie in the late 1950s. The latter chemist has been responsible for the popularization of the ideas, although J. Linnett has also contributed to the utility of the approach.