Seventh Meeting, May 9th, 1884.

THOMAS MUIR, Esq., LL.D., F.R.S.E., President, in the chair.

The Hypothesis of Le Bel and Van 't Hoff.

By Professor A CRUM BROWN, University of Edinburgh.

Arago observed in 1811 that if a plane polarised ray of light be passed vertically through a plate of quartz cut at right angles to the crystallographic axis, the ray emerges plane polarised but with its plane of polarisation inclined at an angle to the original plane of polarisation, this angle (or the amount of rotation of the plane of polarisation about the direction of the ray) being proportional to the thickness of the plate. Biot further showed that in some quartz crystals this rotation is in one sense, in others in the opposite. In 1821 Herschel proved that the sense of this rotation was connected with the inclination of the so-called plagiedral faces to the faces of the prism. In 1830 Naumann gave a very complete account of the crystallography of quartz, showed that the two kinds of crystals are mirror images of each other, and gave to this relation the name of Enantiomorphism. Quartz long remained the only known solid crystalline substance having the property of rotating the plane of polarisation in the way above described. In 1853 Rammelsberg discovered that the crystals of sodium chlorate are enantiomorph, and next year Marbach showed that they rotate the plane of polarisation, and that the two sets of enantiomorph crystals rotate the plane in opposite senses, so that, like quartz, sodium chlorate is enantiomorph optically as well as crystallographically.

The same relation has since been observed in some other substances.

All these substances show optical enantiomorphism while they are in the solid, crystalline state. But if they are fused or dissolved, the liquid has no rotating action on the plane of polarisation.

It is interesting to notice that these crystals are all either regular (sodium chlorate, sodium bromate) or uniaxial (quartz). But there

are many substances, whose *solutions* possess optical activity, as the property of rotating the plane of polarisation is called. In them this property must therefore depend on the structure of the molecules, and not on the way in which these are arranged in the crystal.

Pasteur in an elaborate series of papers worked out the enantiomorphic relations especially in the case of tartaric acid. He showed that besides the ordinary tartaric acid (the solution of which rotates the plane of polarisation to the right) there is its enantiomorph—left-handed tartaric acid, that racemic acid is an optically inactive compound of these two opposite tartaric acids, and that there is a fourth form which is also optically inactive, but which cannot be separated as racemic acid can, into a right and a left-handed component. It is interesting to notice that in this and in all other cases where optical activity is observed in the liquid or dissolved state, the crystals of the substance (if it can be obtained in crystals) are biaxial, while as already stated optically active *crystals* are regular or uniaxial—in other words crystallographic enantiomorphism depends in the latter on tetartohedry, in the former on hemihedry.

It is obvious that optical activity in the dissolved state, that is optical activity of the molecules, must depend on the structure of the molecules, that is, on the chemical constitution of the substance.

The hypothesis as to the relative position of the atoms in the molecule of an organic compound, published nearly simultaneously by Le Bel in Paris, and by Van 't Hoff in Rotterdam, gives a plausible explanation of this relation. I shall state the main points of the theory without adhering closely to the order in which either of its authors has developed it.

An atom of carbon can combine with four atoms of hydrogen, or four atoms of chlorine, or four atoms of any so-called *monad* element or compound radical. It can also combine with several different monad atoms or compound radicals in such a manner that the sum of them is four. So that $Ca\beta\gamma\delta$ may be taken to represent a compound of carbon where a, β, γ, δ stand each for a monad atom or compound radical. When a, β, γ and δ are all different the carbon atom is said to be asymmetric. Now, all subtances optically active in solution (or in the liquid state) whose chemical constitution is known contain an asymmetric carbon atom. The converse of this is not true--we know substances with an asymmetric carbon atom which

have not been observed to possess any action on the plane of polarisation. Now, if we suppose the four atoms (leaving, for the meantime, compound radicals out of consideration) a, β, γ and δ to be situated around the atom of carbon, the simplest supposition is that if they are all of the same kind (that is if the compound be $Caaaa$) the carbon atom C will occupy the centre of figure of a regular tetrahedron while the atoms a, a, a, a combined with it occupy the apices. Now, if all the atoms combined with the carbon atom are not of the same kind, we may reasonably assume that the tetrahedron, at the apices of which these atoms are, will not be a regular tetrahedron, because each atom will have its own appropriate distance from C. As long, however, as they are not *all* different there will be only one figure; but if they are all different there will be two possible figures with a, β, γ, δ at the apices and each of them at its appropriate distance from C, and these two figures will be enantiomorph. That this is so will be at once seen if we consider any one face of the tetrahedron—say that which has a, β, γ, at its corners. Looking at this face from the outside—that is, with δ further from us than the face in question—we may have the order

$$\beta \qquad\qquad\qquad \beta$$

$$a \qquad\qquad \gamma \quad \text{or} \quad \gamma \qquad\qquad a \quad ,$$
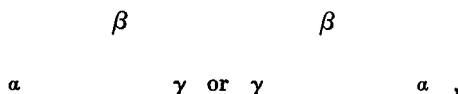
the one being the mirror image of the other.

On this supposition as to the relative position of the atoms, a compound containing an asymmetric carbon atom can exist in one or other of two forms precisely similar in every respect, except that they are enantiomorph.

And we can easily see why substances which have an asymmetric carbon atom are not always optically active. In any ordinary way of making such a substance it is plainly as likely that the one form should be produced as the other. Therefore, as the number of molecules in any quantity of the substance that we can deal with is practically infinite, the ratio of the number of the one kind to that of the other kind will be practically unity, and, therefore, the rotatory effects will precisely balance one another. So that we cannot expect an optically active substance to be produced from optically inactive materials without the intervention of some agent which can act differently on the two enantiomorphs, and enable us to obtain one or both of them separately out of the mixture. Of such agents we have several kinds.

(1) Crystallisation. The two enantiomorphs may crystallise in identical forms, but usually there are present certain faces on one side of the one and on the other side of the other, distinguishing them. In such cases, if the two enantiomorphs do not unite together, we can pick out the two sorts of crystals and thus separate the two substances. Further, if we prepare a super-saturated solution of one of the enantiomorphs, we find (in some cases, at all events) that crystallisation is caused by the addition of a crystal of the same kind, but not of the other kind; so that if we prepare a supersaturated solution of the mixture and drop into it a crystal of the right-handed sort, only the right-handed substance will crystallise out. In this way, separation has been effected by dropping simultaneously into such a supersaturated solution, at different parts of the vessel containing it, two crystals, one of the one sort the other of the other, when each substance crystallised out separately at the place where the crystal of its own kind was placed.
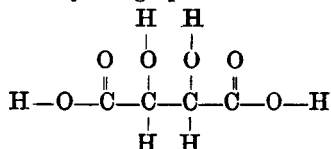
(2) The action of another optically active substance. An example will make this mode of separation clear. Right-handed tartaric acid forms a definite crystalline compound with left-handed asparagine; left-handed tartaric acid with left-handed asparagine gives an uncrystallisable gummy substance. We might illustrate this by an analogy. Right-handed and left-handed men can both use tools of the sort that Professor Tait calls amphicheiral, such as chisels, knives, axes, and planes, but the case is different if you give them right or left-handed tools such as scissors or screws. The right-handed man with the left-handed tool is as awkward as the tartaric acid with the wrong kind of asparagine.

(3) Fermentation. Fermentation takes place in many solutions in the presence of growing fungi. The nature of the chemical change depends, of course, on the nature of the dissolved substance and also on the kind of fungus.

M. Le Bel found that some of the fungi act more readily on one than on the other of two enantiomorph substances. These fungi are, in fact, not indifferent or amphicheiral but pick out the one kind of molecules and cause their oxidation while leaving the other. This may give us some idea how it is that plants and animals often contain optically active substances.
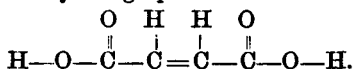
Tartaric acid is peculiarly interesting in connection with this

theory, both because its optical, chemical, and crystallographical properties have been very fully examined, and also because it is an example of a special case. The constitution of tartaric acid is represented by the graphic formula

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

Here the two middle atoms of carbon are both asymmetric and precisely similar to one another in their relation to the rest of the compound. Here, then, we should expect the following forms:—(a) Right-handed, in which both asymmetric carbon atoms are right-handed. (b) Left-handed, in which both are left-handed. (c) Inactive, in which one is right and the other left, that is to say, the one is the mirror image of the other. (d) Inactive by compensation—a mixture (or compound) of a and b. Now, this is exactly what we have. No other case has been investigated in which there are two precisely similar asymmetric carbon atoms, and no other case is known where there is an inactive form besides the mixture (or compound) of the two enantiomorphs.

The theory also gives a plausible explanation of the existence of two different acids, maleic and fumaric, both having the constitution indicated by the graphic formula

$$
\begin{array}{c}
\text{O}\quad\text{H}\quad\text{H}\quad\text{O} \\
\ \|\quad\ |\quad\ |\quad\ \| \\
\text{H}-\text{O}-\text{C}-\text{C}=\text{C}-\text{C}-\text{O}-\text{H}.
\end{array}
$$

and yielding by the addition of bromine, two isomeric acids, the one corresponding to inactive tartaric acid, the other to racemic acid (the compound of the two active tartaric acids).