THESIS

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PART I.

THE ROTATION - DISPERSION OF OPTICALLY ACTIVE COMPOUNDS

In view of the nature of the work to be described, it is of considerable interest to trace the history of the observations on double refraction and polarisation of light, which culminated in the discovery by Biot, that certain organic compounds could rotate its plane of polarisation. The result was the opening up of a rich field of investigation for chemists, and developments were rapid in most directions. A short history is therefore appended, narrating events as far as possible in historical sequence, and presenting in broad outline the main facts about the subject of optical activity, down to the present day.

Towards the end of the seventeenth century, Erasmus Bartholinus, (CF. Phil. Trans. Jan. 16th, 1670/71, No. 67, p. 2039), a Danish philosopher, discovered that when a ray of light is refracted by a crystal of calcite, it forms two refracted rays, termed ordinary and extraordinary rays. The phenomenon is termed double refraction, and is exhibited by other substances such as tourmaline. Historically calcite was the starting point for the development of the whole subject.

A few years later Huygens, who founded the wave theory of light and published a treatise twelve years later in 1690, confirmed and extended the above experiment. By passing these rays through a second crystal he found they acquired new properties. It was not till 1808, that Etienne Louis Malus discovered that when light is reflected from the surface of glass, water or other transparent medium, at a particular angle, that it acquired the same properties as the rays transmitted through calcite. The term "polarisation", was applied by him to the alteration in the properties of light thus produced. The term arises from the emission theory held by him at the time, on which he attributed a kind of polarity to the light corpuscles. The particular angle of incidence is called the "polarising angle", while the plane passing through the incident ray and the normal to the reflecting surface was termed the "plane of polarisation".

Arago found in 1811, that quartz rotated the plane of polarisation of a beam traversing it in the direction of the optic axis. Other crystals were possessed of the same property. With Fresnel he made the classic experiments on interference with two rhombs, and demonstrated that light was propagated, not in the direction in which the light travelled, as Young and Huygens had supposed, but contra in a transverse direction.

Biot noted that some quartz crystals rotate polarised light in one direction, while others rotate it in the opposite direction. He further found that the amount of the rotation was proportional to the thickness of the quartz plate, and increased, according to a certain law, the shorter the wave length used. He made the more fruitful discovery in 1815, that certain naturally occurring organic substances, such as oil of turpentine in the liquid or gaseous state, besides solutions of sugar, tartaric acid, camphor etc., also rotate the plane of polarisation of light. Substances which possess this property are said to be "optically active". Fused quartz is inactive, and whereas the activity of quartz crystals was attributed to the crystalline structure, the rotation produced by solutions, wherein the molecules move freely, must be ascribed to the structure of the molecules themselves. This was first grasped completely by Pasteur but definitely formulated only at a later period, and resulted in a wonderful development on the chemical side.

Mitscherlich drew attention to the relation between crystalline form and chemical constitution. The recognition by Haüy of two varieties of quartz with hemihedral facets on opposite sides when similarly oriented, along with the previous observations of Biot, were correlated by Herschel (Trans. Camb. Phil. Soc. 1821 1, 43). He showed that the crystals with hemihedral facets on different sides, were respectively the d and l rotating variety.

Berzelius emphasised the close relationship of racemic and tartaric acid. The chief difference between them lay in the fact, that racemic acid was optically inactive while tartaric acid and its salts were dextro-rotatory. The crystallographic examination of their salts by Mitscherlich failed to furnish an explanation. It was not till 1848 that Pasteur, remembering Herschel's work on the relationship between hemihedrism and optical rotation in quartz made his brilliant discovery of the nature of racemic acid. He simultaneously isolated laevo tartaric acid for the first time, by mechanically separating the two forms of crystals present in sodium ammonium racemate, on slow evaporation, and converting these to the free acids.

While the significance of molecular structure, for which we are principally indebted to Kekulé, was not then appreciated, Pasteur in spite of the inadequacy of the theories of his time, grasped nevertheless the relationship of object and mirror image which exists in d and l tartaric acid. To him also we owe the term "asymmetric", not strictly correct, to describe enantiomorphously related objects.

Following Kekulé's idea of the tetravalency of carbon, Van't Hoff and Le Bel formulated the conditions in which asymmetry could exist, namely when a carbon atom was joined to four different groups. The former adopted the tetrahedral structure of the carbon atom, to represent it from the new point of view.

Theoretical considerations made it clear, that atoms other than those of carbon, could serve as a centre of asymmetry. The correctness of the view was first demonstrated by Le Bel himself, when he showed that a solution of isobutyl propyl ethyl ammonium chloride became optically active, as the result of the action of certain moulds. Pope and Peachey (Chem. Soc. Trans. 1899 75 1127) resolved an analogous compound by means of Reychler's d. camphor sulphonic acid, a modified method of that first suggested by Pasteur, and the one most generally employed to-day for resolving racemic bodies. Smiles (Chem. Soc. Trans. 1900 77, 1174) and Pope and Peachey (ibid. 1900 77 1072) obtained compounds whose optical activity was due to the presence of an asymmetric sulphur atom. While a compound having a selenium atom as a centre of optical activity was resolved by Pope and Neville in 1902. Compounds which owe their activity to an atom of silicon, tin, phosphorus have likewise been obtained. To Werner, who has made the greatest advances in this subject, we owe the resolution into active components, of complex chromium, iron, rhodium and cobalt derivatives, during the last few years. The result is, that our knowledge of the structure of these inorganic complexes now rests on a basis, almost as sound as that of purely organic type.

For the first time the resolution of an asymmetric arsenic compound into optically active components was accomplished last year by Mills and Raper (J.C.S. 127 2479 1925), and Phillips (J.C.S. 1925 127 2552) has resolved ethyl p. toluene sulphinate, whose activity is difficult to reconcile with the constitution ascribed by the old theories of valency. The later electronic theories have, according to the author, provided a satisfactory explanation.

Three different methods of resolution of racemic compounds into their optically active components were employed by Pasteur. These were,- mechanical separation of the two forms of crystals present; the use of moulds, whereby one of the active forms was preferentially destroyed; and the combination of a racemic mixture with an active substance followed by fractional crystallisation, and the removal of the active agent employed. Marckwald and McKenzie (Ber. 1899, 32, 2130) found that one form of mandelic acid was esterified more quickly than its isomer on heating the inactive acid with menthol for a short time. The unchanged mandelic acid was optically active. Dakin (J. Physiol. 30, 253, 1904) found that, if lipase were allowed to act on an optically inactive mixture of the two methyl mandelates the dextro component was hydrolised more rapidly. Lipase had no hydrolysing action on l menthyl mandelate or d-bornyl mandelate but later (ibid. 32, 199, 1905) was used for the hydrolysis of esters which contained an asymmetric carbon atom present in the alkyl group. McKenzie (Chem. Soc. Trans. 1905 87 1373) and in other papers has made use of the process known as "asymmetric synthesis" whereby, for example, when l-menthyl pyruvate was reduced to l-menthyl lactate, the lactic acid, obtained from the latter, was slightly active. Marckwald (Ber. 1904 37 4696), by heating the acid brucine salt of methyl ethyl malonic acid, obtained some slightly active valeric acid. Recently (Z. Physiol. Chem. 1923 126 308), a method of resolving racemic alcohols into their active components by means of digitonin is reported. A double compound of digitonin with alcohol is formed, and separation effected by re-crystallisation. The active alcohol is obtained by distillation in a vacuum or with steam. Mitchell (J.C.S. 127 208 1925) has found, that emulsin hydrolyses l-bornyl glucoside three times as fast as d bornyl glucoside. The method has been suggested for the resolution of the higher alcohols.

Let us now return to the work of Biot. When he made the discovery, that certain organic compounds possess the property now known as optical rotatory power, he was then of the opinion that, the rotation value was unaffected by change of external conditions, such as temperature, solvent, concentration or colour of light used. Later work showed clearly that this was not the case, but contra the changes produced by such variations are highly complex. Biot himself established in the case of quartz that the deviation which polarised light undergoes is greater the shorter the wave length. He made the further discovery that tartaric acid in solution offers an exception, to the behaviour shown by quartz. This acid in question exhibits what is now known as anomalous rotation-dispersion.

When he detected that a solution of camphor deviates certain colours of light to a different extent from turpentine, he followed out the observation by passing polarised light through these two tubes balanced one against the other (Ann. Chim. Phys. 1852 iii 36 431), and observed the dispersion phenomena. In the above case and with camphor dissolved in turpentine the same phenomena were observed, as with a solution of tartaric acid.

The exact way in which variation in rotation takes place with light used, was determined for a solution of tartaric acid by Arndtsen (Ann. Chim. Phys. 1858 iii 54 403), using the different rays of the solar spectrum. Biot did not conclude from his results as Arndtsen later did, that anomalous rotation-dispersion resulted from the presence, in the tartaric acid solution, of two substances with opposite rotations and unequal dispersions. The formation of such a body having a reversed rotatory power to that of the parent dextro tartaric acid, which has two similar dextro-rotating groups, is not easy to grasp. Anent this Nasini and Gennari (Zeit. Physikal Chem. 1896 <u>19</u> 113), remark on the difficulty of isolation and identification of such a body, a difficulty not yet overcome.

In a later paper (ibid. 1896 <u>19</u> 130), the same authors with reference to the anomalous rotation dispersion of nicotine-acetate in water, adopt a similar view to Arndtsen. Winther (Zeit. physikal. Chem. 1906 <u>55</u> 278) takes the view that the existence of single or double molecules are the cause of the anomalies. In solution of electrolytes, he suggests also, that the existence of dissociated and undissociated molecules may be responsible, or the formation of a complex between the active substance and the solvent.

Picard and Kenyon (Trans. Chem. Soc. <u>105</u> 837 1914) found that an ester such as <u>d</u>- β-octyl acetate with only one asymmetric carbon atom in the molecule, exhibited anomalous rotation dispersion. If then, as Frankland (Trans. Chem. Soc. 1919 636) points out, this be due to the presence of reversibly related iso-dynamic forms, as

Armstrong and Walker (Proc. Royal Soc. 1913 A 88 388) suggest from their observations of the behaviour of fructose in solution, then a laevo ester with dextro rotation is postulated. So far no dextro-rotating laevo ester is known and the supposition of its existence is improbable.

The supposition of the existence of dynamic isomerides has been supported by Lowry and Dickson (Trans. Faraday Soc. 1914 10 60) and polymerisation suggested as an alternative hypothesis. Lowry in his Bakerian Lecture to the Royal Society 1921 attempts to establish his conclusions in the first place mathematically, from the form of the dispersion curve in tartrates, using Drude's equation with two terms. Which he states, "expresses mathematically the suggestion of two substances opposing one another." In the second place, chemical evidence, whereby the existence of two forms of nitrocamphor was proved, is sought for, but is lacking in the case of tartrates. Patterson (Trans. Chem. Soc. 1916 109 1204), from rotation data obtained by Lowry himself (Trans. Chem. Soc. 75 215 1899) for nitrocamphor, in solution in various solvents and at different concentrations, has shown the absurdity of the hypothesis of dynamic isomerism. He has demonstrated, contrary to the view of Armstrong and Walker, that solvent, temperature and concentration influence on rotation, exists apart altogether from dynamic isomerism. Patterson (ibid. 1224) has further pointed out that "It has been shown in a good many cases now, that, on heating, the rotation of an active substance may increase to reach a maximum value and then diminish again on further heating. This occurs for many homogeneous substances, and it occurs also for their solutions. It seems impossible that this behaviour could be explained by the assumption that the influence of temperature change is merely to alter the equilibrium between two dynamic isomerides, one of which has a low rotation and the other a high rotation. A maximum could hardly be accounted for in this way, and it need scarcely be pointed out that if the suggestion, in favour of which strong evidence has been brought forward, be true, namely, that the change of rotation of an active substance with alteration of temperature is periodic - that there may be in the T.R.* curve, sufficiently extended, several maximum and minimum values - Armstrong and Walker's views become less and less in accordance with facts."

It was as a result of their views on the anomalous behaviour of some substances, in regard to their rotatory dispersive powers, that Armstrong and Walker (Proc. Royal Soc. 1913 A 88 392) introduced what they term the

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*Temperature-Rotation

"characteristic diagram". Its use for the purposes of co-ordinating rotation data of a substance, of its derivatives and even of related substances, in different conditions, has justified the name. To construct the diagram a reference line is drawn with a slope of unity, and along it are plotted the various specific rotations observed for a particular colour. The points for other colours are then plotted on the ordinates passing through the points already located on the reference line. The values may be those obtained with variations of solvent, temperature or concentration. The original method has been modified by Patterson (T <u>109</u> 1181 1916), in such a way, that a reduction in size is effected. This is accomplished by plotting along a horizontal reference line, for a particular colour, the degrees of rotation. Vertically on either side of this line are plotted the differences in rotation between the other colours and that used as reference. The points for the other colours are then found to lie on or approximately on straight lines, all of which intersect the reference line over a short range, but not actually at one point. In calculating the dispersion coefficient for the reference line and any other colour the zero of rotation is neglected, and the point at which these straight lines intersect is chosen as zero. It has been termed the "rational zero". The dispersion ratio for these two colours is the quotient of the respective rotation values after subtraction of the value of the rational zero from each.

Modern work on optical activity has disclosed, in general, the very important fact that if, under two entirely different sets of circumstances (temperature, concentration, solvent), the rotations for some particular colour, say sodium yellow, are the same, then the rotations for all the other colours also will be the same or very nearly the same, each to each. This is the lesson of the characteristic diagram, and it holds not merely for one and the same substance in different sets of circumstances, but also for derivatives of that active substance.

From the characteristic diagram we are thus able to foretell for a group of related compounds that if by varying the external conditions we can produce a certain rotation for one colour of light, the rotations for other colours will have certain definite values. But the characteristic diagram, unfortunately, does not indicate the physical conditions necessary to bring about a certain effect, or how they may be produced. Further, the characteristic diagram, although of a remarkably general character, is only an approximation, and, as far as can be judged at present, there are, probably, definite limits to its application. Thus for many substances, the rotation passes through a maximum or minimum value with change of temperature, and the data at present available are insufficient to show whether the rotation values on both sides of such a maximum fall upon a single characteristic diagram or not. It is clear that the difference between the rotation values for two colours of light - what may be called the dispersion - is directly proportional to either value, if calculated from the point of intersection for these two colours - the rational zero. Using the rational zero, a dispersion coefficient may be arrived at which shows very fair constancy under widely differing circumstances and may in future prove to be definitely characteristic of a particular substance or group of substances.

The experimental difficulties encountered in examining the rotation of an active substance over a wide range of temperature are considerable, and therefore only a comparatively short part of the T-R curves for most active compounds has been ascertained. It has been suggested, however, (J.C.S. 1913 103 148), that this difficulty can be at least partly overcome by piecing together T-R curves for solutions of the active compound in question, or derivatives of it, just as a characteristic diagram is constructed by piecing together data of different kinds - the evidence being indeed just the same in both cases. The question, similar to that already referred to, then arises, as to whether the dispersion-coefficient derived from such T-R curves would have the same value as for the mother-substance, when calculated from the rational zero. It was with a view to collect further evidence of this kind that the work described below was undertaken.

For our purpose it is desirable to study substances the rotations of which vary as much as possible with change of external conditions. Some previous work had shown that benzyl tartrate has a fairly high rotation, and, moreover, that the maximum in the T-R curve lies at a moderate and easily ascertainable temperature (J., 1913, 103, 148). We therefore thought it worth while to examine in the first place dibenzyl dimethoxysuccinate, hoping that its rotation would be both high and easily variable.

Dibenzyl dimethoxysuccinate was prepared from d-dimethoxysuccinic acid (J., 1901, 79, 959) (1 mol.) by heating with pure benzyl alcohol (4 mols.) at 120° for about 16 hours and allowing the water formed to distil off. The excess of alcohol was removed under diminished pressure; the crude ester was washed with dilute sodium carbonate solution, taken up in chloroform, dried over calcium chloride, and distilled (yield 70%). It was slightly coloured and fairly mobile. Purified by careful distillation, it boiled at 180-190°/3 mm.; $n_D^{19^\circ} = 1.5321$ (Found: C, 66.8; H, 6.1. $C_{20}H_{22}O_6$ requires C, 67.0; H, 6.1%).

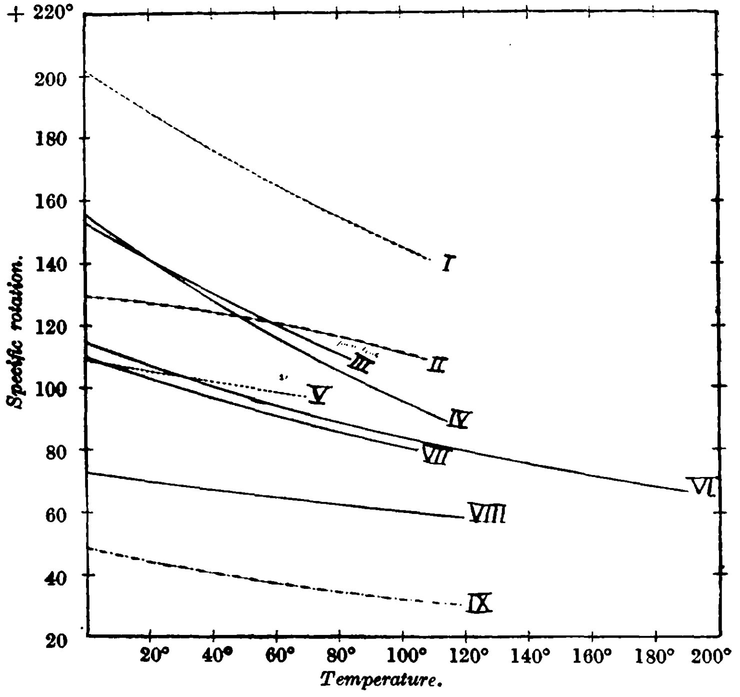
The rotation of this ester was examined for six different wave-lengths of light at temperatures ranging from 0-100°. In the case of the homogeneous substance, the examination was continued up to 174°. The results are shown in Fig. 1, which gives the curves obtained for mercury green light alone. It will be seen that the specific rotation of the homogeneous benzyl dimethoxysuccinate, which has a high value of about 115° at zero, gradually falls to reach a value of 68° at a temperature of 180°, the appearance of the curve suggesting a maximum value at some temperature considerably below zero and a minimum value at a temperature possibly in the neighbourhood of 250°.

The influence of solvents upon this ester is also apparent from the diagram. Acetylene tetrabromide lowers the rotation of the ester considerably. m-Xylene lowers it only slightly. Nitrotoluene and quinoline both raise the rotation markedly. The general appearance of the curves is very similar to what has been observed already for the rotation of ethyl tartrate, but the displacement of a maximum or minimum value is not so obvious.

For purposes of comparison, the temperature rotation curves of some other related compounds were examined. Benzyl tartrate (J., 1913, 103, 176) in quinoline has a much lower rotation than benzyl dimethoxysuccinate, but the general appearance of the curve is similar. The rotation of methyl dimethoxysuccinic acid in acetone is

Fig. 1.

Influence of solvents on the rotations of various related compounds.



I. d-*Dimethoxysuccinic acid in pyridine*, p = 7·8435. II. *Methyl* d-*dimethoxysuccinate in quinoline*, p = 5·5020. III. *Benzyl* d-*dimethoxysuccinate in quinoline*, p = 5·1758. IV. *Benzyl* d-*dimethoxysuccinate in* o-*nitrotoluene*, p = 4·860. V. d-*Dimethoxysuccinic acid in acetone*, p = 15·982. VI. *Benzyl* d-*dimethoxysuccinate* (*homogeneous*). VII. *Benzyl* d-*dimethoxysuccinate in* m-*xylene*, p = 6·6875. VIII. *Benzyl* d-*dimethoxysuccinate in acetylene tetrabromide*, p = 3·0660. IX. *Benzyl tartrate in quinoline*, p = 9·4489.

considerably higher, but the curve is again of a similar form, the rotation gradually diminishing as the temperature rises. Dimethoxysuccinic acid dissolved in pyridine gives again a T-R curve of a similar form, the rotation, however, being much higher. Methyl dimethoxysuccinate dissolved in quinoline, shows, for all the colours of light examined, a behaviour suggesting a maximum at a temperature in the neighbourhood of zero. It is clear, however, that any fundamental type of curve for these different compounds is not displaced to nearly so great an extent as is the curve for ethyl tartrate. All these curves, with the possible exception of that for methyl dimethoxysuccinate in quinoline, suggest that the T-R curve would rise to a maximum at lower temperatures than those examined. Homogeneous ethyl tartrate and the same ester dissolved in a number of solvents exhibited just the opposite behaviour. For homogeneous ethyl tartrate and for the ester in some solvents, the maximum is actually apparent. In some other solvents such as quinoline, pyridine, and benzaldehyde, the curves obtained suggest that a maximum value would lie, in these solvents, at a much lower temperature. On plotting on a characteristic diagram the results obtained with benzyl dimethoxysuccinate in the homogeneous condition and in the solvents mentioned, it is found that the data lie fairly well upon straight lines, which for green and yellow light would intersect in the neighbourhood of a point corresponding to the rotation + 9°. Table I gives the necessary data and the rational dispersion coefficients calculated therefrom.

TABLE I.

Dispersion Coefficients for Benzyl d-Dimethoxysuccinate.

$[a]_y/[a]_g$ is the rational dispersion coefficient for the rational zero $[a]$ = + 9°.

Physical state	t°	$[a]_y$	$[a]_g$	$[a]_y/[a]_g$
Homogeneous	100°	72.72°	82.84°	0.8630
"	139.5	65.98	74.82	0.8659
In quinoline	0	134.9	154.59	0.8648
"	69.2	100.4	115.02	0.8621
In nitrotoluene	13.6	127.06	145.51	0.8648
"	72	95.13	108.25	0.8678
In acetylene tetrabromide	14	62.25	70.62	0.8642
" "	44.2	58.77	66.63	0.8636
In m-xylene	43.7	83.11	95.04	0.8614
"	69	76.73	87.31	0.8649

It will be observed that the coefficient is very constant, differences only occurring in the third decimal place. Its mean value is 0.8642.

In Table II are shown similar dispersion coefficients for the other substances which have been examined and it will be seen that the dispersion coefficient is slightly higher than before, having a mean value of about 0.876 when the values are calculated from a rational zero of + 9°.

The data of Tables I and II have reference, as will be apparent from Fig. 1, to a region of the T-R curves to the right of the maximum. It is of interest now to compare them with similar data for ethyl tartrate applying to T-R curves on the other side of the maximum, namely, between

TABLE II

Dispersion Coefficients for *d*-Dimethoxysuccinic Acid and for Methyl *d*-Dimethoxysuccinate.

$[a]_y/[a]_g$ is the rational dispersion coefficient for the rational zero $a = + 9^\circ$.

Physical state	t°	$[a]_y$	$[a]_g$	$[a]_y/[a]_g$
d-Dimethoxysuccinic acid in pyridine...	0°	180.96°	204.38°	0.8801
" "	69	142.37	161.24	0.8761
In acetone	12	94.00	106.29	0.8737
"	30.5	91.96	103.75	0.8756
Methyl *d*-dimethoxysuccinate in quinoline..	0	114.55	129.40	0.8766
Methyl *d*-dimethoxysuccinate in quinoline..	67	105.67	119.39	0.8757

temperatures of 40° and 140° (J., 1916, *109*, 119). The rational zero then found was + 7.92°, very close, therefore, to that (+ 9°) obtained from our present experiments. The mean value of the rational dispersion coefficient was 0.8660, again close to the values found above. Our results lend support, therefore, to the idea that even when the data are taken from T-R curves apparently on different sides of the maximum rotation, the rational dispersion-coefficient shows something like a real constancy.

ROTATION OF NICOTINE

Since it was not found possible to vary the rotation of the dimethoxysuccinates as much as we had hoped, we next undertook an examination of nicotine, the rotation of which is known to vary to some considerable extent, but has not hitherto been examined very completely in regard to change of colour, temperature, and concentration. Previous workers have given the following values for the constants of the homogeneous substance:

	$[\alpha]^{20^\circ}_{D}$	$d^{20^\circ}_{4^\circ}$
Landolt ("Das Optische Drehungsvermogen", 2nd ed., 1898, p. 159)	161.55°	1.01101
Genari (Z. physikal. Chem., 1896, 19, 130)	162.84	1.01071
Winther (ibid, 1907, 60, 563)	163.85	-
Jephcott (J., 1919, 105, 105)	168.61	1.00925

The first three purified their nicotine by vacuum distillation only. In the last case the nicotine was purified by means of the zinc chloride double salt (Vohl, J. pr. Chem., 1870, 2, 331). We used 95% nicotine, purified it by preparation of the double salt with zinc chloride, decomposed this in sodium hydroxide, dried the nicotine over solid sodium hydroxide, and then distilled it under reduced pressure, using a Claisen flask with a long side arm, and a receiver of the type described in J. Soc. Chem. Ind., 1924, <u>43</u>, 283, thus avoiding completely any contact of the hot vapour or liquid with cork or rubber. A colourless, odourless liquid was obtained. Two separate preparations gave: (1) $[\alpha]_{D}^{20^\circ}$ 168.02°, $d_{4^\circ}^{20^\circ}$ 1.0095; (2) $[\alpha]_{D}^{20^\circ}$ 167.78°, $d_{4^\circ}^{20^\circ}$ 1.0100. The homogeneous substance was then examined for six colours of light over a range of temperature from 0-100°, in polarimeter tubes having a side arm to allow of expansion of the liquid. In order to prevent oxidation of the nicotine by air, a slow current of hydrogen was passed into the side arm. This proved entirely satisfactory; no coloration of the solution due to oxidation of the nicotine took place even at 100°, at which temperature oxidation in presence of air is extremely rapid. The data obtained, when plotted on a diagram, indicate that the change of rotation of nicotine with temperature is only slight, but the shape of the curves suggests the occurrence of a minimum at a temperature probably in the neighbourhood of 170° or thereabouts.

Nicotine was then examined in a number of solvents. <u>o</u>-Nitrotoluene as a solvent diminishes to some slight extent the rotation of nicotine, which is then almost unaffected by temperature change. In ethyl acetate, the rotation is depressed almost to the same extent, but not quite so much as in o-nitrotoluene, the temperature coefficient being again very small. α-Bromonaphthalene raises the rotation of nicotine, the temperature coefficient becoming somewhat greater at the same time - the rotation becomes more negative as the temperature rises. In quinoline, nicotine has a rotation at zero of - 152°. It falls steadily until at 100° the value is - 179°. This temperature-rotation curve is therefore quite in agreement with the others. Water raises the rotation of nicotine considerably, the value at zero being - 90°. Heating lowers the value much as in quinoline. Formamide also was used as a solvent, and in this case the rotation fell from - 35.6° at zero to - 77.5°. The formamide which we had used, however, was found to contain some formic acid; nevertheless, the curve obtained, as in many other cases, fits in along with those for the other solvents. We had hoped to raise the rotation of nicotine into the neighbourhood of $[\alpha] = 0^\circ$ in order to be able to examine a definite region of anomalous dispersion, but we have found no "inert" solvent which is capable of producing this effect. In addition to those quoted, the specific rotations of nicotine, dissolved in benzaldehyde, carbon disulphide, methyl-ethyl ketone, carbon tetrachloride and ether, were determined for green light at room temperature. The values obtained ranged from - 40° to - 60°, so it was not considered worth while to continue the examination. It is one of the interesting things, however, about the study of optical activity in solution that a solvent which combines chemically with the active compound behaves in very much the same way as one which would normally be regarded as indifferent; otherwise the characteristic diagram would be impossible. The increase in the rotation of the nicotine in the experiment just mentioned was doubtless partly due to the formamide itself and partly due to the action of the formic acid which it contained. Solution of nicotine in an excess[x] of 3.2095 N-aqueous sulphuric acid raised the rotation at 0° to 30.45°, and, on heating, the rotation gradually fell to 19.5° at 90°.

From the data for the various solutions examined, the characteristic diagram shown in Fig. 2 is obtained. It will be seen that the data obtained lie in a fairly satisfactory manner on the lines of the diagram. The data for the rotation of nicotine in excess of sulphuric acid are in agreement with the others. It seems clear from the diagram

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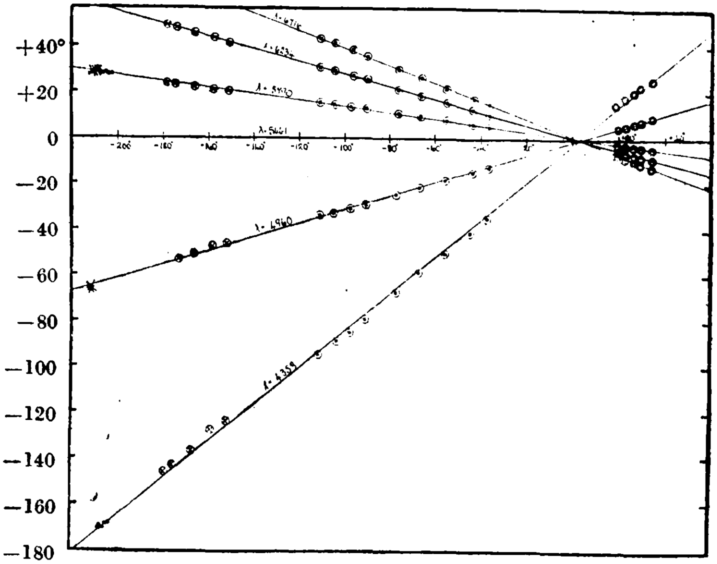
[x] Such that all the nicotine existed, presumably, as sulphate.

Fig. 2.



Characteristic diagram of nicotine in ◎ sulphuric acid (excess), ⊙ formamide, ⊕ water, ⊕ quinoline, ✱ o-nitrotoluene, • homogeneous.

that if the rotation for green light could be made to take on a value in the neighbourhood of + 3° or 4°, the rotation dispersion would be visibly anomalous; the lines of the characteristic diagram intersect over a range. The behaviour of nicotine may therefore be said to be normal, inasmuch as it conforms to that observed for the large majority of - if not indeed for all - active compounds.

The dispersion coefficients, $[\alpha]_{5790}/[\alpha]_{5461}$, calculated for nicotine from these data using the rational zero + 3° are shown in Table III. The values found show a very fair constancy, the mean value being 0.8674.

TABLE III.

Physical State	t	Nicotine Intersecting at = + 3° $[\alpha]_y$	$[\alpha]_g$	Rational Dispersion Coefficient Hg_y/Hg_g
Homogeneous	0°	-175.56	-202.8	.8676
"	71.5°	-179.29	-207.05	.8679
In ethyl acetate	15.2°	-181.03	-209.42	.8664
" " "	40.8°	-182.61	-210.52	.8693
In Water	24.5°	-83.41	- 97.22	.8623
" "	47.5°	-89.69	-104.43	.8628
In Brom.napthalene	12.6°	-163.49	-188.92	.8727
" " "	41.1°	-166.70	-191.36	.8731
In excess H_2SO_4	0°	+ 30.30	+ 34.46	.8678
" " "	66.8°	+ 20.02	+ 22.70	.8640
In formamide containing formic acid	15.5°	- 37.36	- 43.66	.8650
" " "	99°	- 66.43	- 76.87	.8693
In o nitrotoluene	14.10°	-182.1	-211.0	.8671
" "	40.8	-182.55	-211.37	.8658
In quinoline	80°	-151.60	-174.90	.8690
" "	99.2°	-154.54	-178.31	.8689

The colours of light used were as follows :

	r_1.	r_2.	y.	g.	b.	v.
λ	6716·3	6234·3	5790·3	5460·7	4959·7	4358·3

Homogeneous benzyl d-*dimethoxysuccinate.* Densities determined : 1·1730 at 16·4°; 1·1551 at 41°; 1·1320 at 70·75°; 1·1064 at 100°.

t.	*d*.	$[\alpha]_{r_1}$.	$[\alpha]_{r_2}$.	$[\alpha]_y$.	$[\alpha]_g$.	$[\alpha]_b$.	$[\alpha]_v$.
0°	1·1813	72·83°	85·16°	100·6°	114·17°	148·6°	193·3°
16·3	1·1732	69·91	80·25	94·99	108·05	135·5	181·2
44·4	1·1523	62·29	73·42	86·14	98·54	123·8	166·1
70·5	1·1324	56·99	68·08	79·65	90·20	114·1	152·7
100	1·1064	52·40	61·64	72·72	82·84	104·0	139·8
139·5	1·0685	47·09	55·80	65·98	74·82	93·84	127·5
174·5	1·0321	43·31	51·45	60·32	68·58	86·21	117·6

Benzyl d-*dimethoxysuccinate in quinoline, p* = 5·1758. Readings for some colours could not be taken at 100° owing to the darkening of the quinoline in solution. Densities determined : 1·0982 at 17·5°; 1·0740 at 48·5°; 1·0511 at 76°; 1·0312 at 100°.

t.	*d*.	$[\alpha]_{r_1}$.	$[\alpha]_{r_2}$.	$[\alpha]_y$.	$[\alpha]_g$.	$[\alpha]_b$.	$[\alpha]_v$.
0°	1·1148	97·05°	114·3°	134·9°	154·6°	—	—
15·2	1·1020	90·64	105·3	126·6	142·9	178·8°	243·9°
44·2	1·0775	80·33	93·96	108·7	128·0	158·4	216·1
69·2	1·0566	72·97	84·30	100·4	115·0	142·0	198·8
100	1·0312	67·66	73·69	—	—	—	—

Benzyl d-*dimethoxysuccinate in nitrotoluene, p* = 4·860. Densities determined : 1·1682 at 16·7°; 1·1413 at 43·4°; 1·1150 at 70·7°; 1·0874 at 100°.

t.	*d*.	$[\alpha]_{r_1}$.	$[\alpha]_{r_2}$.	$[\alpha]_y$.	$[\alpha]_g$.	$[\alpha]_b$.
0°	1·1843	98·51°	115·2°	137·0°	155·5°	197·0°
13·6	1·1709	90·50	107·0	127·0	145·5	184·0
43·5	1·1411	79·13	93·2	109·0	124·2	158·4
72	1·1139	68·53	80·4	95·13	108·3	137·1
100	1·0874	61·12	71·2	83·45	95·8	119·0

Benzyl d-*dimethoxysuccinate in acetylene tetrabromide, p* = 3·066. Densities determined : 2·8405 at 16·2°; 2·7853 at 42°; 2·7184 at 72·8°; 2·6651 at 98·8°.

t.	*d*.	$[\alpha]_{r_1}$.	$[\alpha]_{r_2}$.	$[\alpha]_y$.	$[\alpha]_g$.	$[\alpha]_v$.
0°	2·8755	47·18°	53·99°	63·18°	72·48°	118·2°
14·0	2·8452	45·40	53·73	62·25	70·62	116·2
44·2	2·7804	43·46	49·74	58·77	66·63	111·6
70·6	2·7238	40·59	47·42	55·92	63·34	105·4
98·8	2·6651	38·67	44·79	53·24	60·46	100·8

Benzyl d-*dimethoxysuccinate in* m-*xylene, p* = 6·6875. Densities determined : 0·8865 at 14·2°; 0·8630 at 42·2°; 0·8375 at 71°; 0·8122 at 99°.

t.	*d*.	$[\alpha]_{r_1}$.	$[\alpha]_{r_2}$.	$[\alpha]_y$.	$[\alpha]_g$.	$[\alpha]_b$.	$[\alpha]_v$.
16·9°	0·8843	68·91°	77·68°	91·10°	103·5°	131·8°	175·3°
43·7	0·8614	60·22	70·31	83·11	95·04	120·7	160·0
69	0·8392	55·13	64·82	76·73	87·31	111·4	147·7
98·7	0·8126	50·47	59·58	70·39	80·28	102·4	135·4

d-*Dimethoxysuccinic acid in pyridine, p* = 7·8435. Densities determined : 1·0137 at 15°; 0·9865 at 41·8°; 0·9621 at 66·7°; 0·9293 at 98·7°.

t.	*d*.	$[\alpha]_{r_1}$.	$[\alpha]_{r_2}$.	$[\alpha]_y$.	$[\alpha]_g$.	$[\alpha]_b$.	$[\alpha]_v$.
0°	1·0287	129·9°	152·8°	181·0°	204·4°	255·3°	336·3°
14·8	1·0140	122·6	143·6	170·1	192·0	241·2	318·9
46·4	0·9819	111·4	130·1	151·3	172·6	218·0	287·8
69	0·9592	103·1	120·2	142·4	161·2	201·1	268·4
99	0·9293	92·8	110·0	128·2	146·1	184·0	243·5

d-*Dimethoxysuccinic acid in acetone,* $p = 15{\cdot}982$. Densities determined: 0·8558 at 21·5°; 0·8433 at 33°; 0·8327 at 42·8°.

t.	*d.*	$[\alpha]_{r_1}$.	$[\alpha]_{r_2}$.	$[\alpha]_y$.	$[\alpha]_g$.
0°	0·8787	70·08°	81·82°	95·36°	108·5°
12	0·8656	70·24	80·08	94·00	106·3
30·5	0·8459	68·15	76·52	91·96	103·8
46·6	0·8283	65·95	73·12	88·98	100·8

Methyl d-*dimethoxysuccinate in quinoline,* $p = 5{\cdot}502$. Densities determined: 1·1026 at 14°; 1·0804 at 40·7°; 1·0582 at 68·3°; 1·0326 at 100·2°.

t.	*d.*	$[\alpha]_{r_1}$.	$[\alpha]_{r_2}$.	$[\alpha]_y$.	$[\alpha]_g$.	$[\alpha]_v$.
0°	1·1138	84·04°	97·74°	114·6°	129·4°	211·5°
13·5	1·1030	83·54	97·05	114·0	129·4	211·7
36·3	1·0844	81·79	94·69	111·0	125·9	208·5
67	1·0595	77·36	88·51	105·7	119·4	198·0
99·6	1·0332	—	80·92	98·2	110·8	unreadable

Benzyl tartrate in quinoline, $p = 9{\cdot}4489$. Densities determined: 1·1080 at 17°; 1·0878 at 40·2; 1·0627 at 72°; 1·0408 at 98·9°.

t.	*d.*	$[\alpha]_{r_1}$.	$[\alpha]_{r_2}$.	$[\alpha]_y$.	$[\alpha]_g$.
0°	1·1213	31·34°	37·79°	43·56°	48·88°
13·5	1·1103	29·92	34·60	40·51	45·58
48·8	1·0818	25·26	30·46	34·89	38·63
74·2	1·0610	21·95	27·73	31·69	34·86
98·9	1·0408	21·57	25·04	30·29	32·15

Nicotine in formamide solution. The formamide contained some formic acid and caused a rise in rotation in the absolute sense from that obtained with pure formamide, $p = 18{\cdot}5040$. Densities determined: 1·1328 at 14·9°; 1·1061 at 50·8°; 1·0877 at 73·7°; 1·0660 at 99·3°.

t.	*d.*	$[\alpha]_{r_1}$.	$[\alpha]_{r_2}$.	$[\alpha]_y$.	$[\alpha]_g$.	$[\alpha]_b$.	$[\alpha]_v$.
0°	1·1433	−20·99°	−25·57°	−30·77°	−36·30°	−49·35°	−73·88°
16·0	1·1325	26·01	30·97	37·36	43·66	58·89	86·99
44·6	1·1103	33·29	39·52	47·16	55·15	73·25	106·0
70·4	1·0899	39·82	47·90	56·72	66·25	87·12	124·8
99	1·0665	47·68	56·50	66·43	76·87	102·1	144·1

Solution of nicotine in o-*nitrotoluene,* $p = 4{\cdot}7337$. Densities determined: 1·1582 at 15·7°; 1·1322 at 43°; 1·1024 at 75°; 1·0789 at 99°.

t.	*d.*	$[\alpha]_{r_1}$.	$[\alpha]_{r_2}$.	$[\alpha]_y$.	$[\alpha]_g$.	$[\alpha]_b$.
0°	1·1733	−128·4°	−153·7°	−184·1°	−211·0°	−277·3°
14·1	1·1598	129·4	154·5	182·1	211·0	278·3
40·8	1·1346	130·7	154·3	182·7	211·1	277·2
74·4	1·1025	130·6	154·7	182·6	211·4	277·6
99·2	1·0878	129·9	153·9	182·2	210·4	—

Solution of nicotine in quinoline, $p = 9{\cdot}1365$. Densities determined: 1·0888 at 15·3°; 1·0626 at 48·9°; 1·0413 at 75·2°; 1·0217 at 99·4°.

t.	*d.*	$[\alpha]_{r_1}$.	$[\alpha]_{r_2}$.	$[\alpha]_y$.	$[\alpha]_g$.	$[\alpha]_b$.	$[\alpha]_v$.
0°	1·1010	−93·75°	−110·3°	−131·3°	−151·3°	−197·2°	−274·9°
17	1·0878	96·59	114·8	137·1	158·1	205·4	287·1
43·7	1·0665	102·4	121·0	144·5	166·5	216·9	302·8
80	1·0375	107·4	127·2	151·6	174·9	227·8	317·6
99·2	1·0220	109·4	129·7	154·5	178·3	226·6	324·2

Nicotine in a-bromonaphthalene. Some naphthalene was also present as impurity. No rotations could be observed at 0° owing to partial solidification of the mixture, $p = 4{\cdot}3213$. Densities determined: 1·4668 at 10·7°; 1·4335 at 45·2°; 1·4081 at 70·4°; 1·3788 at 100°.

t.	*d.*	$[\alpha]_{r_1}$.	$[\alpha]_{r_2}$.	$[\alpha]_y$.	$[\alpha]_g$.	$[\alpha]_b$.	$[\alpha]_v$.
12·6°	1·4650	−111·4°	−133·6°	−163·5°	−188·9°	−241·2°	−337·9°
41·1	1·4367	117·1	139·0	166·7	191·4	244·7	342·3
69·6	1·4085	119·9	140·3	168·1	192·6	252·2	345·9
99·2	1·3800	121·1	141·0	167·4	194·5	254·1	343·8

Homogeneous nicotine. Densities determined: 1·0124 at 14·8°; 0·99037 at 41·0°; 0·9688 at 70°; 0·9449 at 99·2°.

t.	*d.*	$[\alpha]_y$.	$[\alpha]_g$.	$[\alpha]_v$.
0°	1·0212	−175·6°	−202·8°	−371·2°
14·2	1·0108	176·4	204·2	372·8
39	0·9925	177·9	206·0	376·1
71·5	0·9673	179·3	207·1	377·0
99	0·9453	179·7	207·2	377·1

Nicotine in ethyl acetate. The rotation values for the highest temperature show a sudden rise in the absolute sense; this may be due in part to loss of solvent at that temperature, $p = 10{\cdot}701$. Densities determined: 0·9143 at 15°; 0·8893 at 37·7°; 0·8569 at 64·7°.

t.	*d.*	$[\alpha]_{r_1}$.	$[\alpha]_{r_2}$.	$[\alpha]_y$.	$[\alpha]_g$.	$[\alpha]_b$.	$[\alpha]_v$.
0°	0·9294	−127·7°	−151·0°	−180·7°	−208·2°	−268·8°	−376·8°
15·2	0·9135	129·0	152·1	181·0	209·4	269·1	378·2
40·8	0·8855	127·0	153·7	182·6	210·5	274·0	380·9
60	0·8626	116·2	141·3	171·0	198·1	253·2	355·9

Nicotine in water, $p = 9{\cdot}3930$. Densities determined: 1·0060 at 15·1°; 1·0003 at 32·8°; 0·9912 at 52·6°; 0·9820 at 68·5°.

t.	*d.*	$[\alpha]_{r_1}$.	$[\alpha]_{r_2}$.	$[\alpha]_y$.	$[\alpha]_g$.	$[\alpha]_b$.	$[\alpha]_v$.
0°	1·0098	−54·57°	−64·68°	−77·15°	−90·25°	−119·0°	−170·0°
24·5	1·0031	58·74	70·15	83·41	97·22	127·5	182·4
47·5	0·9935	63·07	75·40	89·69	104·4	137·3	194·7
67·6	0·9827	68·08	80·18	95·63	111·1	144·7	205·4

Nicotine in excess of sulphuric acid. To 3·5241 g. of nicotine were added 24 c.c. of $3{\cdot}2095N\text{-}H_2SO_4$, $p = 11{\cdot}880$. Densities determined: 1·1085 at 13·8°; 1·0920 at 46·8°; 1·0798 at 67°; 1·0645 at 90°.

t.	*d.*	$[\alpha]_{r_1}$.	$[\alpha]_{r_2}$.	$[\alpha]_y$.	$[\alpha]_g$.	$[\alpha]_b$.	$[\alpha]_v$.
0°	1·1145	+22·10°	+25·63°	+30·30°	+34·46°	+43·43°	+58·06°
26·6	1·1027	18·46	21·56	25·48	29·39	37·45	49·61
44·8	1·0931	16·41	19·30	22·86	26·23	33·06	44·56
66·8	1·0800	14·37	16·76	20·02	22·70	28·74	38·58
90	1·0645	12·16	14·33	17·05	19·42	24·56	32·86

PART II

OPTICAL SUPERPOSITION

In the case of molecules containing two similar asymmetric carbon atoms, Van't Hoff (1875)[x] assumed, that the rotation of each is unaffected by the nature of the group to which it is joined. Later in his book, "Die Lagerung der Atome im Raume", English edition page 160, the above assumption is extended to molecules containing several asymmetric carbon atoms. The view expressed by him being, that the rotatory power of a compound as a whole, was simply the algebraic sum of the rotations of the several active groups present. The hypothesis is now known as the "Principle of Optical Superposition".

The truth of the hypothesis was tested, separately and simultaneously, by Guye and Walden, who concluded from their experimental results, that Van't Hoff's assumption was justified. Their method of procedure was as follows. Isomeric amyl esters were made in three different ways; (a) from an active acid and inactive alcohol, (b) from an inactive acid and an active alcohol, (c) from an active acid and an active alcohol. A modification of the above method was employed, in the case of amyl ethers. Thus the rotation of di-laevo-amyl ether was found, and from racemic sodium-amylate by interaction with laevo-amyl-

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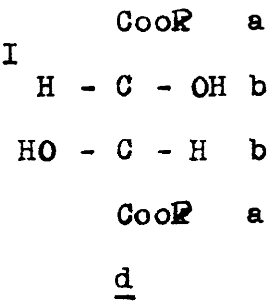
[x] A bibliography on optical superposition will be found at the end.

bromide, was obtained another ether. The latter compound was found to have a rotation equal to half of that of the first. This fact was accepted by these authors, as a proof of the above hypothesis.

Rosanoff (1906) points out the fallacies in the work of Guye and Walden, who were dealing with mixtures, and that the results have no bearing on the problem of optical superposition. What these authors had done was to study solvent influence on active bodies and their data fail to corroborate the truth of the principle. The same criticism has been made by Patterson and Kaye, on the work of Gadamer and his collaborators (1901, 1904), who believed from their results that the principle was contradicted. Rosanoff makes the suggestion (loc. cit. 526) that, "The optical rotatory power of an asymmetric carbon atom depends upon the composition, constitution, and configuration of each of its four groups." Somewhat the same idea had been expressed by Patterson and Taylor (1905). A consideration of the influence which the arrangement of the constituent groups exerts on the properties of an organic compound, lends support to the views expressed, and suggests the invalidity of Van't Hoff's principle. The latter authors point out (1906) that Guye and Walden, while working with mixtures of uncertain composition, have assumed the point they wished to prove.

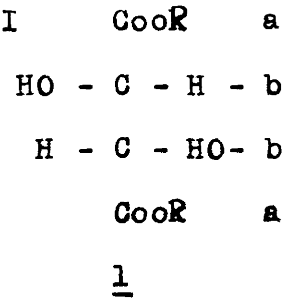
Rosanoff (1906) suggested as the most direct method of attack on the problem, the comparison of rotations of active derivatives of substances which exist in d, l and i forms. Patterson and Kaye (1905) had started on a similar line of investigation with the menthyl tartrates, the object being to compare the specific rotations of these substances. Suppose these active esters to be represented as follows:-

I



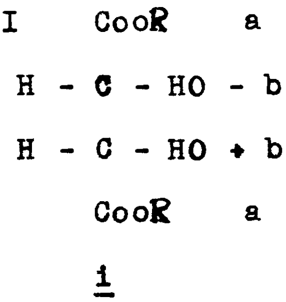
$$\begin{array}{rcll} & \mathrm{CooR} & & a \\ \mathrm{H} - & \mathrm{C} & - \mathrm{OH} & b \\ \mathrm{HO} - & \mathrm{C} & - \mathrm{H} & b \\ & \mathrm{CooR} & & a \\ & \underline{d} & & \end{array}$$

II



$$\begin{array}{rcll} & \mathrm{CooR} & & a \\ \mathrm{HO} - & \mathrm{C} & - \mathrm{H} - & b \\ \mathrm{H} - & \mathrm{C} & - \mathrm{HO} - & b \\ & \mathrm{CooR} & & a \\ & \underline{l} & & \end{array}$$

III



$$\begin{array}{rcll} & \mathrm{CooR} & & a \\ \mathrm{H} - & \mathrm{C} & - \mathrm{HO} - & b \\ \mathrm{H} - & \mathrm{C} & - \mathrm{HO} + & b \\ & \mathrm{CooR} & & a \\ & \underline{i} & & \end{array}$$

Formula I represents an ester of d-tartaric acid, while II and III represent the same esters of l and i tartaric acid respectively. Suppose the principle is correct and we assume the rotation of each carbon atom of the acid as b, and that of each active alcohol radicle, which is then unaffected by the acid radicle, as a. Then from the above the value of the rotation of I is 2a + 2b, that of II is 2a-2b, while that of III is 2a. The mean value of rotation of I and II is 2a, which is the same as that of III. This relationship should hold in practice if the principle is true. On the other hand Patterson and Patterson (1915) have shown that, "even if the mutual influence of the different centres were very great indeed and the principle of optical superposition altogether violated, the mean of the rotations of I and II might, owing to a compensation of effects, be exactly equal to that of the compound III." There is one difficulty, perhaps in this method, namely, solvent influence, and also whether all three exist in the same state in one solvent. Even if different states of molecular complexity were found to exist their influence on rotation is altogether unknown.

Adopting the same method as that described above Tschugaev and Glebko (1907), from data obtained by them, are of the opinion that the principle is correct, as a first approximation. The same opinion is also held by Hudson, who along with his collaborators, has published a series of important papers on the sugars, in the Journal of the American Chemical Society, and particularly in the later series, dating from 1924, on "Relations between Rotatory Power and Structure in the Sugar Group", some interesting computations have been made to demonstrate these relationships. The results, of potential value in other directions, have been accepted as an indication of the truth of Van't Hoff's principle and are of direct interest on that account.

Hudson states (1924) that "the theory holds as a first approximation at least, among the halogen acyl aldoses" while in other cases (1925), the principle is regarded as applying, without qualification, to the rotations of the synthetic glucosides of the aliphatic alcohols and the compound sugars. The data of Hudson, Table I, can hardly be said to bear out his own views.

Hudson assumes that the principle of optical superposition is true and adopts the following method of procedure. A sugar which exists in α and β forms, say penta-acetyl glucose, is taken. If the rotations of the end carbon atom be written A_{Ac} and $-A_{Ac}$ respectively for the two forms, and $B_{glucose}$ be chosen to represent the rotation of the rest of the chain, then the molecular rotation of α form is $B_{glucose} + A_{Ac}$, and that of the β form is $B_{glucose} - A_{Ac}$. The mean of these two quantities gives the value of $B_{glucose}$ and this value should be independent of the nature of substituent on the end carbon atom, provided the end carbon atom alone is affected in this way. The mean difference of the molecular rotations is A_{Ac}, which should be constant for all aldehyde sugars and for derivatives, wherein the groups directly attached to the end carbon atom are unchanged.

In just the same way the value A_{Cl}. is calculated from the rotation of one form of chlor-acetyl glucose, and from the known rotations of the α and β forms of penta-acetyl glucose. Similar methods of calculation are applied to sugars containing from five to twelve carbon atoms in the molecule, and it is concluded (1924), that "the rotation of the end asymmetric carbon atom of a halogen or nitro-acyl aldose is approximately a constant quantity for the various aldoses." From general considerations the results would appear improbable and the values quoted in Table I, from the first paper in the series, support the latter view.

TABLE I.

Substance	Mol. wt.	$[\alpha]$ in chloroform	$[M]_D$	Rotation of the end C atom	Average A
Chloro-acetyl xylose	294	+ 165	48,500	+38,300	+ 37,800 A_{Cl}.
Chlor-acetyl glucose	366	166	60,800	40,100	
Do. do. mannose	366	90	32,900	27,100	
" " lactose*	654	72	47,100	30,200	Excluding
" " maltose	654	159	104,000	41,300	the value
" " cellobrose	654	73	47,700	38,900	for chloro-
1st " " galactose	366	212	77,600	52,200	acetyl
2nd " " galactose	366	-78	-28,500	-32,000	mannose

*The value for chloro-acetyl lactose has subsequently been revised (1925) and the value 38,100 is quoted for A_{Cl}.

Inspection shows large differences in the values for A_{Cl}, and these cannot be regarded as in agreement with the principle. It is perhaps unfortunate, from the author's point of view, that the rotation values, collected from different sources, should not all have been observed in the same solvent. It is only fair to state, however, that in other instances, the rotation values calculated for the end carbon atom show good agreement with experimental values. That such agreement should exist is somewhat puzzling.

On applying Van't Hoff's principle to the ketose sugars, the rotation values for the known penta-acetates of fructose are on calculation by the above method found to be,

$$[\alpha]^{20}_{D} = -5^{\circ} \text{ and } -103^{\circ},$$

while those determined are:

$$[\alpha]^{20}_{D} = +34.7 \text{ and } -121^{\circ}.$$

The values bear little relation to one another and so the aid of a different oxide-ring structure is invoked. This point will be brought up later.

Hudson's conclusion (1924, 488) in agreement with that of Haworth and Leitch (J.C.S. 1922 <u>121</u> 1921) as to the nature of the biose of amygdalin,though interesting,cannot be accepted as a proof of the principle, on account of the mode of procedure. The rotation data, collected from various sources, embody the mean values of different workers and muta-rotation of the sugars has also to be reckoned with. It is to be noted that the same author (1924, 474) accepts the final equilibrium rotation value of a sugar, while (1924, 488) the stable rotation value is not accepted, but one differing widely from it. This difficulty occurs in some of his earlier communications.

Hudson (1924, 2601) quoted the following values:-

TABLE II

			Mean already found for other sugars.
β fluoro-acetyl l arabinose	A_F	8,300	9,800
" chloro " "	A_{Cl}	41,900	37,800
" bromo " "	A_{Br}	67,200	59,300
" iodo " "	A_I	100,700	85,400

Except for the value of A_F the agreement is poor.

The values for the rotations of halogen-acetyl arabinoses calculated and observed are as follows:-

TABLE III

	Calc.	Found
Fluoro	144	138
Chloro	231	244
Bromo	264	287
iodo	299	339

Hudson adds "the calculated value for the iodo-compound is much lower than the observed, a fact which may prove of much theoretical importance." Yet (loc. cit. 2591-2592) he remarks, "the halogen-acetyl derivatives of arabinose fall into line with those of the other sugars, by conforming, in first approximation at least, to Van't Hoff's principle of optical superposition." It is suggested that the discrepancy between the values for A_I, is due to a difference in ring structure of the sugars concerned, namely arabinose and glucose. Yet the values of A_F for these sugars are in fair agreement, and it is pointed out indeed, that the value of A_F for arabinose and xylose are in close agreement, suggesting a similar ring structure. However, a different oxide-ring structure from arabinose cannot be assigned to glucose on these grounds, for (1924, 465) we find A_{Cl} and A_{Br} for glucose and xylose in comparatively good agreement. Thus the facts might serve equally well to prove or disprove the point at issue, and earlier, attention has been drawn to the same difficulty in the case of fructose. The arguments adduced, may therefore not be regarded as consistent and stronger evidence for different ring systems is required.

In this connection the recent paper by Haworth, Charlton and Peat (J.C.S. Jan. 1926, p. 89) is of interest, where evidence is adduced for the amylene-oxide structure of glucose in its normal form. It seems that more chemical evidence of the latter type will be required, before definite conclusions on ring structure can be arrived at. The lack of such knowledge gives too much scope to the method of calculation adopted by Hudson.

Thus (1925, 272) the same author suggests that the α and β forms of mannose, rhamnose and lyxose have different ring structures because the difference in rotation between these forms is smaller than Van't Hoff's principle demands. Measurements in support of this theory are awaited with the interest which the idea engenders. The conception of so many different rings certainly does not simplify the relationships existing amongst the sugars.

Anhydro menthyl and methyl glucosides prepared from 16 dibromo 235 triacetyl glucose, by interaction with the respective alcohols followed by treatment with caustic soda solution, are assigned different ring structures on the basis of rotation, though prepared by the same method. Thus Fischer and Zach (Ber. 1912, <u>45</u>, 456) record $[\alpha]_D$ = -137° for 6 anhydro methyl-glucoside. Calculation if a β derivative gives $[\alpha]_D = -32^\circ$, while if an α derivative $[\alpha]_D = +178^\circ$. The above conclusion is arrived at from the data quoted. The principle of optical superposition has been shown to be untenable in a number of cases, and meantime, the figures just quoted could equally well be cited against the truth of it.

To sum up, it is suggested that the methods adopted by Hudson to prove the truth of the hypothesis are of limited application, till the types of ring structure, present in the various sugars, are known with certainty. Further the rotation values, collected from numerous sources, while of value for correlation in definite cases, are on the other hand unreliable to test a principle so subtle.

A further test of the validity of the principle has been made, by the method which at present seems most likely to give satisfactory results. The bornyl esters of <u>d</u>, <u>l</u> and <u>i</u> dimethoxy-succinic acids have been prepared, with the object of comparing the mean value of the specific rotations of the two former, with that of the third, under similar conditions. If the principle holds accurately these values should be identical. It has been pointed out already, however, that even a complete agreement, is not of necessity a proof of the principle. Whereas a small though definitely established difference proves the principle to be false.

Bornyl <u>l</u>-dimethoxy succinate was prepared by mixing 10 gms. of dimethyl <u>l</u>-dimethoxy succinate MP 51°, obtained by the method of Patterson and Patterson (J.C.S. 1915 <u>107</u> 142), with 60 grams borneol in a distilling flask. Dry hydrogen-chloride was then passed into the mixture at the ordinary temperature, for an hour, when partial liquefaction took place. (Cf. Patterson and Dickinson J.C.S. 1901, 79 280). The flask was then heated at 100° in an oil bath for 24 hours. The stream of dry hydrogen-chloride was passed continuously and the sublimation of borneol caused some difficulty. The product was distilled at low pressure up to 200° to remove borneol. The fraction boiling at 265°/15 m.m. was collected and 6 gms. of fairly pure ester obtained, readily soluble in common organic solvents. The ester was recrystallised from aqueous alcohol 75% strength. MP 70°.

C	theory	69.33	found	69.14
H	"	9.33	"	9.42

Bornyl d-dimethoxy succinate was prepared and purified in the same way. MP 103. It is readily soluble in the common organic solvents. C found 69.21. H found 9.32.

Bornyl i-dimethoxy succinate was prepared, not from the methyl ester but from i-dimethoxy succinic acid itself MP 162°, which in turn was got by hydrolysis of the methyl ester. Ten grams of the acid were mixed with 60 grams borneol and the same procedure followed as before. The ester is much less soluble in alcohol than the others, but is readily soluble in common organic solvents. C found 69.47. H found 9.37.

The rotation of the esters has been examined for five different solvents over a range of temperature. On account of their rather high melting points, the esters were not polarimetrically examined in the homogeneous state. The data will be found at the end, while the following table summarises the results, with regard to the main point under discussion.

TABLE IV.

Specific rotation of bornyl esters of dimethoxy succinic acids.

Physical Condition	t°	c	I d ester	II l ester	III i ester	IV Mean of I & II	Δ IV-III
In alcohol	0	4.5	130.97°	-37.88°	44.73°	46.55°	1.82°
	20	"	126.04	35.32	43.49	45.36	1.87
In pyridine	0	5	141.31	55.86	37.06	42.73	5.67
	20	"	134.50	52.61	36.46	40.94	4.48
In benzene	20	5	127.42	45.46	39.20	40.98	1.78
In chloroform	0	5	128.60	28.09	50.65	50.25	- .40
	22	"	121.84	26.45	47.97	47.69	- .28
Ethylene bromide	20	7	130.90	26.23	49.18	52.34	3.16

If the hypothesis of Van't Hoff regarding optical superposition be correct, the mean of the rotations of the *d* and *l* forms should have the same value as that of the ester of the *i* acid. It will be seen that the values we have obtained, in this series of compounds, with the exception of the solutions in pyridine and ethylene bromide, do not in fact differ much from what the principle would require. Nevertheless the following points are to be noted.

(1) That in each solvent for which observations are quoted at two different temperatures, the differences are in the same sense. This seems to show that the differences are not due to experimental error.

(2) That the differences are not the same in the various solvents used, seems also to favour the view, that the results are not due to any constant error such as impurity of one or more of the esters used, but that they are really due to invalidity of the principle.

(3) The effect of change of temperature upon these differences seems truly to be significant.

Table V. shows the data for these three esters dissolved in chloroform and in alcohol, values in the latter case being taken from smoothed temperature rotation curves.

TABLE V.

Variations in Δ with change of temperature.

In Chloroform		In alcohol	
t^o	Δ	t^o	Δ
0	-0.40	0	1.8
22	-0.28	20	1.6
44.8	+0.36	60	0.3

It will be observed, that in chloroform the difference which at first is negative becomes less negative as the temperature increases and changes to a positive value at higher temperatures. The difference in the case of the alcohol also diminishes gradually as the temperature rises. It thus appears, that in chloroform one could realise a condition of affairs, in which the difference would be zero and Van't Hoff's assumption would thus hold completely. Although this temperature is not actually reached in alcohol, it seems clear that it also might easily be realised. The fact that the differences observed in the present experiments is dependent upon the temperature in this way, seems a strong proof that Van't Hoff's supposition cannot be regarded as a general principle. Thus, although in the cases presently recorded the agreement of the experimental data with the requirements of the principle is fairly close, in other cases very wide differences have been found.

EXPERIMENTAL

The Ethylene bromide was purified by washing with dilute NaOH solution followed by water and drying over fused calcium chloride. It was then distilled, frozen and freed from liquid by decantation. After melting it was again distilled and fraction BP 130° C collected.

Benzene was shaken with concentrated sulphuric acid and then washed with dilute sodium hydroxide followed by water, dried over fused calcium chloride and distilled, frozen twice and again distilled. Fraction BP 80° C. was collected.

Pyridine of good quality was refluxed over solid caustic potash, the liquid decanted and fractionally distilled. BP of the fraction used was 115.5° C.

Chloroform was treated with concentrated sulphuric acid to remove alcohol, washed with water and dried over fused calcium chloride. The fraction of BP 61° C was used as solvent.

Absolute alcohol was refluxed over quick-lime and distilled in a column. The fraction boiling at 78°-78.5°C was collected.

The colours of light used were as follows:-

y	g	v
5790.3	5460.7	4358.3

Bornyl d. dimethoxy succinate in chloroform

Densities determined 1.4649 at 13°C; 1.4449 at 25°; 1.4110 at 43.4. $p = 3.4310$

t	d	α_y	$[\alpha]_y$	α_g	$[\alpha]_g$	α_v	$[\alpha]_v$
0°	1.4874	8.76	111.43	10.11	128.60	16.66	211.92
22°	1.4495	8.24	107.50	9.34	121.84	15.34	200.14
44.7°	1.4090	7.68	103.05	8.78	117.80	14.40	193.21

Bornyl l dimethoxy-succinate in Chloroform

Densities determined 1.4585 at 17.8°; 1.4378 at 30°; 1.4120 at 44°. p = 3.4315.

t	d	α y	$[\alpha]$y	α g	$[\alpha]$g	α v	$[\alpha]$v
0°	1.4883	-1.86	-23.64	-2.21	-28.09	-3.30	-41.95
22°	1.4515	-1.67	21.76	+2.03	+26.45	3.07	39.99
44.7°	1.4110	-1.60	21.44	1.93	25.86	2.80	37.51

Bornyl i dimethoxy succinate in Chloroform

Densities determined 1.4590 at 17°; 1.4339 at 32°; 1.4116 at 44°. p = 3.4282.

t	d	α y	$[\alpha]$y	α g	$[\alpha]$g	α v	$[\alpha]$v
0°	1.4880	3.52	44.79	3.98	50.65	6.63	84.37
22°	1.4560	3.23	41.99	3.69	47.97	6.15	79.95
44.8°	1.4104	3.10	41.59	3.40	45.61	5.80	77.81

Bornyl d dimethoxy succinate in Benzene

Densities determined .8947 at 10°; .8714 at 32°; .8470 at 58°. p = 5.6115.

t	d	α y	$[\alpha]$y	α g	$[\alpha]$g	α v	$[\alpha]$v
20°	.8839	8.34	109.10	9.74	127.42	16.27	212.84
39.2°	.8640	7.93	106.10	9.21	123.20	15.22	203.62
57°	.8456	7.67	104.80	8.78	120.0	14.38	196.51

Bornyl i dimethoxy succinate in Benzene

Densities determined .8859 at 20.5°; .8663 at 39.1; .8496 at 55°. p = 5.5854.

t	d	α y	$[\alpha]$y	α g	$[\alpha]$g	α v	$[\alpha]$v
20°	.8861	2.69	35.27	2.99	39.20	4.98	65.27
39°	.8665	2.54	34.04	2.87	38.47	4.84	64.87
56°	.8485	2.46	33.66	2.79	38.17	4.72	64.58

Bornyl l - dimethoxy succinate in Benzene

Densities determined .8814 at 24°; .8669 at 38.2; .8463 at 57.7. p = 5.6116.

t	d	α y	$[\alpha]$y	αg	$[\alpha]$g	α v	$[\alpha]$v
20°	.8852	-3.08	-40.23	-3.48	-45.46	-5.64	-73.67
38.7°	.8661	2.89	38.57	3.25	43.37	5.25	70.07
56.5°	.8476	2.70	36.81	3.05	41.58	4.95	67.48

Bornyl l dimethoxy succinate in Alcohol

Densities determined .8099 at 14.7°; .8006 at 26.7; .7887 at 40.6; .7767 at 53.7. p = 5.5874.

t	d	α y	$[\alpha]$y	αg	$[\alpha]$g	α v	$[\alpha]$v
0°	.8220	-2.19	-30.95	-2.68	-37.88	-4.16	-58.80
20°	.8055	2.00	28.83	2.45	35.32	3.87	55.79
39.4°	.7896	1.83	26.91	2.25	33.08	3.51	51.61
55°	.7760	1.69	25.28	2.09	31.26	3.27	48.91

Bornyl d dimethoxy succinate in Alcohol

Densities determined .8088 at 12.2; .7892 at 36; .7808 at 45.5; .7698 at 58°. p = 5.5774.

t	d	α y	$[\alpha]$y	αg	$[\alpha]$g	α v	$[\alpha]$v
0°	.8192	8.13	115.51	9.22	130.97	15.15	215.25
20°	.8022	7.65	110.95	8.69	126.04	14.35	208.13
38.8°	.7863	7.23	106.94	8.17	120.84	13.55	200.41
54°	.7735	6.86	103.12	7.77	116.70	12.91	194.06

Bornyl i dimethoxy succinate in Alcohol

Densities determined .8037 at 17.6; .7916 at 31.8; .7800 at 45.5; .7689 at 58°. p = 5.5830.

t	d	α y	$[\alpha]$y	α g	$[\alpha]$g	α v	$[\alpha]$ v
0°	.8188	2.84	40.33	3.15	44.73	5.38	76.40
20°	.8017	2.70	39.14	3.00	43.49	5.08	73.64
38.5°	.7858	2.55	37.70	2.89	42.73	4.82	71.26
54.2°	.7722	2.41	36.25	2.80	42.12	4.61	69.34

Rotation of Bornyl d dimethoxy succinate in pyridine

Densities determined .9908 at 14°; .9738 at 31.6°; .9553 at 50.3. p = 5.0458.

t	d	α y	$[\alpha]$y	α g	$[\alpha]$g	α v	$[\alpha]$v
0°	1.0042	9.56	122.48	11.03	141.31	18.01	230.73
20°	.9848	9.04	118.04	10.30	134.50	16.92	220.93
44.2°	.9613	8.47	113.26	9.52	127.3	15.68	209.67

Bornyl i dimethoxy succinate in pyridine

Densities determined .9883 at 15.7; .9703 at 34.5°; .9522 at 52.3. p = 5.0453.

t	d	α ~~$[\alpha]$~~y	$[\alpha]$y	α g	$[\alpha]$g	α v	$[\alpha]$v
0°	1.0034	2.53	32.44	2.89	37.06	4.76	61.04
20°	.9841	2.45	32.02	2.79	36.46	4.63	60.50
44.6°	.9600	2.30	30.80	2.64	35.35	4.45	59.59

Bornyl l dimethoxy succinate in pyridine

Densities determined .9892 at 15°; .9724 at 32.5°; .9551 at 50°. p = 5.0482.

t	d	α y	$[\alpha]$y	αg	$[\alpha]$g	αv	$[\alpha]$v
0°	1.0036	-3.79	-48.56	-4.36	-55.86	-6.85	87.77
20°	.9845	+3.53	46.08	+4.03	52.61	6.31	82.38
45.5	.9596	3.17	42.44	3.59	48.07	5.65	75.65

Bornyl l dimethoxy succinate in ethylene bromide

Densities determined 2.0980 at 11°; 2.0481 at 37°; 1.9982 at 61.5; 1.9668 at 78°; 1.9241 at 98°. p = 3.3511.

t	d	α y	$[\alpha]$y	αg	$[\alpha]$g	αv	$[\alpha]$v
20°	2.0814	-2.49	-23.16	-2.82	-26.23	-4.31	-40.10
44.3	2.0336	2.27	21.61	2.57	24.46	3.83	36.45
73.8°	1.9740	1.95	19.11	2.22	21.75	3.23	31.65
99.5°	1.9216	1.69	17.0	1.98	19.92	2.66	26.76

Bornyl d dimethoxy succinate in ethylene bromide

Densities determined 2.0963 at 12.3°; 2.0475 at 37°; 2.0058 at 57.1°; 1.9725 at 74.6°; 1.9231 at 98.5°. p = 3.3518.

t	d	α y	$[\alpha]$y	αg	$[\alpha]$g	α v	$[\alpha]$v
20°	2.0810	12.27	114.14	14.07	136.75	23.18	215.63
45.5°	2.0304	11.32	107.89	12.99	123.80	21.31	203.1
73°	1.9746	10.59	103.72	11.94	116.94	19.17	187.76
99.7°	1.9200	9.74	98.06	11.07	111.42	17.37	174.87

Bornyl i dimethoxy succinate in ethylene bromide

Densities determined 2.0922 at 13°; 2.0503 at 33.7°;
2.0057 at 56.7°; 1.9680 at 75.5°; 1.9188 at 98.5°.
$p = 3.3382$.

t	d	y	y	g	g	v	v
20°	2.0786	4.72	44.14	5.26	49.18	8.95	83.69
43.7°	2.0306	4.41	42.20	4.95	47.36	8.51	81.43
73°	1.9704	4.09	40.30	4.59	45.23	8.03	79.13
99°	1.9180	3.86	39.06	4.37	44.22	7.41	74.98

I desire to thank Miss J. M. Semple (Mrs. McCulloch) for the preparation of the crude bornyl esters.

When this work was completed, some doubt arose as to the optical purity of the borneol from which these esters had been prepared. The esters themselves had been crystallised repeatedly till melting point and rotation were constant and were therefore presumably pure, even if the borneol from which they were made had not been quite pure. To establish this point approximately equal quantities of the three esters were mixed and hydrolysed by alcoholic potash and the borneol recovered. Without recrystallisation it had M.P. 205° (uncorrected) and 208·7° (corrected). The rotation of the borneol was then determined in alcoholic solution with c = 12·268 when the following values for rotation were obtained:-

$$[\alpha]_{5461}^{19\cdot5} = 44\cdot63$$

$$[\alpha]_{5790}^{19\cdot5} = 38\cdot72$$

$$[\alpha]_{D}^{19\cdot5} = 37\cdot66$$

$$[\alpha]_{4358}^{19\cdot5} = 76\cdot14$$

The above results leave no doubt as to the purity of the borneol contained in the esters.

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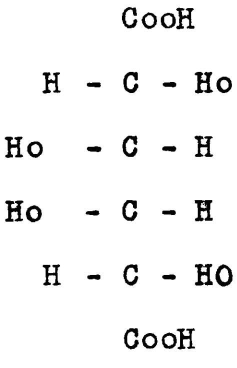
PART III.

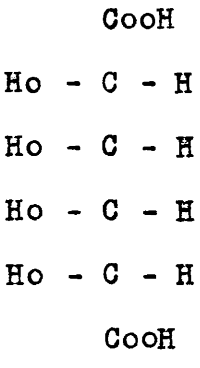
OPTICAL SUPERPOSITION

In continuation of the work described in Part II, some alkaloidal salts of mucic and allomucic acid have been prepared and used as a further test of the principle of optical superposition. The allomucic acid was prepared by the isomerisation of mucic acid. The following configurations have been assigned to these acids, both of which are optically inactive.



$$\begin{array}{c} \mathrm{CooH} \\ \mathrm{H - C - Ho} \\ \mathrm{Ho - C - H} \\ \mathrm{Ho - C - H} \\ \mathrm{H - C - HO} \\ \mathrm{CooH} \end{array}$$

Mucic Acid



$$\begin{array}{c} \mathrm{CooH} \\ \mathrm{Ho - C - H} \\ \mathrm{Ho - C - H} \\ \mathrm{Ho - C - H} \\ \mathrm{Ho - C - H} \\ \mathrm{CooH} \end{array}$$

Allomucic Acid

It will be evident from what has been stated previously that, according to Van't Hoff, the optical activity of any derivatives of these acids would be uninfluenced by the arrangement of the groups about the asymmetric carbon atoms. If such were the case then no difference in optical activity beyond that due to experimental error should be found in similar derivatives of each acid. A definite difference on the other hand disproves the theory. Such active derivatives of these acids therefore ought to furnish an excellent test of the principle.

In practice many difficulties arise since both acids are of high melting point and particularly insoluble. Thus mucic acid dissolves in 60-80 parts of boiling water, while allomucic acid dissolves in 10-12 parts, both being insoluble in common organic solvents. Both acids give readily a soluble lactone when heated in solution.

Practically the only available methods for esterification are those of Fischer or Fischer-Speier. In preparing menthyl esters for both acids by either method the product in each case was identical. The acid from the above ester has not been recovered so far. It is of interest to remember that a definite phenyl-hydrazide can readily be obtained for either acid and this would suggest the preparation of derivatives from an active hydrazine, only such hydrazides are likely to be too insoluble for examination in solution.

The use of the acid chloride with an alcohol or sodium alcoholate is not feasible since phosphorus penta-chloride converts mucic acid to chlor-muconic acid (Bode A. 132 95), while mucic acid heated for three hours with thionyl chloride at the boiling point of the latter reagent remained unchanged.

The employment of the silver salts of these acids with an alkyl halide is unsafe owing to the fact that in the preparation of halogen alkyls of suitable alcohols such as menthol, sec-octyl alcohol or borneol racemisation~~s~~ tends to occur. Cf. Pickard and Kenyon J.C.S. 1911 99 45; Ber. 1912 45 1592; also McKenzie and Tudhope J. Biol. Chem. 62 551 1924-25.

The tetramethyl dimethyl ester of mucic acid has been prepared by Karrer and Peyer (Helv. Chim. Acta 5 577), but no indication of yield is given and experiment has shown it to be so small as to be negligible. At present diazomethane is being used as methylating agent. It is of value that the tetramethyl derivative of the acid is more soluble and also its salts than those of the parent acid. The tetra-acetyl derivative of mucic acid has been prepared according to the method of Maquenne (Bull. Soc. Chim. II 48 719) and is readily soluble in hot alcohol. It forms no salts and is immediately hydrolised by alkali.

Neutral salts of menthylamine, strychnine and brucine have meantime been prepared for each acid and their activities compared under comparable conditions. These salts crystallised well from water and so this method was used for purification. The salts are little soluble in most solvents but those of strychnine and brucine show a fairly large solubility in benzyl alcohol. The menthyl-amine salts are least soluble in water while those of codeine and morphine are difficult to crystallise from aqueous solution and so far have not been obtained pure. In each case the acid was recovered from the salt and recognised by its melting point or that of its phenylhydrazide or both. The acid was in each case unchanged and the melting point of the bases was also unaltered and the activity in the case of brucine unimpaired.

EXPERIMENTAL

Allomucic acid was prepared according to Fischer (Ber. 1891 24 2136) by heating mucic acid dissolved in pyridine and water, for three hours in a copper autoclave at 140° under pressure not exceeding four atmospheres. The pyridine prevents lactone formation. In this connection Hac and Bodina (Bull. Soc. Chim. 1925 IV 37 1242) have shown that in a silver vessel no isomerisation occurs, while in the presence of nickel only eight per cent. of the mucic acid is isomerised to allomucic acid. In a copper vessel about fourteen per cent. of the mucic acid is converted. Holleman (Rec. trav. Chim. 17 323) has shown that no allomucic acid is obtained from heating mucic acid with ten per cent caustic alkali.

According to Fischer only an amorphous product is produced in the autoclave. In the present experiments a substance was extracted from the amorphous powder and was readily soluble in organic solvents but insoluble in water. It contained nitrogen and crystallised from acetone and water, M.P. 58°.

At the end of three hours the acids still in solution were converted to barium salts and the pyridine removed. The free acids were liberated by addition of the exact equivalent of sulphuric acid. On evaporation to small bulk most of the mucic acid separated out and the acids still in solution were then converted to their lead salts. From the latter the free acids were again liberated by hydrogen sulphide and finally separated as a result of the large difference in their solubilities in water. The allomucic acid melted at 172-173°.

MENTHYL-MUCATE:

Mucic acid (1 mol.) and menthol (6 mols.) were heated together at 120° in an oil bath while a current of dry hydrogen chloride was passed in. The heating was continued for 36 hours and the excess menthol removed under reduced pressure. The ester was then extracted with acetone and recrystallised from alcohol as very fine needles M.P. 165. 2 gms. acid furnished .9 gm. of the pure ester. The latter is readily soluble in ether, benzene, chloroform etc. but much less soluble in alcohol. Analysis agreed with that for a dimenthyl-mucate. Different preparations gave the same result.

The same substance was obtained by heating the above quantities in a sealed tube with .75 gm. dry hydrogen chloride for twenty-four hours at 140°-150°. Allomucic acid treated in the same way gave a product with the same rotation and melting point and there was no lowering of melting-point produced on mixing the product from each acid. So far the acid has not been isolated.

$$[\alpha]^{19.4}_{5461} = -111.30$$

No ester could be obtained from sec-octyl alcohol.

MENTHYLAMINE SALTS:

To one molecule of mucic acid in hot water was added a small excess over two molecules of menthylamine, and the mixture heated till solution was complete. On filtering and allowing to cool a well crystallised salt was obtained. Recrystallised from water it melted at 198°, with decomposition. $C_6H_{10}O_8 \cdot 2\,C_{10}H_{21}N$ requires N = 5.38

found N = 5.31, 5.43

The salt of allomucic acid prepared in the same way melted at 173° with decomposition. N found 5.46, 5.44. Both salts were sparingly soluble in water. Examined in methyl alcohol in a 4 dcm. tube with C = 1, the following values were found for specific rotation.

Mucic acid salt $[\alpha]^{18.5}_{5461} = -26.00$

Allomucic acid salt $[\alpha]^{18.5}_{5461} = -33.75$

BRUCINE SALTS

The brucine salts prepared as above from the purified base M.P. 177° were crystallised as needles from water and dried in vacuo. The mucic acid salt started frothing at 150° while that of the allomucic acid decomposed at 170° and softened below this temperature.

$2\ C_{23}H_{26}O_4N_2,\ C_6H_{10}O_8$ requires N	= 5.61
Mucic acid found	5.64, 5.76
Allomucic acid found	5.73 5.76

The salts examined in benzyl alcohol for C = 5, gave

for mucic acid $[\alpha]^{17}_{5461} = 1.35$

Allomucic Acid $[\alpha]^{17}_{5461} = -1.10$

The rotation values are remarkably low considering that the activity of the base was unimpaired on recovery.

STRYCHNINE SALTS.

Prepared in the same way as the brucine salts they were crystallised from water and formed beautiful needle shaped crystals. The salt of mucic acid browned at 200° and finally decomposed at 273°. The allomucic acid salt browned at 189° and decomposed at 269°. $2\ C_{21}H_{22}N_2O_2 \cdot C_6H_{10}O_8$ already prepared by Ruhemann and Dufton for mucic acid (J.C.S. 59 750) requires N = 6.38.

Mucic acid salt found	6.35, 6.43
Allomucic acid salt found	6.38, 6.45

Examined in benzyl alcohol C = 3.5

Mucic Acid $[\alpha]^{17.5}_{5461} = 7.93$

Allomucic Acid $[\alpha]^{17.5}_{5461} = 7.07$

The results show a wide departure from the requirements of the principle of optical superposition. It is specially to be noted that in all three cases the allomucic acid salt has the smaller absolute rotation value. On account of the smallness of the rotation value in the case of the brucine salts it would appear unwise to attempt to draw any definite conclusions from the results, in view of the fact that Tykociner (Rec. trav. Chim. 1 146-148) has stated that the specific rotation of neutral salts of brucine and strychnine are about -34° and -36° respectively. After dilution of the original solution with benzyl alcohol the mucic acid salts of both bases on standing became turbid and a very fine precipitate settled on the walls of the containing vessel. A change in rotation also occurred. These salts will be further investigated. The preparation of suitable esters for each acid would be much more satisfactory to test the point at issue. Till more suitable derivatives have been obtained it seems better to withhold judgment in the case of these acids, in so far as they affect the theory of optical superposition.

In conclusion I desire to thank Professor T. S. Patterson, my supervisor, for his kindness and help during the course of this work.
