

LXXXV.—*Optical Activity and Enantiomorphism of Molecular and Crystal Structure.*

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THE view may be regarded as axiomatic that the property of optical activity is wholly restricted to substances possessing an enantiomorphous structure, that is, a structure which is non-superposable with its mirror image. It is convenient to divide optically active substances into two classes: first, those in which the rotatory power is limited to the crystalline state of aggregation, as, for example, quartz; secondly, those in which the activity persists when the crystalline structure is destroyed by dissolving, liquefying, or vaporising the substance, for example, seignette salt, camphor, and turpentine. The prevailing view concerning these two classes is that in the first the seat of the activity lies in an enantiomorphous, spiral grouping of the molecules in the crystal edifice, which breaks down on dissolution, whilst in the second class the activity is referred to an enantiomorphous configuration of the atoms within the chemical molecule, which configuration is independent of the state of aggregation.

The objects of the present paper are: first, to point out that the theory of crystal structure is incapable of accounting for the activity of many substances of the first class by a spiral grouping of molecules, from which it follows that the molecular configuration must be enantiomorphous in the same sense as is recognised for substances of the second class; secondly, to indicate for such sub-

stances chemical constitutions of an enantiomorphous character which seem to be in harmony with the general chemical behaviour of the substances concerned.

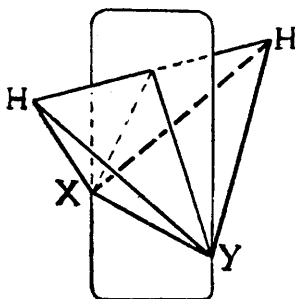
Before proceeding to the main theme it will be necessary to discuss separately the general nature of molecular and crystal structure which shall exhibit enantiomorphism.

Conditions Necessary for Optical Activity of Molecular Structure.

In the simpler carbon compounds the essential difference between an enantiomorphous configuration and one which is superposable with its mirror image is that the latter possesses a plane of symmetry, for example, CH_2XY possesses a plane of symmetry, whereas CHXYZ does not, and is, in fact, enantiomorphous. In view of the enormous number of compounds of these types which have been investigated, it is not surprising that chemists came to the conclusion that any structure devoid of a plane of symmetry is necessarily enantiomorphous. This is erroneous. The complete conditions for geometrical enantiomorphism have been long recognised by crystallographers, and are three in number: the molecular configuration must not only be devoid of (1) a plane of symmetry, but also (2) of a centre of symmetry, and (3) of an alternating axis of symmetry. The presence of any one of these three elements of symmetry suffices to render a configuration superposable with its mirror image. The precise meanings of these three terms will now be explained and illustrated by concrete examples.

Plane of Symmetry.—When a configuration can be divided into

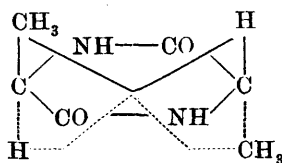
FIG. 1



two halves so that the reflection of one half across a mirror, placed in contact with the plane of the section, restores the missing half, there is a plane of symmetry. Thus, in a disubstituted product of methane, CH_2XY , there is a plane of symmetry cutting the C, X, and Y atoms into equal halves, and each hydrogen atom is symmetrically

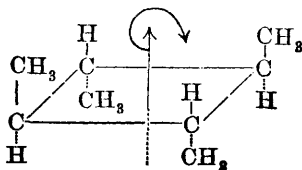
disposed on opposite sides of the plane. Although containing no other symmetry, the substance is superposable with its mirror image, and therefore is incapable of existence in optically active forms.

Centre of Symmetry.—This involves similarity about the centre of the molecule in the following sense: lines drawn through the centre of the whole molecule to each and every atom meet a similar atom when produced in the opposite direction. Thus, in *trans*-1:4-diketo-2:5-dimethylpiperazine (alanyl anhydride) any line drawn through the centre of the ring to any atom (either above, below, or in the ring) meets a similar atom similarly environed, when produced backwards. In the figure given, lines have been



drawn connecting pairs of *trans*-hydrogen atoms and methyl groups to indicate the symmetry about the centre ("centrosymmetry") by the presence of which optical activity is precluded (E. Fischer, *Ber.*, 1906, **39**, 467, 3981).

Alternating Axis of Symmetry.—This peculiar element of symmetry is illustrated by, say, 1:3-*cis*-2:4-*trans*-tetramethylcyclobutane. If any hydrogen atom or methyl group be rotated through an angle of 90° about the vertical axis indicated, and then reflected across the horizontal plane (that is, the plane perpendicular to the



axis of rotation), it comes into superposition with a corresponding hydrogen atom or methyl group, and the same is true of the molecule as a whole. The similar atoms or groups are seen to alternate successively above and below the plane of reflection; hence the term alternating. The molecule is superposable with its mirror image by virtue of the alternating axis of symmetry.

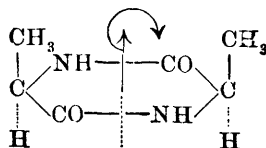
In the illustration just given there are evidently two vertical planes of symmetry cutting diagonally through the ring carbon atoms, and it might be objected that the presence of these two planes of symmetry are in reality the cause of the superposability. If, however, the methyl groups be replaced alternately by the groups CXYZ and CXZY, there would be no longer any planes of

symmetry, and the molecule, although possessing no less than eight asymmetric carbon atoms, would be an inactive, internally compensated compound by virtue of the alternating axis of symmetry, which would, in fact, be the sole element of symmetry.

In configurations possessing alternating axes of symmetry, the successive rotations must be $360^\circ/n$, where n is an even number. When $n=2$, the alternating axis is equivalent to a centre of symmetry; where $n=6, 10, 14$, etc., the alternating axis also involves a centre of symmetry, but where $n=4$ (as above), 8, 12, etc., this does not hold.

In testing a new configuration as to the elements of symmetry actually present, it must be understood that in the case of single linkings the atoms or groups must be rotated into as symmetrical positions as possible, since experience has proved that atoms or groups invariably take up such a symmetrical, favourable configuration by virtue of free rotations about single linkings.

Although an enantiomorphous configuration must be devoid of all the three elements discussed, it need not necessarily be totally devoid of symmetry, that is, asymmetric in the literal sense. For example, the *cis*-form of 1:4-diketo-2:5-dimethylpiperazine, although optically active, possesses an ordinary (as opposed to alter-



nating) axis of symmetry. It is seen that by simply rotating the whole molecule through 180° about the axis indicated, each atom comes into congruence with a similar atom, and the molecule as a whole presents the same aspect before and after the rotation. The above axis is termed digonal, because the rotation is $360^\circ/2$. Substances can be easily formulated exhibiting trigonal (rotation = $360^\circ/3$), tetragonal, pentagonal, etc., axes of symmetry, of an enantiomorphous character.

It is almost needless to add that in every case where the constitution of a substance, exhibiting optical activity in the non-crystalline condition, has been established, the molecular configuration is devoid of plane, centre, and alternating axis of symmetry. For example, the two optically active forms of tartaric acid are configurationally devoid of all symmetry whatsoever. The internally compensated meso-form has either a plane of symmetry or a centre of symmetry, according as to which of the two possible favourable configurations is taken up by the molecule by virtue of

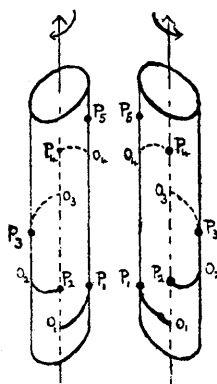
the free rotation about the single bond between the two central carbon atoms.

Conditions Necessary for Optical Activity in the Crystal.

The optical activity of a crystal may be theoretically due to two causes: first, an enantiomorphous configuration of the molecule, for example, in crystals of tartaric acid and sucrose; secondly, an enantiomorphous, spiral grouping of non-enantiomorphous molecules, for example, in crystals of quartz and cinnabar.

Now, with substances of the second class, the theory of crystal structure demands that the arrangement of molecules must possess "screw axes of symmetry." Suppose points (each representing the mean position of a molecule) be distributed on the surface of a

FIG. 2.



cylinder so that a point P_2 is obtained from P_1 by the following operations. First rotate P_1 through 90° clockwise about the axis of the cylinder to the point O_1 , then translate O_1 any given distance parallel to the cylinder axis to P_2 . Treating P_2 in the same way, points P_3, P_4 (at the back of the cylinder), P_5 , etc., are located. It is obvious that P_5 lies vertically above P_1 ; further, all the points lie on a spiral. By effecting the rotation in the opposite direction (counter clockwise), but carrying out the translations in the same direction as previously, a spiral enantiomorphous with the former is obtained. When an arrangement of points is of such a nature as the one outlined, it is said to possess screw axes of symmetry.

Now in a crystal the angle of rotation may not only be 90° , that is, $360^\circ/4$, but also $360^\circ/2$, $360^\circ/3$, and $360^\circ/6$; any other values but these are inadmissible, since they would contravene the fundamental law of geometrical crystallography. The screw axes

mentioned are known respectively as tetragonal, digonal, trigonal, and hexagonal.

The character of the digonal screw axis is especially important for the present subject. By a rotation of the point P_1 through 180° , followed by a translation equal to half P_1P_5 , the point P_3 is located, and a subsequent operation discovers the point P_5 . Now the points P_3 and P_5 are successively obtained, no matter in which direction the rotation is effected; there is no physical difference, then, between a rotation of $+180^\circ$ and one of -180° , and the two arrangements are no longer distinguishable by an enantiomorphous, spiral nature. Any assemblage of points possessing no other screw axes save digonal can only be endowed with optical activity providing the points themselves (that is, the molecules) are enantiomorphous.

Crystals belonging to the rhombic, monoclinic, and triclinic systems cannot possess screw axes other than digonal. Again, in the sodium chlorate class of the cubic system, although the point-assemblages exhibit trigonal screw axes, the latter are always paired, each *d*-spiral being accompanied by a *l*-spiral axis. Now optical activity has been recorded in three rhombic, three monoclinic, and four substances having the symmetry of sodium chlorate. Among these ten cases there are four which admittedly have an enantiomorphous molecular configuration, namely, seignette salt, sucrose, rhamnose, and tartaric acid. The remaining six substances, which must equally possess enantiomorphous configurations, are: magnesium sulphate, $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$; sodium dihydrogen phosphate, $\text{NaH}_2\text{PO}_4 \cdot \text{H}_2\text{O}$; Schlippe's salt, $\text{Na}_3\text{SbS}_4 \cdot 9\text{H}_2\text{O}$; sodium uranyl acetate, $\text{NaUO}_2(\text{C}_2\text{H}_3\text{O}_2)_3$; sodium chlorate and sodium bromate.

Co-ordination and Valency.

The work of Werner and the views expressed by him on his theory of co-ordination seem to show that whilst the co-ordination number of an element is not the same as its valency, yet, like valency, it is constant for a large series of compounds, and the atoms or groups associated in co-ordination with the element have themselves a monad or dyad character. Thus, the groups Cl , NO_2 , OH , NH_3 , H_2O are monad, whilst the groups $\text{C}_2\text{H}_4(\text{NH}_2)_2$, CO_3 , C_2O_4 are dyad. In this way the co-ordination number for cobalt is six, no matter whether it be associated with six NH_3 -groups or with three ethylenediamine groups. It seems therefore likely that the oxygen atom will have double the co-ordination value of that of chlorine, hydroxyl, or NO_2 , just as it has double the valency value. It will follow therefore that in the groups $(\text{ClO}_3)'$, $(\text{NO}_3)'$, $(\text{CO}_3)''$, the co-ordination number of Cl , N , and C will be six, and

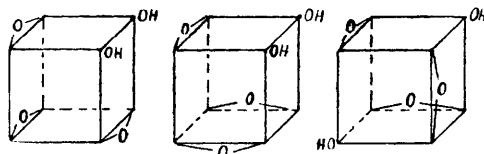
the co-ordination figure will be an octahedron, each oxygen atom being represented as attached to two adjacent corners of the octahedron. Again, in the groups OsO_4 , $(\text{ClO}_4)'$, $(\text{SO}_4)''$, $(\text{PO}_4)'''$, $(\text{SiO}_4)''''$, the co-ordination number will be eight, and the co-ordination figure a cube, where each oxygen atom influences, or is attached to, two adjacent corners.

Constitution of Substances with Co-ordination Number Eight.

To this category belong all the substances previously mentioned excepting sodium chlorate and bromate. The constitutions suggested will be best illustrated by treating the heptahydrated magnesium sulphate in some detail.

Magnesium Sulphate, $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$.—This salt loses six molecules of water of crystallisation much more easily than the seventh, which requires a temperature of 200° . Again, the naturally occurring monohydrated salt, kieserite, requires prolonged boiling with water before it will dissolve. There appears, then, every good reason for supposing that one of the seven molecules of water is water of constitution, and is presumably bound to the acidic portion of the molecule, with the result that one of the doubly co-ordinated oxygen atoms is developed and forms two hydroxyl groups; the constitution may therefore be written $[\text{SO}_3 \cdot 2\text{OH}]\text{Mg} \cdot 6\text{H}_2\text{O}$. Now there are three possible spacial formulæ for the co-ordinated portion of the molecule:

FIG. 3.



In the first two formulæ the hydroxyl groups occupy *cis*-positions, but in the third formula, *trans*-positions. The first formula possesses two planes of symmetry, the second, a single plane of symmetry; so neither is of an enantiomorphous character. The third *trans*-formula, although possessing a trigonal axis of symmetry, has neither plane, centre, nor axis of alternating symmetry, and is consequently non-superposable with its mirror image. It is accordingly suggested that the *trans*-formula represents the stereochemical constitution of the acidic radicle of magnesium sulphate, and confers enantiomorphism on the molecule as a whole. Since in solution the magnesium is separately ionisable, it lies of necessity outside the co-ordination sphere of the sulphur, and it appears

reasonable to suppose that it is in turn co-ordinatively surrounded by the six molecules of water of crystallisation.

Sodium Dihydrogen Phosphate, $\text{NaH}_2\text{PO}_4 \cdot \text{H}_2\text{O}$.—The constitution of this compound would appear to be analogous to that of the foregoing, namely, $[\text{PO}_3 \cdot 2\text{OH}]\text{NaH}_2$, in which, as before, the hydroxyl groups occupy the *trans*-position.

Schlippe's Salt, $\text{Na}_3\text{SbS}_4 \cdot 9\text{H}_2\text{O}$.—No data exist concerning a possible division of the water into water of constitution and of crystallisation. Enantiomorphous formulæ are, indeed, obtainable by taking one, two, three, or four molecules as water of constitution, each molecule forming with a corresponding double bond sulphur atom the groups SH and OH. The number of possible spacial formulæ are respectively: one active and one inactive, four active and four inactive, two active and two inactive, one active and four inactive. In view of this, it is impossible to indicate any particular formula for this salt.

Sodium Uranyl Acetate, $\text{NaUO}_2(\text{C}_2\text{H}_3\text{O}_2)_3$.—If, as seems likely, the sodium atom be supposed to lie outside the co-ordination sphere of the uranium, the co-ordination number of the latter becomes seven, and it becomes impossible to indicate, a priori, any likely configuration. If, on the other hand, the unlikely assumption be made that the sodium makes up the eighth co-ordination number, the number of possible spacial formulæ can be easily worked out and proves to be four—three active and one inactive.

Collateral Evidence in Favour of the Constitutions Suggested.

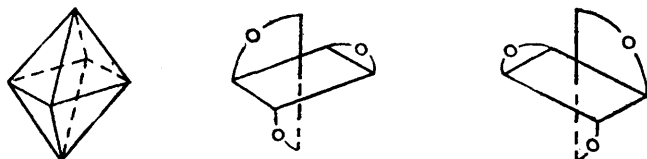
The constitutions which have been suggested for the first two compounds discussed are based fundamentally on the assumption that a certain amount of water of constitution is included in the acidic part of the molecule, and confers on it enantiomorphism. Now there are, as a matter of fact, two possible spacial formulæ for the anhydrous group (SO_4), both of which possess planes of symmetry; with neither of these possible configurations, then, would optical activity be expected. This expectation is fully in accordance with the facts, for there is only one case known of optical activity amongst the large class of anhydrous sulphates, orthophosphates, orthosilicates, periodates, perruthenates, etc., namely, potassium lithium sulphate, KLiSO_4 . This substance crystallises in the hexagonal system in a class which admits of the presence of hexagonal screw axes, and accordingly even in this case no enantiomorphism of molecular configuration is called for.

The lowering of the symmetry of the molecular configuration by the presence of a molecule of water of crystallisation is of quite frequent occurrence, as is evidenced by the appearance of mono-

hydrated salts in enantiomorphous forms. Thus, the mono-hydrated lithium sulphate, $\text{Li}_2\text{SO}_4 \cdot \text{H}_2\text{O}$, is one of the classical examples of enantiomorphism in the monoclinic system. The proof of the presence of optical activity in such a crystal is a somewhat laborious process, since the rotatory power can only be observed in two sections, which have to be ground with great accuracy. It is proposed to undertake this work when the necessary grinding instrument has been obtained.

Constitution of Substances with Co-ordination Number Six.

The two substances to be considered are sodium chlorate and its analogue sodium bromate, which must naturally have a similar constitution. Since the co-ordination number is six, the co-ordination figure is a regular octahedron, at the centre of which is situated the chlorine atom, with its six co-ordination valencies directed towards the six corners. When the six valencies are satisfied by three doubly bound oxygen atoms, the group ClO_3 becomes enantiomorphous:



The above constitution is analogous to the one suggested by Werner for the complex chromium oxalate group in the optically active potassium chromium oxalate.

Constitution of the Substances in the State of Solution.

The question must now be considered whether the substances under discussion retain the same constitution when dissolved or liquefied, or whether a radical change takes place so as to yield a molecule with a different formula. There appears to be only one available source of evidence in this connexion, namely, ionisation phenomena, which, in fact, point to the conclusion that there is no change of constitution when the substances are dissolved. Sodium chlorate, for example, undergoes electrolytic dissociation into ClO_3 and Na ions, that is, into the co-ordinated and the unco-ordinated parts of the molecules. Again, a solution of magnesium sulphate contains Mg and SO_4 ions, and since the prevailing tendency of opinion is to assume that each ion is surrounded by an envelope of several water molecules, the single water molecule which was received into the co-ordination sphere may perhaps be looked upon

as constituting one of the relatively large number which surround the SO_4 ion in solution.

If the constitution remains unaltered during the passage of the substance into solution, some explanation must be forthcoming of the inactivity of the solution. This inactivity is probably due to autoracemisation. That there is nothing inherently improbable in this view will perhaps be generally admitted if the constitution of the compounds be compared with those of the substances which have been successfully resolved by Werner. The latter are very prone to racemisation, although the bivalent groups attached to the central atom are of a complex character; representative examples of such groups are ethylenediamine, dipyridyl, and C_2O_4 . In particular, the optically active antipodes of potassium chromic oxalate, $\text{K}_3\text{Cr}(\text{C}_2\text{O}_4)_3 \cdot \text{H}_2\text{O}$, are completely racemised in aqueous solution in seventy-five minutes (Werner, *Ber.*, 1912, **45**, 3063). Now racemisation in such a molecule involves either a flipping of the molecule or a loosening of one of the attachments of each of two (C_2O_4) groups, a rotation of each group about the free ends through an angle of 60° , and a subsequent coupling up. If this process is so easy with a group like C_2O_4 , how much more readily should it occur with doubly bound oxygen atoms, especially as it could be brought about by alternate hydroxylation and dehydration. It is conceivable that autoracemisation should be practically instantaneous on dissolving the crystal. Since no previous experiments appear to have been carried out on this subject, it is proposed to investigate the point, although a positive result is perhaps not to be hoped for.

The reverse change, that is, the crystallisation of the inactive supersaturated solution so as to yield either one or the other crystalline antipode, is equally feasible. When the substance crystallises, the solid phase may be either a conglomerate of active crystals or a racemate. In the former case the accidental appearance of a surplus of *d*- over *l*-crystals will be automatically accompanied by a racemisation of *l*- into *d*-molecules in solution, so that the solution remains inactive.

The Relationship of Sodium Chlorate and Sodium Nitrate.

The crystalline forms of these two substances are not isomorphous at the ordinary temperature, but at higher temperatures sodium chlorate crystallises in a second modification, isomorphous with the well-known rhombohedral form of sodium nitrate. It must therefore be concluded that the two substances have a similar constitution, and the question must now be entertained why sodium nitrate is not optically active. The absence of rotatory power in

crystals of sodium nitrate receives a satisfactory explanation if it be assumed to be a racemate, that is, a molecular compound of the two antipodes, which in the free state would be isomorphous with sodium chlorate. Some confirmation of the correctness of this view is derived from the following interesting consideration: If a *d*- and an *l*-molecule of sodium nitrate, having configurations similar to those given for sodium chlorate, be allowed to interpenetrate in the most symmetrical way possible, then the symmetry of the racemic molecule thus obtained is found to be identical in every respect with that of a crystal of sodium nitrate, and, moreover, is in complete harmony with the rhombohedral form.

Again, the dimorphism of sodium chlorate now acquires a new significance. The rhombohedral modification of this salt, being isomorphous with the racemic nitrate, must itself also be a racemic compound; and the "dimorphism" of sodium chlorate becomes precisely analogous to that of sodium ammonium tartrate, that is, there is a transition temperature above and below which the racemate and the conglomerate of optical antipodes are the stable phases respectively. The crystalline form, composition, and physical properties of mixed crystals of sodium chlorate and nitrate are also in full accord with the present interpretation. Mallard (*Bull. Soc. franç. Min.*, 1884, 7, 352) has found that at the ordinary temperature the rhombohedral sodium nitrate will take up as much as 22.5 per cent. of sodium chlorate; the optically active, cubic sodium chlorate, however, does not appreciably dissolve the nitrate.

In conclusion, we wish to express our grateful thanks to Prof. H. Hilton for much valuable advice on the theory of crystal structure.

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