LXXX.—*Isomeric Partially Racemic Salts containing Quinquevalent Nitrogen. Parts I—VI. Hydrindamine Bromocamphorsulphonates, Chlorocamphorsulphonates, and cis- π -Camphanates.*

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THIS paper contains an account of the preparation and investigation of three pairs of isomeric partially racemic salts, the isomerism of which is apparently of a kind different from any yet recorded.

All these salts have been obtained from α -hydrindamine,* a primary base easily prepared by reducing α -hydrindoxime (compare Revis and Kipping, Trans., 1897, 71, 250).

Hydrindamine contains an asymmetric carbon group, as will be seen from its formula,

and the synthetical base is therefore composed of equal quantities of enantiomorphous components.

When this base is combined with various optically active acids, it shows an altogether unusual behaviour, giving in some cases what appears to be a homogeneous partially racemic salt, in others a mixture of unequal quantities of two isomeric salts; the latter are not the ordinary isomerides which are obtained from most externally compensated bases under such conditions, that is to say, they do not represent salts of the separate enantiomorphously related components of the base, but are both comparable to partially racemic substances.

The results of the examination of these remarkable isomerides may be briefly summarised as follows.

Hydrindamine and α -bromocamphorsulphonic acid unite to form *unequal* quantities of two hydrated salts, which contain different quantities of water of crystallisation; the anhydrous salts both have the molecular formula $C_9H_{11}N, C_{10}H_{14}BrO \cdot SO_3H$. The more sparingly soluble " α -salt" separates from water in opaque, bulky masses of minute needles, whereas the more readily soluble " β -salt" crystallises in well-defined, transparent prisms, absolutely different in appearance

* The letter α - which is used here to distinguish this base from β -hydrindamine is not employed again, as to do so might cause confusion with the α -salts, which are described later.

from the crystals of its isomeride. The two salts have different specific rotations.

Hydrindamine and α -chlorocamphorsulphonic acid unite to form unequal quantities of two isomeric salts which are respectively analogous to those of the bromo-acid; the more sparingly soluble α -salt is isomeric with the corresponding bromo-salt, from which it cannot be distinguished by inspection. The β -chloro-salt bears a close relationship to the β -bromo salt, but differs from the latter in at least one important respect; when crystallised from water, it is deposited either in what may be termed the normal form of transparent, well-defined prisms, closely resembling, and doubtless isomeric with, the crystals of the β -bromo-salt, or it is obtained in opaque masses indistinguishable by inspection from those of the α -chloro-salt; these two varieties, so different in appearance, both represent β -salt, and although convertible one into the other by crystallisation, undergo this change in a rather bewildering manner, and under conditions which have not yet been established. The conversion of either of these α -salts (bromo- or chloro-) into the corresponding β -salt, or *vice versa*, by crystallisation only, has never been observed. The specific rotations of the α - and β -chloro-salts are practically the same in dilute aqueous or alcoholic solution, but different in other solvents.

Hydrindamine and *cis*- π -camphanic acid (Kipping, Trans., 1896, 69, 913) give apparently unequal quantities of two isomeric anhydrous salts of the composition $C_9H_{11}N, C_{10}H_{14}O_4$, which are indistinguishable in appearance, but differ in melting point and other properties; the more sparingly soluble α -salt melts at about 193° , the β -isomeride at about 173° , and the two compounds seem to be partially, but slowly, converted one into the other in aqueous solution. The two isomerides have widely different specific rotations in methyl alcoholic solution, but in dilute aqueous solution they give practically the same value; the α -salt shows mutarotation in a very marked manner, but apparently the β -salt does not.

The question now to be discussed is, how to account for the existence of these isomerides. In doing so, it will be convenient to take a particular case, such as that of the hydrindamine bromocamphorsulphonates, with which most of the experiments have been made, the behaviour of the other salts being considered only when there is some important difference to note.

The most natural conclusion, namely, that the externally compensated base is resolved into its enantiomorphous components by fractional crystallisation of its salts with these optically active acids, will first be examined, and, as evidence against this view, the fact that the isomerides are obtained in very unequal quantities may first be quoted. Further, the base regenerated from the α -salt is optically inactive, and

is identical in this, and in every respect, with the base regenerated from the β -salt, and also with externally compensated hydrindamine prepared directly from hydrindoxime ; this is proved by the fact that the salts obtained by combining the regenerated bases with optically inactive or active substances are identical. It may therefore be concluded, provisionally, at any rate, that the externally compensated base has not been resolved into its enantiomorphous components.

Granting this to be so, the formation of the isomerides might be explained by assuming that the salts of the sulphonic acids are merely differently hydrated varieties of one substance ; this is not the case, however, because these salts are not convertible one into the other by crystallisation, they have different specific rotations in aqueous solution, and the anhydrous compounds have different melting points ; moreover, such an assumption would not explain the existence of the isomeric anhydrous *cis*- π -camphanates. For similar reasons, the isomerides cannot be regarded as different crystallographic forms of one individual compound.

The view that the β -salts of the sulphonic acids are derived from an acid physically or chemically isomeric with the acid of the α -salt might next be adopted, especially as these β -salts are formed in comparatively small quantities ; it is shown, however, that the acid regenerated from the β -salt is identical with that of the α -salt ; also that the behaviour of the salts themselves towards ferric chloride, phenyl isocyanate, piperidine, &c., is such as to practically exclude the possibility of the existence in the β -salt of a tautomeric form of the acid which might change when liberated from the base : the existence of the isomeric *cis*- π -camphanates, and many other facts, show that the isomerism is not due to the acid ion of the salts ; further, the β -salt of any one of the acids is converted into the α -salt on repeatedly evaporating it with small quantities of externally compensated hydrindamine.

As these facts seem to prove that the isomerism is due to the hydrindamine, and as the base obtained from the α -salt is nevertheless identical with that regenerated from the β -salt, it might be assumed that the α - and β -isomerides are actually the salts of enantiomorphously related bases, but that the latter undergo rapid racemisation at ordinary temperatures when liberated from the acid. That this explanation will not suffice is proved (*a*) by the fact that the salts are obtained in unequal quantities, (*b*) by the fact that the *cis*- π -camphanates afford optically inactive hydrindamine hydrochloride when decomposed directly with hydrochloric acid, and (*c*) by the values obtained for the molecular rotations of the salts in dilute aqueous solution. These three facts may be discussed a little, as they are all of considerable importance.

With regard to (*a*), it is quite possible that an externally com-

pensated base might yield unequal quantities of the salts of its enantiomorphous components provided that the one salt were convertible into the other during crystallisation as in the case recently recorded by Pope and Peachey (Proc., 1900, 16, 116); but the isomeric hydrindamine bromo- and chloro-camphorsulphonates are not thus convertible one into the other; they may be repeatedly recrystallised from water or other solvents without undergoing change. In order to account for the formation of unequal quantities of the α - and β -isomerides on the assumption that they contain enantiomorphously related basic components, it would be necessary to assume further that the one enantiomorphous base is transformed into the other in aqueous solution before it combines with the acid; manifestly, this view cannot be adopted.

The fact (*b*) that either of the *cis*- π -camphanates, when directly treated with hydrochloric acid, gives an optically inactive hydrindamine hydrochloride is of importance from its bearing on this question. Admitting the ionic dissociation hypothesis, it must be concluded that the base ions of any one of the sulphonic salts, if optically active, are incapable of racemisation, as the isomerides are not mutually convertible in very dilute aqueous solution; consequently, it seems very improbable that racemisation could occur in the direct conversion of one of the *cis*- π -camphanates into the hydrochloride, a reaction which may be regarded as a mere interchange of ions.

The fact (*c*) that the values of the molecular rotations of the salts exclude the assumption that the isomerides contain enantiomorphously related bases will be obvious from the following considerations.

The molecular rotation of bromocamphorsulphonic acid in aqueous solution is approximately $[M]_D + 270$, a value which has been established by numerous observations by Kipping and Pope (Trans., 1893, 63, 548), Walden (*Zeit. physikal. Chem.*, 1894, 15, 196), and also by some made for the purposes of this paper; this value seems to be practically independent—as it should be—of the nature of the base with which the acid may be combined, salts such as potassium, ammonium, morphine, and phenylparatolyliodonium bromocamphorsulphonates giving almost identical molecular rotations.

Now the molecular rotations of the α - and β -bromocamphorsulphonates are $[M]_D + 268$ and $+220$ respectively, both being determined in approximately 1 per cent. aqueous solution; the former then is normal on the assumption that the base is optically inactive and that ionic dissociation is sufficiently complete to give the true value of the acid ion; the latter, however, is about 19 per cent. too low,—more than can be attributed to experimental error.

To account for this abnormal value, it might be suggested (1) that the salt contains *l*-hydrindamine, (2) that the β -salt contains optically

inactive base, but gives an acid ion which is not that of ordinary bromocamphorsulphonic acid, (3) that the salt is not sufficiently dissociated. The first view is untenable, because it would necessitate the further assumption that some of the *d*-hydrindamine of the externally compensated base passes into the *l*-isomeride before the base combines with the acid; also because the β -salt of the chloro-acid, which is doubtless very closely analogous to this β -bromo-salt, gives a practically normal molecular rotation—or, if not, a value which indicates the presence of a *dextro*rotatory base; also because the molecular rotations of the isomeric *cis*- π -camphanates are both apparently normal on the assumption that they both contain optically inactive base.

The second possible explanation of the abnormal molecular rotation of the β -bromo-salt, namely, that this compound contains an isomeric bromocamphorsulphonic acid, has been shown to be untenable, and is further disproved by the arguments just advanced.

The third possible view is not contrary to any direct evidence, and may therefore be accepted for the present.

Reviewing the whole of the experimental evidence, it seems to be proved that the isomeric compounds in question do not represent salts of the enantiomorphously related bases, but that they all contain optically inactive, externally compensated hydrindamine.

How, then, can the existence of such isomerides be accounted for?

To assume that there are two isomeric optically inactive hydrindamines is out of the question, since the base of the α -salt is identical with that of the β -isomeride; further, the base regenerated from the α -salt gives *both* isomerides when it is again neutralised with the acid.

To assume that hydrindamine does not contain an asymmetric carbon group, and has not the constitution assigned to it, leaves the matter just where it was; moreover, the method of formation of the base, its conversion into trimethylhydrindamine iodide (Kipping and Hall, this vol., p. 467), and the decomposition of the last-named substance into indene and trimethylamine hydriodide (*loc. cit.*), are facts of such importance that there can be no hesitation in accepting the constitutional formula which has been assigned to the base above.

Since, then, it must be admitted that the isomerides are formed by the combination of one and the same externally compensated base with one and the same acid, their isomerism must be ascribed to a difference in configuration caused by the union of their identical components in different ways; further, since the isomerides are essentially different not only in the crystalline state, but also in solution, the difference in configuration must extend to their chemical molecules.

An explanation which at one time suggested itself was, that the

two salts were comparable to ordinary stereoisomerides. Although the nitrogen atom is only singly linked to carbon, it seemed possible that stereoisomeric forms might exist, in consequence of the great size of the acid molecule, which, by colliding with the hydrindamine ring in various directions, might limit the rotation of the nitrogen atom; since, however, the salts do not immediately change one into the other in dilute aqueous solution, when, owing to ionic dissociation, the acid ion is no longer united to the nitrogen atom, this view of their isomerism had to be abandoned.

Now, there seems to be no doubt that the isomerides are both ordinary salts, formed by the mere addition of the ions of the acid to the base; in this process, according to the usually accepted view, the two acid ions become directly united to the tervalent nitrogen atom, which then becomes quinquevalent. Two questions therefore suggest themselves in connection with this process: firstly, are the two affinities or valencies of the nitrogen atom which are concerned in such an union identically, or differently, situated with regard to the other three (which are generally regarded as arranged symmetrically in one plane)? Secondly, does the negative ion of the acid necessarily combine with or take up one particular nitrogen valency, or may it occupy either of the two which may be concerned?

From the results of work which has been done in connection with the stereochemistry of nitrogen, definite answers to these questions cannot yet be drawn; there certainly seems to be a considerable difference of opinion in regard to the first question—which would probably determine the second,—and in any case the experimental evidence admits of no conclusive interpretation. Under these circumstances, judging by analogy with carbon—if it be permissible to do so—it seems probable that when a symmetrical primary, secondary, or tertiary base combines with an optically inactive acid or halogen alkyl compound, the ions or groups do not attach themselves to one particular nitrogen valency, but are equally distributed between two.

If this view be adopted, it will be obvious that the nitrogen atom of a base in which there is an asymmetric carbon group may show a behaviour altogether different from that of the nitrogen atom of a symmetrical compound; for, whereas in the latter case combination would naturally give rise to *equal* quantities of isomerides which may be represented by

the former would probably give *unequal* quantities of the two isomerides

because of the enantiomorphous carbon group, with respect to which X and Y cannot be identically situated.

In the case of the combination of hydrogen cyanide with an aldehyde, for example, direct addition to the group $\text{X}\cdot\text{CHO}$ takes place, and whether the forms

are produced in equal or unequal quantities depends entirely on the configuration of the part X; if this be symmetrical, equal quantities of enantiomorphously related groups are formed, but if it be asymmetrical, unequal quantities of new enantiomorphous groups are produced, and two different substances result, until possibly in extreme cases the influence of X may be sufficient to ensure the formation of only one kind of new asymmetric group.

Now, in the case of the hydroxycyanides formulated above, it is known that the two forms are enantiomorphously related so long as X is not enantiomorphous; but in the case of the supposed isomerides of the symmetrical base, it is not possible to say whether this would be so or not until it is known whether the two nitrogen valencies carrying X and Y are symmetrically situated or not with regard to the other three. When, however, an optically active base such as one of the components of externally compensated hydrindamine, combines with an optically active acid, it is obvious that the two isomerides *cannot* be enantiomorphously related, whatever the configuration of the nitrogen atom; consequently, they might be expected to differ in ordinary properties, and possibly to be separable by crystallisation.

Granting that the one component of externally compensated hydrindamine might thus give rise to two isomerides, its antipodes would naturally do so likewise, and in this way four different substances might be initially produced by the union of the base with the acid, as may be indicated by the following formulæ:

Of these four isomerides, no two are enantiomorphously related, since the group X is common to all, and unless the directions of the three valencies of the nitrogen atom, by which it is united to carbon and to the acid ions respectively, are all situated in a plane at right angles to the plane about which the whole nitrogen group may be free to rotate, no two of these forms could become identical by such a rotation of the nitrogen atom.

These considerations lead to a possible explanation of the existence of the isomeric hydrindamine salts, which is based on two assumptions only; firstly, that the acid negative ion does not necessarily take up one particular nitrogen valency, and secondly, that the directions of the valencies carrying the acid ions are such that they cannot become identical by the free rotation of the nitrogen atom.

The two salts actually isolated from the products of the neutralisation of the acid and the base both contain externally compensated hydrindamine; consequently, they are composite in character, and each may be regarded as a mixture of two of the above four isomerides; further, as a salt composed of D and D₁ or of L and L₁ would contain optically active base, the isomerides may be regarded as consisting of DL and D₁L₁, or of D₁L and DL₁ respectively.

This view, that each salt is made up of two enantiomorphous components which are not enantiomorphously related, and which nevertheless are not separable by fractional crystallisation within certain limits of temperature, might have been considered to be highly improbable, were it not for the existence of partially racemic salts, with which such isomerides as the above are in many ways comparable; there only remains therefore for consideration the important question as to how far the explanation here suggested accords with the facts observed in the study of these isomerides.

This accordance is satisfactory; taking the most important facts in order, the formation of unequal quantities of the two isomerides may first be dealt with.

On examining the formulæ already given, it will be seen that the two forms D and D₁ should be produced in unequal quantities in consequence of the asymmetry of the hydrindamine molecule; for the

same reason, this is true of the forms L and L_1 . Now if the group X were not enantiomorphous, the two forms D and L would probably be enantiomorphously related, as would also the forms D_1 and L_1 ; consequently, the formation of equal quantities of D and L would be expected, and so also of D_1 and L_1 . The fact that, in the case under consideration, the group X is enantiomorphous, would not apparently condition the formation of unequal quantities of D and L, and the relation between these forms being closer than that between D and L_1 , they might unite to form one of the isomeric salts, the union of D_1 and L_1 producing the other; the two partially racemic salts would thus be formed in unequal quantities.

These arguments may seem somewhat speculative, merely because they are applied to nitrogen, whereas had they been used in the case of carbon they might have been accepted without question; the essential difference between the two cases lies in the fact that with nitrogen it is not possible to say whether the two forms

stand in the relation of object and mirror image when Y represents any non-enantiomorphous group; if they do so, the analogy with carbon is essentially complete.

The fact that the isomerides derived from the sulphonic acids retain their individuality in aqueous and other solvents seems also to be in accordance with the suggested view of their nature.

On referring again to the formulæ on p. 868, it will be seen that hydrolytic dissociation might bring about the partial transformation of one salt into the other; for if D, for example, were to be resolved into acid and base, recombination might give D_1 as well as D; similarly, L might be partially converted into L_1 ; thus the partially racemic salt DL might be changed partly or completely into D_1L_1 , or *vice versâ*, by dissolving in water and then evaporating.

So far as can be ascertained, the isomeric salts of the sulphonic acids do not undergo hydrolytic dissociation to an appreciable extent, and in accordance with this conclusion these salts are not convertible one into the other by solution in water. The *cis*- π -camphanates, however, do undergo hydrolytic dissociation, and experiment shows that they are also slowly converted one into the other in aqueous solution.

As regards electrolytic dissociation, the case is altogether different, since to whatever extent this change may occur, it would seem that each of the four forms, D, D_1 , L, and L_1 , should be regenerated

unchanged by the recombination of its ions ; in this respect, therefore, the facts are again in agreement with the explanation which has been put forward.

The fact that the base regenerated from one of the salts yields both isomerides on recombination with the acid would be a necessary consequence of the above explanation, and need not be discussed.

The partial conversion of the one isomeride into the other by treating it with an aqueous solution of the externally compensated base is also a consequence of this explanation ; in aqueous solution, the given salt undergoes ionic dissociation, and, on concentrating again, the acid ions unite, not only with the base ions of the original salt, but also with those of the added base ; all the four isomerides, D, D₁, L, and L₁, will thus be formed, a condition of equilibrium will be attained, and, on evaporating, the two salts will result. If also the more readily soluble isomeride be repeatedly evaporated with small quantities of externally compensated base, it will be finally almost completely transformed into the more sparingly soluble α -salt, as is found to be the case.

With reference to the optical behaviour of these isomerides, it is not easy to decide whether their properties are or are not in accordance with the above view of their isomerism ; an inspection of the formulæ on p. 868 will show that when the salts undergo ionic dissociation, the forms D and L give rise to base ions which are either enantiomorphously related or else only partially so, according to the configuration of the nitrogen atom ; this is true also of the base ions of D₁ and L₁. In the first case, the molecular rotations of the α - and β -salts should be identical and equal to that of the contained acid ; in the second case, they would probably not be identical, but their mean should be the molecular rotation of the acid ; it is assumed, of course, that the solutions are sufficiently dilute to give the rotations of the ions only.

As a matter of fact, the molecular rotations of all the isomerides, with the exception of the β -salt of the bromo-acid, are practically the same as those of the acid which they contain, and no satisfactory explanation of this exception is forthcoming, unless it be assumed that dissociation is far too incomplete to allow of a normal result being obtained ; several objections to such an assumption might, of course, be advanced, but there are still so many facts in connection with optical activity which require explanation, that the apparently abnormal behaviour of the β -bromo-salt may for the present be passed over.

Much more extraordinary is the behaviour of the α -salt of *cis*- π -camphanic acid ; this isomeride, as already stated, shows a marked mutarotation in certain cases, and its specific rotation in methyl

alcoholic solution of a fixed concentration varies within very wide limits ; in the case of both isomerides, *different samples of one and the same salt, having the same melting point, have been found to differ greatly in specific rotation when examined in solutions of the same concentration in 99.8 per cent. methyl alcohol.* So far these facts, which are apparently unique, remain unaccounted for ; it is not impossible that a partial separation of the D and L components by repeated crystallisation may have occurred in such cases, but there is no direct evidence at present that any such change has taken place.

Having now dealt with the more important experimental data in relation to the explanation which has been suggested to account for the formation and properties of these isomeric salts, it will be manifest that much still remains to be done before any definite conclusion can be arrived at as to the validity of the view which has been advanced ; with this object, various investigations have already been commenced, and it is hoped that other instances of such partially racemic isomeric salts may soon be described. There is, however, one very obvious objection which might be raised to the view in question—namely, that if it be adopted, all nitrogen bases, whether optically active or not, should give rise to two salts on combination with an acid or with an alkyl iodide ; this objection may be briefly considered.

Dealing in the first place with optically inactive bases and acids, if it be assumed that the two nitrogen valencies concerned in salt formation be symmetrically situated with respect to the other three, the two isomeric salts would be enantiomorphously related, and would not, therefore, be separable by crystallisation if they showed the ordinary behaviour of such isomerides ; they would, of course, be formed in equal quantities.

If, however, the base, or the acid, were enantiomorphous, unequal quantities of non-enantiomorphously related isomerides would probably be produced ; the question then arises, Would such isomerides be separable by fractional crystallisation ? because, if so, it might be concluded that their formation would have been observed long before now. Bearing in mind the existence of partially racemic salts, it seems very probable that such isomerides would not be separable by the ordinary methods ; even if they were, it would probably be with great difficulty. Since, moreover, hydrolytic dissociation might bring about the conversion of one form into the other, it is probable that in the great majority of cases it would be impossible to isolate the more readily soluble modification, except with the aid of non-hydrolytic solvents. Since, finally, one of the isomerides may be produced in comparatively very small quantities, it might easily escape detection ; many instances, drawn from cases of ordinary isomerism, might be quoted in support of this statement, but it is unnecessary to do so.

Dealing next with the salt produced by the combination of an enantiomorphous base with an enantiomorphous acid, it is again possible that such a substance may consist of unequal quantities of two isomerides which are not enantiomorphously related; such isomerides would be similar to the D and D₁ forms discussed above, and with regard to the possibility of separating them, much the same may be said as in the case just considered. Although it might seem probable that such isomerides would differ to a greater extent than when only one of the components (acid or base) is enantiomorphous, the comparatively small number of such salts which have been examined, and their lack of definite characteristics, might be quoted as a possible reason why isomerism of this kind has not yet been observed. It is also conceivable that the two isomerides D and D₁ might be so similar that they could not be separated, and yet that by union with L and L₁ respectively they might give rise to very different partially racemic salts, just as enantiomorphously related substances give rise to ordinary racemic compounds.

Passing, lastly, to the case of externally compensated bases combining with an optically active acid, it is known already that they may behave in three different ways: (1) They may form only one partially racemic salt; (2) they may give two salts, corresponding with the enantiomorphously related bases, which *are* separable by crystallisation; (3) they may give two isomeric partially racemic salts, such as those described in this paper.

Whether, in these three cases, the original product consists of four, or of only two, isomerides, is a question which has still to be answered, and one which involves considerations regarding the stereochemistry of the nitrogen atom.

EXPERIMENTAL.

I. *Isomeric Hydrindamine Bromocamphorsulphonates.*

An aqueous solution of bromocamphorsulphonic acid is neutralised with hydrindamine, partly dissolved and partly suspended in water, and concentrated on the water-bath; on cooling, the solution becomes semi-solid, owing to the separation of a felted, opaque mass of needles; this product is separated by filtration, the mother liquors again concentrated, and allowed to crystallise. These processes having been repeated several times, the last mother liquors give a deposit differing in appearance from previous ones, and on further fractional crystallisation from water or very dilute alcohol, two different products are finally obtained in a state of purity. The intermediate deposits are again fractionally crystallised, but they consist principally of the more

sparingly soluble salt, and only small quantities of the less soluble compound are obtained from them.

α-Salt.

The more sparingly soluble salt, which will be subsequently referred to as the *α*-salt, usually separates from cold or tepid water in bulky, felted masses of very slender, concentrically-grouped needles, but it is deposited as an oil if the solution be too concentrated and separation occur too quickly. Very occasionally, when evaporation of a nearly saturated solution takes place slowly at the ordinary temperature, the salt separates at, or near, the surface of the liquid in large, transparent, compact, but ill-defined prisms. It dissolves fairly easily in cold methyl or ethyl alcohol, and in hot water, but it is only moderately soluble in cold ethyl acetate and cold water; it crystallises from ethereal alcohol in long, transparent, ill-defined prisms.

The moss-like crystals obtained from aqueous, and the prisms deposited from alcoholic, solution, contain water of crystallisation, and when dried on porous earthenware, and then quickly heated, they usually liquefy partially or completely at about 100°; the compact prisms, more rarely obtained, do not liquefy at 100°, but slowly become opaque. On exposure to the air at ordinary temperatures, the crystals effloresce, but so slowly that they continue to lose in weight during many days, and even when dried in the air until constant they still contain water of crystallisation, and liquefy or become pasty when heated at 100°. After prolonged drying at 100°, the *α*-salt shows a constant and fairly definite melting point, namely, 149—151°.

Numerous determinations of the water of crystallisation were made, but they did not give very satisfactory results; it would seem that the freshly crystallised salt contains $1\frac{3}{4}$ mols. H_2O , whereas the air-dried crystals contain less than $1\frac{1}{2}$ mols.

One gram of salt from ethereal alcohol, dried over night in the air, lost 0.0669 gram H_2O . $H_2O = 6.69$ per cent.

With samples air-dried until constant in weight, the following results were obtained:

0.5 lost 0.0272 H_2O at 100° during 72 hours. $H_2O = 5.44$ per cent.

1.0 „ 0.0509 H_2O „ „ 100 „ . $H_2O = 5.09$ „

0.5 „ 0.0265 H_2O „ „ 60 „ . $H_2O = 5.3$ „

$C_{10}H_{14}BrO \cdot SO_3H, C_9H_{11}N + 1\frac{3}{4}H_2O$ requires $H_2O = 6.62$ per cent.

$C_{10}H_{14}BrO \cdot SO_3H, C_9H_{11}N + 1\frac{1}{2}H_2O$ „ $H_2O = 5.7$ „

$C_{10}H_{14}BrO \cdot SO_3H, C_9H_{11}N + 1\frac{1}{4}H_2O$ „ $H_2O = 4.82$ „

The disagreement between the observed and the calculated results in the case of the air-dried salt may perhaps be due to the difficulty of

ascertaining when efflorescence has ceased, and to the prolonged heating at 100° required to expel the last traces of water; on the other hand, it might be taken as an indication that the salt is not homogeneous.

Bromine determinations in a sample of the salt dried at 100° gave the following results:

0.1629 gave 0.0704 AgBr. Br = 18.3 per cent.

0.1449 „ 0.0626 AgBr. Br = 18.4 „

$C_{10}H_{14}BrO \cdot SO_3H, C_9H_{11}N$ requires Br = 18.0 per cent.

The air-dried salt is readily soluble in boiling benzene and very readily soluble in cold chloroform, but it does not seem to crystallise from either solvent, except by gradual absorption of moisture from the air with formation of the ordinary hydrated crystals; on evaporating a benzene or chloroform solution, the salt is deposited as a gum-like mass.

β -Salt.

The more readily soluble hydrindamine bromocamphorsulphonate, which is hereafter referred to as the β -salt, nearly always separates from cold or tepid water in small, compact, fairly well-defined transparent prisms, which often form concentrically grouped masses; the appearance of these crystals is always absolutely different from that of the opaque, felted masses of the α -salt, but they are not easily distinguished by mere inspection from the compact prisms of the latter which are occasionally obtained. The crystals of the β -salt become opaque but do not liquefy at 100° , and they do not effloresce appreciably on exposure to the air; they become opaque when warmed in contact with their saturated aqueous solution. After having been dried at 100° , they have a constant and fairly definite melting point, namely, $129-130^{\circ}$. The β -salt is more readily soluble in cold water than the α -compound, and, like the latter, it is deposited as an oil from warm saturated solutions; it dissolves freely in cold alcohol and ethyl acetate.

The air-dried salt contains $\frac{3}{4}$ mol. of water of crystallisation:

0.5 lost 0.0129 H_2O at 100° during 60 hours. $H_2O = 2.58$.

1.6612 „ 0.0453 H_2O „ 96 „ $H_2O = 2.72$.

0.8328 „ 0.0228 H_2O „ 48 „ $H_2O = 2.73$.

$C_{10}H_{14}BrO \cdot SO_3H, C_9H_{11}N + \frac{3}{4}H_2O$ requires $H_2O = 2.73$ per cent.

Bromine determinations in the salt dried at 100° gave the following results:

0.2000 gave 0.0874 AgBr. Br = 18.5.

0.2072 „ 0.0873 AgBr. Br = 18.0.

$C_{10}H_{14}BrO \cdot SO_3H, C_9H_{11}N$ requires Br = 18.0 per cent.

The air-dried salt is readily soluble in benzene or hot chloroform, but on allowing such solutions to evaporate, it is deposited as a gum which gradually crystallises owing to absorption of water; no particular effort was made to obtain anhydrous crystals either in this case or in that of the α -salt.

Molecular Weight Determinations, $C_{10}H_{14}BrO \cdot SO_3H, C_9H_{11}N = 444$.

Molecular weight determinations were made by the cryoscopic method in dilute aqueous solution; the results show that the salts are isomeric and that both are largely dissociated.

α -Salt.

Weight of solvent.	Weight of substance.	Grams substance in 100 grams solvent.	Depression of freezing point.	M. W.
25 grams	0.2	0.8	0.075	203
25 „	0.2	0.8	0.067	227

Taking the water of crystallisation in the sample as 5.2 per cent., the average result for the anhydrous salt would be M.W. = 204.

β -Salt.

Weight of solvent.	Weight of substance.	Grams substance in 100 grams solvent.	Depression of freezing point.	M. W.
25 grams	0.3	1.2	0.100	228
25 „	0.2	0.8	0.065	234
25 „	0.3	1.2	0.090	253

The water of crystallisation in the β -salt being 2.7 per cent., the average value for the molecular weight of the anhydrous salt would be 232.

The Salts do not contain Enantiomorphously Related Bases.

Having obtained these isomeric salts by the combination of externally compensated hydrindamine with bromocamphorsulphonic acid, it seemed most probable that the former had been resolved into its optically active components. Accordingly, a sample (10 grams) of the pure α -salt was treated with excess of barium hydroxide, and the liberated base separated by steam distillation; the distillate, after the addition of a little alcohol to dissolve the oily base, occupied about 100 c.c., and a portion of it, on examination in a 200 mm. tube, was found to give no appreciable rotation.

Of course, this result did not prove that a resolution of the externally compensated base had not occurred, as the specific rotation of its

optically active components might have been too small to detect except in a very concentrated solution, and with a very sensitive polarimeter; or the specific rotation might even be *nil* in spite of the base being an optically active compound. So, in order to ascertain whether this was or was not the case, a portion of the base which had been regenerated from the α -salt was converted into its hydrochloride; the latter melted at the same temperature as the hydrochloride of the externally compensated base, and was identical with the latter in all ordinary properties. Another portion of the regenerated base was converted into its benzoyl derivative by the Schotten-Baumann method; the product, after recrystallisation, was identical in melting point and appearance with the benzoyl derivative of ordinary hydrindamine (Reis and Kipping, *Trans.*, 1897, **71**, 251), and a small quantity of it, examined optically in benzene solution, gave no appreciable rotation.

These observations seemed to prove that the base regenerated from the α -salt was really an externally compensated compound, identical with the base obtained directly from hydrindoxime, but the evidence was not absolutely conclusive. Both the hydrochloride and the benzoyl derivative of the externally compensated base might possibly be mere mixtures, and not racemic substances, and by a further possibility, the melting points of these compounds might be practically identical respectively with those of the optically active hydrochloride and benzoyl derivative. As, moreover, it is very difficult to make sure that the α -salt is perfectly free from the more sparingly soluble β -salt, owing to the ill-defined character of its crystals, and the sample used might conceivably have contained a little of the β -salt even after repeated crystallisation, it seemed necessary to examine the latter, as being a much better characterised substance.

A carefully purified sample (4 grams) of the β -salt was, therefore, decomposed as described in the case of the α -compound. The aqueous alcoholic solution of the regenerated base, which measured less than 50 c.c., produced no appreciable rotation in a 200 mm. tube, and the base was found to be identical in every respect with that obtained from the α -salt.

In spite of the apparently conclusive results of these experiments, it seemed advisable to apply a crucial test, namely, to ascertain whether the base of the one salt would differ from that of the other, if combined with an optically active substance. For this purpose, samples of the two bases were separately treated with *d*-camphoric acid; the salts thus obtained were identical in melting point and in ordinary properties. Similar experiments were made, using *cis*- π -camphanic acid (p. 903) as the optically active substance; again, the base from the α -salt gave the same product as that obtained with the base from the β -salt.

These facts prove that the bases regenerated from the two salts are not enantiomorphous, and that their optical inactivity is not merely a fortuitous instance of very low specific rotatory power.

Relative Quantities of the Two Isomerides.

Another fact which accords with this conclusion is, that the two isomeric salts are not obtained in even approximately equal quantities. After repeated fractional crystallisation of the original mixtures, carried as far as possible, with the object of ascertaining roughly the relative proportions of the isomerides, there is always obtained at least four times as much of the α - as of the β -salt.

The Salts are not merely Different Crystalline Varieties.

The formation of the two isomerides could hardly be attributed to a difference in the degree of hydration of their crystals, as they are both deposited from water at the ordinary temperature, apparently under the same conditions; moreover, the (completely dehydrated) salts have different melting points and different specific rotatory powers.

Dimorphism is also out of the question for similar reasons, and it may be explicitly stated that, although the two salts have been crystallised over and over again during the time they have been under investigation, the partial conversion of one into the other has never been observed except under the particular conditions described later (p. 882). It must again be noted, however, to avoid misunderstanding, that very occasionally, under conditions not precisely ascertained, the α -salt crystallises from cold water in compact prisms, difficult to distinguish from those of the β -salt by mere inspection, but which have nevertheless the melting point and other specific properties of the α -salt.

Examination of the Acid contained in the Salts.

The possibility that the bromocamphorsulphonic acid might be the cause of the formation of the two salts may next be considered. The acid used in these experiments was prepared from purified ammonium bromocamphorsulphonate (Kipping and Pope, *Trans.*, 1895, 67, 358), and although in the course of work with this acid and its derivatives no indication of the presence of any isomeride had ever been observed, it was desirable to obtain experimental proof that the acid of the α -salt is really identical with that of the β -isomeride.

As the latter is formed in much the smaller quantity, it would be in this compound, if anywhere, that the isomeric acid would be found. The pure β -salt was therefore decomposed with barium

hydroxide, the base separated, the barium salt converted into ammonium salt, and the latter isolated; it was identical with ordinary ammonium bromocamphorsulphonate in all outward properties, and had the same specific rotatory power as the latter. Further, when triturated with phosphorus pentabromide, it gave a sulphonic bromide identical with the compound obtained from ordinary ammonium bromocamphorsulphonate.

The Base from one Salt gives both Isomerides when combined with the Acid.

The next experiments which were made had the object of ascertaining whether the base regenerated from one of the salts would, or would not, give the same salt when neutralised again with bromocamphorsulphonic acid.

A sample of the α -salt, which had the correct melting point, was first carefully fractionally crystallised from water, and it was proved that the last mother liquors did not deposit even traces of the more readily soluble β -salt. A quantity of the same sample was then decomposed with barium hydroxide, the base distilled in steam, and the distillate neutralised with bromocamphorsulphonic acid; on then submitting the product to fractional crystallisation from water, the first and several subsequent deposits were found to be the α -salt, but the last mother liquors deposited crystals of the β -salt, and, as far as could be judged, the proportion of the two isomerides was just about the same as that in which they are formed from the ordinary externally compensated base.

The β -salt was then treated in a similar manner; on fractional crystallisation from water, it afforded no indication of the presence of the isomeride, but when decomposed with barium hydroxide it yielded a base from which, on neutralising with bromocamphorsulphonic acid and fractionally crystallising, both the α - and β -salts were obtained; in this case, again, the relative weights of the two salts seemed to be just about the same as usual.

The Free Base does not undergo Racemisation.

These last experiments, and many other facts already recorded, might be explained by assuming that the base is actually resolved into its enantiomorphously related components when its salt with bromocamphorsulphonic acid is fractionally crystallised, but that when liberated from its salt, or during steam distillation, the optically active substance racemises.

Although the mechanism of racemisation is not yet capable of satisfactory explanation, it is conceivable that, in the case of a primary

base such as hydrindamine, this change might be brought about as the result of the existence of tautomeric modifications, which might cause a transformation of one enantiomorphous form into the other in the following manner :

These changes do not require further explanation, and it will be seen that the possibility of racemisation would depend here upon the direct union of the amino-group with the asymmetric carbon group ; it seems not unlikely that changes such as these actually occur in the racemisation of β -aspartic acid, for example, and in the case of other optically active amino-compounds of this class, many of which are converted into the inactive modifications comparatively easily.

Considering, now, whether this assumption of the occurrence of racemisation would explain the existence of the isomeric salts, one very important objection immediately suggests itself, namely, the fact that the two compounds are formed in such very unequal quantities when the base is neutralised with the acid. Although it has been recently shown by Marckwald and McKenzie (*Ber.*, 1899, 32, 2130) that in the combination of the enantiomorphously related mandelic acids with menthol, the two antipodes have a different reaction velocity, and after a certain period of interaction give a product consisting of unequal quantities of the two menthyl mandelates, the difference is only very small, and it is extremely unlikely that any analogous difference in the case of the combination of the two enantiomorphous hydrindamines with bromocamphorsulphonic acid could lead to the production of such unequal quantities of their salts, even if at the same time the free base were undergoing rapid autoracemisation. These remarks apply, of course, only if hydrolytic dissociation be excluded ; if, however, hydrolytic dissociation were to accompany autoracemisation, one of the salts should be partially or completely converted into the other on recrystallisation from water.

The experimental evidence which can be advanced against the view that optically active hydrindamine may undergo autoracemisation is not of much weight in the case of the two bromocamphorsulphonates, and merely amounts to this : that on decomposing either the α - or the β -salt with barium hydroxide in cold aqueous solution, and then quickly extracting the base with ether, the ethereal solution is found to show no appreciable optical activity. This experiment merely

proves that if autoracemisation takes place at all, it must occur with great rapidity, even at low temperatures, a conclusion which can hardly be regarded with favour. But the arguments just advanced, the optical behaviour of the two salts, and further experimental evidence which will be brought forward later, show conclusively that an explanation of the isomerism of the two salts, based on the assumption of autoracemisation, is quite out of the question.

The Isomeric Salts are derived from one and the same Acid.

If autoracemisation of the base be excluded, and the α - and β -salts contain one and the same externally compensated hydrindamine, it might be concluded that the acid must be the cause of the isomerism. This possibility has already been considered superficially, and it has been shown that the acid obtained, after a series of operations, from the β -salt is identical with ordinary bromocamphorsulphonic acid (p. 877).

An inspection of the following formula,

which has previously been assigned to α -bromocamphorsulphonic acid (Kipping, Trans., 1896, 69, 913), will, however, make it obvious that there are certain ways in which this acid might possibly give rise to two salts, and yet appear to be a single individual. For reasons which will be evident when the molecular rotations of the hydrindamine salts have been dealt with, it seemed at one time very probable that the acid of the β -salt was really different, in some way, from that of the α -isomeric; it was consequently necessary to make a number of experiments, in order to exclude this possibility.

The existence of desmotropic forms of the acid, namely, a ketonic $\cdot\text{CHBr}\cdot\text{CO}\cdot$ and an enolic $\cdot\text{CBr}\cdot\text{C}(\text{OH})\cdot$, is perhaps the simplest of the possible explanations which might suggest itself, as the α -salt might be regarded as derived from one, the β -salt from the other modification.

Such a view does not seem to commend itself for many reasons, and firstly on theoretical grounds, since, so far as is known, camphor itself, and its simple substitution derivatives which contain the group $\cdot\text{CHX}\cdot\text{CO}\cdot$, do not exhibit the phenomenon of desmotropism.

The experimental evidence which can be brought forward against this view also seems to be conclusive. If the supposed desmotropic acids were so stable that aqueous solutions of their hydrindamine salts might be boiled without converting the one into the other, it seems

most unlikely that mere displacement of the hydrindamine by barium and ammonium successively in hot aqueous solution would bring about such a change, and yet the ammonium bromocamphorsulphonate prepared from the β -salt by the usual method is identical with ordinary ammonium bromocamphorsulphonate (p. 877).

It can also be proved that when this displacement occurs at temperatures below 20° the result is the same:—A sample of the β -salt was treated with a large excess of concentrated ammonia in the cold, and the liberated organic base extracted with ether; the aqueous solution of the ammonium salt was then evaporated almost to dryness at the ordinary temperature, concentrated ammonia added, and the solution again repeatedly extracted with ether. After evaporating at the ordinary temperature, the ammonium bromocamphorsulphonate was obtained in crystals, which were identical with those of the ordinary ammonium salt in outward and in optical properties.

Now, as a general rule, desmotropic forms are easily converted one into the other by a change of temperature, or with the aid of a trace of piperidine (Schiff, *Ber.*, 1898, 31, 601) or of sodium ethoxide. Accordingly, attempts were made to convert the α - into the β -salt and *vice versa*, but without success, and it was thus found that the two isomerides do not show the ordinary behaviour of desmotropic forms in any way whatever.

The salts, as already stated, are not changed when they are repeatedly crystallised from water or other solvents, nor when heated to fusion in their water of crystallisation. Ferric chloride, so reliable a reagent in most cases for the detection of the enolic modification, gives no coloration with either the α - or the β -salt in aqueous or in alcoholic solutions.

Neither of the salts interacts with phenyl isocyanate; samples of each, dried at 100° , were left in contact with this reagent during several days, but neither underwent any change; portions which had been treated in this way, and then merely washed with ether on porous earthenware, showed the melting points of 130° and 150° respectively, and after dissolving in water and filtering from diphenylcarbamide, the solutions, on evaporation, gave the α - and β -salts respectively in an unchanged condition. Had either of the salts been derived from an enolic form of bromocamphorsulphonic acid, it is probable that it would have interacted with the phenyl isocyanate.

Samples of the dehydrated salts were also separately recrystallised from benzene in presence of traces of piperidine; no change, however, was brought about in either case, and after recrystallisation from water (an operation which is known to have no effect on either salt), the two compounds still had their original properties, and were apparently quite free from isomeride.

The only other manner, apparently, in which the bromocamphor-sulphonic acid might be accountable for the formation of two hydrindamine salts, would be the existence of two stereoisomeric forms represented by the formulæ

but it will be obvious that such an assumption is quite untenable for many reasons which it is unnecessary to specify.

It has thus been shown that the isomeric hydrindamine bromocamphorsulphonates are derived from one acid only, and that their isomerism is in no way referable to the existence of physically or chemically different forms of this acid; this conclusion does not rest merely on the experimental evidence recorded in this paper, but is supported by such an array of facts, which cannot conveniently be discussed here, that it may be regarded as final.

Conversion of the β - into the α -Salt.

Although all attempts to convert one of the hydrindamine salts into the isomeride by crystallisation, or by dissolution in and evaporation with solvents, were unsuccessful, it was found that the β -salt could be almost entirely transformed into the isomeride by repeatedly evaporating its aqueous solution with externally compensated hydrindamine; the operation is so simple that further description is unnecessary.

In a similar manner, the α -salt may be partly converted into the β -isomeride.

That in this process hydrolytic dissociation plays no part is proved by the fact that in absence of added base, the change does not occur; it can also be shown in other ways that the salts do not undergo hydrolytic dissociation to any appreciable extent. The conversion of one isomeride into the other under the conditions just stated is therefore a process essentially different from that in which this partial transformation is brought about by first liberating the base, and then treating again with fresh bromocamphorsulphonic acid (p. 878).

Two diametrically opposite views might be held as to the interpretation of the fact just recorded. On the one hand, it might be considered as conclusive evidence that the α - and β -salts are not derived from physically or chemically isomeric acids, since base alone is added during the transformation. On the other hand, it might be assumed that the presence of free base causes a change to take place in the physical or chemical character of the acid; if the presence of a trace of piperidine may bring about the conversion of an enolic form

into the ketonic isomeride, the free base, hydrindamine, might play a similar part. The possibility of the latter view being adopted made it necessary to show by the experiments already recorded that bromocamphorsulphonic acid exists only in the one form.

Hydrindamine is composed of Two Enantiomorphous Modifications only.

Another very natural conclusion which might be drawn from the fact that the β -salt is converted into the α -isomeride on evaporation with fresh quantities of the externally compensated base would be, perhaps, that the hydrindamine supplied to the acid during this process is different, partly or entirely, from the base to which the acid is already united.

To conclude that one enantiomorphous base displaces the other would, of course, necessitate the further assumption that the two isomeric salts correspond in the ordinary manner with the two enantiomorphously related bases, a view which has already been discussed and shown to be untenable.

The question as to whether the base exists in two modifications which are not enantiomorphously related has not yet been raised, and, in fact, it is hardly necessary to consider it. If the hydrindene and benzene chains did not lie in one plane, there might, of course, be two stereoisomeric hydrindones, as represented roughly by the following formulæ:

and each of these would give rise to two different optically active bases. There would thus be two different externally compensated hydrindamines, which would be related to one another in much the same way as optically inactive bornylamine and neobornylamine, for example; the two externally compensated compounds would then be different altogether, and would necessarily give different salts and other derivatives, just as do the optically active bornylamines (Forster, Trans., 1898, 73, 386).

As it has already been shown that the base of the α -salt is identical, chemically and physically, with that of the β -isomeride, the possible existence of isomeric inactive hydrindamines need not be further discussed.

The results of the experiments which have now been described may be briefly summarised as follows: Externally compensated hydrindamine, which is a mixture of two enantiomorphously related forms,

combines with *d*-bromocamphorsulphonic acid, giving unequal quantities of two isomeric salts. The base and the acid of which one salt is composed are identical respectively, both physically and chemically, with the components of its isomeride.

II. *Specific and Molecular Rotations of the Hydrindamine Bromocamphorsulphonates.*

The optical examination of the α - and β -salts described in the preceding section shows that the isomerides have different specific rotations in methyl alcohol, chloroform, and aqueous solutions, that of the α -compound being in all cases considerably higher than that of the isomeride.

Methyl Alcohol Solutions.—The samples were dried at 100° until practically constant in weight; 1 gram of each was then separately dissolved in 99 per cent. methyl alcohol, the solution diluted to 25 c.c., and examined in a 200 mm. tube at about 16°.

α -Salt		$\alpha + 5^{\circ} 19'$	$[\alpha]_D + 66.6^{\circ}$	$[M]_D + 296$
β -Salt		$\alpha \quad 4^{\circ} 25'$	$[\alpha]_D \quad 55.2$	$[M]_D \quad 245$

Optical examination was next made in more dilute solutions, 0.5 gram being used, the samples of salt, solvent, and all other conditions being the same as before.

α -Salt		$\alpha + 2^{\circ} 36'$	$[\alpha]_D + 65.0^{\circ}$	$[M]_D + 289$
β -Salt		$\alpha \quad 2^{\circ} 12'$	$[\alpha]_D \quad 55.0^{\circ}$	$[M]_D \quad 244$

These values show that the change in concentration from about 4 to 2 per cent. produces no appreciable effect on the specific rotation.

Chloroform Solutions.— α -Salt: 0.5 gram of the anhydrous salt was dissolved in, and made up to 25 c.c. with chloroform, the solution being examined in a 200 mm. tube. β -Salt: 0.5 gram of air dried salt containing 2.7 per cent. of water was treated in the same way: the molecular rotation is calculated for the anhydrous compound.

α -Salt		$\alpha + 1^{\circ} 53'$	$[\alpha]_D + 47.3^{\circ}$	$[M]_D + 210$
β -Salt		$\alpha \quad 1^{\circ} 40'$	$[\alpha]_D \quad 41.5^{\circ}$	$[M]_D \quad 190$

Aqueous Solutions.

Observations were next made in dilute aqueous solutions: 0.25 gram of each of the dehydrated salts was dissolved, the solution made up to 25 c.c., and examined in a 200 mm. tube at about 16°.

α -Salt		$\alpha + 1^{\circ} 10'$	$[\alpha]_D + 58.3^{\circ}$	$[M]_D + 259$
β -Salt		$\alpha \quad 0^{\circ} 58'$	$[\alpha]_D \quad 48.3^{\circ}$	$[M]_D \quad 214$

Now the molecular rotation, $[M]_D$, of bromocamphorsulphonic acid in aqueous solution is +270, and it might therefore be inferred from these results that the base of the β -salt is levorotatory, whilst that of the α -compound is either very feebly levorotatory or optically inactive; but, in view of the rather large experimental error which is unavoidable in dealing with such dilute solutions, it was necessary to make further determinations with different samples of the two salts before much weight could be attached to the results.

In the first of this new series of experiments, the samples were again dried at 100° until constant in weight, an operation which lasted during many hours; the following results were then obtained, the samples marked with an asterisk being different from the other two; a 200 mm. tube was used in all cases.

α -Salt.

Weight of substance.	Volume of solution.	α_D .	$[\alpha]_D$.	$[M]_D$.
0.9331	25 c.c.	+4°43'	+63.1°	+280
0.2333	"	1°8'	60.5	268
*0.4735	"	2°31'	60.7	270

β -Salt.

0.8100	25 c.c.	+3°31'	+54.3°	+241
0.2025	"	0°52'	53.5	237
*0.4862	"	2°6'	54.0	240

These results confirm those previously obtained in the case of the α -salt within the limits of experimental error, but in the case of the β -salt, the values of the molecular rotation are about 10 per cent. higher than that previously found. As it seemed possible that this disagreement might be the result of such prolonged heating at 100°, fresh determinations were made with air-dried samples of the two salts, and the combined water was determined in other portions of the same samples; the following results were thus obtained, using water as solvent and a 200 mm. tube.

The specific and molecular rotations are calculated for the anhydrous salts.

α -Salt.

Weight of substance.	Volume of solution.	α_D .	$[\alpha]_D$.	$[M]_D$.
0.2500	25 c.c.	+1°8'	+59.7°	+265
0.5000	"	2°17'	60.3	268

The sample of the α -salt contained 5.3 per cent. of water.

β -Salt.

Weight of substance.	Volume of solution.	α_D .	$[\alpha]_D$.	$[M]_D$.
0.2500	25 c.c.	+ 0°59'	+ 50.3°	+ 223
0.5000	„	1°54'	49.0	218

The sample of the β -salt contained 2.76 per cent. of water.

The samples marked above with an asterisk were the same respectively as those used in the last experiments, but the marked samples were dehydrated before the specific rotations were determined; it would seem, therefore, that prolonged heating at 100° raises the specific rotation of the β -salt to a very slight extent, but has no effect on that of the α -salt. If such a change really does occur, it does not consist in the conversion of the β - into the α -isomeride, because on evaporating an aqueous solution of a sample of the β -salt which has been heated during several days at 100°, the crystalline deposit does not show the presence of even traces of the α -compound.

Accepting the values for the molecular rotations obtained in the last series of experiments, which are probably the most trustworthy, and assuming that they are practically the same as those of the fully dissociated salts, it might be provisionally assumed that the base ion of the α -salt is optically inactive, whereas that of the β -salt shows a molecular rotation of about -50° .

At this stage of the investigation, for reasons which will be obvious, it seemed desirable to ascertain whether the value obtained for the molecular rotation of bromocamphorsulphonic acid in the case of salts analogous to the hydrindamine compounds would correspond with that deduced from an examination of its metallic salts; ammonium bromocamphorsulphonate and aniline bromocamphorsulphonate were therefore examined in 1 to 4 per cent. aqueous solutions with the following results:

Ammonium bromocamphorsulphonate.

Weight of salt.	Volume of solution.	α_D .	$[\alpha]_D$.	$[M]_D$.
1 gram	25 c.c.	+ 6°47'	+ 84.8°	+ 278
0.5 „	„	3°24'	84.8°	278
0.25 „	„	1°40'	83.5°	274

Aniline bromocamphorsulphonate.

Weight of salt.	Volume of solution.	α_D .	$[\alpha]_D$.	$[M]_D$.
0.5 gram	25 c.c.	+ 2°39'	+ 66.3	+ 268
0.25 „	„	1°20'	67.0	271

These results are practically identical with those obtained by Walden (*loc. cit.*) and therefore do not afford any good reason for reject-

ing the provisional assumption just made, namely, that the molecular rotation of the α -salt is normal on the supposition that the base is optically inactive, whereas that of the β -salt indicates the presence of lævorotatory hydrindamine.

But it has already been shown that the β -salt must be regarded as partially racemic because the base contained in it is identical with ordinary hydrindamine; further, it cannot be assumed that the β -salt contains lævorotatory base without also assuming that the α -salt contains the dextrorotatory isomeride, in which case the molecular rotation of the α -salt could hardly be $[M]_D = +268$. Even the assumption that optically active hydrindamine undergoes almost instantaneous racemisation would not account for the existence of a (β -)salt containing lævorotatory base and a more sparingly soluble (α -)salt containing optically inactive hydrindamine. For these reasons, the abnormal molecular rotation of the β -salt cannot be explained in this simple way.

The existence in the β -salt of an isomeric bromocamphorsulphonic acid, which in the ionic state has a molecular rotation $[M]_D +220$ is another explanation which might suggest itself, and it was for this reason that it was so necessary to prove by the experiments already recorded that the molecular rotation of the acid of the β -salt is identical with that of ordinary bromocamphorsulphonic acid.

The assumption that the abnormal molecular rotation of the β -salt is due to hydrolytic dissociation might also be made, but even if it were in itself sufficient, it would be in direct conflict with the experimental evidence; so far as can be inferred from the fact that aqueous solutions of the β -salt do not acquire an acid reaction on prolonged boiling, the salt does not undergo hydrolytic dissociation to any appreciable extent; moreover, even in the case of a salt such as morphine bromocamphorsulphonate, which is a salt of a comparatively feeble base, the normal molecular rotation is obtained in dilute aqueous solution (Walden, *Zeit. physikal. Chem.*, 1894, 15, 206).

The last explanation which may be considered is the possibility that the β -salt does not undergo ionic dissociation in 1 per cent. aqueous solution to a sufficient extent to give the normal molecular rotation of its acid ion.

Now Walden has shown that even in very dilute aqueous solutions the metallic salts of bromocamphorsulphonic acid are only dissociated to the extent of 80—90 per cent.; he also found that the extent of dissociation, for solutions of equivalent concentration, varies with the nature of the solvent, being, for example, only about 80 per cent. in the case of the barium salt, but reaching 90 per cent. in the case of the potassium salt, these being the results of determinations in the most dilute solutions which he examined.

As it is very improbable that the salts of hydrindamine with bromocamphorsulphonic acid would be more highly dissociated than the potassium salt of this acid, it may be safely concluded that the former are only partially ionised even in the most dilute solutions (1 per cent.) which were examined, more especially as even these solutions contained about three times as many equivalents of the salt as the most dilute solutions of potassium bromocamphorsulphonate investigated by Walden.

Now, in the case of the metallic salts of bromocamphorsulphonic acid, the molecular rotations vary very little with the extent of dissociation, a difference of about 20 per cent. in the latter making a difference of only 1 or 2 per cent. in the former; it might be thought, therefore, that the value obtained for the molecular rotation of the β -salt in 1 per cent. solution, in which dissociation is probably far from complete, might nevertheless be almost identical with the value which would be obtained in infinitely dilute solution.

This, however, is not a necessary consequence by any means. The β -salt differs profoundly from the metallic salts of bromocamphorsulphonic acid, inasmuch as it contains enantiomorphous base ions, and the union of the latter with the acid ions may give salt molecules which have a molecular rotation widely different from that of the algebraic sum of the molecular rotations of the ions; consequently a small difference in the extent of the dissociation might make a very considerable difference in the observed molecular rotation.

If, then, it could be shown that the specific rotation of the β -salt increased as the concentration of the aqueous solutions diminished, the whole difficulty would be overcome. Unfortunately, however, the solubility of the salt in cold water is so small that solutions containing more than about 2 per cent. cannot be examined, and with those containing less than 1 per cent. the experimental error would be too large; for these reasons, it was impossible to trace the influence of concentration by employing aqueous solutions only.

As the addition of hydrindamine for the purpose of diminishing the ionic dissociation would have been inadmissible, since the free base brings about the partial conversion of one isomeride into the other, and as its salts might do so likewise, this method was also excluded.

Experiments were therefore made in aqueous methyl alcoholic solution as follows: 2 grams of β -salt, containing 2.7 per cent. of water, were dissolved in water containing just sufficient methyl alcohol to prevent crystallisation on diluting with water to 25 c.c.; this solution was examined in a 100 mm. tube.

$$\alpha + 4^{\circ}8' \quad [\alpha]_D + 53.1^{\circ} \quad [M]_D + 236.$$

2.4635 grams of the same sample were dissolved in 99 per cent. methyl

alcohol, the solution diluted to 25 c.c., and examined in a 200 mm. tube :

$$\alpha + 10^{\circ}25' \quad [\alpha]_D + 54.2^{\circ} \quad [M]_D + 241$$

The specific and molecular rotations are calculated for the anhydrous salt in both cases.

Since the specific rotation of the β -salt is about $[\alpha]_D + 55^{\circ}$ in a 2 per cent. solution in methyl alcohol, and about $+50^{\circ}$ in 1 per cent. aqueous solution, the results of these experiments afford no indication as to whether the specific rotation increases or decreases as concentration diminishes ; from experiments made with aqueous solutions containing about 0.4 per cent. of salt, it would seem that the latter is true, but the experimental error was too large to admit of any positive conclusion being drawn.

The results of the optical examination of this pair of isomerides, taken as a whole, cannot, therefore, be regarded as strictly in accordance with the view that the β -salt is partially racemic, although they confirm this conclusion as regards the α -salt. On the other hand, the view that the β -isomeride is a salt of lævorotatory hydrindamine is so beset with improbabilities that it could not be maintained ; in addition to the reasons already stated against it, there is the obvious relation between the β -salts of the bromo- and chloro-acids, which practically settles the matter, since the value for the molecular rotation of the β -chloro-salt is approximately normal on the assumption that it is partially racemic.

III. *Isomeric Hydrindamine Chlorocamphorsulphonates.*

The interesting case of isomerism observed in the study of the hydrindamine bromocamphorsulphonates led naturally to the examination of other salts of the externally compensated base, and the close relationship between the sulphonic acids of bromo- and chloro-camphor (Kipping and Pope, *Trans.*, 1893, **63**, 548) seemed to justify the conclusion that the hydrindamine salts of chlorocamphorsulphonic acid would be obtainable in isomeric forms, corresponding with those of the salts of the bromo-acid.

Experiment showed this to be the case, and the preparation and investigation of the isomeric partially racemic hydrindamine chlorocamphorsulphonates are described in this section.

The analogy between the salts of the chloro-acid and the corresponding isomerides of the bromo-acid is on the whole very complete ; nevertheless, the β -salt of the former differs from that of the latter in one important particular, as it exists in two differently hydrated crystalline modifications which show an interesting behaviour.

The two salts are prepared by neutralising an aqueous solution of chlorocamphorsulphonic acid with hydrindamine, which is partly dissolved and partly suspended in water; the solution is then concentrated if necessary and allowed to cool. The first and several subsequent deposits seem to be homogeneous, and consist of bulky masses of very slender needles, but on further concentration the character of the crystalline deposit begins to change, and finally compact, transparent prisms are often obtained; by systematic crystallisation from water or very dilute alcohol, two different products may be isolated.

α -Salt.

The more sparingly soluble salt, which doubtless corresponds with the α -salt of the bromo-acid, invariably separates from warm or cold water in bulky, opaque, or translucent masses consisting of very small, concentrically grouped needles, which under the microscope are quite transparent and appear to be fairly well defined.

These crystals liquefy almost immediately—in less than 5 minutes—in their water of crystallisation when they are heated at about 100° in a water-oven, giving a brittle, vitreous mass, from which the rest of the water is expelled only on prolonged heating; on exposure to the air, they gradually effloresce, and continue to lose in weight during many days, but even when efflorescence has ceased they still liquefy in their water of crystallisation when heated at 100° . In appearance and in all ordinary properties, this salt is difficult to distinguish from the α -salt of the bromo-acid, but as a rule its crystals are rather larger and more definite. Compact, ill-defined prisms, such as are sometimes observed in the case of the α -bromo-salt (p. 873), have never been obtained with this compound, although it has been repeatedly crystallised from water under different conditions; it also differs from the α -salt of the bromo-acid, inasmuch as it is deposited in a crystalline, and not in an oily condition, from warm saturated aqueous solutions.

The α -salt of hydrindamine and chlorocamphorsulphonic acid is only sparingly soluble in cold water, but it dissolves freely on warming, and is also readily soluble in cold chloroform and ethyl alcohol; it crystallises from methyl alcohol in long, transparent, efflorescent prisms, which often attain a length of several centimetres, but its solutions in chloroform give, on spontaneous evaporation, a vitreous or gum-like mass which apparently only becomes crystalline as the result of the absorption of atmospheric moisture. The anhydrous salt is only sparingly soluble in hot ethyl acetate, but in presence of a small quantity of water it dissolves freely, separating again on cooling in opaque masses.

The anhydrous salt has not a very definite melting point; it begins to sinter at about 160° , and then melts fairly sharply at about 165 — 166° (corr.); it does not darken in colour appreciably when heated at 100° during several days.

The water of crystallisation was determined in two different samples. The first was prepared by crystallisation from methyl alcohol, and dried on porous earthenware during about 12 hours only.

0.5 lost 0.0413 H_2O at 100° during 72 hours. $\text{H}_2\text{O} = 8.26$.

0.5 „ 0.0414 H_2O „ „ „ $\text{H}_2\text{O} = 8.28$.

The second sample was prepared in a similar manner, but was dried in the air until constant in weight.

1.0015 lost 0.0713 H_2O at 100° during 72 hours. $\text{H}_2\text{O} = 7.1$.

1.000 „ 0.0701 H_2O „ „ „ $\text{H}_2\text{O} = 7.0$.

$\text{C}_{10}\text{H}_{14}\text{ClO}\cdot\text{SO}_3\text{H}\cdot\text{C}_9\text{H}_{11}\text{N} + 2\text{H}_2\text{O}$ requires $\text{H}_2\text{O} = 8.3$ per cent.

$\text{C}_{10}\text{H}_{14}\text{ClO}\cdot\text{SO}_3\text{H}\cdot\text{C}_9\text{H}_{11}\text{N} + 1\frac{3}{4}\text{H}_2\text{O}$ „ $\text{H}_2\text{O} = 7.3$ „

These results seem to show that the salt crystallises with $2\text{H}_2\text{O}$, of which it loses $\frac{1}{4}$ mol. on exposure to the air; the experimental results agree with the calculated much more closely than in the case of the α -salt of the bromo-acid, and it may also be noted that the two salts do not seem to be equally hydrated, although the difference is very small.

Determinations made by Carius' method with samples dried at 100° until constant gave the following results:

0.2844 gave 0.1037 AgCl . $\text{Cl} = 9.0$.

0.1360 „ 0.0526 AgCl . $\text{Cl} = 9.4$.

$\text{C}_{10}\text{H}_{14}\text{ClO}\cdot\text{SO}_3\text{H}\cdot\text{C}_9\text{H}_{11}\text{N}$ requires $\text{Cl} = 8.8$ per cent.

β -Salt.

The hydrindamine chlorocamphorsulphonate, which is deposited from the mother liquors of the α -salt, gives, after further fractional crystallisation, a product which in some respects is very similar to the β -salt of the corresponding bromo-acid. This product is very often deposited from aqueous solution in the form of small, lustrous, compact, transparent, well-defined prisms, which are indistinguishable in appearance from the crystals of the β -salt of the bromo-acid, and, like the latter, become opaque when warmed in contact with their mother liquor.

Very great difficulty and uncertainty, however, were first experienced with this β -salt, as for a long time it seemed impossible to obtain it free from the α -isomeride.

Owing to the great difference in appearance between the opaque

masses of slender needles of the α -salt and the small, transparent crystals of the β -isomeride, and owing to the fact that the melting points of the salts cannot be determined until the samples have been dried at 100° for many hours, the best method of testing the purity of a sample supposed to be the β -salt, at any rate, in the case of the hydrindamine bromocamphorsulphonate, is to recrystallise the sample from cold or tepid water; if any α -salt is then deposited, its presence can be immediately detected by mere inspection, as it forms opaque, white patches on the transparent prisms.

Now on recrystallising, the compact prisms of the β -chloro-salt from water—in order to ensure the purity of the preparation—the salt was often deposited again in its original, apparently pure, condition, and as this recrystallisation, with or without fractionating, could often be repeated many times without the bulky crystals of the supposed α -compound making their appearance, it seemed that the latter was absent; on continuing this testing, however, under apparently the same conditions as before, small, opaque masses of needles, looking exactly like crystals of the α -salt would be deposited among the transparent prisms, sometimes simultaneously with the latter, generally only towards the end of the crystallisation; the opaque masses having been separated mechanically and the prisms again dissolved, the solution again deposited what were obviously two different kinds of crystals, and in some cases the opaque masses which appeared to be crystals of the α -salt were deposited alone.

As these recrystallisations were often carried out without altering, intentionally or appreciably, the quantity of water present, the solutions being of such a strength that the salt only separated after they had cooled to nearly atmospheric temperature, and as two kinds of crystals were certainly obtained, the presence of the α -salt seemed to be the only explanation of the difficulty, and repeated attempts were made to get rid of this compound by fractional crystallisation, combined with a mechanical separation of the opaque masses, whenever they appeared.

The β -Salt Crystallises in Two Differently Hydrated Forms.

Finding that these operations failed to alter the character of the deposits, the crystals, which were supposed to be those of the α -salt, were collected and examined. They consisted of bulky masses of transparent needles, indistinguishable in appearance, even under the microscope, from the crystals of the α -salt, and on recrystallisation from water or dilute methyl alcohol, they were deposited apparently unchanged, the only slight difference which could be observed between them and the crystals of the α -salt was, that when heated in a water-

even they did not liquefy in their water of crystallisation except after some time (20—30 minutes), whereas the α -salt invariably does so in the course of a few minutes, even when it is thoroughly air-dried.

Although it seemed very improbable that this β -salt of the chloro-acid would differ from the β -salt of the bromo-acid to any considerable extent, the above observations doubtless indicated the existence of two different crystalline varieties of the latter, and as the result of further experiments, this view was fully confirmed.

The one crystalline form of the β -salt, which is called the A variety, as already stated, is very similar to, in fact indistinguishable from, the ordinary crystalline form of the β -salt of the bromo-acid (p. 874), and consists of small, lustrous, transparent, well-defined prisms, which are often massed together concentrically; these crystals do not seem to effloresce, and they become constant in weight after a few days' exposure to the air; they then contain about 3·7 per cent. of water, which is expelled on prolonged heating at 100°:

0·5	lost 0·019	H ₂ O at 100° during 72 hours.	H ₂ O = 3·9.
0·5190	„ 0·0195	H ₂ O „ „ „	H ₂ O = 3·7.
1·1885	„ 0·0444	H ₂ O „ „ „	H ₂ O = 3·7.
C ₁₀ H ₁₄ ClO·SO ₃ H, C ₉ H ₁₁ N + H ₂ O requires H ₂ O = 4·3 per cent.			
C ₁₀ H ₁₄ ClO·SO ₃ H, C ₉ H ₁₁ N + $\frac{3}{4}$ H ₂ O „ H ₂ O = 3·2 „			

As the crystals of the β -salt of the bromo-acid give results which agree well with those required for $\frac{3}{4}$ mol. H₂O, it is rather surprising that this corresponding form of the β -salt of the chloro acid should give values which are not in good agreement with the theoretical ones; for reasons which will appear later, it is possible that this is due to the presence of the other hydrated form of the β -salt.

The second crystalline form of the β -salt, the B variety, separates from water or dilute methyl alcohol in opaque masses of slender, transparent needles, indistinguishable by inspection from the crystals of the α -salts of the chloro- and bromo-acids but absolutely different in appearance from the crystals of the A variety of this salt.

These crystals do not effloresce appreciably, and when air-dried they contain about 5·4 per cent. of water of crystallisation, which is only very slowly expelled at 100°, as the salt gradually liquefies at first, and then forms a vitreous mass.

0·5	lost 0·0265	H ₂ O at 115° (4 hours), at 100° (12 hours).	H ₂ O = 5·3.
0·4	„ 0·0222	H ₂ O „ 100° during 16 hours.	H ₂ O = 5·5.
C ₁₀ H ₁₄ ClO·SO ₃ H, C ₉ H ₁₁ N + $1\frac{1}{4}$ H ₂ O requires H ₂ O = 5·3 per cent.			

These results agree satisfactorily with those required by the above formula, but too much weight should not be attached to them, as it is difficult to ascertain whether this B variety of the β -salt is, or is not,

free from the A form; the two kinds of crystals are often deposited together, and the presence of the A form might easily pass undetected.

Now since a determination of the water of crystallisation in the B variety of the β -salt, for the reason just given, may not be considered conclusive proof of its non-identity with the α -salt, and as, so far, no other evidence has been advanced to show that the two substances are really different, it is necessary to state fully the facts which have led to the conclusion that the β -salt crystallises in two differently hydrated forms. The existence of any ordinary compound in two such forms is of course in no way remarkable, but in view of the possible conversion of one of these partially racemic salts into the other by crystallisation (compare the hydrindamine *cis*- π -camphanates, p. 869), of the curious relation between the two crystalline hydrates of the β -salt, of the fact that the β -salt of the bromo-acid seems to exist in only one form, and of the great similarity between the α -salt of the chloro-acid and the B variety of the β -salt, it cannot be denied that some further evidence is required in order to prove that the A and B crystalline varieties both represent β -salt.

Generally speaking, of course, it is a very simple matter to ascertain whether a substance which gives two kinds of crystals is a mixture or is dimorphous, but in this particular instance there were many difficulties in the way. It is useless, for example, to take the melting point of either the α - or the β -salt, unless the crystals have been thoroughly dehydrated at 100° , an operation which requires about 24 hours. Further, the β -salt, even when thus treated, does not appear to have a definite melting point. Crystals of the A variety which have been heated at 100° during only a few hours or during several days, sometimes melt fairly sharply at about 130° , but other samples only sinter at about 140° and do not melt completely until about 165° . Most samples, in fact, behave much as they might be expected to do if they were really mixtures of the α - and β -salts. This indefinite melting point may possibly be caused by the presence of water, as the dehydrated salt is very hygroscopic, or by the presence of two different crystalline varieties of the anhydrous salt, or by slight decomposition; but after the many determinations which have been made with various samples, it is impossible to believe that it is due to the presence of the α -salt.

Another difficulty in settling this question of the existence of two forms of the β -salt was owing to the fact that the B variety varies very much in appearance and behaviour, according to the conditions under which it is deposited; although generally it forms opaque masses of minute needles, which, when dried on porous earthenware, do not liquefy in the water oven until after some time (30–60 minutes), in other cases, when it has been deposited more slowly, it forms slightly

larger transparent prisms which, like the crystals of the α -salt, liquefy completely in the course of a few minutes.

These statements merely show that a conclusion could not be hastily formed, and the evidence which is relied on to establish the existence of the two varieties of the β -salt has still to be given.

In the first place, then, the two forms A and B often change one into the other on recrystallisation from water or dilute methyl alcohol. Although the variety A may be recrystallised several times, 8, 10, or more, consecutively, without showing the presence of traces of the variety B in the deposit, and although, similarly, the variety B may often be recrystallised several times without passing into the form A, repeated crystallisation, without intentionally altering the quantity of solvent will cause, or, at any rate, has done hitherto, the conversion of one variety into the other, either partially or entirely. The α -salt has been repeatedly crystallised under the same conditions as the β -salt, but it has never yet been observed to give crystals resembling those of the A variety of the β -salt.

In the second place, the specific rotations of the two varieties A and B, calculated for the anhydrous salts, are identical within the limits of experimental error, whilst the specific rotation of the α -salt is lower than that of the β -salt (compare following section).

There can, therefore, be no doubt that the variety B of the β -salt is not the same substance as the α -salt in spite of their outward similarity. The conditions which determine the formation of one or the other variety of the β -salt have not been satisfactorily determined, although presumably it is primarily a question of temperature. Experiments were made to ascertain the influence of a change in temperature, and it was found that when an aqueous solution of the β -salt was cooled to 0° before the separation of oil or of crystals commenced, the form B was deposited, and this occurred repeatedly. The same solution, when concentrated a little, and then allowed to crystallise at the ordinary temperature, gave crystals of the A variety three times consecutively. Moreover, solutions which are beginning to deposit the variety B, if warmed gently to about 20° without dissolving the whole of B, will often deposit the variety A on subsequent cooling.

On the other hand, the variety B often separates when the solutions crystallise at about 15° , at which temperature A is usually deposited. The presence of crystals of one or other variety in the solution does not seem to have any effect on the nature of the subsequent deposit. Solutions from which the form A has been deposited, and in which the crystals are still immersed, if left alone, will sometimes give specks of opaque B in the course of a few hours, but in other cases nothing of the kind happens, even after keeping during several days. The crystals of A in contact with the solution will also remain unaltered for

several days, but at the end of this time usually begin to change in appearance and become opaque at the edges. Whether this is due to the formation of a thin deposit of the B variety or to an actual change in the crystals themselves is difficult to determine. This conflicting evidence seems to show that the temperature at which the one variety changes into the other is within the limits of ordinary atmospheric temperatures, but it would also appear that the concentration of the solution has some effect. A solution which has given one of the two forms, if merely warmed until all the crystals have dissolved, will generally give the same variety again and again, and only on repeating these operations a number of times does the change into the other variety occur. The whole behaviour of the β -salt requires, in fact, a more complete investigation before it can be stated with certainty what are the conditions which determine the formation of one or other of these different hydrates.

It seemed probable, at one time, that the change which the β -salt sometimes undergoes on recrystallisation, might be caused by the resolution of the partially racemic compound into the two salts of the enantiomorphous bases, since Ladenburg has shown (*Ber.*, 1899, 32, 50) that partially racemic strychnine racemate has a definite transition temperature at which such a change occurs; the experiments described in the following section show, however, that this is not the case, and that the two varieties of the β -salt are both partially racemic.

As regards the ordinary properties of the β -salt little need be said; it is only sparingly soluble in cold water, but dissolves freely in cold ethyl or methyl alcohol.

Molecular Weight Determinations.

The molecular weight of the isomeric hydrindamine chlorocamphor-sulphonates was determined in dilute aqueous solution by the cryoscopic method; the results show that the two salts are largely dissociated, the values obtained being approximately half the calculated value.

	Weight of solvent.	Weight of substance.	Grams substance in 100 grams solvent.	Depression of freezing point.	M. W.
α -Salt	25 grams	0.3	1.2	0.100	227
	25 "	0.2	0.8	0.080	190
	25 "	0.3	1.2	0.100	227
β -Salt	25 "	0.3	1.2	0.110	207

Taking the water of crystallisation to be 7.0 per cent. in the α -salt and 3.7 per cent. in the β -salt (variety A), the values would become

$$\alpha\text{-Salt : M.W.} = 200. \qquad \beta\text{-Salt : M.W.} = 199.$$

Conversion of β - into α -Salt.

The close relationship between the isomeric hydrindamine bromocamphorsulphonates and chlorocamphorsulphonates rendered it almost certain that the β -salt of the chloro-, like that of the bromo-acid, would be converted into the α -isomeride on evaporation with the externally compensated base; experiment showed this to be so. If, after evaporating almost to dryness 5—8 times, small quantities of base being added after each evaporation, the residue is crystallised from water, it is deposited in needles identical in appearance with the crystals of the α -salt, and when these needles have been dried for about 30 hours at 100° , they have no longer the indefinite melting point of the β -salt, but liquefy fairly sharply at 162 — 165° .

IV. Specific and Molecular Rotations of the Hydrindamine Chlorocamphorsulphonates.

The determination of the specific rotations of the isomeric hydrindamine chlorocamphorsulphonates was undertaken with two objects; in the first place, in order to prove that the β -salt, in spite of its apparent behaviour to the contrary, is not really converted into the α -isomeride on repeated crystallisation from water; and in the second place, in order to ascertain whether the analogy between the salts of the bromo- and chloro-acids would extend to their optical behaviour.

The first of these points, namely, the homogeneity and unalterability of the β -salt, had of course to be settled before the second could be considered, and the experiments which were made for this purpose may now be described.

A sample of the β -salt, which had been prepared by repeated recrystallisation from water, and which consisted entirely of the (A) variety so far as could be ascertained, was separated by further crystallisation into two approximately equal fractions, I and II, both of which were apparently identical with the original sample; the specific rotations of these two fractions were then determined in aqueous solution, the air-dried salt being used; both fractions contained 3.7 per cent. of water. A 200 mm. tube was used and the volume of the solution was 25 c.c. in both cases.

 β -Salt. (A) Variety.

			Calc. for anhydrous salt.	
	α_D .	$[\alpha]_D$.	$[\alpha]_D$.	$[M]_D$.
I. 0.25	58'	+48.3°	+50.2°	+201°
0.5	1°57'	48.8	50.7	202
II. 0.25	57'	47.5	49.3	197
0.25	59'	49.1	50.9	203
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A sample of the β salt, which had been deposited in the opaque, bulky crystals of the B variety, and which was indistinguishable from the α -salt in appearance, was then examined. The observations were made in aqueous solution in a 200 mm. tube, the volume of the solution being 25 c.c.; the air-dried salt, which was afterwards found to contain 5.2 per cent. of water of crystallisation, was employed.

	$[\alpha]$	$[\alpha]_D$	Calc. for anhydrous salt.	
			$[\alpha]_D$	$[M]_D$
0.5 gram	+1°56'	+48.4°	+51°	+200
0.5 „	1°55'	47.9	50.5	202

Another sample of the variety B, obtained in a different crystallisation, was also examined under the same conditions, with the following result:

$$0.5 \text{ gram} \dots\dots\dots \alpha + 1^\circ 58'. \quad [\alpha]_D + 49.1^\circ.$$

The water of crystallisation in this (air-dried) sample was not determined, but taking it to be 5.2 per cent., as in the previous case, the values for the anhydrous salt would be

$$[\alpha]_D + 51.8^\circ. \quad [M]_D + 207.$$

These results, under ordinary circumstances, would be sufficient to establish the chemical identity of the two different crystalline varieties of the β -salt, especially as the samples recovered from the solutions used in the above experiments could be converted one into the other just as can ordinary preparations of the β -salt.

It must be stated, however, that in one case the examination of the crystalline variety B led to very different results; two portions of one and the same sample, which contained 5.2 per cent. of water, were separately dissolved in cold water, the solutions diluted to 25 c.c., and examined in a 200 mm. tube.

	α_D	$[\alpha]_D$	Calc. for anhydrous salt.	
			$[\alpha]_D$	$[M]_D$
0.25 gram	+1°6'	+54.5°	+57.4°	+229
0.25 „	1°4'	53.5	56.4	225

It will be seen that these values differ very widely from all those previously obtained, and as the difference could not be caused by the presence of the α -salt—which has a lower specific rotation than the β -salt—it seemed possible that a partial resolution of the β -salt had been accomplished. In order to confirm or disprove this view, the sample used in the last two experiments was fractionally crystallised from water, and again obtained, after one or two unsuccessful attempts, as the crystalline variety B. The latter was separated, roughly dried in the air, and examined again under the same conditions

as before (volume = 25 c.c. ; column = 200 mm.). The sample was found to contain 6·8 per cent. of water.

		α_D	$[\alpha]_D$	Calc. for anhydrous salt.	
				$[\alpha]_D$	$[M]_D$
I.	0·5 gram.....	+1°58'	+49·15°	+52·6°	+210
II.	0·4 „	1°34'	48·9	52·4	209

These results agree moderately well with those obtained for the specific rotation of the original samples of the variety A, but the very abnormal values obtained for the variety B in the preceding experiment, combined with the extraordinary behaviour of the isomeric hydrindamine *cis*- π -camphanates (compare pp. 910, *et seq.*), raised suspicion as to the homogeneity of the β -salt and the constancy of its specific rotation in the two different crystalline forms.

A fresh sample of the β -salt was, therefore, crystallised from water and separated into three fractions. The first deposit consisted of the variety A ; it was dried in the air until constant, and it was then taken as containing 3·7 per cent. of water. The second crop consisted of the variety B, and when air-dried contained 5·5 per cent. of water. The third crop also consisted of the variety B, and when air-dried contained 6·0 per cent. of water.

The specific rotations of the air-dried fractions were determined in aqueous solution ; volume = 25 c.c. ; column of liquid, 200 mm.

		α	$[\alpha]_D$	Calc. for anhydrous salt.	
				$[\alpha]_D$	$[M]_D$
I.	(A). 0·5 gram	+1°52'	+46·7°	+48·5°	+194
II.	(B). 0·5 „	1 56	49·0	51·8	207
III.	(B). 0·5 „	1 52	46·6	49·5	198

The first fraction (A variety), crystallised again from water, gave a deposit of the variety A ; this was dried in the air, and examined under the same conditions as above.

0·5 gram (variety A). α +1°55'. $[\alpha]_D$ +47·95°.

This sample was found to contain 3·45 per cent. of water, so that the specific and molecular rotations of the anhydrous salt are :

$[\alpha]_D$ +49·6°. $[M]_D$ +198°.

It may be concluded from these results, firstly, that the two crystalline varieties of the β -salt become identical in solution, and that neither is identical with the α -salt ; secondly, that the formation of the crystalline variety (B) of the β -salt is not caused by a resolution of that salt into different optically active components which are separable by fractional crystallisation.

It will, perhaps, be noted that the results obtained in all these experiments with the β -salt, excluding the two very abnormal values on p. 898, which are possibly due to some large experimental error, vary from $[\alpha]_D + 48.5^\circ$ to $+52.6^\circ$ in solutions of practically the same concentration; this want of agreement is probably caused in some measure by unavoidable errors introduced in allowing for the water of crystallisation. During the prolonged heating at 100° , which is required before the salt becomes fairly constant in weight, it evidently undergoes slight decomposition, and on subsequent treatment with water, it gives a slightly coloured and faintly turbid solution; hence the loss, which is attributed to water of crystallisation, may be partly due to other changes.

Specific and Molecular Rotations of the Isomeric Salts.

For the second main object of the optical examination of these compounds, namely, the comparison of the specific and molecular rotations of the α - and β -salts with one another, and with those of the corresponding salts of the bromo-acid, experiments were made in three different solvents, as in the case of the last-named compounds.

The specific rotation of the α -salt was first determined in aqueous solution with an air-dried sample containing 7.05 per cent. of water of crystallisation; the volume of the solution was 25 c.c., and a 200 mm. tube was employed in all cases.

		Calc. for anhydrous salt.			
		α_D	$[\alpha]_D$	$[\alpha]_D$	$[M]_D$
(1)	0.25 gram	$+52'$	$+43.3^\circ$	$+46.5^\circ$	+186
(2)	0.25 „	$48'.5$	40.3	43.3	173
(3)	0.25 „	$54'$	45.0	48.3	193
(a)	0.5 „	$1^\circ 43'$	43.0	46.2	185
(b)	0.5 „	$1^\circ 46'$	44.1	47.5	190

Excepting (2), the results are sufficiently concordant, and give for the molecular rotation $[M]_D$ a mean value +188.

Now the mean value for the molecular rotation of the β -salt, calculated from the most concordant results given above, is +202, so that in dilute aqueous solution the two isomerides have but slightly different molecular rotations; this difference practically disappears in dilute alcoholic solutions, but becomes more marked in chloroform solutions.

Alcoholic Solutions. α -Salt.—An air-dried sample containing 7.05 per cent. of water was used in these experiments; the solvent was 99.8 per cent. ethyl alcohol, volume of the solution 25 c.c., and length of the tube 200 mm.

		Calc. for anhydrous salt.			
		α_D	$[\alpha]_D$	$[\alpha]_D$	$[M]_D$
1 gram	$+4^{\circ}12'$	$+52.6^{\circ}$	$+56.6^{\circ}$	$+226$	
1 „	$4^{\circ}8'$	51.7	55.6	222	

β -Salt.—This salt was examined under exactly the same conditions, but three different samples were used, and one of them (1) had been dried at 100° ; the other two (2 and 3) were air-dried samples of the crystalline variety A, and were taken as containing 3.7 per cent. of water.

		Calc. for anhydrous salt.			
		α_D	$[\alpha]_D$	$[\alpha]_D$	$[M]_D$
(1) 0.5190 gram	$+2^{\circ}13'.5$	$+53.6^{\circ}$	$+53.6^{\circ}$	$+214$	
(2) 0.5 „	$2^{\circ}8'$	53.4	55.4	221	
(3) 1.0 „	$4^{\circ}11'$	52.5	54.5	218	

It is possible that prolonged heating at 100° may effect the specific rotation of the β -chloro-salt, just as it seems to do in the case of the β -bromo-salt, and, neglecting the result of experiment (1), the specific and molecular rotations of the isomeric chloro-salts become practically identical.

Chloroform Solution.—Air-dried samples were used in both cases; the volume of the chloroform solution was 25 c.c., and a 200 mm. tube was used.

α -Salt: 0.5 gram	$\alpha_D + 1^{\circ}16'$	$[\alpha]_D + 31.3^{\circ}$
β -Salt: 0.5 „	$\alpha_D + 1^{\circ}42'$	$[\alpha]_D + 42.5^{\circ}$

As the variety (A) of the β -salt was used, it may be taken as containing 3.7 per cent. of water; the α -salt contained 7.05 per cent. The values for the anhydrous substances would therefore be the following:

α -Salt:	$[\alpha]_D + 33.6^{\circ}$	$[M]_D + 134$
β -Salt:	$[\alpha]_D + 44.1^{\circ}$	$[M]_D + 176$

Molecular Rotation of Chlorocamphorsulphonic Acid.

Before comparing the molecular rotations of the isomeric salts of chlorocamphorsulphonic acid with those of the corresponding derivatives of the bromo-acid, it was necessary to determine the molecular rotation of the first-named acid.

The only data available for this purpose were those obtained some time ago by Kipping and Pope, who determined the specific rotations of the sodium and barium salts of chlorocamphorsulphonic acid in aqueous solution (Trans., 1893, 63, 601). The values then obtained were $[\alpha]_D + 63.8^{\circ}$ in the case of the sodium salt and $[\alpha]_D + 46.8^{\circ}$ in that

of the barium salt, from which the molecular rotation $[M]_D$ is calculated to be +184 and +177 respectively.

For the purpose of obtaining further information on this point, ammonium chlorocamphorsulphonate was prepared; this salt, judging by analogy, should give in 1—2 per cent. aqueous solution values for the molecular rotation of the acid which could be satisfactorily compared with those obtained in the case of the isomeric hydrindamine salts and also with those of the hydrindamine bromocamphorsulphonates.

Samples of this ammonium salt, dried at 100° , were examined optically in aqueous solution in a 200 mm. tube.

Weight of salt.	Volume of solution.	α_D .	$[\alpha]_D$.	$[M]_D$.
0.25 gram.	25 c.c.	+1°19.5'	+66.25°	+187
0.25 "	"	1°18.5'	65.5	185
0.5 "	"	2°41'	67.0	190

The mean of these concordant results gives a molecular rotation $[M]_D + 187$, a value which agrees well with those obtained in the case of the sodium and barium salts, but which is a little higher than both of these, just as the molecular rotation of the bromo-acid, deduced from an examination of its ammonium salt, is a trifle higher than the value obtained by Walden (compare p. 886).

On now comparing the molecular rotations of the isomeric hydrindamine salts of chlorocamphorsulphonic acid with the value just obtained, it will be seen that the α -salt shows the normal behaviour, whilst the molecular rotation of the β -salt is a little too high.

α -Salt: $[M]_D + 188$. Acid: $[M]_D + 187$. β -Salt: $[M]_D + 202$.

The difference in the case of the latter, however, is almost insignificant, and the only reason why attention is drawn to it is because in the case of the hydrindamine bromocamphorsulphonates, the conditions are reversed, the β -salt having a molecular rotation below the normal value (compare p. 885).

Considering the results of the optical examination as a whole, the behaviour of the hydrindamine chlorocamphorsulphonates is obviously analogous to that of the isomeric salts of the bromo-acid, and the results also show that the two chloro-salts are both partially racemic substances; any possibility of a resolution of the externally compensated base having occurred in the case of the salts of the bromo-acid is thus excluded, as there can be no doubt that the isomerism of the chloro-salts is due to the same cause as that of the α - and β -bromo-salts.

V.—*Hydrindamine cis- π -Camphanates.*

In order, if possible, to obtain further examples of isomeric partially racemic salts, the investigation of which might help to explain the existence of the isomeric hydrindamine bromo- and chlorocamphorsulphonates, it seemed desirable in the first place to try and prepare such isomerides from the same base as before, namely, externally compensated hydrindamine, but using an acid altogether different from those already employed.

Now optically active monobasic acids which give stable, well-crystallised salts, with the exception of the sulphonic acids of camphor and its derivatives, are not easily obtainable, but among the new derivatives of camphor recently investigated there occurred an acid which seemed suitable for the purpose in view, namely, *cis- π -camphanic acid* (Trans., 1896, 69, 943).

cis- π -Camphanic acid, as previously shown, is a lactonic monocarboxylic acid of the composition $C_{10}H_{14}O_4$; as it is practically insoluble in cold water and only sparingly soluble in most ordinary organic solvents, it seemed probable that it might give, with externally compensated hydrindamine, salts which would crystallise readily, and which might possibly exist in isomeric forms. Experiment showed this supposition to be well founded, and the properties of two isomeric hydrindamine *cis- π -camphanates* are described in this section of the paper.

Before passing to the consideration of these salts, it may be stated that the acid is a well-defined substance which shows very great stability in many ways, and the lactonic ring contained in it is not readily hydrolysed by sodium hydroxide solution at ordinary temperatures; it is, at the same time, a comparatively feeble acid, and some of its salts, as, for example, its quinoline and ammonium salts (*loc. cit.*), undergo hydrolytic dissociation very readily in aqueous solution.

The study of the isomeric hydrindamine *cis- π -camphanates* has shown that these two compounds are both partially racemic salts, and their formation may therefore be explained in the same way as that of the isomeric hydrindamine bromocamphorsulphonates (p. 868) and chlorocamphorsulphonates, namely, by assuming that the negative acid ion becomes united to nitrogen valencies, which being those of a nitrogen atom contained in an enantiomorphous compound, are necessarily differently situated.

In accordance with this view, the more readily soluble salt can be partially converted into the isomeride by repeated evaporation with an aqueous solution of the externally compensated base.

The isomeric hydrindamine *cis- π -camphanates* differ, however, from

the salts of the sulphonic acids in undergoing hydrolytic dissociation to some extent in aqueous and in aqueous alcoholic solutions, and this difference in behaviour has the important consequence that the salts are partially converted one into the other on solution in these solvents; this, for the reasons already given (p. 869), was to be expected.

Owing to the fact that *cis*- π -camphanic acid is practically insoluble in cold water, it was easy to prove that its isomeric salts do not represent salts of enantiomorphous hydrindamines (p. 909); the question of the possible autoracemisation of the optically active base being considered as an explanation of the formation of the various isomeric salts described in these papers is therefore definitely answered in the negative.

Preparation of the Salts.

cis- π -Camphanic acid is dissolved in methyl alcohol and an aqueous or alcoholic solution of hydrindamine is added until a permanent alkaline reaction is obtained; on evaporating the solution to a small volume and then adding methyl alcohol, and allowing to cool, the salt is deposited in colourless needles, and by repeated fractional crystallisation at different temperatures, preferably from ethyl alcohol, the product is separated into two components.

α -Salt.

The more sparingly soluble salt, hereafter referred to as the α -compound, melts almost sharply at about 193°, when it is heated fairly quickly from about 100°, but as it slowly decomposes and turns brown even at comparatively low temperatures, its melting point depends to some extent on the rate of heating. It crystallises from ethyl alcohol and other solvents in slender, concentrically grouped prisms or needles, which are deeply striated, and appear to consist of bundles of smaller crystals, and it dissolves fairly easily in boiling alcohol and water, but is only sparingly soluble in cold ethyl acetate, ether, or boiling chloroform. When crystallised from methyl alcohol containing acetone, it soon darkens in colour, and after some time a considerable quantity of tarry matter is formed.

β -Salt.

The more readily soluble salt, which will be referred to as the β -salt, melts and decomposes slightly at about 173°, but here again the melting point depends to some extent on the rate of heating; in appearance, and in all other ordinary properties, the β -salt resembles the α -compound very closely, but its crystals are usually smaller and its solubility is greater than that of the latter.

The relative quantities of the two salts obtained after repeated fractional crystallisation were determined in one experiment and found to be 1·8 grams of the pure α -salt and 3·1 grams of the β -compound, together with about 2·0 grams of a mixture of the two melting at about 168°. In spite of the difference in melting point of the two salts, it is, however, a very difficult matter—if not impossible—to make sure that the β -compound is free from the α -salt, as its melting point is not very much altered by the presence of a small quantity of the latter, and a mixture of approximately equal quantities of the two salts only sinters at about 165°, melting almost completely at about 170°. For this reason, the fraction melting at about 168°, referred to above, must not be considered to represent β -salt; it is more probably a mixture of approximately equal quantities of the two components.

It will be seen from these numbers that the quantities of the α - and β -salts are probably much more nearly equal than in the case of the α - and β -salts of hydrindamine bromocamphorsulphonic acid, and that whereas in the latter case the relative quantity of the β -salt is very small, the β -*cis*- π -camphanate is probably formed in rather larger quantities than the α -salt.

The Salts are Isomeric.

Since *cis*- π -camphanic acid is a lactonic monocarboxylic acid, which when boiled with a solution of sodium hydroxide is converted into a salt of a hydroxydicarboxylic acid (Kipping, *Trans.*, 1896, **69**, 945), little interest could be attached to these two salts until it had been proved that they are isomeric, for the one might have been derived from the lactonic monocarboxylic acid, the other from the hydroxydicarboxylic acid.

Now the percentage composition of the normal salt of a *cis*- π -camphanic acid differs but little from that of the normal salt of the hydroxydicarboxylic acid, as will be seen from the following numbers :

$C_{10}H_{14}O_4, C_9H_{11}N$ requires C = 68·8; H = 7·5; N = 4·2 per cent.

$C_{10}H_{16}O_5, 2C_9H_{11}N$ „ C = 69·8; H = 7·6; N = 6·9 „

The results of combustions would not, therefore, decide satisfactorily between the two possible formulæ, and nitrogen determinations would probably have given results intermediate between the two values 4·2 and 6·9.

Under these circumstances, the following methods were adopted to establish the isomerism of the two compounds :

Firstly, both salts were separately dissolved in methyl alcohol, the solutions rendered distinctly alkaline with hydrindamine, and then

heated on the water-bath in closed vessels during about 3 hours; at the end of this time, both solutions, which were still alkaline, were allowed to evaporate spontaneously. The deposits melted at 173° and 193° respectively, showing that the two salts had not been appreciably changed by this treatment; had one of them been derived from a mono-, the other from a di-carboxylic acid, the former should have been converted into the latter under the conditions of the experiment, and the solution should have become neutral.

Both salts are anhydrous. After recrystallisation from methyl alcohol and ether, finely divided samples were dried in the air during 2 days and then heated at 100° during 1 hour; the α -salt lost only 0.8 per cent., the β -salt 1.8 per cent., the percentage of water required for $C_{10}H_{14}O_4 \cdot C_9H_{11}N + \frac{1}{2}H_2O$ being 2.6 per cent. On further heating at 100° , both salts continued to lose in weight very slowly, and after 24 hours heating, the total loss amounted to 4.2 per cent. in the case of the α - and 8.4 per cent. in the case of the β -compound; as, however, both compounds had turned brown, the β -salt especially, and their weights had not become constant, it must be concluded that the loss on heating is due to decomposition and volatilisation of the base.

For the further analysis of the two compounds, the samples were dried over sulphuric acid.

The determination of the percentage of hydrindamine in the two salts offered the best means of deciding between the two possible formulæ, and this was done in two ways.

In the first method, a weighed quantity of the salt was treated with excess of a solution of barium hydroxide in a current of steam, the base collected in hydrochloric acid, the solution evaporated to dryness, and the residue of hydrindamine hydrochloride weighed; the results were as follows:

α -Salt. 0.4 gave 0.1924 $C_9H_{11}N, HCl$. $C_9H_{11}N = 37.7$.

β -Salt. 0.4 „ 0.1984 $C_9H_{11}N, HCl$. $C_9H_{11}N = 39.1$.

$C_{10}H_{14}O_4 \cdot C_9H_{11}N$ requires $C_9H_{11}N = 40.2$ per cent.

$C_{10}H_{16}O_5 \cdot 2C_9H_{11}N$ „ $C_9H_{11}N = 51.3$ „

Control experiments were made with hydrindamine hydrochloride under exactly the same conditions, and the following results were obtained:

0.2008 gave 0.1954 $C_9H_{11}N, HCl$ or 97 per cent. of the theoretical.

0.1969 „ 0.1835 $C_9H_{11}N, HCl$ „ 93 „ „ „

In the second analytical method, a weighed quantity of the salt was dissolved in the smallest possible quantity of hot methyl alcohol, the solution treated with a slight excess of concentrated hydrobromic

acid, and then evaporated, first on a water-bath until nearly dry, and then over potash and sulphuric acid; after about 2 days, the residues were nearly constant in weight, but a further loss of about 2 milligrams occurred in the course of about a fortnight.

α -Salt. 0.3 gave 0.3741 $C_9H_{11}N, HBr + C_{10}H_{14}O_4$.

β -Salt. 0.3 „ 0.3745 $C_9H_{11}N, HBr + C_{10}H_{14}O_4$.

Calculated for $C_{10}H_{14}O_4, C_9H_{11}N$ residue = 0.3734.

„ „ $C_{10}H_{16}O_5, 2C_9H_{11}N$ „ = 0.4305.

These results, especially those obtained by the last method, which is the more satisfactory of the two, prove that the two salts are isomeric, and that they are both normal salts of the lactonic monocarboxylic acid; it may also be stated that the acid which is liberated from the two salts on addition of hydrobromic acid is unchanged *cis*- π -camphanic acid, easily recognisable by its highly characteristic crystalline form.

Both the α - and β -Salts give Optically Inactive Base.

The next point to decide was whether the externally compensated base had been resolved into its enantiomorphous components by fractional crystallisation of the salts which it forms with *cis*- π -camphanic acid. For this purpose, a small quantity (0.4 gram) of the α -salt was decomposed with aqueous barium hydroxide, the base separated by steam distillation and collected in hydrochloric acid; the solution of the hydrochloride was concentrated to about 15 c.c. and then examined in a 200 mm. tube, but no rotation could be observed; a repetition of the experiment, using a larger quantity of the salt, gave the same result.

It is obvious, then, that the externally compensated base has not been resolved into its optically active components, and consequently it seems very probable that the isomerism of these two salts is due to the same cause as that which holds in the case of the α - and β -salts of the bromo- and chloro-camphorsulphonic acids.

For this reason, it seemed quite unnecessary to repeat all the experiments which were made in the case of the bromo-salts in order to prove that the isomerides contain one and the same base.

Conversion of the β - into the α -Salt.

The conversion of the β - into the more sparingly soluble α -isomeride can be accomplished by evaporating its aqueous or alcoholic solution with a small quantity of hydrindamine; the change, however, does not take place very readily, possibly because the quantity of the β -salt in equilibrium with the α -isomeride is larger than in the case of the bromocamphorsulphonic salts; after one or two evaporations, the

product melts over a wide range of temperature, and is doubtless a mixture of the two isomerides, but on repeated treatment, its melting point rises, becomes more definite, and finally reaches that of the α -salt.

Hydrolytic Dissociation of the Two Salts.

The α - and β -salts of *cis*- π -camphanic acid differ from the hydrindamine bromo- and chloro-camphorsulphonates in undergoing hydrolytic dissociation in aqueous and alcoholic solutions; on boiling a solution of either salt in dilute methyl alcohol, hydrindamine is slowly evolved, a litmus paper suspended in the vapour very slowly turns blue, and the solution acquires an acid reaction.

Hydrolytic dissociation takes place to such a limited extent, however, that, judging by their melting points, the salts are not appreciably altered by crystallisation from methyl or ethyl alcohol; even when their solutions in a large volume of these solvents have been heated for some time and then evaporated almost to dryness, the crystalline deposits, after having been merely spread on porous earthenware, have the melting points of the original preparations. This statement does not imply that the salts are unchanged; it is, as already mentioned, a matter of considerable difficulty to prove that the β -salt is really free from its isomeride.

In discussing the nature of these isomeric salts, it was pointed out that, according to the explanation suggested, hydrolytic dissociation should bring about the partial conversion of one isomeride into the other; experiments were therefore made in order to ascertain whether this could be done in the case of these *cis*- π -camphanates, which are doubtless hydrolytically dissociated to some extent.

For this purpose, an aqueous solution of the β -salt was heated during several hours on the water-bath, then evaporated to dryness, and the residue recrystallised from a small quantity of alcohol; the deposit sintered at about 165° , and did not melt completely until about 175° ; on repeating the above treatment, the deposit melted through approximately the same range of temperature; there is thus presumptive evidence that a partial conversion of the β - into the α -salt had occurred. Since, under the above conditions, some hydrindamine is lost during evaporation, the indefinite melting point of the product might possibly have been due to the presence of *cis*- π -camphanic acid, and, as a matter of fact, on *repeatedly* evaporating such a solution of the β -salt, and then crystallising from alcohol, the first deposit consists almost entirely of crystals of this acid.

In order to try and eliminate this source of inaccuracy, the experiment was carried out differently. A small quantity of the β -salt was dissolved in hot water, the solution placed in a closed vessel and

left at the ordinary temperature during several days; the solution was then allowed to evaporate to dryness spontaneously. The deposit thus obtained was evidently a mixture of the α - and β -salts, as it melted from about 165—180°.

The α -salt, treated with water in an exactly similar manner, seems to be partially converted into the β -salt, as the deposit thus obtained melts from about 185—190°; the change, however, seems to be only a very partial one, probably because the β -salt which is produced is gradually reconverted into the α -isomeride during the slow crystallisation.

The Enantiomorphous Hydrindamines have not been separated.

The determinations of the specific rotations of the isomeric hydrindamine bromocamphorsulphonates and chlorocamphorsulphonates, and the fact that the α - and β -isomerides do not change one into the other on solution in a large volume of water, prove that, if these isomerides are really the salts of enantiomorphous hydrindamines, the optically active base does not undergo autoracemisation when its salts are electrolytically dissociated. Now the salts of *cis*- π -camphanic acid probably do undergo a partial change one into the other in aqueous solution, as just stated, but this is doubtless the result of hydrolytic dissociation only. Since, then, it may be taken as proved that the base ions do not racemise, if the base of the α - or β -salt of any one of the three acids can be transferred to an optically inactive acid without being at any time set free from combination, an examination of the new salt would show whether the base was or was not optically active, and thus the question of the possibility of the salts being those of enantiomorphously related bases would be definitely settled.

In the case of the salts of the sulphonic acids, it was not very easy to carry out such an experiment satisfactorily, as the acids are both very readily soluble in water, and could not well be separated from the new salt; but *cis*- π -camphanic acid being practically insoluble, its isomeric salts were very suitable for the purpose in view, and were therefore examined as follows.

A quantity (2 grams) of the β -salt, in a finely divided condition, was triturated with excess of concentrated hydrochloric acid, and after keeping for a few minutes the liberated *cis*- π -camphanic acid was separated by filtration from the solution of hydrindamine hydrochloride; the residue was washed with a little ice-cold water, and the combined filtrate and washings, having been made up to about 15 c.c., were examined in a 200 mm. tube. The average of eight concordant readings gave $\alpha - 0^{\circ}6'$.

This feeble levorotation was certainly due to the presence of a small

quantity of *cis*- π -camphanic acid, which is not absolutely insoluble in cold water, and which has a specific rotation of about -24° in dilute aqueous solution.

The contents of the tube and washings were then evaporated to dryness, the residual hydrindamine hydrochloride dissolved in cold water, and the solution filtered from a very small deposit of *cis*- π -camphanic acid. On then diluting to about 15 c.c., and again examining the solution in a 200 mm. tube, it gave $\alpha -0.2'$ and the same rotation, within the limits of experimental error, was shown by a cold saturated aqueous solution of *cis*- π -camphanic acid.

It is thus proved that the base of the β -salt is optically inactive, and a similar experiment with a small quantity of the α -salt gave the same result; as the base was at no time in the free state during the conversion of these salts into the hydrochloride, and as the base does not undergo autoracemisation in a state of combination, it is thus proved that the α - and β -salts of *cis*- π -camphanic acid both contain equal quantities of *d*- and *l*-hydrindamines.

VI.—*Specific and Molecular Rotations of the Hydrindamine cis- π -Camphanates.*

Of the results obtained in the study of the isomeric salts which have now been described, not the least interesting and, at the same time, the most difficult to explain satisfactorily, are those which have accrued during the optical examination of the isomeric hydrindamine *cis*- π -camphanates.

From the numerous observations which have been made, and which are recorded in this section, it would seem that different preparations of the α -salt, all of which have the same, and a fairly sharp, melting point, have totally different specific rotations in methyl alcoholic solution, the values ranging from $[\alpha]_D -8^\circ$ to $+20^\circ$; different samples of the β -salt also gave values ranging from $[\alpha]_D -10^\circ$ to -20° , although the samples melted at the same temperature.

Now, in the case of the β -salt, this comparatively small variation in specific rotation might possibly be due to the presence of small quantities of the α -isomeride, but in the case of the latter, where the difference in the specific rotation of different preparations is most marked, no such explanation is possible, as the quantity of β -salt which would be required to produce the observed result would be so large that its presence could not fail to be detected by ordinary examination.

Another remarkable fact brought to light is that the α -salt shows mutarotation in methyl alcoholic solution in a very marked manner,

whilst in the case of the β -isomeride a corresponding change has not been detected with certainty.

This difference in behaviour between two salts, otherwise so similar, recalls another instance already recorded, namely, the existence of two differently hydrated forms of the β -salt of hydrindamine chloro-camphorsulphonate and of only one form of the corresponding compound of the bromo-acid.

The discussion of these results is best postponed until the experimental data have been given, but it may be stated here that in dilute aqueous solution, the molecular rotations of the isomeric hydrindamine *cis*- π -camphanates appear to be normal on the assumption that the salts are both partially racemic substances.

Specific Rotation of the α -Salt.

The determination of the specific rotation of the α -salt was found to be a matter of considerable difficulty, and a large number of experiments had to be made.

The sample which was first examined had been heated at 100° for some time, and as slight decomposition had occurred, the result may not be very trustworthy; the solvent was 99.8 per cent. methyl alcohol, the volume of the solution 25 c.c., and the column of liquid 200 mm.

Exp. I. 0.2991 gram. $\alpha + 43.3$ $[\alpha]_D + 30^\circ$.

For the next determination, a different sample, obtained by crystallisation from ethereal alcohol, was used; this preparation was dried over sulphuric acid, the solvent and other conditions remaining the same.

Exp. II. 0.3 gram. $\alpha + 18$. $[\alpha]_D + 12.5^\circ$.

This result differed so widely from the preceding one that a third specimen of the α -salt was prepared; the sample, which melted sharply at 193° was dried at 100° during a few minutes only, and examined under the same conditions as before.

Exp. III. 0.3 gram. $\alpha - 3$. $[\alpha]_D - 2^\circ$.

Here again, an entirely different value was obtained, although the three preparations used in these three experiments had all exactly the same melting point, and seemed in other respects to consist of pure α -salt.

Now, it has already been pointed out that the α -salt is partially transformed into the β -isomeride on solution in water, owing to the occurrence of hydrolytic dissociation (p. 908), but so far as can be ascertained, the change is comparatively limited, even when the solution has been kept during several days; consequently, it seemed very improb-

able that mere solution in methyl alcohol would bring about a similar transformation to such an extent as to appreciably alter the specific rotation, especially as it had been proved that alcoholic solutions of the α -salt might be heated and evaporated without the melting point of the salt being obviously changed.

However, in order to ascertain whether prolonged treatment with such alcoholic solvents produced any change in the specific rotation, the whole of the solution used in Exp. III, together with the washings of the tube, &c., was evaporated nearly to dryness, again diluted to 25 c.c. with 99.8 per cent. methyl alcohol, and examined as before in a 200 mm. tube.

Exp. IV. 0.3 gram. $\alpha \pm 0$.

This result bears out the view that the α -salt undergoes no appreciable change into the (laevorotatory) β -salt when it is dissolved in and heated with methyl alcohol.

The experimental error in dealing with such feebly active solutions is of course so large that little weight can be attached to the actual numerical results of Exps. III and IV, but it is obvious that if any change in specific rotation occurs it is a very small one.

As it appeared from the first three determinations that samples of the α -salt of identical melting point may have a specific rotation ranging over very wide limits, a second series of experiments was made.

A fresh sample of the α -salt was prepared, dried over sulphuric acid, and examined in a 200 mm. tube in 99.8 per cent. methyl alcoholic solution; volume = 25 c.c.

Exp. V. 0.6 gram. $\alpha + 5'$. $[\alpha]_D + 1.7^\circ$.

A portion of this sample was then fractionally crystallised from methyl alcohol; it was thus separated into three fractions and a mother liquor, which, however, did not contain a large quantity of the salt.

The whole of each of the three fractions was then separately dissolved in 99.8 per cent. methyl alcohol and examined in a 200 mm. tube; volume of solution = 25 c.c. in each case. The results were as follows:

			α .	$[\alpha]_D$.
Exp. VI.	1st fraction	0.3170 gram	28'	+18.5°
„ VII.	2nd „	0.4510 „	+12'	+ 5.5°
„ VIII.	3rd „	0.3875 „	+23'	+12.3°

These three fractions and the parent substance (Exp. V) all melted sharply and simultaneously at about 193°, and yet there is again a great difference in their specific rotations; moreover, the

specific rotation of all three fractions is very much higher than that of the parent substance.

In the course of these experiments, there seemed to be indications of the occurrence of mutarotation, the first readings sometimes showing a smaller dextrorotation than the later ones; for this reason, the observations in Exps. VI to VIII were not taken until some time after the solutions had been prepared, but in the case of Exps. I and V no particular attention was paid to this matter as mutarotation had not been suspected.

Mutarotation of the α -Salt.

In order to study this supposed mutarotation and, if possible, to obtain some fairly concordant values for the specific rotation of the α -salt, a considerable quantity of a fresh sample was obtained by repeated crystallisation from methyl alcohol; this sample was then separated by further crystallisation from methyl alcohol into three fractions, a very small quantity only being left in the mother liquor. All the crystallisations were carried out as quickly as possible, the first and second deposits being obtained by merely cooling the alcoholic solution, and the third by cooling after rapidly boiling off some of the solvent.

The three fractions and the parent substance all melted sharply and simultaneously at 193° , and the residue from the mother liquor sintered only a few degrees lower, namely, at about 188° .

The samples were dried for a few minutes at 100° , and then over sulphuric acid.

For the determination of the specific rotation, 99.8 per cent. methyl alcohol was again employed, the volume being 25 c.c. and the column of liquid 200 mm.

				α .	$[\alpha]_D$.
Exp. IX.	Fraction I.	0.3 gram.	$\left\{ \begin{matrix} (i) \\ (f) \end{matrix} \right.$	$+27^{\circ}0$ $36^{\circ}5$	$+18^{\circ}7$ $25^{\circ}4$
,, X.	,, II.	0.3	$\left\{ \begin{matrix} (i) \\ (f) \end{matrix} \right.$	$17^{\circ}7$ $29^{\circ}7$	$12^{\circ}3$ $20^{\circ}6$
		0.3	$\left\{ \begin{matrix} (i) \\ (f) \end{matrix} \right.$	$31^{\circ}7$	$22^{\circ}1$
,, XI.	,, III.	0.3	$\left\{ \begin{matrix} (i) \\ (f) \end{matrix} \right.$	$15^{\circ}8$ $36^{\circ}0$	$11^{\circ}0$ $25^{\circ}0$

The mean of the first 6—8 readings, taken as soon as possible after dissolving the salt, gives the value for what may be considered to be approximately the initial specific rotation. These values are given first, under (i), but as the rotation increases in the course of a few minutes, it is not possible to determine them very accurately. After about an hour's time, or less, the rotation apparently becomes

constant, and the average of the readings then taken gives the final value (α).

It is obvious from these results that the α -salt shows mutarotation in methyl alcoholic solution in a very marked manner, the initial value for the specific rotation being less than half the final value in Exp. XI. The agreement between the final results obtained with the three different fractions, considering the large experimental error, is also fairly satisfactory, and might be taken as an indication that the α -salt is a stable and homogeneous substance.

In order to check these results and study more closely this change in specific rotation, the following experiments were next made.

A sample of α -salt which, judging by its melting point, was free from its isomeride, was crystallised three times from hot ethyl alcohol; the most sparingly soluble portion and two successive deposits from the mother liquors all seemed to be pure α -salt.

The most sparingly soluble portion was then examined in 99.8 per cent. methyl alcoholic solution in a 200 mm. tube, 0.3 gram of the salt being used, and the volume of the solution 25 c.c.

Exp. XII.—The average of the first seven readings, which ranged from $\alpha + 3'$ to $+11'$, and which rose almost continuously, gave

$$\alpha + 7' \qquad [\alpha]_D + 4.8^\circ$$

This is a much lower result than any of the initial values given before, perhaps owing to the fact that the salt was very finely divided and dissolved very quickly, so that all the readings were taken within less than 5 minutes after pouring the alcohol on to the salt.

The average of six readings taken about 15 minutes later gave

$$\alpha + 25' \qquad [\alpha]_D + 17.3^\circ$$

Thirty minutes later still, that is to say, about 50 minutes after solution commenced, the average of six readings gave

$$\alpha + 34' \qquad [\alpha]_D + 23.6^\circ$$

The solution was then left in the polarimeter tube overnight and examined the next morning, when the average reading was

$$\alpha + 30' \qquad [\alpha]_D + 20.8^\circ$$

After a further lapse of 24 hours, the average reading was again

$$\alpha + 30' \qquad [\alpha]_D + 20.8^\circ$$

The value $[\alpha]_D + 23.6^\circ$ compares well with the results obtained in Exps. IX to XI, and the difference between it and the last result,

$[\alpha]_D + 20.8^\circ$, is practically within the limits of experimental error, as changes of temperature no doubt occurred.

A consideration of the results recorded in Exps. I to XII would, perhaps, lead to the conclusion that, in spite of the statement on p. 913, the observations in Exps. VI to VIII had been taken before mutarotation had ceased. Such a view would, of course, explain in a great measure the differences in the observed values for the specific rotation of the α -salt. Fortunately, an opportunity occurred to set all such doubts at rest, as will be seen from the results of the following experiments.

A sample of the α -salt, prepared directly from the acid by evaporating the latter with an aqueous solution of externally compensated base, and then fractionally crystallising from ethyl alcohol, was finally obtained in a very fine state of division and was dried over sulphuric acid; this sample melted almost sharply at about 193° , and showed no sign of sintering even at 190° .

Exp. XIII. 0.4 gram of this sample was then dissolved in 99.8 per cent. methyl alcohol, the solution diluted to 25 c.c. and examined in a 200 mm. tube.

The average of the first seven readings taken in less than 5 minutes after first adding the solvent was

$$\alpha - 15' \qquad [\alpha]_D - 7.8^\circ$$

The solution was left in the tube and examined 15 minutes, 30 minutes, and 15 hours later, but no appreciable change in rotation was observed, the greatest difference between the average readings taken at the four different times being only about $4'$, when at the end of 15 hours the specific rotation had apparently become $[\alpha]_D - 5.7^\circ$. This difference is so small that it may be neglected.

The melting point of the original sample was again taken, and also that of the deposit obtained on evaporating practically to dryness the solution of the salt used in this experiment; the two specimens melted sharply and simultaneously at about 193° , and the deposit from the methyl alcoholic solution appeared to be a pure homogeneous compound.

It is thus proved conclusively that different samples of the α -salt, all melting at the same temperature and apparently pure, may have a specific rotation $[\alpha]_D$ ranging from about -8° to $+25^\circ$, and that these widely different values are obtained even when sufficient time has been allowed for the ordinary mutarotation of the salt to have taken place.

Now it has been observed by Lowry, by whom the term mutarotation was first employed in connection with such changes (Trans., 1899, 75, 211), that chloroform solutions of nitrocamphor which ordinarily

exhibit the phenomenon of mutarotation, sometimes fail to do so spontaneously and remain unchanged during several days; but that when such labile solutions are disturbed or warmed, mutarotation sets in and takes its normal course.

In order to ascertain whether anything of this kind occurred in the case of the α -salt, the methyl alcoholic solution of the salt used in Exp. XIII was kept for some days, then heated for some time on the water-bath and after cooling, diluted to its original volume; on examination, it was found to show the same rotation as before, namely, $[\alpha]_D - 7^\circ$.

It may be concluded from this result that the different values obtained for the specific rotation of the α -salt cannot be attributed to the non-occurrence or only partial occurrence of mutarotation; the question arises then what other explanation can be advanced?

A satisfactory answer to this question, and to another, namely, what is the cause of the mutarotation of the α -salt, cannot be given; the second point, however, will be considered later on, when the results of the examination of the β -salt have been described.

Specific Rotation of the β -Salt.

The first samples of the β -salt of hydrindamine and *cis*- π -camphanic acid which were examined optically, did not give very concordant results, but the values for the specific rotation which were obtained with different preparations were not so widely different as in the case of those of the α -salt.

The samples used in these experiments were all dried over sulphuric acid, but sometimes they were previously heated for a few minutes on a water-oven in order to expel adherent alcohol or ether. The determinations were all made with a 200 mm. tube, and in the following experiments the given weight of substance was dissolved in 99.8 per cent. methyl alcohol, the solution being diluted to 25 c.c.

Exp. XIV.	0.2970 gram	$\alpha - 15'$	$[\alpha]_D - 10.3^\circ$
Exp. XV.	0.3 „	$\alpha - 13'$	$[\alpha]_D - 9.0^\circ$
Exp. XVI.	0.6 „	$\alpha - 30.5'$	$[\alpha]_D - 10.6^\circ$

The following determinations were made in ethyl alcohol (98 per cent.) solution, all other conditions remaining unchanged:

Exp. XVII.	0.3 gram	$\alpha - 9'$	$[\alpha]_D - 6.2^\circ$
Exp. XVIII.	0.3 „	$\alpha - 14'$	$[\alpha]_D - 9.7^\circ$

All the samples used above melted almost sharply at about 173° , and they were all different preparations, the last two results being obtained with successive fractions from one series of crystallisations.

As the experimental error in all these determinations is rather

large owing to the very feeble rotation, the above results might have been taken to be sufficiently concordant; but in the light of the experience gained in studying the α -salt, it seemed possible that the values actually obtained might not represent the true specific rotation of the β -salt.

In order, therefore, to further test the value of the above results, a considerable quantity of a fresh sample of the β -salt was prepared; this sample, judged by its melting point, was free from the isomeride, and had the specific rotation $[\alpha]_D - 15.2^\circ$ when examined in methyl alcohol in a 200 mm. tube; volume of solution, 25 c.c.

Exp. XIX. 0.3 gram. $\alpha - 22'$. $[\alpha]_D - 15.2^\circ$.

This sample was then fractionally crystallised from methyl alcohol in such a way that a small quantity (about 15 per cent. of the whole) of the most sparingly soluble portion was separated; the remainder was obtained in two fractions, which were separately examined in methyl alcoholic solution in a 200 mm. tube; volume of solution, 25 c.c.

Exp. XX. Fraction I. 0.242 gram $\alpha - 13'$ $[\alpha]_D - 11.2^\circ$

Exp. XXI. „ II. 0.3 „ $\alpha - 23'$ $[\alpha]_D - 16.0^\circ$

In these experiments, not only was the specific rotation of the original sample found to be considerably higher than that of any previous preparation, but there were also indications that the sample had been resolved into dissimilar parts on fractional crystallisation.

The next attempt to obtain a constant value for the specific rotation of the β -salt was made in the following manner. A sample, melting at 173° , which had been very carefully prepared, was dissolved in hot ethyl alcohol; by merely cooling the solution, separating consecutive deposits, and then precipitating with ether as completely as possible, this sample was separated into three fractions, which are numbered in the order in which they were obtained. Their specific rotations were then determined in methyl alcoholic solution in a 200 mm. tube, the volume of the solution being 25 c.c.

Exp. XXII. Fraction I. $\begin{cases} 0.3 \text{ gram} & \alpha - 20' & [\alpha]_D - 13.8^\circ \\ 0.6 & \text{„} & \alpha - 44 & [\alpha]_D - 15.2^\circ \end{cases}$

Exp. XXIII. „ II. 0.3 „ $\alpha - 30'$ $[\alpha]_D - 20.8^\circ$

Exp. XXIV. „ III. 0.3 „ $\alpha - 29'$ $[\alpha]_D - 20.0^\circ$

In spite of the considerable difference between their specific rotations, the fractions I and II melted simultaneously at 173° , and the presence of α -salt in the former could not be detected; the sample of salt recovered on evaporating the methyl alcoholic solutions which were used for these determinations also melted at the same temperature as before, and simultaneously with the original preparation.

As this method of rapid crystallisation had given two consecutive fractions having the same specific rotation, and also a value which was considerably higher than that of any previous preparation, it seemed that a repetition of this process was all that was necessary in order to finally determine the specific rotation of the β -salt.

Accordingly, a fresh sample of carefully recrystallised β -salt was prepared; it melted sharply at 173° , and had the specific rotation $[\alpha]_D -13.3$ (see below, Exp. XXV). It was dissolved in hot ethyl alcohol, and then by cooling, and finally by adding ether to the solution, the sample was separated into three successive fractions, which are numbered in the order in which they were deposited. The specific rotation of the original sample and of the three fractions was then determined in ethyl alcoholic solution in a 200 mm. tube, the volume of the liquid being 25 c.c. in all cases:

Exp. XXV.	Original sample.	0.3 gram	$\alpha -19'$	$[\alpha]_D -13.3^{\circ}$
	Fraction I.	0.3 „	$\alpha -15'$	$[\alpha]_D -10.4^{\circ}$
	„ II.	0.3 „	$\alpha -15'$	$[\alpha]_D -10.4^{\circ}$
	„ III.	0.3 „	$\alpha -15'$	$[\alpha]_D -10.4^{\circ}$

These results differ entirely from those obtained in the last series of fractional crystallisations, and the most soluble portions have now the same specific rotation as the first deposit. All these, as well as all previous examples, had the same melting point, and yet the specific rotation ranges from about -10° to -20° .

The following explanation of these results may be suggested. In the first place, it is not impossible that even when the β -salt shows its normal melting point, it may nevertheless contain a small proportion of the α -isomeride. When a sample of the β -salt melting at 173° is intimately mixed with an approximately *equal* quantity of the α -salt, there certainly results a mixture which has a very indefinite melting point, and which does not liquefy completely until about 180° , but it is quite possible that the samples supposed to be β -salt already contain variable quantities of the α -isomeride, and that the melting point is not appreciably altered by a small change in the quantity of the latter; as already stated, the melting point of the β -salt is not very sharp, and although so many preparations have been found to melt at this constant temperature, it is not thereby proved that the α -isomeride is altogether absent.

The difficulty of obtaining samples of the β -salt free from its isomeride may, in its turn, be due to conversion of a little of the former into the latter during crystallisation; although it is true that the sample recovered on evaporating a dilute solution in ethyl or methyl alcohol has the same melting point as before, it does not necessarily follow that no change has occurred during this process;

repeated evaporation with alcohol, as already stated, does bring about the conversion of the β -salt into the α -isomeride to some extent, and this change takes place in a greater degree on evaporating an aqueous solution only once.

In the case of the α -salt, similar explanations of the much greater difference in the specific rotations of different samples could not be considered as in any way probable, and it is possible, therefore, that the difficulty of obtaining a constant specific rotation may be due to the same cause in both cases.

Mutarotation not shown by the β -Salt.

Before passing on to describe the results of the optical examination of the α - and β -salts in aqueous solution, attention may be drawn to one important difference in the behaviour of the two isomerides, namely, that the latter, unlike the former, does not show any definite sign of mutarotation. Although many solutions of the β -salt have been examined, observations taken as soon as possible after solution gave essentially the same results as those taken after the lapse of several hours or even days: only in one case, namely, in that of Exp. XXII, were even faint indications of mutarotation observable. The average of the first eight readings in the first determination made with this sample gave $[\alpha]_D - 9.3^\circ$, whilst the average of ten readings taken about two hours afterwards gave $[\alpha]_D - 13.8^\circ$; in the second determination, however, using the same sample and a solution containing twice as much salt, the average of the readings taken as quickly as possible, was the same as that of those taken the next day. As the difference in the one case just referred to is almost within the limits of experimental error, it must be concluded either that the β -salt does not show mutarotation at all, or that the change takes place so quickly that it cannot be followed experimentally. Considering the close relationship between the two isomerides, it is difficult to say which alternative is to be preferred.

The cause of the mutarotation in the case of the α -salt is not apparent; it is very improbable, in fact almost impossible, that it could be due to the hydrolysis of the lactone ring in alcoholic solution, for the following reasons:—The α -salt does not combine with another molecule of hydrindamine, even when it is heated with a solution containing excess of that base; solutions of the acid itself do not show mutarotation in methyl alcoholic solution; solutions of ammonium *cis*- π -camphanate containing free ammonia do not show mutarotation, and this is also true of the piperidine salt in presence of free piperidine.

It is also improbable that the change in rotation is due to the

hydration of the base in any way, because, if this were so, the β -salt should behave in a similar manner; that is to say, the change should take place with approximately the same rapidity, and thus be capable of experimental verification.

The phenomenon of mutarotation, however, being still obscure, even in the case of compounds of known constitution, it would not be justifiable to conclude that because the β -salt does not behave similarly to the α -salt in this respect, it must necessarily differ from the latter in constitution.

Specific Rotation in Aqueous Solution.

Although it did not seem very probable that the hydrindamine salts of *cis*- π -camphanic acid would be dissociated in dilute aqueous solution to a sufficient extent to give molecular rotations comparable with those of other salts of this acid, it seemed interesting to examine them optically under these conditions, partly for purposes of comparison, partly in order to try and follow polarimetrically the conversion of one into the other, which, for the reasons already stated, doubtless takes place. That this conversion would probably take place most rapidly in dilute aqueous solution is, perhaps, a proposition which admits of some discussion; for when the salts are electrolytically dissociated, they are, according to the author's views, no longer capable of being converted one into the other, and it would therefore depend on the amount of this dissociation, as well as on the extent of hydrolytic dissociation, whether the transformation of one isomeride into the other could take place at all, and, if so, the rate at which it would occur.

The following experiments were made, in order to obtain information on these points.

α -Salt.—A sample of the α -salt, melting at the right temperature, was recrystallised from alcohol and dried over sulphuric acid; 0.25 gram, dissolved in water, the solution diluted to 25 c.c. and examined in a 200 mm. tube, gave

$$\alpha - 20' \quad [\alpha]_D - 16.7^\circ.$$

The wide differences shown by different preparations of the α -salt in methyl alcoholic solution made it necessary to confirm this result, and a second determination was therefore made with a specimen obtained by recrystallising the sample just used three times from ethyl alcohol; 0.25 gram was dissolved, the other conditions remaining the same.

$$\alpha - 19' \quad [\alpha]_D - 15.8^\circ.$$

The specific rotation of this last specimen in methyl alcoholic solution, was $+20.8^\circ$ at its maximum, so that the results of the last two concordant determinations in aqueous solution may be accepted.

It may be mentioned that the α -salt did not show mutarotation in aqueous solution; the average of the readings taken as soon as possible was practically identical with that of observations made 1 hour later, and no change in rotation occurred, even on keeping the aqueous solution at the ordinary temperature during 4 days; this fact does not warrant any conclusion as to the stability of the α -salt in aqueous solution, as will be seen from the data obtained in the case of the β -salt.

β -Salt.—The specific rotation of this salt in aqueous solution was determined with the aid of two different preparations, which, however, had both the same specific rotation, -10.6° in methyl alcoholic solution; both samples had the melting point of the β -salt.

0.25 gram dissolved in water, the solution diluted to 25 c.c. and examined in a 200 mm. tube, gave

$$\alpha - 18' \quad [\alpha]_D - 15^\circ.$$

On keeping the solution at the ordinary temperature, no appreciable change in rotation took place in the course of 4 or 5 days, but on then evaporating the solution and allowing to crystallise, the deposit did not fuse at the melting point of the β -salt, but sintered at about 168° , and was not completely liquefied until the temperature had risen to about 178° .

0.6 gram dissolved in water, examined under the same conditions as in the last experiment, gave

$$\alpha - 46' \quad [\alpha]_D - 15.9^\circ.$$

These results are not only sufficiently concordant to be accepted as correct, but are also practically identical with those obtained in the case of the α -salt.

This last fact, of course, rendered it impossible to ascertain by optical examination whether any conversion of one isomeride into the other took place on keeping their dilute aqueous solutions at the ordinary temperature, but that the identity of their specific rotations is not due to the two isomerides becoming identical in aqueous solution seems to be proved by the further fact that even solutions which have been kept for some time do not yield, on evaporation, products having the same, or even approximately the same, melting point, although both appear to be mixtures. The identity of their specific rotations in aqueous solution may, however, be taken as further evidence of the optical inactivity of the basic components of the two salts.

Molecular Rotations of the Isomeric Salts.

In the case of the hydrindamine bromo- and chloro-camphorsulphonates, it was possible to compare their molecular rotations with

those of the acid and of other salts, and the results thus obtained have already been discussed. In order to make a similar comparison in the case of the salts of *cis*- π -camphanic acid, it was first necessary to determine the molecular rotation of the acid by an examination of its salts with optically inactive bases.

In the first place, the acid itself was examined in order to ascertain whether it showed mutarotation in methyl alcoholic solution comparable with that exhibited by the α -salt.

0.5 gram of very finely divided acid was dissolved in methyl alcohol (99.8 per cent.), the solution diluted to 25 c.c., and examined as quickly as possible in a 200 mm. tube; the average of eight concordant readings gave:

$$\alpha - 25' \quad [\alpha]_D - 10.5.$$

The same solution, examined about 24 hours later, gave:

$$\alpha - 27' \quad [\alpha]_D - 11.3^\circ,$$

and 24 hours later still, practically the same result was obtained; as the initial and final values are the same within the limits of experimental error, it must be concluded that the acid does not show mutarotation under these conditions.

The acid being almost insoluble in water, the determination of its molecular rotation was made in dilute aqueous ammonia and in dilute aqueous solutions of other bases comparable to hydrindamine.

0.25 gram of the acid was dissolved in water, with the addition of a few drops of ammonia, the solution diluted to 25 c.c., and examined in a 200 mm. tube; the average reading was $\alpha - 29'$, from which

$$[\alpha]_D - 24.1^\circ \quad [M]_D - 48.$$

The addition of more ammonia to the solution had no appreciable effect on the specific rotation.

Piperidine cis- π -Camphanate.—0.25 gram of this salt was examined in aqueous solution; volume, 25 c.c.; tube, 200 mm.

$$\alpha - 24' \quad [\alpha]_D - 20^\circ \quad [M]_D - 56.$$

Benzylamine cis- π -Camphanate.—This salt was not isolated for the purpose, but a solution of 0.5 gram of the acid in water and a little benzylamine was diluted to 25 c.c., and examined in a 200 mm. tube; the specific and molecular rotations are calculated for the acid.

$$\alpha - 1^\circ 6' \quad [\alpha]_D 27.5^\circ \quad [M]_D - 54.4.$$

These results are not very concordant, but the large experimental error, and the probability that the ammonium, piperidine, and benzylamine salts are only very partially dissociated, have to be taken into consideration.

The specific rotations of the hydrindamine *cis*- π -camphanates in aqueous solution being practically identical, and equal to -16° , their molecular rotations are -53° , a value which is practically the average of those obtained in the case of the three salts just examined. This agreement is sufficiently close to be taken as confirmatory evidence of the view that the isomeric hydrindamine *cis*- π -camphanates are both partially racemic salts.

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