

STEREOCHEMISTRY.

THE present report deals with the progress of stereochemistry during the two years which have elapsed since the last report on this branch of chemistry appeared. Some of the more striking developments which have taken place during this period have been mentioned in the report on Organic Chemistry for 1908, but, in order to secure continuity, it will in some cases be necessary to refer to these again.

The past two years have been marked by great activity on the part of the numerous workers in this most interesting and productive field, and the output of important work has been so great that it is difficult, within the narrow limits of this report, to do justice even to all the work which has an obvious bearing on general progress; consequently a number of researches which have added to the sum of our knowledge must of necessity be left unmentioned.

A good deal of attention has been paid to the problem of effecting a complete asymmetric synthesis, and a number of papers have been published in which an account is given of attempts made to bring this about by the use of circularly polarised light, or of a combination of magnetic and electric fields; hitherto all these attempts have led to negative results, but the use of emulsin for effecting asymmetric synthesis has been made successfully in a number of cases.

The allied problem of separating the synthetic mixture of enantiomorphous isomerides has also attracted attention, and the work of Ostromisslensky has shown it in a new aspect, since it is clear that a separation can be effected without the actual use of one of the enantiomorphs, or even of an optically active substance, but merely by using a substance isomorphous with the active substance.

The attempts to verify experimentally van't Hoff's prediction, that optical activity could be due to enantiomorphism of the molecule without being assignable to a single asymmetric atom, have now been brought to a successful issue. The resolution of two substances of this class has been announced: first, 1-methylcyclohexylidene-4-acetic acid, by Perkin, Pope, and Wallach, and, secondly, 4-oximinocyclohexanecarboxylic acid, by Mills and Miss Bain. In both cases the molecule is devoid of a plane of symmetry, but contains no atom which is asymmetric according

to any of the accepted definitions of an asymmetric atom. The case of 4-oximinocyclohexanecarboxylic acid acquires additional interest on account of its important bearing on the Hantzsch-Werner hypothesis concerning the isomerism of oximes.

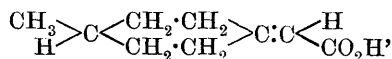
The study of the quantitative relations of optical activity has been the subject of a very large number of communications, the general trend of which has been to demonstrate, first, the importance of the chemical character of the groups in the molecule as distinct from their mass, and, secondly, that the value of the rotatory power is more dependent on the solvent, on temperature, and on the wave-length of the light used than had hitherto been suspected.

The Walden inversion and the closely allied subject of racemisation have received a great deal of attention, and, in regard to the former, the results obtained have complicated matters very considerably by showing that some of the conclusions deduced from Walden's original observations and from Fischer's work in 1907 are not applicable in other cases, but, at the same time, new facts lend support to other conclusions, and these will probably be found universally applicable. Thus it appears that the Walden inversion is dependent on the presence of a carboxyl group attached to the asymmetric carbon atom, and that it is never caused by the action of phosphorus pentachloride.

A very large number of new optically active substances have been prepared, and among them a second compound owing its activity to silicon.

The investigations which have added a new type of molecular structure causing optical activity to those already known may be considered first.

The acid resolved by Marckwald and Meth,¹ melting at 40—41°, and stated by them to be 1-methylcyclohexylidene-4-acetic acid,



has eventually been proved² to be the isomeric 1-methyl- Δ^3 -cyclohexene-4-acetic acid, whilst the acid prepared by Perkin and Pope and by Wallach, melting at 66°, possesses the structure represented by the above formula.

This acid has been resolved³ by the fractional crystallisation of its brucine salt from dilute alcohol. The complete separation of the two salts was found to be extremely difficult, owing to the formation of mixed crystals of the salts dA/B and lA/B , but both the active acids have been obtained pure, melting at 52·5—53°, and having $[\alpha]_D \pm 81^\circ$ in 0·7 per cent. solution in absolute alcohol.

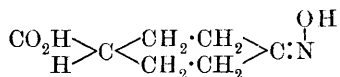
¹ *Ber.*, 1906, **39**, 1171; *A.*, 1906, i, 360.

² See *Trans.*, 1909, **95**, 1791, for references.

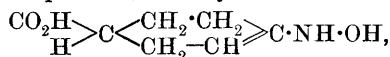
³ Perkin, Pope, and Wallach, *ibid.*, 1789.

The racemic acid melts at 66° , and a mixture of this with one of the active acids can be found melting at as low a temperature as $43-44.5^{\circ}$; hence the melting-point curve for mixtures of the *d*- and *l*-acids must be of the same type as that of the dimethyl tartrates.

Another exceedingly interesting example of a substance owing its activity to enantiomorphism of the molecule has been found in 4-oximinocyclohexanecarboxylic acid,



A preliminary account⁴ only has appeared, in which the resolution of the acid by fractional crystallisation of its quinine salt from ethyl acetate is described. The sodium salt, after removal of the quinine, was found to show a rotation of -4.4° in aqueous solution in a 2-dcm. tube, and this activity was at once destroyed by the addition of acid. Further details of this work will be awaited with interest, since the behaviour of this substance has an important bearing, not only on the demonstration of a new type of molecular structure capable of causing optical activity, but also on the Hantzsch-Werner hypothesis of the stereoisomerism of oximes, which would receive the very strongest confirmation if this acid can be proved to have the structure assigned to it above, and, at the same time, to exhibit optical activity. In this case the molecule can only be devoid of a plane of symmetry if the hydroxyl group attached to the nitrogen atom is deflected to the right or left in the plane of the ring. An alternative formula containing an asymmetric carbon atom seems possible, namely:



but if this were the constitution, it is not easy to understand why acidification should cause the disappearance of activity, whereas this can be explained with the aid of the oximino-formula.

It has long been recognised that molecular asymmetry or enantiomorphism of the molecule is the essential cause of activity, although the asymmetry could usually be referred to a single atom, four valencies of which were occupied in linking four different groups; in the cases mentioned above a somewhat modified definition of an asymmetric atom would include the case of the atom $\begin{array}{c} \text{CH}_3 \\ \text{H} \end{array} \text{C} <$

in the first case,^{4a} and $\begin{array}{c} \text{CO}_2\text{H} \\ \text{H} \end{array} \text{C} <$ in the second.

The problem of effecting a complete asymmetric synthesis, that is, producing an optically active substance without the aid of another

⁴ W. H. Mills and Miss A. M. Bain, *Proc.*, 1909, **25**, 177.

^{4a} See A. E. Everest, *Chem. News*, 1909, **100**, 295; *A.*, 1910, ii, 6.

optically active substance, has been attacked vigorously, but hitherto without success.

Several reactions which are influenced by light have been carried out in circularly polarised light; thus, the acids $\text{CN}\cdot\text{CMeEt}\cdot\text{CO}_2\text{H}$ and $\text{CO}_2\text{H}\cdot\text{CClMe}\cdot\text{CClMe}\cdot\text{CO}_2\text{H}$ lose carbon dioxide under the influence of light in presence of uranium salts, yet when the incident light had been passed through a magnetic field the product was inactive.⁵ Similarly, the change of *r-o*-nitrobenzaldehydediamyl-acetal in solution in *r*-amyl alcohol into amyl *o*-nitrosobenzoate under the influence of circularly polarised light gave rise to an inactive compound,⁶ and the exposure of copper racemate to circularly polarised light also gave no result.⁷

The experiments first mentioned have been criticised by A. Byk,⁸ who points out, quite correctly, that the combination of ordinary light and a magnetic field would not be expected to give any result, since the light is not circularly polarised.

The union of bromine with methyl fumarate and with methyl cinnamate has also been carried out under the influence of superposed magnetic and electrostatic fields,⁹ but the products were inactive.

A large number of syntheses, which, to distinguish them from the above, may be described as partial asymmetric syntheses, and in which an optically active substance is used, have been carried out. When the union of benzaldehyde and hydrocyanic acid is brought about under the catalytic action of emulsin, *d*-benzaldehyde-cyanohydrin is produced, and from this pure *l*-mandelic acid can be obtained.¹⁰ A number of other aldehydes also give optically active cyanohydrins under the influence of emulsin.¹¹

Emulsin is also found to destroy *d*-benzaldehyde-cyanohydrin more rapidly than its antimeride, so that the latter is in excess when emulsin acts on the synthetic *dl*-mixture.¹²

Syntheses of active substituted glycollic acids have been effected by the action of Grignard's reagent on *d*-amyl pyruvate and on *d*-amyl phenylglyoxylate.¹³ A comparison of the results now obtained with those previously obtained leads to the conclusion that the greater the optical activity of the active group present

⁵ F. Henle and H. Haakh, *Ann. Report*, 1908, 107.

⁶ P. Freundler, *Ber.*, 1909, **42**, 233; *A.*, i, 164.

⁷ A. Cotton, *J. Chim. Phys.*, 1909, **7**, 81; *A.*, ii, 278.

⁸ *Ber.*, 1909, **42**, 141; *A.*, i, 130.

⁹ P. A. Guye and G. Drouguine, *J. Chim. Phys.*, 1909, **7**, 97; *A.*, ii, 278.

¹⁰ L. Rosenthaler, *Biochem. Zeitsch.*, 1909, **14**, 238; *A.*, i, 74; S. J. M. Auld, *Trans.*, 1909, **95**, 927.

¹¹ L. Rosenthaler, *Biochem. Zeitsch.*, 1909, **17**, 257; *A.*, i, 622.

¹² K. Feist, *Arch. Pharm.*, 1909, **247**, 226; *A.*, i, 589.

¹³ A. McKenzie and H. A. Müller, *Trans.*, 1909, **95**, 544.

in a molecule during the asymmetric synthesis the greater is its directive influence on that synthesis. Mandelic acid having $[\alpha]_D -15.6^\circ$ has been obtained by the reduction of *l*-menthyl phenylglyoxylate and subsequent hydrolysis, racemisation during the action of potassium hydroxide having been prevented by acetylation of the hydroxyl group.

Some very interesting observations have been recorded on the separation of *d* + *l*-mixtures of enantiomorphous compounds. Thus, a crystal of *l*-asparagine added to a supersaturated solution of sodium ammonium *dl*-tartrate causes the separation of a quantity of the *d*-tartrate, with which it is isomorphous, and so does a crystal of any alkali salt of *d*-tartaric acid.¹⁴ A crystal of the *l*-tartrate causes the deposit of a crop of levorotatory crystals. Further, it was found that it is not necessary that the nucleating material should itself be active if it be isomorphous with the tartrate, and therefore presumably tetartohedral; thus, a crystal of glycine added to the supersaturated solution of *dl*-asparagine causes a deposit of either the *d*- or *l*-compound, the same crystal always producing a crop of crystals having a rotatory power of the same sign.

These observations afford another method of distinguishing a racemic compound from a *dl*-mixture; from a supersaturated solution of the former the crystals deposited when the solution is nucleated with a suitable material would be inactive, whereas the latter would yield an active deposit under the same conditions.

A large number of experiments on the slow, spontaneous crystallisation of solutions of sodium ammonium *dl*-tartrate were described in 1898, and now further interesting observations on this subject are recorded.¹⁵ When the solutions were allowed to evaporate in the laboratory, the first deposits obtained were usually dextrorotatory; thus, for example, in one series of experiments dealing with nineteen solutions, sixteen gave dextrorotatory deposits; when the solutions were allowed to evaporate in desiccators so as to exclude dust, the proportion of dextrorotatory deposits were smaller, thus in two series of experiments it was 5 to 4 and 11 to 8. It seems therefore probable that the preferential deposition of dextrorotatory material is caused by inoculation by the dust of the laboratory, or by the presence of an extremely minute excess of *a*-tartrate, which is very difficult to remove completely from the racemate. The deposit would naturally be expected to have the same sign of rotation as that of the first crystal actually formed from the solution.

A new aspect of the difficulties attending the resolution of acids and bases by the crystallisation of a salt with an active base or

¹⁴ I. Ostromisslensky, *Ber.*, 1908, **41**, 3035; *A.*, 1908, ii, 913.

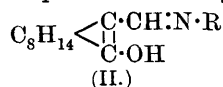
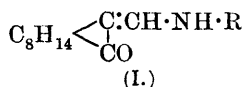
F. S. Kipping and W. J. Pope, *Trans.*, 1909, **95**, 103.

acid has been revealed by experiments that have shown that when a base can be resolved by means of an active acid this active base is not necessarily capable of resolving the *dl*-acid.¹⁶ Thus, *d*-methylhydrindamine was used to resolve *dl*-sulphobenzylethylpropylsiliclyl oxide, but the active acid does not resolve *dl*-methylhydrindamine, and the latter is not resolved by *d*-mandelic acid, whereas either the *d*- or *l*-base is capable of resolving *dl*-mandelic acid.

It is therefore clear that the mixture *dAdB* + *dAlB* does not always behave in the same way as *dAdB* + *lAdB*; one of these pairs may form a partly racemic salt, and therefore the constituents cannot be separated by crystallisation, while the other pair does not, and is therefore separable.

A new method for determining whether a primary or secondary amine is or is not externally compensated has been based on the use of oxymethylenecamphor.¹⁷

The method is identical in principle with that involving the use of an active acid chloride,¹⁸ but is more convenient, since oxymethylenecamphor is readily obtainable. This substance condenses readily with amines to form crystalline compounds of the type (I):



which can be separated into two components if the amine used is externally compensated.

The compounds derived from primary amines usually exhibit marked mutarotation, which, it is suggested, is due to the existence of the dynamic isomerides (I) and (II).

This view is supported by the following facts: first, equilibrium is reached in a few minutes in the presence of a small quantity of sodium ethoxide, and, secondly, the derivative of methylaniline shows no mutarotation.

The compounds derived from *o*- and *p*-nitroanilines do not exhibit mutarotation, whereas that of *m*-nitroaniline does; this, it is suggested, is due to the suppression of one dynamic isomeride by the strongly acidic nitro-group, which is more closely associated with the imino-group in the ortho- and para- than in the meta-derivative.

The case of *ac*-tetrahydronaphthylamine is interesting; the compound from this substance and oxymethylenecamphor appears to be homogeneous, but exhibits mutarotation. These observations can readily be explained on the same assumption as that which was adopted¹⁹ to account for the fact that this substance undergoes

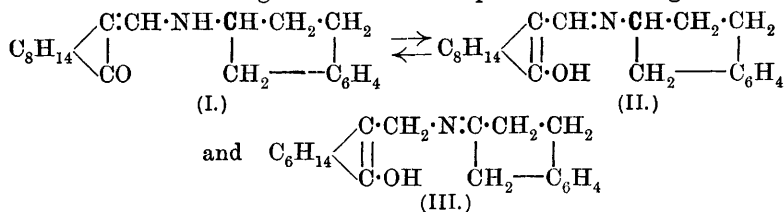
¹⁶ Kipping, *Trans.*, 1909, **95**, 408.

¹⁷ W. J. Pope and J. Read, *ibid.*, 171.

¹⁸ F. S. Kipping and A. H. Salway, *ibid.*, 1904, **85**, 438.

¹⁹ W. J. Pope and A. W. Harvey, *Trans.*, 1901, **79**, 74.

almost complete racemisation when liberated from its salts. In this case the following scheme would represent the changes:



Thus, owing to a tendency for the nitrogen to become doubly linked to the (asymmetric) carbon atom in the ring, the compound (I) is converted into two forms (II and III), of which the latter is no longer asymmetric as regards the tetrahydronaphthylamine part of the molecule, and consequently in solution the *d*-form would be readily converted into the *l*-form and vice versa, and no separation would be effected.

Several amino-acids have been resolved by the action of yeast in the presence of sugar,²⁰ and the optical antimerides of the natural substances have been thus obtained. Thus, *d*-phenylalanine, *d*-serine, *l*-phenylaminoacetic acid (impure), and α -amino- α -methylbutyric acid have been prepared.

Methylisoserine was readily resolved in the form of its benzoyl derivative by means of quinine or brucine,²¹ and the formyl derivative of α -amino-*n*-hexoic acid similarly by the use of brucine.²²

Synthetic α - and β -cincholeuponic acids have been resolved by means of brucine, and *d*- β -cincholeuponic acid, to obtain which the brucine salt of the acetyl derivative was used, is found to be identical with the acid obtained from quinine and cinchonine.²³

In spite of the fact that difficulties have been encountered so frequently in the resolution of sulphonic acids, *dl*-camphorsulphonic acid from synthetic camphor can be resolved readily by means of brucine.²⁴

Our knowledge of racemic, pseudo-racemic, and partly racemic compounds has been extended, for, in addition to the interesting work of Kipping already mentioned, the following observations are recorded.

Tetrahydroquinaldine hydrogen tartrate forms a partly racemic salt above 59°, but below this temperature the two salts are separable by crystallisation.²⁵

The melting-point curve of the *l*-menthyl *d*- and *l*-mandelates

²⁰ F. Ehrlich and A. Wendel, *Zeitsch. Ver. deut. Zuckerind.*, 1908, 198; *A.*, 1908, i, 268.

²¹ F. W. Kay, *Annalen*, 1908, 362, 325; *A.*, 1908, i, 772.

²² D. Marko, *ibid.*, 333; *A.*, 1908, i, 772.

²³ A. Wohl and R. Maag, *Ber.*, 1909, 42, 627; *A.*, i, 254.

²⁴ B. Rewald, *ibid.*, 3136; *A.*, i, 811.

²⁵ A. Ladenburg and W. Herrmann, *Ber.*, 1908, 41, 966; *A.*, 1908, i, 364.

examined in 1907²⁶ showed that a definite partly racemic compound was formed. The solubility in alcohol of *l*-menthyl *dl*-mandelate in presence of each of the *d*- and *l*-mandelates separately has now been examined at different temperatures. The curve is of the ordinary double salt type, and there is no evidence of the existence of a transition point between 35° and -15°.²⁷

Further information concerning the melting-point curves of pseudo-racemic mixtures has been acquired by the study of certain *d*- and *r*-amyl derivatives.²⁸ The melting-point curve of a pseudo-racemic mixture is usually a horizontal straight line, and this is true in the following cases: *d*- and *r*-1-amyl 3-nitrophthalates, the compounds themselves and mixtures of them melting at 116°, *d*- and *r*-2-amyl 3-nitrophthalates melting at 155°, *d*- and *r*-amyl phenylcarbamates melting at 31°, and *d*- and *r*- β -methylvaleramides melting at 126°. The melting-point curve of a pseudo-racemic mixture had been found to show a maximum in the case of the carboximes, and the first instance of a minimum has now been observed in the case of *d*- and *r*-amyl carbamates.

The problem of racemisation, especially when it occurs during chemical transformations, and the allied problem of the Walden inversion continue to attract attention, and many valuable contributions to our knowledge of the mechanism of these processes have to be noted.

It is found²⁹ that if *d*-amyl alcohol is converted into *d*-amyl bromide by means of phosphorus tribromide, the bromide obtained has $[\alpha]_D$ 4.25°, but when hydrobromic acid is used the value of $[\alpha]_D$ is only 3.68°. Therefore partial racemisation occurs during the action of hydrobromic acid. If now *d*-amyl bromide is converted into *d*-amyl acetate by the action of silver acetate at 150°, and the latter hydrolysed by means of 22 per cent. sodium hydroxide solution, the amyl alcohol obtained shows a rotation of only -1.08° in a 5 cm. tube instead of -2.29°. The racemisation has not taken place during the hydrolysis of the *d*-amyl acetate, since if this is prepared directly from the alcohol and acid and hydrolysed, the alcohol is recovered with unchanged rotation. Further, if the *d*-amyl bromide is converted into the iodide, and the latter into the acetate by the action of potassium acetate, the amyl alcohol obtained on hydrolysis has a rotatory power of -2.13°, whereas if silver acetate is used instead of potassium acetate, the alcohol obtained finally has a rotatory power of -1.53°. The racemisation therefore takes place during the action of silver acetate on the bromide, and, to a less extent, on

²⁶ *Ann. Report*, 1907, 185.

²⁷ A. Findlay and Miss E. M. Hickmans, *Trans.*, 1909, **95**, 1386.

²⁸ W. Marckwald and E. Nolda, *Ber.*, 1909, **42**, 1583; *A.*, i, 350.

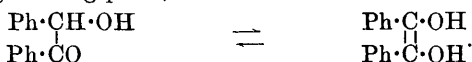
²⁹ W. Marckwald and E. Nolda, *loc. cit.*

the iodide. This case therefore closely resembles the Walden inversion.

Another case which resembles the Walden inversion was found in the action of nitrous acid or of nitrosyl bromide on active phenyl-aminoacetic acid, when inactive mandelic or phenylbromoacetic acid was produced. It is noteworthy that in this case racemisation was almost complete when the ethyl ester of the active amino-acid was used.³⁰

The study of *l*-benzoin and its derivatives has revealed a number of cases in which racemisation takes place very readily.³¹ *l*-Benzoin itself is stable in the cold, but is rapidly racemised in presence of an alkaline catalyst; its methyl and ethyl ethers show the same behaviour, the former being completely racemised in the cold by a 0.113*N*-solution of alcoholic potash in five minutes. The ethers are also racemised by heat.

The racemisation in these cases is readily explained by keto-enolic change taking place, thus:



This view is supported by independent evidence³² that benzoin can react as the enolic form.

The change of *l*-pinene into dipentene under the influence of aqueous-alcoholic sulphuric acid has been examined, and it has been shown that active terpineol and an ether are first formed; these are then converted into *l*-limonene and then finally into dipentene.³³

A similar case of almost complete racemisation was observed when synthetic active terpineols were dehydrated by the action of magnesium methyl iodide in the cold, or of anhydrous oxalic acid at 100°; the dipentene produced showed a specific rotatory power of only 5°.³⁴

The change of *l*-amygdalin into a mixture of unequal quantities of *d*- and *l*-amygdalin (the prefixes *d*- and *l*- here indicate the character of the mandelic acid obtainable from the amygdalin) has been shown to be brought about by the catalytic action of alkalis, but the change³⁵ is complicated.

A brief summary of our knowledge of the Walden inversion was given in 1907,³⁶ including the work done during that year by

³⁰ E. Fischer and O. Weichhold, *Ber.*, 1908, **41**, 1286; *A.*, 1908, i, 419.

³¹ H. Wren, *Trans.*, 1909, **95**, 1594.

³² W. N. Haworth, *ibid.*, 486.

³³ W. A. Smirnoff, *J. Russ. Phys. Chem. Soc.*, 1909, **41**, 996; *A.*, i, 942.

³⁴ K. Fisher and W. H. Perkin, jun., *Trans.*, 1908, **93**, 1871.

³⁵ J. W. Walker and V. K. Kriebel, *Trans.*, 1909, **95**, 1435.

³⁶ *Ann. Report*, 1907, 190. A more detailed historical account was given by A. McKenzie and G. W. Clough, *Trans.*, 1908, **93**, 811.

Fischer. It appeared then that the following statements were justified.

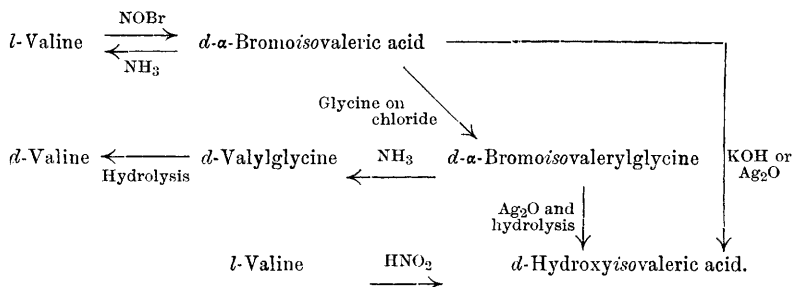
(1) The inversion is dependent on the presence of a carboxyl group attached to the asymmetric carbon atom, and does not take place when the CO_2H group has been converted into CO_2Et or $\text{CO}\cdot\text{NHR}$.

(2) Phosphorus pentachloride, ammonia, nitrous acid, and potassium hydroxide seem to be optically normal in their action, that is, they do not produce inversion, whereas silver oxide and nitrosyl bromide are optically abnormal.

Evidence was also produced showing the probability that the Walden inversion was preceded by the formation of additive compounds, and actually took place during the molecular turmoil attending the breakdown of these complexes.

Subsequent work confirms the first conclusion, but has so altered the second that it is now applicable only to phosphorus pentachloride and nitrosyl bromide.

The first of the observations which introduced disorder into an apparently orderly arrangement was made on *l*-valine,³⁷ with which the following transformations were effected:



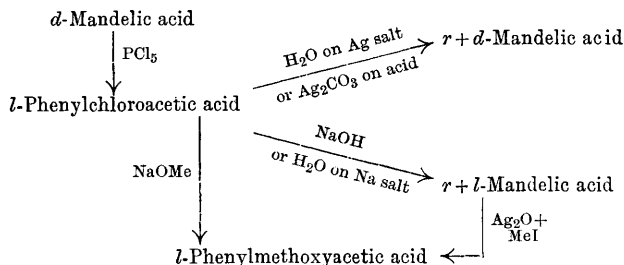
A consideration of the above series of changes shows conclusively that, in this case, ammonia and nitrosyl bromide act in the same way, and so also do potassium hydroxide and silver oxide, whereas in all cases previously examined these reagents acted differently, and, apparently, potassium hydroxide and ammonia were normal in their action while nitrosyl bromide and silver oxide were abnormal.

It seems probable that, in this case, ammonia behaves abnormally, and silver oxide normally, since the behaviour of ammonia is different while that of silver oxide is the same when the carboxyl group is protected by being converted into a $\cdot\text{CO}\cdot\text{NHR}$ group.

Nitrous acid also appears to depart from its usual habit, and to behave abnormally. It is suggested that the differences are due to the *isopropyl* group.

³⁷ E. Fischer and H. Scheibler, *Ber.*, 1908, **41**, 889, 2891; *A.*, 1908, i, 324, 857.

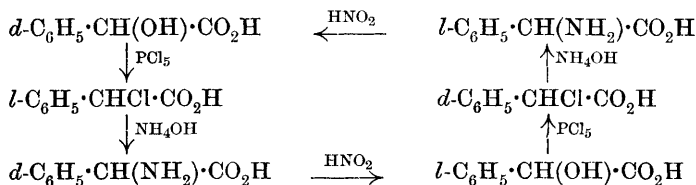
A study of the transformations of active mandelic acid and allied substances³⁸ has shown that the phenyl group also exerts a distinct influence on the course of the Walden inversion, and it certainly favours the occurrence of extensive racemisation during the changes. The following scheme summarises the first series of transformations which were studied:



The action of phosphorus pentachloride on the esters of *d*-mandelic acid yields the esters of *l*-phenylchloroacetic acid, and therefore it is highly probable that this action is optically normal. Consequently the action of silver oxide is also normal, while that of sodium hydroxide is abnormal; thus, the rule which applies in the case of derivatives of malic and propionic acids is reversed here.

It is also concluded that, of the two methylating agents used, sodium methoxide is the one which causes a Walden inversion.

Transformations effected by means of ammonia and of nitrous acid have also been studied by the same workers, and these may be summarised as follows:



As pointed out already, almost complete racemisation takes place during the action of nitrous acid on phenylaminoacetic acid, and this is also true for the action of phosphorus pentachloride and of ammonia, so that the products examined in these cases have only a very feeble rotatory power.

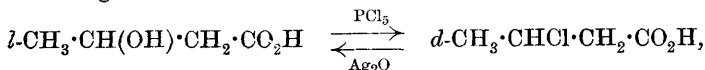
The action of nitrosyl bromide on *l*-phenylaminoacetic acid was also examined, and produced *r*+*d*-phenylbromoacetic acid.

A consideration of the above transformation of *d*- into *l*-mandelic acid shows that a Walden inversion takes place either at one of the three stages or at all three, and that nitrosyl bromide and ammonia behave in the same way. The simplest assumption to make is that

³⁸ A. McKenzie and G. W. Clough, *Trans.*, 1908, 93, 811; 1909, 95, 777.

the action of ammonia is abnormal here as it is in the case of α -bromoisovaleric acid.

No Walden inversion takes place when the asymmetric carbon atom is in the β -position with respect to the carboxyl group, since the following transformations have been effected ³⁹:



and the same result is obtained if the methyl ester is used.

The Walden inversion is therefore a complicated process, the course of which is not determined entirely by the mode of action of the reagent used, but is largely influenced by the group attached to the asymmetric carbon atom, since, for instance, the action of ammonia on a halogen acid produces inversion when a phenyl or isopropyl group is attached to the asymmetric carbon atom, and does not when a methyl group or a $\cdot\text{CH}_2\cdot\text{CO}_2\text{H}$ group is present instead.

The following conclusions, however, have been firmly established by the recent work.

(1) The Walden inversion is dependent on the presence of a carboxyl group attached to the asymmetric carbon atom, and does not take place when the carboxyl group has been converted into $\cdot\text{CO}_2\text{R}$ or $\cdot\text{CO}\cdot\text{NH}\cdot\text{R}$.

(2) The action of phosphorus pentachloride is normal, while that of nitrosyl bromide is abnormal.

A large number of new substances exhibiting optical activity have been prepared in addition to those already mentioned, but many of these must be left unmentioned. Reference has been made to the preparation of optically active terpineols ⁴⁰ and of *l*-benzoin ⁴¹ in the Annual Report for 1908. A number of derivatives of *l*-benzoin have now been prepared, including its methyl and ethyl ethers, carbanilido-*l*-benzoin, and the α -oxime; *d*-benzoin has also been prepared.⁴² The α -oxime of *l*-benzoin exhibits marked mutarotation when dissolved in acetone, acetophenone, or benzaldehyde, but the rotatory power does not change in solution in chloroform, alcohol, or ethyl benzoate. It is suggested that the great increase of rotatory power observed is due to the partial conversion of the α -oxime into the β -oxime, but this could not be isolated.

Two inactive forms of $\alpha\alpha'$ -dihydroxyadipic acid are known; under the action of heat one of these, melting at 146° , gives a dilactone; the other, melting at 174° , gives a lactone-lactide. A study of the configurations of these acids shows that the internally compensated

³⁹ E. Fischer and H. Scheibler, *Ber.*, 1909, **42**, 1219; *A.*, i, 359.

⁴⁰ *Ann. Report*, 1908, 98.

⁴¹ *Ibid.*, 109.

⁴² H. Wren, *Trans.*, 1909, **95**, 1583

(meso) form should give a lactone-lactide, and the externally compensated form should give the dilactone, and this prediction has been verified by the resolution of the isomeride, melting at 146° , into its optically active components by means of cinchonine.⁴³ The isomeride melting at 174° could not be resolved by the same method.

The two optically active forms of thiolactic acid have been isolated by reduction of the corresponding dithiodilactic acids, which were separated by means of *d*- and *l*- α -phenylethylamine.⁴⁴ The thiolactic acids exhibit a very much greater rotatory power, $[\alpha]_D \pm 45.5^{\circ}$, than the lactic acids.

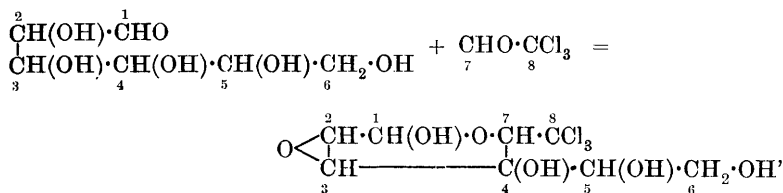
The active prolines have been separated by the crystallisation of the strychnine salts of their *m*-nitrobenzoyl derivatives.⁴⁵

Natural *l*-serine has been converted into the corresponding chloro-acid, and this, when treated with barium hydrosulphide at 100° , and the product oxidised by atmospheric oxygen in presence of ammonia, yields cystine, having $[\alpha]_D - 210^{\circ}$, while natural cystine has $[\alpha]_D - 224^{\circ}$, and the two are therefore the same, allowing for small quantities of impurity in the synthetic product.⁴⁶

It is interesting to note that the two optically active methyl hydrogen mesotartrates have been separated by the crystallisation of their strychnine salts.⁴⁷

The study of optically active reduced naphthoic acids has now been completed by the resolution of Δ^3 -dihydro-2-naphthoic acid by means of menthylamine.⁴⁸ The value of $[M]_D$ for the acid in solution in chloroform is less than that of Δ^2 -dihydro-1-naphthoic acid, but it shows a greater rotatory power than this in solution in benzene. For the purposes of comparison, phenylallylacetic acid, α -phenylvaleric acid, and β -phenyl- α -ethylpropionic acid have also been resolved by means of menthylamine.

Some interesting contributions have been made to our knowledge of the sugar group, including a new method for determining the configuration of three out of the four asymmetric carbon atoms in



⁴³ H. R. Le Sueur, *Trans.*, 1908, **93**, 716.

⁴⁴ J. M. Lovén, *J. pr. Chem.*, 1908, [ij], **78**, 63; *A.*, 1908, i, 714.

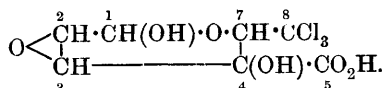
⁴⁵ E. Fischer and G. Zemplén, *Ber.*, 1909, **42**, 2989; *A.*, i, 793.

⁴⁶ E. Fischer and K. Raske, *Ber.*, 1908, **41**, 893; *A.*, 1908, i, 325.

⁴⁷ W. Marckwald and L. Karczag, *Ber.*, 1909, **42**, 1518; *A.*, i, 361.

⁴⁸ R. H. Pickard and J. Yates, *Trans.*, 1909, **95**, 1011.

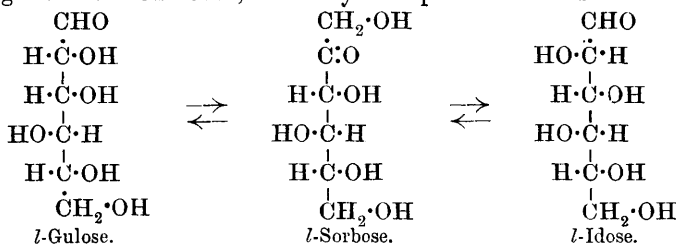
aldohexoses.⁴⁹ Sugars combine with chloral to produce compounds called chloraloses (see equation on p. 122), which on oxidation give chloralic acids of the formula:



The isomerism of the latter depends on the configuration of the three asymmetric atoms numbered 2, 3, and 4 in the original sugar. If, therefore, two sugars give the same chloralic acid, the configuration of these three carbon atoms must be the same.

It is probable, however, that difficulties would arise in the application of this method, owing to the production of two new asymmetric carbon atoms, 1 and 7, during the formation of the chloralose, and it is probable therefore that this would be a mixture in all cases, and, even if one constituent predominated to a large extent, this would not necessarily be the same from two sugars, such as dextrose and *d*-mannose.

An interesting addition has been made to our knowledge of the action of alkalis on sugars. Since dextrose and *d*-mannose are converted by the action of alkalis into lævulose, and a similar change takes place in the case of *d*-galactose, it was to be expected that *l*-gulose and *l*-idose would yield *l*-sorbose under the same treatment, and it has been shown that this change is effected by baryta.⁵⁰ The change is precisely analogous to the well-known changes mentioned above, and may be represented thus:



The four sugars, *l*-gulose, *l*-idose, *d*-talose, and *l*-ribose, have been purified by conversion into various substituted phenylhydrazones and recovering the sugars by treatment with formaldehyde or benzaldehyde. The last was obtained in a crystalline state when recovered from its *p*-bromophenylhydrazone⁵¹; it has $[\alpha]_D$ 18.8°, and shows no mutarotation.

The polyhydric alcohols, *d*-talitol⁵² and β -glucoheptitol,⁵³ have

⁴⁹ M. Hanriot, *Compt. rend.*, 1909, **148**, 487 and 640; *A.*, i, 206, 287.

⁵⁰ W. Alberda van Ekenstein and J. J. Blanksma, *Rec. trav. chim.*, 1908, **27**, 1; *A.*, 1908, i, 136.

⁵¹ *Idem.*; *Chem. Weekblad*, 1908, **5**, 577; *A.*, 1908, i, 951; *ibid.*, 1909, **6**, 373; *A.*, i, 456.

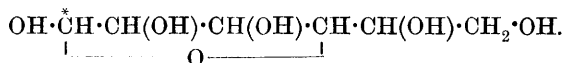
⁵² G. Bertrand and P. Bruneau, *Compt. rend.*, 1908, **146**, 482; *A.*, 1908, i, 249.

⁵³ L. H. Philippe, *ibid.*, 1908, **147**, 1481; *A.*, i, 136.

been prepared in a pure crystalline state by the reduction of *d*-talonic acid and β -glucoheptose respectively.

An interesting relation has been worked out between the rotatory powers of the two dynamic isomerides of aldoses and those of the α - and β -glucosides of the same sugar.⁵⁴

It is assumed that the two forms of a sugar are stereoisomerides on the Tollens' formula, just as the glucosides are:



Then it is found (1) that the difference between the values of $[\text{M}]_D$ of the α - and β -forms of all the aldehydic sugars, and of all their derivatives in which the terminal asymmetric carbon atom (marked *) is not affected, is a nearly constant quantity, and (2) that the sum of the values of $[\text{M}]_D$ for derivatives of the α - and β -forms, in which only the terminal carbon atom is affected, is equal to the sum of the values of $[\text{M}]_D$ for the two forms of the sugar.

If the contribution of the terminal carbon atom to the value of $[\text{M}]_D$ be represented by A, and that of the other asymmetric carbon atoms by B, then the $[\text{M}]_D$ for the α - and β -forms will be represented by $(A+B)$ and $(-A+B)$, and the difference will be $2A$, which is approximately the same for all sugars, since the other asymmetric atoms seem to have little influence on the rotatory power of the terminal carbon atom.

For the corresponding glucosides the values of $[\text{M}]_D$ would be $+A'+B$ and $-A'+B$, since the terminal carbon atom is the only one affected, and the sum ($2B$) should be the same as that for the α - and β -forms of the sugar.

The following numerical data selected from those given will show the degree of agreement obtained, which is only approximate.

The differences between the values of $[\text{M}]_D$ for α - and β -forms are as follows: Glucose, 160; galactose, 157; arabinose, 162.

The sum of the values of $[\text{M}]_D$ for α - and β -glucoses is 232.

„ „ „ „ α - „ β -methylglucosides is 243.
 „ „ „ „ α - „ β -ethylglucosides is 252.

A very large number of papers dealing with the quantitative study of optical rotatory power have appeared, and the result has been to establish still more clearly the complicated nature of the problem. Many factors must be taken into account besides the masses of the group attached to the asymmetric carbon atom, and in some cases the chemical character of a group entirely outweighs the influence of its mass. This was quite clearly shown by Betti's work in 1907,⁵⁵ and several investigations now supply further instances of a similar kind.

⁵⁴ C. S. Hudson, *J. Amer. Chem. Soc.*, 1909, **31**, 66; *A.*, i, 135.

⁵⁵ *Ann. Report*, 1907, 179.

D. A. Chardin and S. Sikorsky⁵⁶ give the details of the examination of derivatives of active amyl and hexyl alcohols undertaken with the view of determining the value of the "atomic product of asymmetry." Fairly consistent values for the atomic product for oxygen can be obtained in this way; thus, the value 129 is obtained from hexyl alcohol, and 132 from amyl alcohol, while theory requires 139. No explanation can be offered of the fact that the sign of the quantity deduced from the two alcohols is different. The values obtained for bromine are, however, much more divergent, and tend to show the limited applicability of the method.

A claim has been made⁵⁷ that the simplified expression $(a-b)(a-c)(a-d)(b-c)(b-d)(c-d)$ gives values for the asymmetry product in better agreement with the actual values of $[M]_D$ found for forty-two derivatives which were examined; but this is controverted very successfully in a later paper,⁵⁸ in which it is shown also that no "rotation equivalents" can be assigned to each group. Assuming the above expression to apply, it is shown mathematically that in a case like that of mandelic and phenylchloropropionic acids the ratio of the values of $[M]_D$ for the methyl and ethyl esters of these two acids should be the same, while the actual ratios found are 0.535 and 1.060 respectively.

Two cases are recorded in which considerable rotatory power is exhibited by compounds in which two of the groups attached to the asymmetric atom have the same weight and differ only in constitution. Thus, cyanopropylisopropylacetic acid was resolved by means of its brucine salt, and found to have $[M]_D$ 182° in toluene solution.⁵⁹ *p*-Tolylbenzylmethylallylammonium hydrogen *d*-tartrate was resolved, and the basic ion was found to exhibit a molecular rotatory power of 246°, which is considerably greater than that of the compounds containing the phenyl and *p*-bromophenyl group in place of the *p*-tolyl group.⁶⁰

A number of papers deal with the influence of unsaturation on rotatory power, but, although it is found that the introduction of an ethylene linking usually increases the value of the rotatory power, this is by no means always the case.

The results obtained with bornyl, menthyl, and amyl esters of phenylpropionic, cinnamic, and phenylpropionic acids are discussed,⁶¹ but no general conclusion can be deduced from them, and it is clear that the influence of unsaturation is in many cases small.

⁵⁵ *J. Russ. Phys. Chem. Soc.*, 1908, **40**, 592; *A.*, 1908, ii, 548; *J. Chim. Phys.*, 1908, **6**, 179 and 584; *A.*, 1908, ii, 470 and 912.

⁵⁷ E. Bose and F. A. Willers, *Zeitsch. physikal. Chem.*, 1909, **65**, 702; *A.*, ii, 361.

⁵⁸ J. W. Walker, *J. Physical Chem.*, 1909, **13**, 574; *A.*, ii, 846.

⁵⁹ E. Fischer and E. Flatau, *Sitzungsber. K. Akad. Wiss. Berlin*, 1909, 876; *A.*, i, 628.

⁶⁰ R. W. Everatt and H. O. Jones, *Trans.*, 1908, **93**, 1789.

⁶¹ T. P. Hilditch, *Trans.*, 1908, **93**, i.

The menthyl esters and brucine salts of a series of nine saturated dibasic acids have also been examined, and here also the influence of constitution is not very marked. In the case of the esters, the rotation of the oxalate is the greatest (-378°), and that of the adipate is next in order of magnitude (-352°), while that of the sebacate is least, 319° . The results with the salts are almost parallel, with the exception of the oxalate, which has the smallest rotatory power.⁶²

The influence of contiguous, unsaturated groups on optical activity is discussed⁶³ and examined in the case of some aromatic esters and salts of camphoric and β -camphorsulphonic acids, and the conclusion is drawn that contiguity of unsaturated groups produces abnormal effects on the optical rotatory power. In both the last-mentioned cases, the original papers should be consulted, since an adequate account of this work cannot be given here.

An account has appeared of an extensive investigation⁶⁴ of the effect of replacing a methyl group or hydrogen atom in an acid by a phenyl group on the rotatory power of the menthyl esters, and the following conclusions are drawn from the results.

(1) The replacement of a methyl group by a phenyl group is usually accompanied by a decrease of rotatory power, as, for example, menthyl crotonate has $[\alpha]_D^{20} -91^\circ$, while menthyl cinnamate has $[\alpha]_D^{20} 77^\circ$

This conclusion does not appear to be justified from the data given, since the values of molecular rotatory power should be compared; these are 204° and 220° respectively. Further, this conclusion is not in agreement with the results obtained with many other compounds, or with those on substituted bornylamines mentioned later, and it is not borne out by the results quoted below.

(2) The assemblage of electronegative (phenyl) groups near the asymmetric system decreases the rotatory power; thus, menthyl β -phenylcinnamate has $[M]_D -137^\circ$, and menthyl α -phenylcinnamate $[M]_D -193^\circ$, compared with 220° for menthyl cinnamate.

(3) The influence of the phenyl group increases as it becomes more distant from the asymmetric system. A comparison of the following three pairs of substances does not, however, appear to bear out this conclusion:

	$[M]_D^{20^\circ}$.	Difference.
Menthyl propionate	-160°	
„ phenylacetate	191	$+31^\circ$
„ butyrate	160	
„ β -phenylpropionate.....	169	$+9$
„ hexoate	165	
„ δ -phenylvalerate	107	-58

A number of acyl-bornylamines have been prepared and their

⁶² T. P. Hilditch, *Trans.*, 1909, **95**, 1578. ⁶³ T. P. Hilditch, *Ibid.*, 331.

⁶⁴ H. Rupe, *Annalen*, 1909, **369**, 311; *A.*, i, 927.

rotatory powers examined⁶⁵ in solution in methyl and ethyl alcohols, in glacial acetic acid, and in pyridine. The compounds now examined, taken in conjunction with the alkylbornylamines examined by Forster,⁶⁶ enable an interesting comparison to be made.

The introduction of an alkyl group into bornylamine increases the dextrorotatory power very considerably, but the difference between the rotatory powers of the various alkyl compounds is not very striking. All the acyl compounds, on the other hand, are levorotatory. The aliphatic acyl derivatives have very different rotatory powers in the different solvents, the order of magnitude being ethyl alcohol, methyl alcohol, acetic acid, pyridine, but the influence of pyridine on the rotatory power of formobornylamide is apparently abnormal. In the aliphatic acyl series, a maximum is found either at the acetyl or the propionyl member in the different solvents.

The members of the aromatic acyl series of compounds are also levorotatory, except in certain cases in pyridine solution, when the compounds become dextrorotatory. The nitrobenzobornylamides are more strongly levorotatory than the toluobornylamides, and the relation between the rotatory powers of the ortho-, meta- and para-compounds is, in some cases, in agreement with theoretical predictions. The original paper should be consulted for the detailed discussion of the results.

The study of certain derivatives of camphorquinone⁶⁷ has led to the production of substances of enormous rotatory power, and to interesting results showing the great influence of unsaturation and of chemical character of the groups present on rotatory power.

Camphorquinone condenses readily with aromatic amines to give compounds of the type $C_8H_{14} \begin{smallmatrix} \diagup C:N \cdot R \\ \diagdown CO \end{smallmatrix}$, and with diamines to give compounds containing two camphorquinone residues.

The results obtained by a study of the rotatory powers of the compounds in pyridine or chloroform solutions bring out the following principles illustrated by the compounds the formulæ and molecular rotatory powers of which are given below.

A conjugated double bond (*a*) acting alone produces a small increase in rotatory power; (*b*) while in co-operation with a benzene ring its influence is greatly increased.

(*a*) is illustrated by a comparison of the rotatory powers of 1 and 2, and of 5 and 6, while (*b*) is illustrated in the same way by comparing the difference between 1 and 2 with that between 3 and 4, and the difference between 5 and 6 with that between 7 and 8.

⁶⁵ P. F. Frankland and F. Barrow, *Trans.*, 1909, **95**, 2017 and 2026.

⁶⁶ *Trans.*, 1899, **75**, 934.

⁶⁷ M. O. Forster and T. Thornley, *ibid.*, 1909, **95**, 942.



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cases there is a maximum of rotatory power in the green, while there is a minimum in the last case.

The coloured xanthates and xanthogenides of menthol and borneol have also been shown to exhibit anomalous rotatory dispersion in the neighbourhood of their absorption bands.⁷⁰

The investigation of the rotatory power of ethyl tartrate in different solvents has been considerably extended by Patterson and his colleagues.

The rotation in fatty halogen derivatives⁷¹ and in aromatic halogen derivatives⁷² has been examined without any very striking results, but the study of aromatic nitro-derivatives⁷³ has yielded the most remarkable results yet obtained. The specific rotatory power of ethyl tartrate in α -nitronaphthalene at infinite dilution is $+65^\circ$, while in *s*-trinitrobenzene under the same conditions it is -30° , thus surpassing both the upper and the lower limits previously observed, in formamide $+30.4^\circ$, and in ethylene dibromide -19° . The dependence of rotatory power on temperature was also investigated, and it has been found that in one solvent the temperature at which a maximum rotatory power occurs is apparently independent of the concentration. A relationship has been established between the maximum rotatory power and the temperature at which it occurs, which relationship appears to be independent of the nature of the solvent and of the concentration. The *l*-v-rotatory power of ethyl tartrate in acetylene tetrabromide decreases very rapidly with increasing temperature, until above 80° the solution becomes dextrorotatory.

Quinoline and benzaldehyde have also been added to the list of solvents examined.⁷⁴ Solutions of ethyl tartrate in the former show a very marked maximum of specific rotatory power of 29° , when the concentration is represented by 44 per cent. of ethyl tartrate, which roughly corresponds with two molecular proportions of quinoline to one of ethyl tartrate. It must, however, be noted that the concentration at which the rotatory power is a maximum is not the same at different temperatures.

The influence of mixed solvents on the rotatory power of ethyl tartrate has also been examined,⁷⁵ the solvents chosen, ethylene dibromide and nitrobenzene, having widely different effects on the rotatory power of the solute, ethyl tartrate, and also very different densities. The influence of each solvent on the rotatory power was

⁷⁰ L. Tschugaeff, *Ber.*, 1909, **42**, 2244; *A.*, ii, 631.

⁷¹ T. S. Patterson and D. Thomson, *Trans.*, 1908, **93**, 355.

⁷² T. S. Patterson and D. P. McDonald, *ibid.*, 936.

⁷³ T. S. Patterson, *ibid.*, 1836.

⁷⁴ T. S. Patterson and D. P. McDonald, *Trans.*, 1909, **95**, 321.

⁷⁵ T. S. Patterson and H. H. Montgomerie, *ibid.*, 1128.

found to be proportional to its volume, and it was possible to calculate the rotatory power of the solutions from their compositions and the known influence of each solvent separately on the rotatory power of the solute.

The method of applying the change in the rotatory power which ethyl tartrate undergoes in different solvents to the investigation of intramolecular change in inactive substances mentioned in 1907⁷⁶ has now been further extended.⁷⁷ The change of piperonal*syn*-oxime, anissynaldoxime, and *ω*-isonitrotoluene into their dynamic isomerides has been studied, and it has been found that the rate at which these changes proceed is an exceedingly sensitive test for the purity of the ethyl tartrate. The change of ammonium thiocyanate and ammonium cyanate did not seem to proceed so regularly as the others. It is possible that this may be due to interaction of the ethyl tartrate with these substances.

Whether we shall ever be able to unravel the complicated problems of the relation between rotatory power and chemical constitution and of the influence of solvents on rotatory power is doubtful at present; but it is clear from what has been said above that much more experimental work will be required before we can even fix upon the data which are to serve as a basis for theoretical discussion, since, if phenomena like those already mentioned are exhibited, it is useless to attempt to discover general laws or to found a theory on the results obtained with light of one wavelength until it has been proved that anomalous rotatory dispersion is not exhibited by the substances or solutions under examination.

The most important contributions to our knowledge of optical activity of silicon and nitrogen compounds have already been mentioned in 1908,⁷⁸ so that a brief reference must suffice here.

A second asymmetric silicon compound, of the same type as the first resolved in 1907, has now been resolved.⁷⁹ This compound, *dl*-sulphobenzylethylisobutylsilicyl oxide, was again resolved by the use of methylhydrindamine, and the two *d*- and *l*-sodium salts were found to have specific rotatory powers of $\pm 10.5^\circ$, which is nearly twice as great as that shown by the corresponding compound containing the propyl instead of the isobutyl group. The differences between salts of *l*-menthylamine, of bornylamine, or of cinchonine with the two acids are again very slight.

No compound containing a single asymmetric silicon atom has yet been resolved, although in the case of *dl*-benzylethylpropylisobutylsilicanesulphonic acid indications were observed that resolution was

⁷⁶ *Ann. Report*, 1907, 184.

⁷⁷ T. S. Patterson and A. McMillan, *Trans.*, 1908, **93**, 1041.

⁷⁸ *Ann. Report*, 1908, 108, 109, 175.

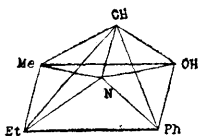
⁷⁹ F. S. Kipping and B. D. W. Luff, *Trans.*, 1908, **93**, 2090.

being effected by crystallisation of the cinchonine hydrogen salt, which gave two fractions of specific rotatory power, $+57.1^\circ$ and $+73.8^\circ$, and this observation is being pursued.⁸⁰

A new type of nitrogen compound exhibiting optical activity has been found in methylethylaniline oxide.⁸¹ The *d*-bromocamphorsulphonate of this base was resolved, and from the solution of the less soluble, *dA/B*, salt the picrate was precipitated and converted into the chloride by treatment with hydrochloric acid. The chloride, $\text{NMeEtPhCl}\cdot\text{OH}$, has $[\text{M}]_D -41^\circ$, and on treatment of the solution of this chloride with baryta the rotatory power falls to -25° (but no racemisation has occurred since the rotatory power rises again to -41° on the addition of hydrochloric acid). This solution, it is assumed, contains the free base, probably $\text{NMeEtPh}(\text{OH})_2$, which contains a nitrogen atom with only four of the five groups actually different.

There is, however, a difference in character between the two hydroxyl groups, since only one of them behaves as a basic hydroxyl group and is replaceable by an acid radicle.

It is easy to account for the occurrence of optical activity in this compound with the aid of the pyramidal configuration for the nitrogen atom, since if one of the hydroxyl groups is situated at the base of the pyramid and the other at the apex, the arrangement



shown in the figure is obtained, is devoid of a plane of symmetry and therefore capable of giving rise to optical activity.

An optically active compound containing two nitrogen atoms, one of which is asymmetric, $\text{C}_7\text{H}_7\cdot\text{NMePhBr}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{NMePh}$, has been resolved⁸² by crystallisation of the *d*-camphorsulphonate and of the *d*-bromocamphorsulphonate, the salt of the *l*-base is much less soluble than that of the *d*-base in the first case, while the reverse is true for the bromocamphorsulphonate.

The iodide of the *l*-base has $[\text{M}]_D -411.5^\circ$, and that of the *d*-base has $+403.2^\circ$ in alcohol. Autoracemisation takes place in solution in chloroform and in alcohol, but takes place much more rapidly in the former case than in the latter.

⁸⁰ F. S. Kipping and H. Davies, *Trans.*, 1909, **95**, 69.

⁸¹ J. Meisenheimer, *Ber.*, 1908, **41**, 3966; *A.*, i, 20.

⁸² E. Wedekind and W. Meyer, *ibid.*, 1909, **42**, 308; *A.*, i, 186.

Further instances are recorded of the formation of two compounds, when an asymmetric nitrogen atom is produced in a compound already containing an asymmetric carbon atom.

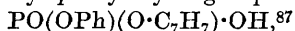
Thus *l*-menthyl iodoacetate combines with *N*-ethyltetrahydroisoquinoline to give two salts, having $[\alpha]_D -44.9^\circ$ and -17.54° respectively. These give betaines, which become inactive very quickly.⁸³ Similar results have also been obtained with *N*-*n*-propyltetrahydroisoquinoline.⁸⁴

It has also been shown that the addition of an alkyl haloid to an active *N*-alkylated coniine or conhydrine and to 2-phenyl-6-methylpiperidine results in the formation of two stereoisomeric quaternary ammonium salts, but that active alkaloids, coniine excepted, yield only one. Such stereoisomerides were obtained only from piperidine derivatives having a heavy substituent in position 2, and it is concluded that this is necessary in order to give the requisite stability to the group attached to the nitrogen atom.

This view is confirmed by obtaining the active *N*-ethyl- α - and β -pipecolines and forming their additive compounds with benzyl bromide or iodide; from these no isomerides could be separated. Similarly, the additive compound of active amyl iodide and 1-methyl-2-pipecoline seemed to be homogeneous. Therefore a methyl or ethyl group attached to the nitrogen atom and a methyl group in position 2 does not seem to confer the requisite stability on the compound.⁸⁵

This conclusion, however, is not necessary, since it is quite possible, as in the case of the cyanohydrin of mannose, that one of the two possible compounds is formed in very small quantities, and so might be entirely overlooked even after very careful examination had been made. Further, a methyl group was found adequate in the first case of this kind examined, namely, the addition of alkyl iodides to methyl-*d*-amylaniline, in which case two well-characterised isomerides are produced.⁸⁶

In the study of phenyl *p*-tolyl hydrogen phosphate,



some indication has been found that asymmetric derivatives of phosphorus can be resolved into their optically active constituents. The salts of this acid, with eight optically active bases, were examined without any indication being obtained that these salts were mixtures; the melting points and specific rotatory powers of the most and least soluble fractions were in each case found to be

⁸³ E. Wedekind and O. Wedekind, *Ber.*, 1908, **41**, 456; *A.*, 1908, i, 258.

⁸⁴ E. Wedekind and F. Ney, *ibid.*, 1909, **42**, 2138; *A.*, i, 514.

⁸⁵ M. Scholtz, *ibid.*, 1908, **41**, 2005; *A.*, 1908, i, 678.

⁸⁶ H. O. Jones, *Trans.*, 1905, **87**, 135.

⁸⁷ F. S. Kipping and B. D. W. Luff, *ibid.*, 1909, **95**, 1993.

identical. Slight indications that the acid was a mixture were obtained from an examination of the salt with *dl*-hydrindamine, but more definite evidence was obtained when the *d*-hydrindamide was examined. This was separated by fractional crystallisation into two fractions, the less soluble melting at 127° and having $[\alpha]_D -17.4^\circ$, while the more soluble melts at 82—88° and has $[\alpha]_D -21.2^\circ$. Similar results were obtained with the *l*-menthylamide. This investigation is being continued, and it seems probable that phosphorus will soon be added to the list of elements which are capable of giving rise to optical activity.

The problem of the isomerism of the cinnamic acids still continues to attract considerable attention, and although several interesting contributions to this subject have appeared, the problem is still far from a satisfactory solution.

It is suggested⁸⁸ that *allocinnamic* acid and the two *isocinnamic* acids are polymorphs. At 105° all three acids are converted into the acid, melting at 42°, and this, when inoculated with the *iso*-cinnamic acid, melting at 58°, or with *allocinnamic* acid, immediately crystallises as a mass of the inoculating acid.

This view is, however, not accepted by E. Erlenmeyer, jun.,⁸⁹ and it has also been shown that a specimen of the *iso*-acid, melting at 58°, was unchanged after keeping for ten or fifteen years in the dark.⁹⁰

A further complication has now been introduced into the problem by the discovery that synthetic cinnamic acid is not a homogeneous substance.⁹¹ By means of fractional crystallisation of the acid, or better by fractional distillation of the ethyl ester, a new acid has been isolated which melts at 128°, has the same molecular formula as cinnamic acid, and therefore is stated to be a new isomeride and is called α -heterocinnamic acid. An amorphous form of this acid is obtained by saponification of the ethyl ester with cold alcoholic potash; this also melts at 128°, but differs from the α -acid in solubility; it is called hetero- β -cinnamic acid, and can be converted into hetero- α -cinnamic acid by repeatedly dissolving it in light petroleum.

It is clear that before the problem of the isomerism of the cinnamic acids can be solved, a careful investigation of the properties of mixtures of the ordinary and *allocinnamic* acids, such as melting point, solubility, and crystalline form, must be carried out. There is at present little or no information on any of these points, and no evidence that the supposed isomerides are not mixed

⁸⁸ E. Biilmann, *Ber.*, 1909, **42**, 182; *A.*, i, 155.

⁸⁹ *Ber.*, 1909, **42**, 521; *A.*, i, 155.

⁹⁰ C. Liebermann, *ibid.*, 1027; *A.*, i, 303.

⁹¹ E. Erlenmeyer, *ibid.*, 502 and 513; *A.*, i, 156.

crystals or even definite molecular compounds, similar to the compound of triphenylmethane and benzene or even to quinhydrone, which may yet give normal values for molecular weight owing to decomposition in solution.

A very large number of isomeric oximes are known, and for the existence of isomeric ketoximes no explanation has been offered except that of stereoisomerism suggested by Hantzsch and Werner. The existence of isomeric aldoximes can be explained on structural grounds, but the existence of isomeric oxygen ethers, such as $C_6H_5 \cdot CH : N \cdot O \cdot C_7H_7$, is definite evidence in favour of the hypothesis of stereoisomerism, although the *N*-substituted aldoximes, $C_6H_5 \cdot CH - N \cdot CH_3$, are very probably derived from the structural

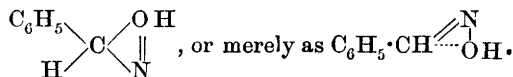


isomeride. Now, although about one hundred and forty of these *N*-substituted aldoximes are known, there is no indication of the existence of isomerides in any but two cases, the methyl derivatives of benzaldoxime and anisaldoxime. These cases have now been re-examined,⁹² and it has been shown in both cases that the supposed isomerides are monohydrated forms of the ordinary *N*-methyl compounds. Consequently, in the case of benzaldoxime, for example, there exist the two oximes, two oxygen ethers (for example, benzyl), and one nitrogen ether.

An examination of the behaviour of the isomeric forms of the oximes of benzaldehyde, of the three nitrobenzaldehydes, and of *p*-triazobenzaldehyde towards diazomethane has shown that the *anti*-aldoximes yield varying amounts, from 6 to 50 per cent., of *O*-methyl ethers, whereas the *syn*-compounds, with one exception, are unchanged.⁹³

The authors are led, therefore, to accept the stereochemical explanation of the isomerism of oximes, although it does not offer a ready explanation of the difference in the behaviour of the *syn*- and *anti*-forms, and suggest a modification of the Hantzsch-Werner hypothesis to account for the stability of the two isomerides.

The view proposed assumes that the carbon atom, doubly linked to the nitrogen atom, exerts some attractive force on the oxygen atom of the hydroxyl group, thus using to some extent the residual valency of the latter. This is represented diagrammatically either as:



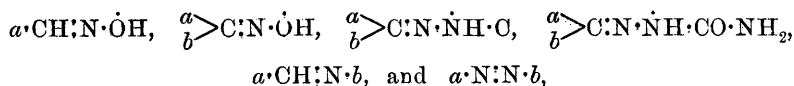
The first method of representation makes the carbon atom

⁹² J. Scheiber, *Annalen*, 1909, **365**, 215; *A.*, i, 391.

⁹³ M. O. Forster and F. P. Dunn, *Trans.*, 1909, **95**, 425.

asymmetric, and is therefore improbable. The second may be regarded favourably on further investigation, since it does in some measure remove the difficulty of accounting for the comparative stability of the two forms.

This view receives support from the fact that among the six types of doubly linked nitrogen compounds:



isomerism has been definitely established in the case of the first four only, and in these the atom, marked with a dot, attached to the nitrogen on the side remote from the double linking is possessed of residual or supplemental valency. It is clear that, in the near future, interesting developments are to be expected in connexion with the Hantzsch-Werner hypothesis of the stereoisomerism of oximes.

H. O. JONES.