The OPTICAL ROTATION of CAMPHOR and some DERIVATIVES.

Thesis submitted for the degree of Ph.D.,
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by

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INTRODUCTION.

The formidable mass of accumulated data relating to the optical rotation of camphor and its derivatives suggests at first sight that this field of research has already been exhausted. Closer examination, however, shows that this is far from being the case; on every side supplementary work is necessary, whilst the field itself is so extensive that a vast expanse of fresh ground remains to be broken. The application of the Drude equation by Lowry and his co-workers has resulted in valuable additions to our knowledge of the dispersion measurements of these compounds, but temperature-rotation data and the effects of solvent action are lacking and, with camphor derivatives in general, even if we except the case of camphor itself, these two highly important factors in rotation have either been neglected altogether or accorded no more than a passing consideration.

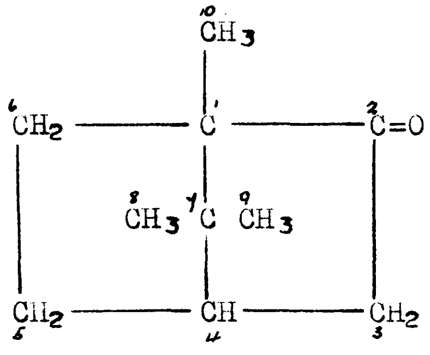
It was in part, therefore, at once the justification and aim in commencing the present work, to repair in some measure this omission and to place on record measurements of these influences which, apart from any resulting theory or generalisation, would have, ipso facto, a real value. In addition, and in this lay the chief incentive to the work, it was believed that investigation of the rotatory power of camphor compounds could scarcely fail to be of interest when referred to characteristic diagrams of the type already studied by Professor Patterson and his colleagues for compounds of a less complex character.

Accordingly, in addition to camphor itself, certain of its sulphonic and halogen derivatives have been selected, and examined in such detail as the merits of each case seemed to require.

Such, therefore, was the object and field of study and I take this opportunity of expressing my sincere thanks to Professor T. S. Patterson, under whose supervision the work was carried out, for the very timely help and encouragement he so often provided. I also desire to express my indebtedness to the Carnegie Trustees for the tenure of a Research Scholarship.

MATERIALS.

The Sulphonic Derivatives of Camphor.



I. The Sulphonic Acids.

The sulphonation of camphor takes a somewhat unexpected course since, containing as it does a reactive methylene group, it might be anticipated that the action of the ordinary sulphonating agents would give rise to substitution at this point. Chlorosulphonic acid and concentrated sulphuric acid produce, however, sulphonation in one of the two median methyl groups (π-substitution; Kipping and Pope, J.C.S., 1893, 548; 1895, 345; 1896, 913; 1897, 7), and though for a stereochemical discussion it would be desirable to specify which of these stereochemically distinct groups is the actual seat of substitution, no information on the point is available nor, indeed, is there any evidence to show that two series of π-substitution products exist. Further, since the direct sulphonation of camphor by these agencies results in racemisation of the product, camphor is replaced in practice by α-chloro- or α-bromocamphor, which can be sulphonated without racemisation. Reduction of the halogenated products so formed yields the active camphor π sulphonic acid which is isolated as the ammonium salt.

In 1898 Reychler (Bull. Soc. Chim., 1898, 19, 120), by treating camphor with a mixture of acetic anhydride and concentrated sulphuric acid, obtained a crystalline sulphonic acid isomeric with the above, and described by him as the *α* derivative. This, however, was shown by Armstrong and Lowry (J.C.S., 1902, T., 1449) to be incorrect, and at present the balance of evidence is in accord with the view that the sulphonic group has in this case entered the molecule at position 10, though position 6 is also a possibility. (Wedekind, Schenk und Stüsser, Ber., 1923, 56, 633-649; Burgess and Lowry, J.C.S., 1925, 127, 271.

Sulphonation in the *α* position has been effected in two ways, (1) by the action of Reychler's sulphonating mixture on β-bromo camphor, the bromine atom appearing to block the 10 position against substitution (Burgess and Lowry, J.C.S., 1925, 271), and (2) by the direct action of methyl chlorosulphonate on camphor (Frèrejacque, C.r., 1926, 183, 607).

This last observation gives rise to an interesting speculation, viz., - is the abnormal course pursued in camphor sulphonation processes due to the presence of a strongly acidic hydroxyl grouping in the reacting system? Added interest is lent to this question in that, as will be shown later, it is precisely in presence of hydroxy compounds of this nature that the optical rotation of camphor is most strongly affected. The action of sulphuric acid and chlorosulphonic acid on camphor would obviously agree with this view, whilst, from the results obtained by Peski (Rec. trav. Chim., 1921, 40, 103), who prepared salts of acetyl sulphuric acid from mixtures of acetic anhydride and sulphuric acid and showed that such a mixture could sulphonate benzene, it is equally obvious that acetyl sulphuric acid - again containing the acidic -OH grouping - is the active agent in the formation of Reychler's acid.

To test this hypothesis, the action of bromine on camphor in acid solution was examined in the hope of isolating π- or β- substituted products. The reaction in sulphuric acid proceeded only very slowly, if at all, at ordinary temperatures, and since application of heat produces disruption of the camphor molecule, this attempt had to be abandoned. In glacial phosphoric acid at room temperature no reaction could be observed, whilst on heating, the reacting mixture separated into two layers, the upper of which consisted of bromine and camphor which had thus been removed from the acidic influence and was brominated in the ordinary way, via the additive compound with bromine, to α brominated products. Bromination in warm acetic acid - a weak acid of the type in question - and in mixtures of acetic and sulphuric acids at 80 - 90°C. gave products from which only α-substituted derivatives could be isolated.

It will be noticed, however, that in these experiments, the acidic hydroxyl group is not contained in the actual substituting agent, so that the negative results obtained only eliminate the exertion of a directive influence by the acids involved when these play a purely solvent rôle. The point is further illustrated by the fact that the halogenation of camphor, when carried out by means of hypochlorous or hypobromous acid, leads to halogenated camphors chemically distinct from the α-substituted derivatives (Wheeler, Ann., 1868, 146, 73: Cazeneuve, Bull. Soc. Chim., [3], 2, 713). Unfortunately, when, as a final test of the hypothesis, camphor was treated with a mixture of acetic anhydride and water-free nitric acid [forming diacetyl orthonitric acid, $(CH_3CO)_2N(OH)_3$ - Ber., 1902, 2526], no action occurred at ordinary temperatures, whilst tetranitromethane - the usual product from heating the nitrating mixture - was formed with great violence when the temperature was raised.

So far, therefore, it has not been found possible to advance any new positive evidence in support of the hypothesis suggested by examination of the literature but the facts of the case are, themselves, sufficiently striking to deserve notice.

For the purpose of examining their optical activity, the camphor sulphonic acids or their salts were prepared by the methods described by Reychler (loc. cit.), Armstrong and Lowry (loc. cit.) and by Kipping and Pope (loc. cit.). Unsuccessful attempts were also made to prepare halogenated camphor-10-sulphonic derivatives by direct chlorination or bromination of the parent acid, the sulphonyl chloride and the methyl ester. The presence of the sulphonic group in the molecule would therefore appear to retard halogenation, though, as Lapworth has shown (J.C.S., 1899, 558), a second halogen atom may be introduced into ammonium-α-bromocamphor-π-sulphonate prepared by sulphonating α-bromocamphor (Kipping and Pope, loc. cit.).

II. The Sulphonyl Chlorides and Amides.

These were prepared by the methods contained in the references already quoted under I. Camphor-10-sulphonyl chloride, however, is obtained in better yield by the action of thionyl chloride (Smiles and Hilditch, J.C.S., 1907, 522) than by means of phosphorus pentachloride (Reychler, loc. cit.). Attempts were made to prepare α-bromocamphor-π-sulphonyl chloride by direct action of excess chlorosulphonic acid on α-bromocamphor (1) alone, (2) in chloroform solution, but in each case so much charring of the materials resulted, that the isolation of the desired product was rendered difficult and was not effected.

All attempts to purify camphor-10-sulphonamide produced, in part, formation of the sulphonanhydramide through elimination of water from the oxygen of the keto group and the two hydrogen atoms attached to nitrogen (Cf. Graham, J.C.S., 1912, 246), so that it was decided to omit this sulphonamide from the list of compounds studied.

III. The Sulphonic Esters.

The esterification of sulphonic acids has been the subject of a number of isolated papers dispersed throughout the literature of the past thirty years. Attention has been focussed almost entirely on the sulphonic derivatives of aromatic compounds, and it is of interest, therefore, to trace the parallelism which exists between aromatic derivatives on the one hand and the aliphatic or hydro-aromatic sulphonic acids of the camphor series on the other. This parallelism was revealed incidentally rather than intentionally in pursuing the present research, and emerged from the difficulties experienced in obtaining good yields of pure products. Moreover, its existence could scarcely have been predicted with safety, nor is it indeed complete, for the conditions of stability and ease of formation of simple sulphonic esters appear to vary considerably from case to case.

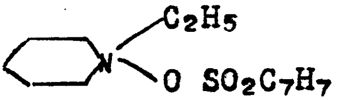
The production and properties of aromatic sulphonic esters have been studied by Ferns and Lapworth (J.C.S., 1912, 273), who conclude that no general method of formation is available. Chief amongst the factors militating against the isolation of the simpler esters at least, is their alkylating tendencies. Thus it is found that, of the following reactions:-

1) $CH_3.C_6H_4.SO_2Cl + NaOCH_2.C_6H_5 \longrightarrow CH_3.C_6H_4SO_2OCH_2.C_6H_5 + NaCl$

2) $CH_3.C_6H_4.SO_2.OCH_2.C_6H_5 + NaOCH_2.C_6H_5 \longrightarrow CH_3.C_6H_4SO_2.ONa + (C_6H_5CH_2)_2O$

(2) is so vigorous in this particular case, that only dibenzyl ether is produced. In contrast, the method gives good results with benzene sulphonyl chloride and sodium menthylate, and with toluene-p-sulphonyl chloride and sodium bornylate, where presumably the alkylating tendency is absent.

The alkylating properties of the esters further prevent the use of pyridine (or tertiary bases) as condensing agent between the sulphonyl chloride and the alcohol. Thus ethyl-p-toluene sulphonate as produced forms a quaternary ammonium salt with pyridine, from which the ester cannot be recovered:-



In addition to the alkylating factor, there are several references in the literature to the ease with which, in some cases, hydrolysis of sulphonyl chlorides proceeds when heated in excess of alcohol (sulphonic acids being produced). Thus Krafft and Roos (Ber., 1892, <u>25</u>, 2257), to surmount this difficulty, in the case of p-halogenated benzene and certain naphthalene sulphonyl chlorides, allowed the reaction to proceed for several days at room temperature. The ready hydrolysis of di iodo benzene sulphonyl chlorides is also noted by Boyle (J.C.S., 1909, 1683; 1910, 211). On the other hand, Armstrong (Proc., 1891, <u>71</u>, 184) prepared several dibromnaphthalene sulphonic esters by boiling the sulphonyl chlorides in excess alcohol.

Schotten-Baumann Application.

In more recent years the application of a modified Schotten-Baumann reaction to the preparation of sulphonic esters has met with good success, and though this application has been attributed to Foldi (Ber., 1920, 53, 1836), it should be noted that it had been previously applied with success by Boyle (J.C.S., 1909, 95, 1683). Foldi acted on molecular proportions of benzene and substituted benzene sulphonyl chlorides with 20·30% aqueous NaOH at 0°C.

About the same time Izmailski and Razenov (J. Russ. Phys. Chem. Soc., 1920, 52, 359; J.C.S., 1923, Ai, 770) obtained good yields of toluene sulphonic esters by a similar method, using 25% NaOH.

The following year Hahn and Walter (Ber., 1921, 54, 1531) prepared these toluene sulphonic esters in good yield by adding powdered KOH at low temperatures ($<10^\circ C$) to equivalents of p-toluene sulphonyl chloride and the alcohol dissolved in ether.

This last method was adopted and extended to other toluene sulphonic esters by Gilman and Beaber (J. Amer. Chem. Soc., 1925, 47, 518).

Turning now to the question of the camphor sulphonic acids, consultation of the literature shows that while references to the more complex esters of these acids are numerous, the only representatives of the simpler cases are the methyl and ethyl esters of camphor-10-sulphonic acid. These were prepared by Edminson and Hilditch (J.C.S., 1910, 223) by heating the sulphonyl chloride with the sodium alkyl oxide dissolved in the corresponding alcohol. Attempts to repeat this procedure were at first unsuccessful but finally, using concentrated solutions of the reagents and with only a few minutes' heating before pouring the reaction mixture into water, the products were obtained in poor yields (methyl 40%; ethyl 25·30%). The poorness of the yield was traced to the formation of ethers which were produced in considerable quantities during the course of the reaction and which presumably result from alkylation processes analogous to those described by Ferns and Lapworth (loc. cit.).

$$C_{10}H_{15}O\ SO_2Cl + NaOCH_3 \longrightarrow C_{10}H_{15}O\ SO_2OCH_3 + NaCl$$

$$C_{10}H_{15}O\ SO_2OCH_3 + NaOCH_3 \longrightarrow C_{10}H_{15}O\ SO_2ONa + CH_3O\ CH_3$$

The yields were further reduced and the production of ethers increased by extending the period of heating.

With a view to finding a more satisfactory method of esterification the following methods, besides ultimately the Schotten-Baumann process, were considered:-

(1) Heating equivalents of <u>acid chloride and alcohol</u>

(a) together (excess alcohol being used),

(b) in benzene,

(c) in presence of pyridine.

(2) The silver salt method.

(3) (a) Heating the acid in excess alcohol containing 3% hydrochloric acid gas in solution.

(b) Heating the acid in excess alcohol in the continuous esterification apparatus of Frankland and Aston (J.C.S., 1901, 79, 517).

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(1) (a) and (b) resulted in partial or complete hydrolysis of the acid chloride despite precautions having been taken to exclude moisture - the acid itself was obtained. Small yields of ester were in a few cases isolated but these were contaminated by impurities resulting from the thermal decomposition of the sulphonyl chloride and also from the action of the hydrochloric acid liberated, on the sulphonic acid itself. In all cases yields were very poor.

(1) (c) was not a practicable method since any ester formed yields an addition compound with pyridine. This was shown in the following way:-

Equivalents of methyl camphor-10-sulphonate and pyridine were mixed at room temperature, when the ester dissolved with development of heat and the appearance of a yellow-green colour in the solution. Gradually this colour faded, and on leaving the mixture to cool in a stoppered flask, a white crystalline solid was deposited. This, on exposure to air, immediately liquified and was consequently not examined further.

(2) The silver salt method yielded the esters, but was not an economic process, nor were good yields obtained.

(3) (a) was unsatisfactory both in the quantity and purity of the product, a small amount of a dark coloured low melting solid being the only product isolated.

(3) (b). This method gave very small yields of the esters — 100 gm. camphor-10-sulphonic acid gave 6 gm. crude ethyl ester — the yields were slightly increased by the addition of a few ccs. of concentrated sulphuric acid.

It is noteworthy that considerable quantities of ether were produced in the process, this taking place at temperatures considerably lower than those required for the decomposition of ethyl sulphuric acid (130 - 140°C). Thus ether was formed at 100 - 110°C. This production of ether is in accordance with the strong alkylating properties of the esters, by decomposition of which the ether most probably results, e.g.,

$$C_{10}H_{15}O\ SO_2OC_2H_5 + HOC_2H_5 \longrightarrow C_{10}H_{15}O\ SO_3H + C_2H_5O\ C_2H_5$$

The results of this experiment, taken in conjunction with those from Exps. (1)(a) and (b), suggest that the "hydrolysis of the sulphonyl chlorides" referred to by Krafft and Roos, Boyle and others (loc. cit.) is probably also due to an alkylation process such as that depicted in the above equation — the production of relatively small quantities of ethers in a bulk of low boiling solvent might readily escape detection. The actual isolation of poor yields of the esters in such cases serves to confirm this view.

The Application of the Schotten-Baumann Reaction.

The optimum conditions for the application of this reaction were first determined for the preparation of methyl camphor-10-sulphonate and thereafter applied in the preparation of other esters.

Preliminary experiments showed that the production or application of heat were detrimental to the yields of the esters, so in all cases the experiments mentioned here were carried out in a freezing mixture, with vigorous agitation of the reagents so as to prevent the development of local heating. For this latter purpose also the solids employed were all in finely divided form.

The following table summarises the results obtained by adding varying concentrations of NaOH (aqueous) to the sulphonyl chloride dissolved (or suspended) in methyl alcohol:-

Acid Chloride	Methyl Alcohol.	NaOH.	Yield (crude)		M.Pt. crude product.
10 gm.	15 cc.	27cc.(10%)	65%	Theor.	50 - 56°C.
10 gm.	15 cc.	12cc.(25%)	90%	"	48 - 52°C.
10 gm.	15 cc.	4cc.(50%)	82%	"	54 - 58°C.
15 gm.	20 cc.	7cc.(50%)	73%	"	56 - 58°C.
5 gm.	7 cc.	1 gm.solid	85%	"	58 - 59°C.
30 gm.	45 cc.	7 gm.solid	90%	"	59 - 60°C.

The M.Pt. of the pure product is 61°C.

The results show that the best conditions for a high and pure yield are obtained using solid NaOH. It was further shown that there was no necessity to have sufficient alcohol present to bring the sulphonyl chloride into complete solution - this indeed lowered the yield — a suspension of the acid chloride in the alcohol is satisfactory.

The quantity of NaOH required for completion of the reaction was found in practice to be somewhat less than two molecular proportions, and since the actual use of two molecular proportions had no harmful effects, this quantity was generally employed.

The general procedure thus evolved is as follows:-

The sulphonyl chloride was dissolved in the hot alcohol (15 cc. per 10 gm. acid chloride) corresponding to the ester required. The solution was quickly cooled, thereby depositing the sulphonyl chloride in finely divided form. The beaker containing the suspension was surrounded by a freezing mixture and vigorously stirred while two equivalents of powdered NaOH were slowly added in small quantities at a time — the temperature being maintained well below 10° C. When the addition was complete the mixture was allowed to stand for half an hour, more alcohol being added if necessary to preserve fluidity, and finally treated with an excess of water. The ester was thus obtained as an oil which immediately solidified on stirring and was collected and washed free from sodium salts at the filter pump.

The quantity and quality of the products resulting from the application of this procedure have been, in general, highly satisfactory, the methyl esters being obtained in yields varying from 80 - 90% theoretical, the ethyl esters from 70 - 85% theoretical.

As will be seen, therefore, from the behaviour of the camphor sulphonic esters described above, the preparation of these esters is subject to the same exigencies as have been found to exist in the formation of aromatic representatives of the class. The success which has attended the application of the Schotten-Baumann procedure in the aromatic series and now also in the aliphatic series, suggests that this may eventually provide the generally efficient method which Ferns and Lapworth believed to be lacking.

Experimental.

Methyl camphor-10-sulphonate was prepared from the sulphonyl chloride (10 gm.), methyl alcohol (15 cc.) and sodium hydroxide (3 gm.) in the manner already described.

The yield of nearly pure ester was 90% theoretical. M.P. 61°C unaffected by admixture with a specimen prepared by Edminson and Hilditch's procedure (loc. cit.).

Ethyl camphor-10-sulphonate - from the sulphonyl chloride (20 gm.), absolute alcohol (30 cc.), and sodium hydroxide (6•5 gm.).

The product was purified by crystallisation from aqueous methylated spirit and had M.P. 46°C unaffected by admixture with an authentic specimen.

Yield 70% theory.

Methyl α chlorocamphor-10-sulphonate - from α-chlorocamphor-10-sulphonyl chloride (10 gm.) (Armstrong and Lowry, J.C.S., 1902, 1451), methyl alcohol (20 cc.), and sodium hydroxide (3 gm.). The product was purified by crystallisation from methylated spirit and then had M.P. 61•5°C. Yield over 90% theoretical.

Cl calculated . . . 12•66%

Cl found . . . . . 12•87%.

Ethyl α-chlorocamphor-10-sulphonate - from the sulphonyl chloride (10 gm.), absolute alcohol (25 cc.) and sodium hydroxide (3 gm.). Recrystallised from spirit, the product had M.P. 56°C. Yield 85 % theory.

Cl calculated . . . 12•06%

Cl found . . . . . 11•95%

Methyl α-bromocamphor-10-sulphonate - from α-bromocamphor-10-sulphonyl chloride (10 gm.) (ibid.), methyl alcohol (20 cc.) and sodium hydroxide (2 gm.). Recrystallised from methyl alcohol the product melted at 64°C. Yield 80 % theory.

Br calculated . . . . 24·59%
Br found . . . . 24·78%

Ethyl α-bromocamphor-10-sulphonate - from the sulphonyl chloride (10 gm.), absolute alcohol (15 cc.) and sodium hydroxide (2 gm.). Recrystallised from spirit the product melted at 61°C. Yield 75 % theory.

Br calculated . . . . 23·57%
Br found . . . . 23·64%

Methyl camphor-π-sulphonate - from camphor-π-sulphonyl chloride (5·5 gm.) (Kipping and Pope, 1895, 345), methyl alcohol (12 cc.) and sodium hydroxide (1·7 gm.). Recrystallised from methyl alcohol the product melted at 109°C. Yield 80% theory.

S calculated . . . . 12·9%
S found . . . . 12·74%

Methyl α-chlorocamphor-π-sulphonate - from α-chlorocamphor-π-sulphonyl chloride (5·5 gm. ibid), methyl alcohol (15 cc.) and sodium hydroxide (1·5 gm.). Recrystallised from methyl alcohol the product melted at 114°C. Yield 80% theory.

Cl calculated . . . . 12·66%
Cl found . . . . 12·94%

Methyl α-bromocamphor-π-sulphonate — from α-bromocamphor-π-sulphonyl chloride (10 gm.), methyl alcohol (25 cc.) and sodium hydroxide (2·5 gm.). Recrystallised from spirit the product melted at 111°C. Yield 85% theory.

Br calculated . . . . 24·6%

Br found . . . . . . 24·7%.

ROTATION MEASUREMENTS.

Camphor.

While examining the chemical action of concentrated sulphuric acid on camphor it was noted that the camphor dissolved in the acid to give laevorotatory solutions. The solutions were all more or less coloured, depending on the concentration of the camphor, but in view of the fact that the latter compound is persistently dextrorotatory in organic and inorganic solvents alike, the observation was sufficiently arresting to merit closer investigation.

It was necessary first to decide whether the negative rotation was due to chemical action or to solvent influence on the part of the sulphuric acid. Experiment showed that the solutions attained their maximum rotation almost immediately and, though in the course of several days their colour deepened perceptibly, the value suffered a decrease of less than 2% and was constant throughout the time taken to make all the observations recorded in the sequel. Further, the camphor was recovered almost quantitatively by precipitation with water whilst the filtrate from this operation had a small rotation of the same magnitude as that of a concentrated solution of camphor in water containing the calculated proportion of sulphuric acid.

These facts indicate that the sulphuric acid plays a rôle at least indistinguishable from an ordinarily solvent one, though in view of the readiness with which, in common with many other ketones, camphor forms additive compounds with nitric acid, phosphoric acid, the halogens etc., the possible formation of a liquid additive compound is not to be excluded.

As the following table shows, the rotation of camphor is negative even in diluted sulphuric acid, though it decreases with increase in the proportion of water in the solvent and finally changes sign:-

Solvent.	Conc.	Temp. °C.	$[\alpha]_g$
Conc. H_2SO_4	2·545	17·1	-74·32
H_2SO_4/H_2O = 4/1 gm.	2·054	15·4	-23·41
H_2SO_4/H_2O = 3/1 gm.	2·045	18·8	-7·335
H_2SO_4/H_2O = 2/1 gm.	2·045	18	+4·4.

The powerful depressing influence thus exerted by sulphuric acid is made clear by comparison with the rotations displayed by camphor in other solvents:-

Solvent.	Conc.	Temp. °C.	$[\alpha]_D$	
Ethylene bromide	5·213	16	+57·37	
Alcohol	5·978	20	43·22	
Chloroform	5·236	16·5	40·49	
Benzene	2·000	20	40·0	†
Pyridine	5·209	16·5	38·21	
n Butyric acid	49·10	20	52·49	*
Propionic acid	60·92	20	50·53	*
Acetic acid	47·52	20	49·37	*
Formic acid	35·89	20	39·93	*
Formic acid	2·000	20	20·5	†

† Lucas, Ann. de Phys., 1928, 447.

* Landolt, "Drehungsvermögen", p.176.

To facilitate comparison with Landolt's values the rotations are given for $[\alpha]_D$, but when allowance is made for the fact that increase in the concentration of camphor in a solvent which diminishes its rotation (estimated as $[\alpha]_D = 55{\cdot}4°$, Landolt, loc. cit.) produces a corresponding increase in the rotation of the solution, it is at once evident from the table that sulphuric acid in depressing the rotation of camphor merely continues and intensifies an effect which is already observable with weak organic acids. Moreover, the magnitude of the depression appears to be related to the strength of the acid.

Of the two other common mineral acids hydrochloric acid, presumably on account of its large water content, does not yield laevorotatory solutions, whilst on addition of camphor to nitric acid, two layers are formed, the upper of which contains camphor and nitric acid in approximately molecular proportions and is weakly laevorotatory, but obviously in this case the effect of aqueous dilution cannot be followed.

With regard to the influence of temperature change on solutions of camphor in sulphuric acid, the chemical action which occurs above 40°C imposed upon this line of investigation very narrow limits, but sufficient evidence was obtained to show that with increase in temperature the rotation diminishes in numerical value, thus conforming to the general observation that camphor solutions increase in positive rotation with temperature increase.

Temp.	Density	$[\alpha]_{r_2}$	$[\alpha]_y$	$[\alpha]_g$
0	1·817	-54·16	-65·51	-75·56
17·1	1·799	-52·38	-64·18	-74·32
32·9	1·782	-51·90	-62·82	-73·84

$p = 2·829$

As was subsequently discovered, the strong depressing solvent action of sulphuric acid on camphor has also been noted by Lucas (Ann. de Phys., 1928, 381) who records the value $[\alpha]_g = -73·1$ for $c = 2·00$. By preliminary treatment of the camphor to remove traces of borneol this author has succeeded in obtaining perfectly clear solutions, but has confined himself to examining the dispersion of a single solution in the concentrated acid. He has also noted that camphor in phosphoric acid solution exhibits a feebly negative rotational value and that for this solution the dispersion curve crosses the zero axis of rotation. Now crossing of the zero axis is one of the criteria for anomalous dispersion, so that could Lucas' curve be sufficiently extended, actual realisation of the full anomalousness might be expected. This, however, involves observations taken in the infra red and is not therefore a generally practicable demonstration of the phenomenon. On the other hand, by utilising the fact recorded in the first table (see p.21) — viz. that, by suitable choice of the proportion of water in the sulphuric acid solvent, any negative rotational region may be realised up to the limit imposed by the concentrated acid —

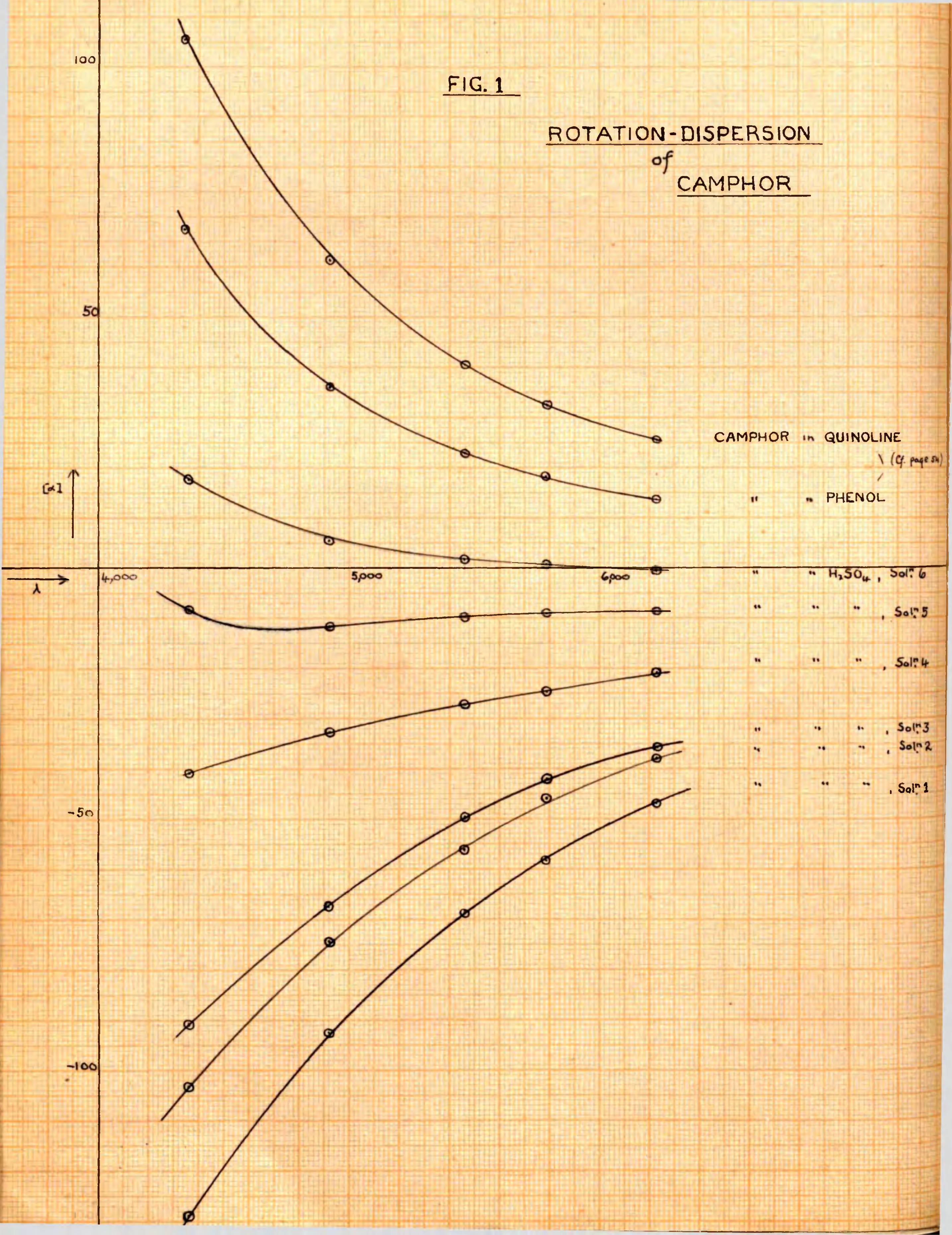


FIG. 1

ROTATION-DISPERSION of CAMPHOR

the complete anomalous region may be brought within the range of the visible spectrum and its gradual development studied.

	Solvent			Temp.					
	H_2SO_4	H_2O	Conc.	°C.	$[\alpha]_{r_2}$	$[\alpha]_y$	$[\alpha]_g$	$[\alpha]_b$	$[\alpha]_v$
1)	-Conc.H_2SO_4 -		2·156	21·5	-46·84	-58·43	-68·64	-92·32	-128·9
2)	20·49 gm	2·50 gm	2·132	24	-37·99	-45·5	-56·28	-74·11	-103·1
3)	12·67 "	2·07 "	2·05	20	-35·6	-41·9	-49·75	-67·32	-90·72
4)	10·19 "	2·5 "	2·036	19	-20·63	-24·56	-27·02	-32·41	-40·77
5)	10·72 "	3·75 "	2·116	17	- 8·507	-8·98	-9·913	-11·81	-8·034
6)	10·03 "	5·03 "	2·02	16	- 0·495	+0·99	+1·98	+5·44	+17·82

The camphor employed was purified by Lucas'[1] procedure, viz., a few drops of concentrated nitric acid were added to a solution of camphor in concentrated sulphuric acid and, after standing for several hours, the camphor was precipitated by addition of water and sublimed. The sulphuric acid used as solvent was the higher boiling distillate from concentrated bench reagent and probably contained some dissolved sulphur trioxide — its density was $d^{20} = 1{\cdot}844$.

The data are represented in graphical form in Fig.I in which there are also included for comparison the dispersion curves for camphor in some organic solvents. Represented thus, the various dispersions are seen to unite in forming a fairly extensive family of curves passing gradually from the extreme form in concentrated sulphuric acid on the one hand, to the opposite form in organic solvents on the other. Intermediate between the two extreme types of curvature and within the negative region of rotation, the dispersion is clearly shown to be anomalous. The curves in this neighbourhood are numbered to correspond with the figures in the table and it will be seen that the dispersion curve for a 2% solution of camphor in 75% sulphuric acid approximately, exhibits both a minimum point and a point of inflexion; 80% and higher concentrations of sulphuric acid yield curves containing no visible anomalousness over the range examined, whilst concentrations between 50 - 70% result in dispersion curves which cross the zero axis and are comparable with Lucas[1] curve for camphor in phosphoric acid.

α Chloro- and α bromo-camphor.

These two compounds may be treated here simultaneously since investigation of the optical rotation of each yielded results of a similar character. For rotation purposes α chlorocamphor was crystallised four times from benzene, α bromocamphor twice from toluene followed by recrystallisation from benzene.

A study of the influences of certain selected solvents upon the rotations of these compounds yielded the following results:-

Solvent	α Chlorocamphor			α Bromocamphor,		
	Temp. °C	conc.	$[\alpha]_g$	Temp. °C	conc.	$[\alpha]_g$
H_2SO_4 conc.	20	2·060	+65·52	17	2·02	+113·9
Benzene	19·5	2·000	87·5	17·5	14·11	152·8
Pyridine		———		17	5·138	162·6
Alcohol	19·5	2·008	121·5	16	10·09	169·3
Tetrachlorethane	20	2·062	129·5	17	5·062	180·7
Ethylene bromide	20	2·036	148·8	17	5·050	192·9

It will be seen, in the first place, that the rotation values generally are higher than those for camphor – a result which may be attributed to the introduction of a new asymmetric carbon atom (the corresponding α' chloro- and α' bromocamphors are known). Moreover, when measured under similar conditions, the values for the bromo derivative exceed those for the chloro derivative. Sulphuric acid again exerts the most powerful depressing solvent influence although the range in each case is smaller than that obtained with camphor. Among the organic solvents, in which a definite solvent order is observable, considerable change in rotation is encountered and for purposes of comparison with compounds to be discussed later, it may be noted that the rotation is highest in ethylene bromide and lowest in benzene.

In these two solvents the effect of temperature was examined for each of the substances in order that the influence of this factor might be ascertained at the most extreme rational limits available. Increase of temperature in all four solutions produced increase in the values of the specific rotation but it was noticeable (cf. T-R tables) that in the benzene solutions the rate of increase was markedly greater than in the ethylene bromide solutions – an observation in harmony with what may, perhaps, be regarded as a fairly general principle, viz., when two solutions of a given active substance increase in rotation with rise of temperature, the rate of increase will be greater in the solution of lower initial rotation. An indication of the general appearance of the T-R curves for these four solutions may be obtained by reference to the composite diagram, Fig. 3, in which the values of $[\alpha]_g$ have been plotted against temperature. It will be seen that in each case an approximately linear relationship is obtained.

$\alpha\alpha'$ Dibromocamphor.

For comparison with the mono α-halogenated camphors, this representative of the di-α-halogenated derivatives was prepared and studied. After five crystallisations from methyl alcohol (conducted in the dark to prevent discoloration) the following rotation values were obtained:-

Solvent.	Conc.	Temp. °C.	$[\alpha]_g$
Sulphuric acid	1·034	14	45·45
Alcohol	2·076	18·5	51·53
Benzene	2·024	18·5	53·35
Tetrachlorethane	2·024	19	59·29
Ethylene bromide	2·002	19	63·45

Lowry (J.C.S., 1898, 587) has already examined the effects of a number of solvents upon the rotation of this compound and has found in each practically constant rotation. As the above table shows, however, at low concentration, where solvent influence is at its greatest, definite changes are observable and further the solvent order is essentially the same as that already found for related substances. The relatively high rotation displayed in concentrated sulphuric acid is at once striking and disappointing and suggests that the potency of this solvent is dependent upon the reactivity of the carbonyl group which is known to be lowered by the presence of an <u>α</u>-halogen — e.g., the keto group in α halogenated camphor does not condense with hydroxylamine and is less vulnerable to oxidative attack, etc.

Reference to the T-R data (p.42) which were obtained for this compound in alcohol solution shows that temperature also has only a slight effect on the rotation — the values obtained appear to lie in the immediate neighbourhood of a maximum point (Fig. 3).

<u>Camphor-10-sulphonic acid (Reychler's Acid).</u>

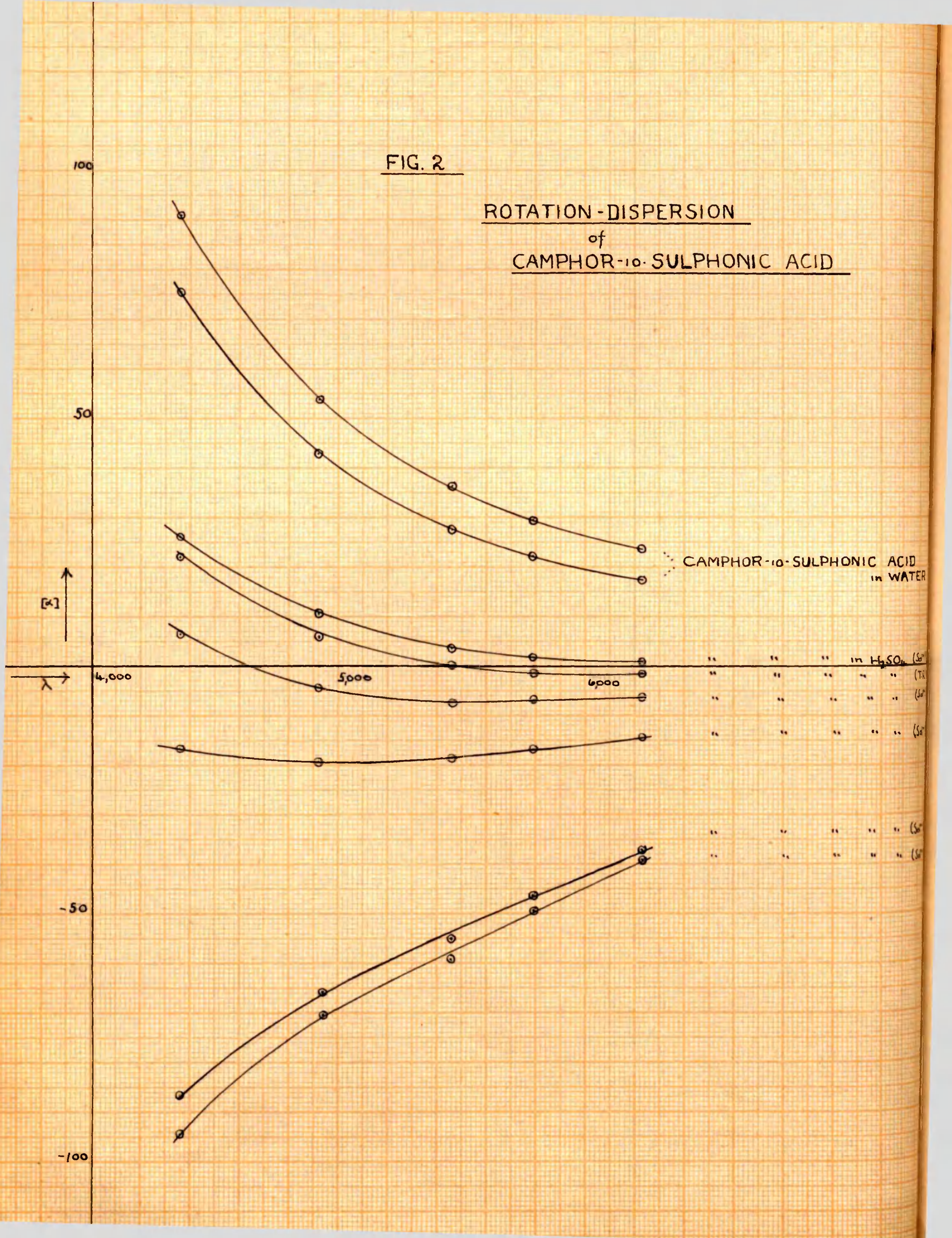
The acid was purified by two crystallisations from glacial acetic acid followed by three further crystallisations from anhydrous ethyl acetate, and before each polarimetric examination the product was heated in an air oven for one hour at 105 - 110°C to remove traces of moisture.

The strong polar character of Reychler's acid resulting in its sparing solubility in organic solvents prevented any attempt to study the effect of these solvents upon its rotatory power. As in the case of camphor, however, sulphuric acid exerts a very powerful depressing influence on the rotation which is again proportional to the aqueous concentration of the solvent acid and is strongly negative in the concentrated solvent. Moreover, unlike camphor, the compound is very soluble in water in which it exhibits strong positive rotations, so that within these fairly wide limits it is possible to realise any desired rotational region. It is, perhaps, not unworthy of note that since acids depress the rotation in the camphor series generally, camphor-10-sulphonic acid may suffer auto rotational depression in solution. Certainly it is the case that the rotations of its methyl and ethyl esters though almost identical with each other (see later) are definitely higher than that of the parent acid, but the question is doubtless complicated by other factors.

In aqueous solution increase in temperature produced increase in rotation for all colours of light examined. The data will be found in the T-R tables inserted at the end of this thesis and when represented in graphical form yield a slightly divergent set of practically straight lines each corresponding to one wave length of light. In sulphuric acid solution the range of investigation was again limited — decomposition begins above 30°C — but as will be seen from the following

FIG. 2

ROTATION-DISPERSION
of
CAMPHOR-10-SULPHONIC ACID



results obtained in aqueous sulphuric acid, the rotation here also increases in a positive sense with rise in temperature:-

Temp.	Density	$[\alpha]_{r_2}$	$[\alpha]_y$	$[\alpha]_g$	$[\alpha]_b$	$[\alpha]_v$
0°C	1·552	-1·771	-1·181	+0·2952	+5·903	+22·14
18°C	1·537	+0·2982	+1·49	+2·683	+8·050	+25·34

p = 3·637.

The solvent effects of sulphuric and diluted sulphuric acids together with the dispersion data for the various solutions are summarised in the next table — no preliminary purification of the active compound being necessary (Cf. camphor) to give colourless solutions:-

	Solvent			Temp.					
	H_2SO_4	H_2O	Conc.	°C.	$[\alpha]_{r_2}$	$[\alpha]_y$	$[\alpha]_g$	$[\alpha]_b$	$[\alpha]_v$
(1)	conc. H_2SO_4*		2·052	19	-38·97	-49·2	-59·44	-70·17	-94·52
(2)	conc. H_2SO_4		2·052	18·8	-37·06	-46·29	-55·07	-65·79	-86·74
(3)	19·80 gm	4·82 gm	2·075	19·6	-14·45	-16·87	-18·79	-19·28	-16·39
(4)	44·24 "	15·09 "	2·054	18·7	-6·327	-6·814	-7·30	-4·38	+6·57
(5)	19·72 "	9·97 "	2·059	14·5	+0·971	+1·942	+3·4	+10·69	+26·23

* $d^{15\cdot3} = 1\cdot8429$

Experiments 1, 3, 4 and 5 were conducted with the main bulk of the higher boiling distillate from bench sulphuric acid (conc.) whilst the sample used in Exp. 2 had a still higher B.P., and contained a greater proportion of dissolved trioxide.

The dispersion data are set out in graphical form in Fig. 2, which also contains the dispersion results obtained from the examinations of temperature change already mentioned.

The family of curves so produced is very similar to that described for camphor. With decreasing wave-length, the rotation in concentrated sulphuric acid solution assumes high negative values whereas in aqueous solution the rotation rises to high positive values. In passing from the one type to the other visible anomalousness is encountered in the negative region: thus with 75% sulphuric acid as solvent, the dispersion curve crosses the zero axis, shows a minimum and possibly also a point of inflexion: a minimum point is also shown in the corresponding curve obtained in 80% sulphuric acid.

In general, therefore, it may be inferred that in the formation of Reychler's acid no very fundamental change has been wrought upon the rotation of the camphor molecule.

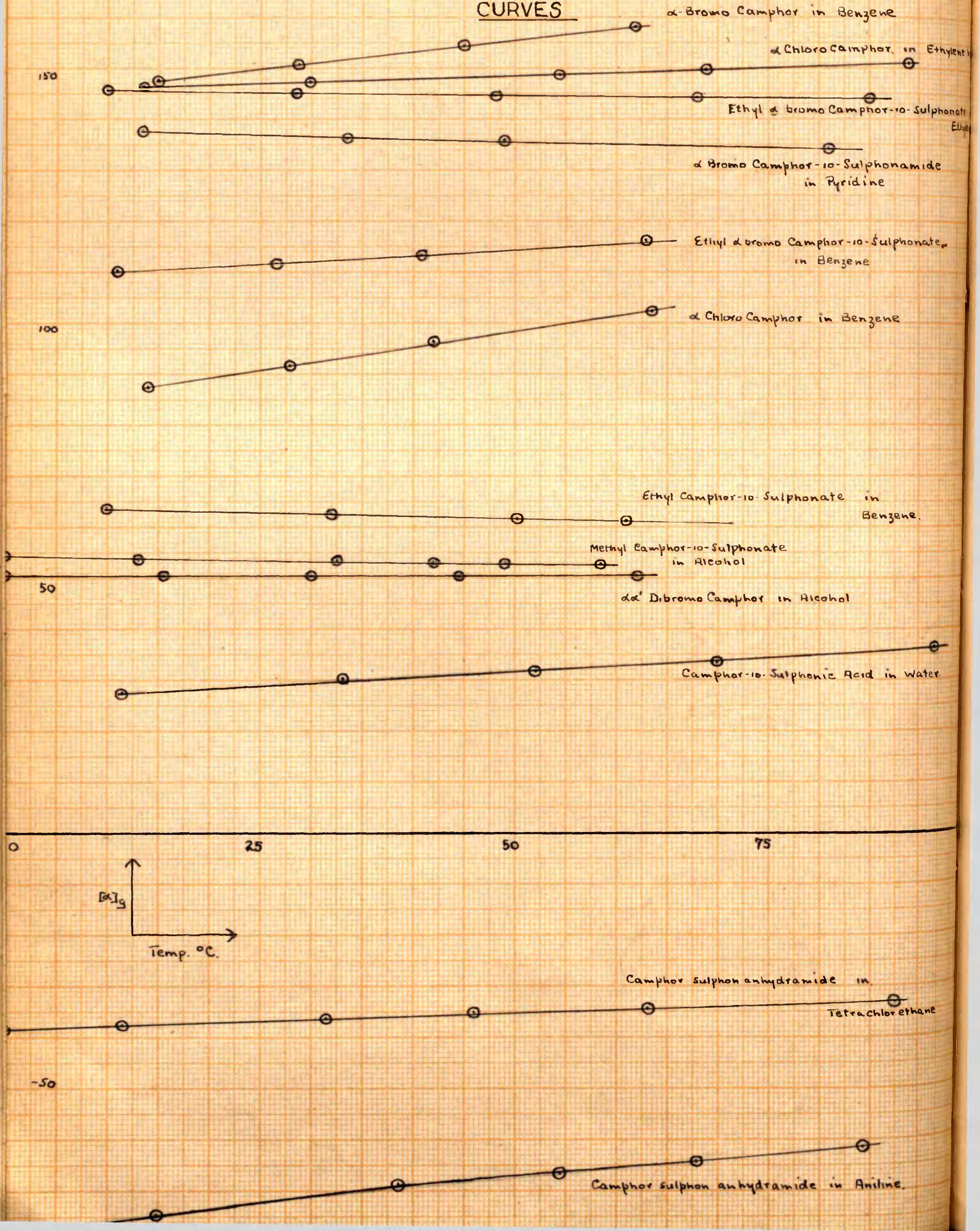
Methyl and ethyl camphor-10-sulphonates.

The two simplest esters of Reychler's acid exhibit rotatory powers which are almost identical and which, except in the case of benzene, are practically constant in the solvents examined:-

	Methyl Ester.			Ethyl Ester.		
Solvent	Temp.	Conc.	$[\alpha]_g$	Temp.	Conc.	$[\alpha]_g$
Alcohol	16·5	5·021	54·18	15·5	5·00	53·00
Chloroform	17	4·928	56·2	16·5	1·124	53·39
Ethylene bromide	16	5·157	56·23	17	1·03	52·43
Nitrobenzene	14	5·032	59·61		—	
Benzene	17	1·030	70·87	14	1·116	70·79

FIG. 3.

VARIOUS TEMPERATURE-ROTATION CURVES

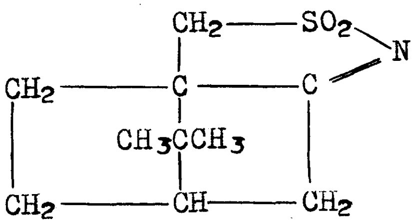


Perhaps the most interesting result is the change in solvent order found here. Whereas in the case of camphor itself, the α halogenated camphors already described and the α halogenated camphor-sulphonic derivatives still to be described benzene solutions exhibit lower rotations than ethylene bromide solutions, the present order is the reverse, the highest rotations being found in benzene. This reverse order is also encountered in the case of methyl camphor-π-sulphonate (see later) but the significance, if any, of these solvent orders cannot be estimated at present.

The influence of temperature was examined for the methyl ester in alcohol solution and for the ethyl ester in benzene solution. In each case temperature increase is accompanied by decrease in specific rotation though in the first case the decrease is very slight, indicating that the T-R curve is here at or just beyond a maximum value (Fig. 3).

Camphorsulphonanhydramide.

Although in this compound the fundamental camphor basis is retained, the molecular structure has been subjected to considerable alteration — a new ring system has been introduced involving the replacement of $>C = O$ by $>C = N —$.



For rotation purposes the material was crystallised four times from glacial acetic acid and dried in the air oven after any adhering solvent had been removed by washing with distilled water. Owing to solubility restrictions no strict comparison of solvent-rotation effects could be made with the other compounds, but as the table shows, similar solvent types act in the same way as with camphor though in the present case all rotations are negative in sign.

Solvent	Temp.	Conc.	$[\alpha]_g$
Sulphuric acid	17	1·162	-99·82
Aniline	16	4·95	-74·54
Nitrobenzene	16·5	3·99	-54·76
Chloroform	14	3·462	-39·56
Tetrachlorethane	17·5	5·116	-37·15

Thus in tetrachlorethane - comparable with ethylene bromide - the highest (positive) rotation is exhibited,whilst in sulphuric acid the lowest rotation is obtained and intermediate values are found in the nitrogen bases (Cf. pyridine, camphor). The depressing effect of sulphuric acid which persists here would indicate that if in the keto compounds the action is connected with the =C=O group, it is also operative with the group =C=N- (Cf. nicotine in H_2SO_4, Patterson and Fulton, J.C.S., 1925, 661).

The change of rotation with temperature was examined in aniline and in tetrachlorethane solutions. Increase of temperature was found to produce an increase in (positive) rotation in each case, the rate of increase being greater in the latter solution whilst in the former the T-R curve appears to become convex to the zero axis.

The Esters and Amide of α Chlorocamphor-10-sulphonic acid.

The methyl and ethyl esters of α chlorocamphor-10-sulphonic acid may conveniently be considered in conjunction with the corresponding amide. Solvent influence on the rotation of the esters is summarised in the next table, the amide being too insoluble to permit of a comparative study:-

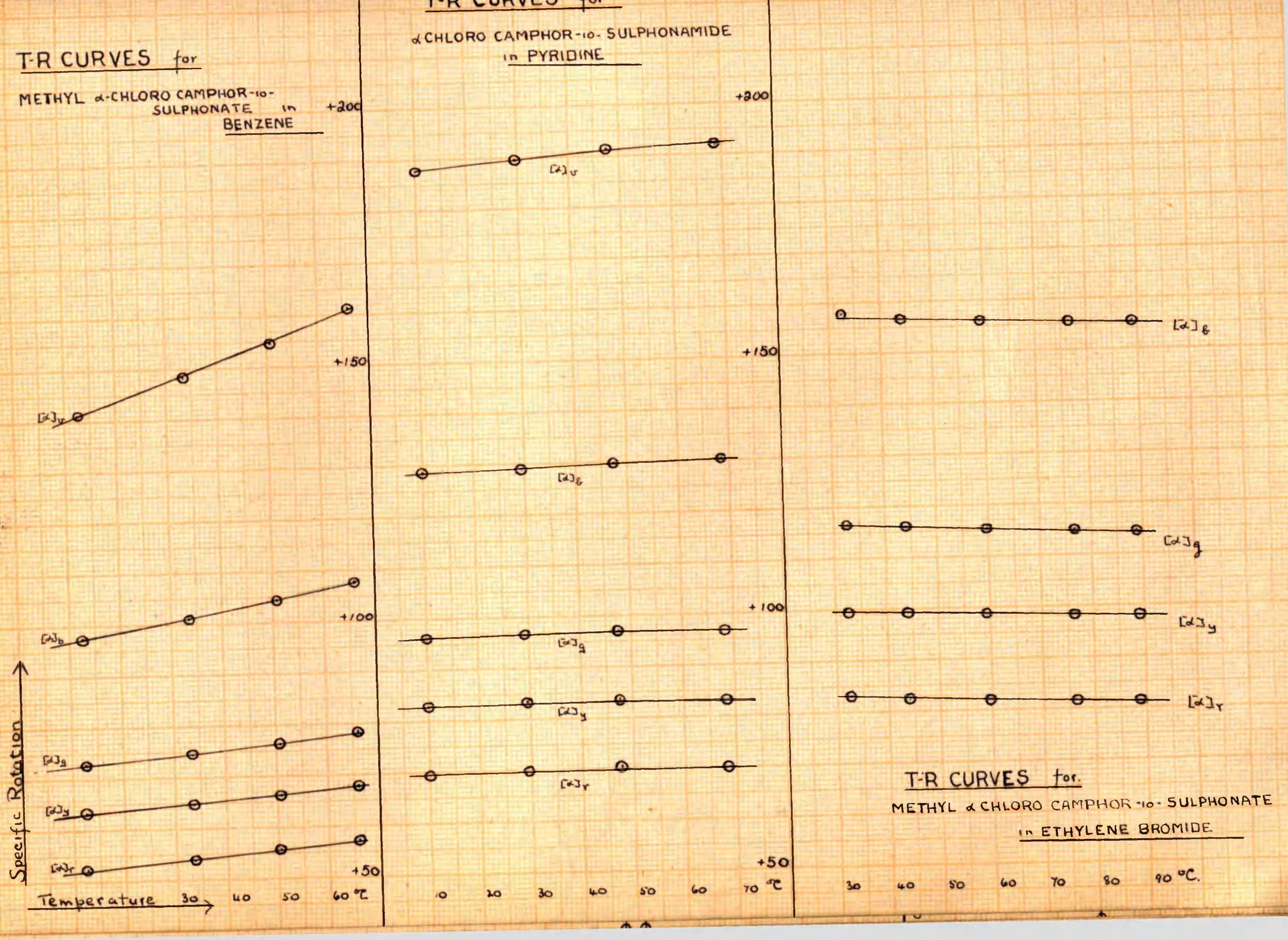
	Methyl Ester.			Ethyl Ester.		
Solvent	Temp.	Conc.	$[\alpha]_g$	Temp.	Conc.	$[\alpha]_g$
Benzene	17·5	1·152	77·27	17	1·068	77·71
Alcohol	17	1·112	109·7	18	1·008	110·2
Chloroform	17·5	1·104	113·2		—	
Ethylene bromide	17·5	1·130	120·3	17	1·084	121·7

Amide in pyridine $C = 1{\cdot}001$; $[\alpha]_g^{16 \cdot 5} = 98{\cdot}91$.

It will be seen that, even more so than in the case of the unhalogenated esters, the rotation values for the two compounds agree very closely. There is, however, a greater rotational range produced by solvent influence and the solvent order is again that found for camphor and the majority of its derivatives examined here.

The examination of temperature change gave results of some interest. Solutions of each ester at approximately the same concentration in benzene gave T-R curves which, as was expected, were practically superimposable, the specific rotation rising appreciably with increase in temperature. In ethylene bromide solution a slight but definite decrease in

FIG. 4.



T-R CURVES for METHYL α-CHLORO CAMPHOR-10-SULPHONATE in BENZENE

T-R CURVES for α CHLORO CAMPHOR-10-SULPHONAMIDE in PYRIDINE

T-R CURVES for METHYL α CHLORO CAMPHOR-10-SULPHONATE in ETHYLENE BROMIDE rotation accompanied temperature increase (only the methyl ester being examined as the other would give similar results). The amide in pyridine solution, for the higher wave lengths of light at least, showed first increase followed by a slight decrease in rotation with continuous increase in temperature. The T-R curve for the amide is evidently just at a maximum value and fits in very well between the curves for the esters in benzene and ethylene bromide respectively. Moreover the whole behaviour is very similar to that already observed among tartrates, for the rotations of the amide being higher than those of the esters in benzene, increase less rapidly (and finally decrease) with rise in temperature but the values are not so high as those of the methyl ester in ethylene bromide for which, consequently, the rotation definitely diminishes with increase in temperature. The data (see tables, p. 43) are represented graphically in Fig. 4.

The Esters and Amide of α Bromocamphor-10-sulphonic acid.

The behaviours of these compounds (methyl and ethyl esters and amide) correspond closely with those of the α chloro derivatives just described, the bromo compounds having throughout higher rotational values. The following table gives the solvent influences:-

	Methyl Ester.			Ethyl Ester.		
Solvent.	Temp.	Conc.	$[\alpha]_g$	Temp.	Conc.	$[\alpha]_g$
Benzene	16	1·01	112·9	18	1·000	113·0
Alcohol	17	1·178	140·1	17	1·000	138·0
Chloroform	16	1·044	141·4	18	1·006	140·2
Ethylene bromide		——		17	1·122	161·4

Amide in pyridine $c = 1·026$; $[\alpha]_g^{16} = 139·3$

With regard to the T-R data the specific rotation of the esters in benzene increased and in ethylene bromide decreased with rise in temperature. The amide in pyridine solution, however, did not show a maximum value but decreased in rotation continuously with increase in temperature, indicating that the maximum had already been passed.

The Camphor-π- derivatives.

Before proceeding to a description of the results obtained with the π-derivatives, it is perhaps desirable to point out that, as will be seen by reference to the structural formula for camphor (p. 3), substitution in this position introduces a new asymmetric carbon atom into the camphor system and consequently in the simple π-derivatives three centres of asymmetry exist, whilst in the α halogenated π-derivatives that number is increased to four.

Methyl camphor-π-sulphonate.

This compound is, unfortunately, the sole representative of the simple π-derivatives examined here — a consequence of the difficulty experienced in obtaining these compounds in quantities suitable for satisfactory purification.

After repeated crystallisation from methyl alcohol the following rotational values were obtained:-

Solvent	Temp.	Conc.	$[\alpha]_g$
Alcohol	18	1·046	106·1
Ethylene bromide	18	1·056	122·2
Benzene	18	1·054	125·2

The solvents fall into the same order as in the case of the esters of Reychler's acid (p. 31) though in the present case the range is slightly greater and the individual values higher. This last fact may, perhaps, be attributed to the new asymmetric centre.

In so far as temperature change is concerned the ester differs markedly from the esters of Reychler's acid in that both in alcohol and in benzene increase of temperature produces increase and not decrease in specific rotation and, in contrast to the generalisation suggested on page 27 , the rate of increase appears to be greater in benzene solution.

The Methyl Ester and Amide of α Chlorocamphor-π-sulphonic acid.

The rotation of the ester was examined in two solvents only, viz. in

(1) benzene, .. $c = 1·038$, $[\alpha]_g^{20°} = 84·78$

(2) ethylene bromide, $c = 1·024$, $[\alpha]_g^{17} = 119·1$

whilst that of the amide was examined in:-

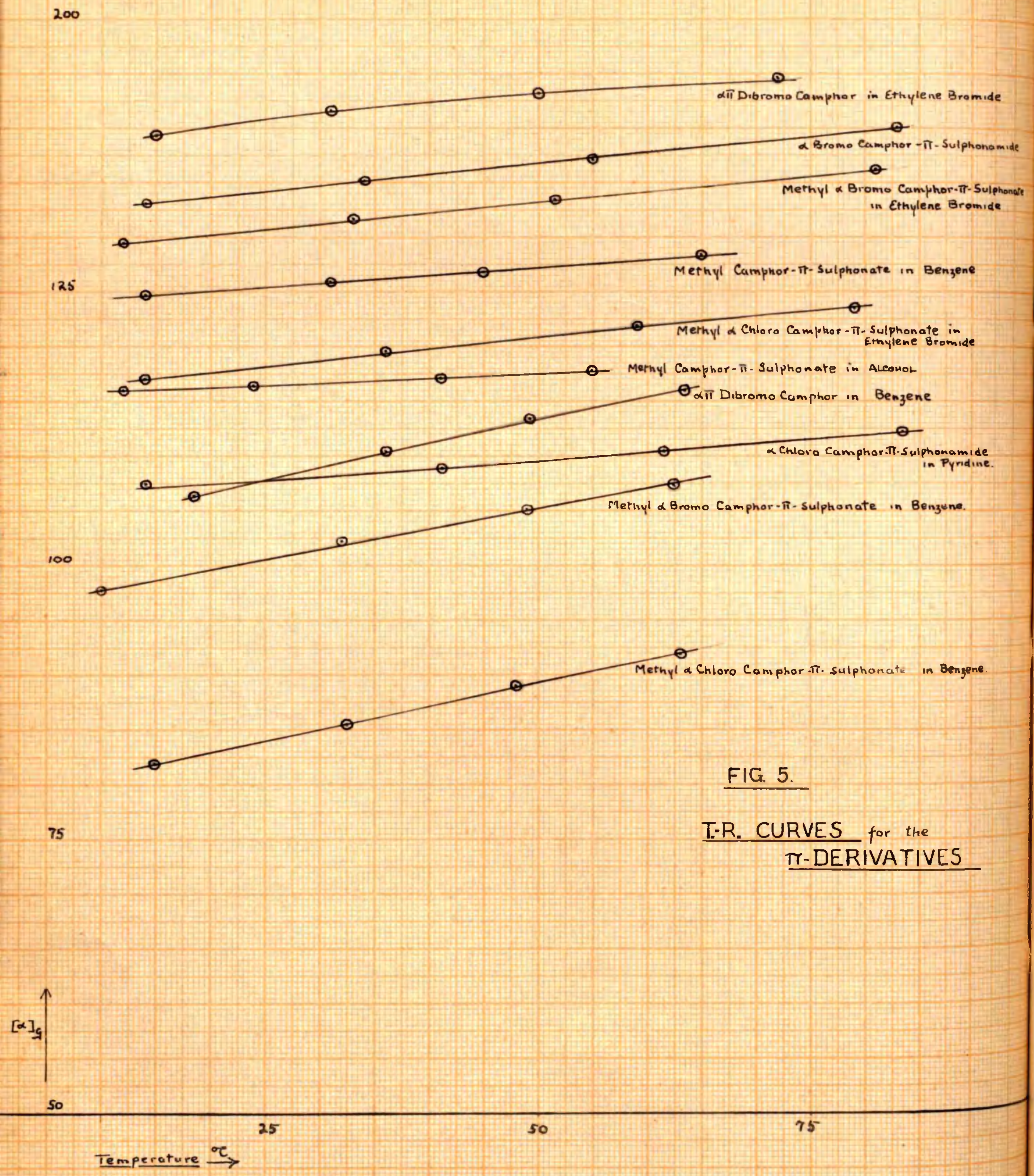


FIG. 5.

T-R. CURVES for the π-DERIVATIVES

pyridine, $c = 0{\cdot}7791$, $[\alpha]_g^{14} = 107{\cdot}5$.

Examination of temperature effect upon each of these solutions (Cf. T-R data) revealed that in contrast to the corresponding α chlorocamphor-10-sulphonyl derivatives increase in temperature produces increase in specific rotation in all cases - the rate of increase being greatest in benzene and least in ethylene bromide solution.

The Methyl Ester and Amide of α Bromocamphor-π-sulphonic acid.

The following table contains the rotation values of the methyl ester in several solvents:-

Solvent	Temp.	Conc.	$[\alpha]_g$
Benzene	16	1·026	100·9
Alcohol	17	1·028	120·6
Chloroform	17	1·044	120·7
Ethylene bromide	16	1·092	131·9

The amide in pyridine solution, $c = 1{\cdot}056$, had $[\alpha]_g^{14} = 133{\cdot}1$.

Temperature-rotation data were obtained for the ester in benzene and in ethylene bromide solutions and for the amide in pyridine solution (p. 47). The results were very similar to those for the chloro compound just described.

α π Dibromocamphor.

This compound was included in the study for comparison with the other halogenated camphors already described. As will be seen from the following table, solvents influence the rotation very markedly:-

Solvent	Temp.	Conc.	$[\alpha]_g$
Sulphuric acid	16	1·056	84·96
Benzene	16	1·032	106·6
Alcohol	16	1·028	127·5
Ethylene bromide	16	1·048	144·1

Concentrated sulphuric acid yields the solution of lowest specific rotation whilst the order among the organic solvents is the same as that found in the majority of cases already studied.

Temperature-rotation change was followed in solutions in benzene and in ethylene bromide - increase in temperature producing increase in specific rotation in both cases, the rate of increase being greatest in the former solvent. In comparison with the other compounds examined the dispersion in the present case was noticeably great, a fact which is referred to later.

Temperature-Rotation Data.

The wave lengths (in ÅU) of the light used are denoted by the following letters:-

r_2	y	g	b	v
6234	5790	5461	4916	4359

p = gm. of solute per 100 gm. solution.

Temp. °C	Density	$[\alpha]_{r_2}$	$[\alpha]_y$	$[\alpha]_g$	$[\alpha]_b$	$[\alpha]_v$
		Camphor-10-sulphonic acid in water			p = 9·709	
11·5	1·029	+17·52	22·21	27·58	42·98	75·44
33·2	1·022	19·08	24·31	30·04	45·65	79·86
52·0	1·014	20·76	26·16	31·93	48·32	83·35
70·0	1·004	22·25	27·57	33·86	51·17	86·76
92·1	0·9892	23·82	29·74	36·18	53·75	90·97

Temp. °C	Density	$[\alpha]_{r_2}$	$[\alpha]_y$	$[\alpha]_g$	$[\alpha]_b$	$[\alpha]_v$
α-Chlorocamphor in benzene p = 6·873.						
14	0·8964	+62·59	74·76	87·34	118·1	178·3
27·8	·8824	65·63	78·72	91·81	124·7	188·4
42	·8672	69·52	82·41	96·36	130·1	197·9
63·5	·8443	72·59	87·34	102·2	139·5	211·6
α-Chlorocamphor in ethylene bromide p = 3·193						
13·5	2·124	103·9	124·4	146·1	200·3	304·5
29·8	2·093	104·7	125·3	147·3	202·1	307·8
54·4	2·044	104·9	126·9	148·9	204·3	311·6
68·8	2·015	105·7	127·5	149·7	205·0	313·9
89·0	1·974	106·4	128·6	150·9	206·9	317·0
α-Bromocamphor in benzene p = 6·688						
15	0·9035	105·1	126·0	147·7	200·9	301·8
28·7	·8896	107·3	128·8	151·0	205·0	309·4
45	·8720	109·6	131·8	154·6	210·1	317·9
61·8	·8537	111·9	134·8	158·1	215·1	326·9
α-Bromocamphor in ethylene bromide p = 3·226						
15	2·144	135·2	162·7	191·1	261·6	406·5
32·5	2·110	136·0	163·9	192·2	264·2	410·1
45	2·084	137·2	164·0	193·0	265·6	412·2
59·5	2·055	137·5	164·3	194·0	266·9	414·6
84·3	2·004	137·8	165·7	195·1	268·1	418·4

Temp. °C	Density	$[\alpha]_{r_2}$	$[\alpha]_y$	$[\alpha]_g$	$[\alpha]_b$	$[\alpha]_v$
αα Dibromocamphor in alcohol p = 5·072						
0	0·8279	30·96	41·23	50·46	77·98	146·2
15·5	·8164	30·94	41·06	50·41	78·03	146·9
30	·8046	31·09	40·89	50·39	78·11	147·2
44·5	·7918	31·28	41·09	50·58	77·82	146·3
62	·7756	31·30	41·15	50·21	77·54	145·7
Methyl camphor-10-sulphonate in alcohol p = 4·793						
0	0·8206	38·30	46·57	54·51	76·28	118·2
13	·8104	37·66	46·5	53·74	75·63	116·9
32·5	·7945	36·93	44·81	53·50	74·67	116·1
42	·7862	36·32	44·79	53·08	74·15	116·6
58·5	·7717	36·16	44·42	52·88	74·01	116·2
Ethyl camphor-10-sulphonate in benzene p = 3·148						
10	0·8945	45·51	54·61	63·71	86·80	131·4
32·2	·8714	44·21	53·10	62·44	85·45	129·6
50·2	·8525	43·79	52·64	61·72	84·55	128·3
61	·8418	43·17	52·13	61·09	83·97	127·4

Temp. °C	Density	$[\alpha]_{r_2}$	$[\alpha]_y$	$[\alpha]_g$	$[\alpha]_b$	$[\alpha]_v$
Camphor-10-sulphonanhydramide in tetrachlorethane						p = 3·162
0	1·614	-29·76	-34·17	-38·58	-47·15	-59·64
11·5	1·597	-29·09	-33·91	-37·75	-46·06	-57·18
31·5	1·567	-28·01	-32·04	-36·21	-44·78	-55·26
46	1·546	-27·36	-31·31	-35·16	-43·6	-53·83
63·1	1·522	-26·88	-30·91	-34·54	-42·21	-51·69
87·5	1·483	-26·12	-29·72	-33·06	-39·97	-49·04
Camphor sulphonanhydramide in aniline						p = 4·839
0	1·047	-60·33	-69·33	-79·09	-99·56	-131·7
14·7	1·035	-55·93	-65·40	-74·64	-94·86	-125·1
38·5	1·015	-52·30	-60·09	-68·87	-87·58	-115·7
54·4	1·001	-50·20	-58·46	-66·73	-83·51	-110·8
67·8	0·9901	-48·15	-56·76	-64·33	-79·87	-105·4
84·2	·9767	-46·43	-54·50	-61·77	-76·72	-100·
Methyl-α-chlorocamphor-10-sulphonate in benzene						p = 2·438
12·5	0·8925	52·29	63·20	72·97	97·38	141·4
33·5	·8708	53·89	64·77	74·78	101·0	148·4
50·5	·8529	55·91	66·41	76·65	104·6	154·8
66	·8375	57·24	67·97	78·66	107·7	161·4

Temp. °C	Density	$[\alpha]_{r_2}$	$[\alpha]_y$	$[\alpha]_g$	$[\alpha]_b$	$[\alpha]_v$
Methyl-α-chlorocamphor-10-sulphonate in ethylene bromide p = 2·007						
32·5	2·125	83·22	99·77	116·6	157·9	235·9
44	2·101	82·56	99·61	116·2	156·7	235·6
59·5	2·070	82·26	98·81	115·3	156·1	234·7
76·5	2·035	81·87	98·37	115·0	156·1	234·4
88·8	2·009	81·37	98·11	114·5	155·6	234·2
Ethyl-α-chlorocamphor-10-sulphonate in benzene p = 2·425						
11	0·8932	51·07	61·16	70·98	94·06	137·4
33	·8708	52·98	64·22	73·98	98·24	144·7
49	·8541	54·31	66·37	76·03	102·0	150·9
65·1	·8376	55·69	68·00	77·82	104·6	156·6
α-Chlorocamphor-10-sulphonamide in pyridine p = 3·682						
10	1·003	69·68	83·05	96·23	128·7	187·9
29·5	0·9856	70·09	83·35	96·79	128·8	189·8
47·7	·9674	70·20	83·70	97·21	130·0	191·3
68·5	·9464	70·13	83·20	96·85	130·2	192·1
Methyl-α-bromocamphor-10-sulphonate in benzene p = 2·62						
11	0·8970	79·52	94·95	111·2	149·7	222·1
30	·8770	81·06	96·83	113·4	152·9	227·2
46·5	·8594	82·45	98·26	115·2	155·2	232·4
59	·8457	83·22	98·74	116·8	156·9	235·8

Temp. °C	Density	$[\alpha]_{r_2}$	$[\alpha]_y$	$[\alpha]_g$	$[\alpha]_b$	$[\alpha]_v$
Ethyl-α-bromocamphor-10-sulphonate in benzene p = 2·386						
11	0·8952	79·58	94·77	110·3	148·6	220·3
26·6	·8790	80·74	96·51	111·7	151·0	224·1
40·8	·8644	81·81	97·86	113·3	153·6	228·4
63	·8418	83·70	99·86	116·1	157·1	234·3
Ethyl-α-bromocamphor-10-sulphonate in ethylene bromide p = 1·939						
10	2·176	103·7	125·0	145·9	197·0	295·6
28·5	2·140	102·8	124·1	145·0	196·2	295·4
48	2·100	102·7	123·4	144·7	196·4	294·8
68	2·059	102·3	123·2	144·3	195·8	295·2
85	2·024	102·5	123·0	144·2	195·8	294·8
α-Bromocamphor-10-sulphonamide in pyridine p = 2·898						
13·5	0·9913	98·56	118·1	137·7	185·1	273·9
33·5	·9809	97·18	116·8	136·1	183·4	271·7
49	·9656	96·49	116·3	136·0	182·5	271·8
81	·9322	95·57	114·8	134·0	182·1	271·4
Methyl camphor-π-sulphonate in alcohol p = 2·811						
12	0·8071	79·07	96·96	116·0	165·9	265·6
24	·7964	79·56	97·16	116·4	166·6	268·0
41	·7818	80·19	98·40	117·1	166·1	269·0
55	·7688	80·39	98·63	117·7	167·4	270·7

Methyl camphor-π-sulphonate in benzene p = 2·302

Temp. °C	Density	$[\alpha]_{r_2}$	$[\alpha]_y$	$[\alpha]_g$	$[\alpha]_b$	$[\alpha]_v$
14	0·8902	85·37	104·0	124·7	179·9	291·2
31	·8734	86·1	105·1	125·9	180·9	293·1
45	·8614	86·66	105·5	126·7	181·5	294·3
65	·8392	88·31	107·6	128·4	184·7	296·6

Methyl-α-chlorocamphor-π-sulphonate in benzene p = 2·013

Temp. °C	Density	$[\alpha]_{r_2}$	$[\alpha]_y$	$[\alpha]_g$	$[\alpha]_b$	$[\alpha]_v$
14·8	0·8900	57·22	69·44	82·00	116·9	192·3
32·5	·8712	60·59	73·43	85·55	122·3	200·6
48	·8549	62·47	75·91	89·00	126·8	207·0
63	·8385	64·43	78·14	91·85	131·1	214·5

Methyl-α-chlorocamphor-π-sulphonate in ethylene bromide p = 1·527

Temp. °C	Density	$[\alpha]_{r_2}$	$[\alpha]_y$	$[\alpha]_g$	$[\alpha]_b$	$[\alpha]_v$
14	2·154	82·10	99·19	117·0	165·5	263·4
36	2·109	83·66	100·5	119·6	170·5	271·0
59	2·062	84·55	102·6	121·9	172·1	274·6
79	2·019	85·92	104·3	123·4	174·5	278·1

α-Chlorocamphor-π-sulphonamide in pyridine p = 0·7861

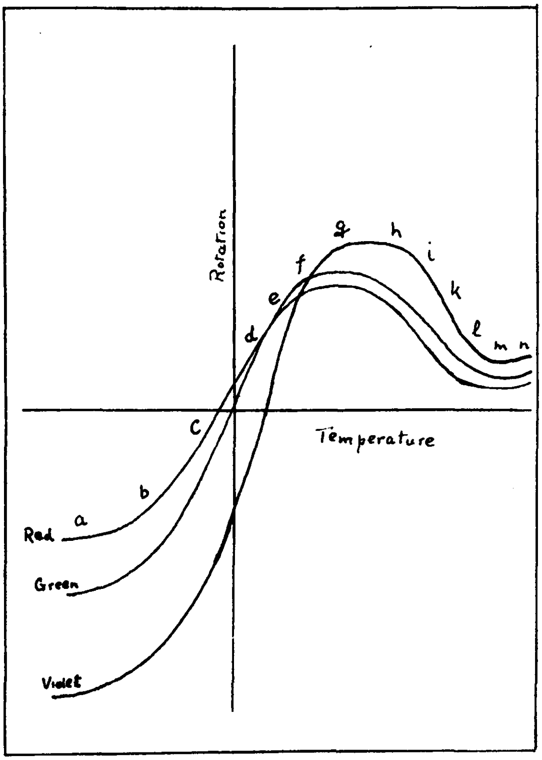
Temp. °C	Density	$[\alpha]_{r_2}$	$[\alpha]_y$	$[\alpha]_g$	$[\alpha]_b$	$[\alpha]_v$
14	0·9913	74·59	92·23	107·5	150·8	243·9
41·2	·9645	75·84	93·15	108·8	153·3	247·3
61·5	·9441	76·63	93·48	110·4	155·0	249·3
83·5	·9206	76·00	94·99	112·3	156·3	253·0

Temp. °C	Density	$[\alpha]_{r_2}$	$[\alpha]_y$	$[\alpha]_g$	$[\alpha]_b$	$[\alpha]_v$
$\alpha{\cdot}\pi$-Dibromocamphor in benzene						p = 2·004
18·5	0·8882	73·38	88·84	106·4	154·5	258·8
36	·8698	75·67	92·15	110·5	159·6	267·2
49·2	·8551	77·69	94·48	113·4	163·8	273·2
63·3	·8399	79·84	96·56	115·9	167·5	279·3
$\alpha{\cdot}\pi$-Dibromocamphor in ethylene bromide						p = 0·8226
15	2·147	95·92	116·4	139·4	200·3	327·7
31	2·115	97·34	117·9	141·6	202·9	331·5
50	2·075	98·11	119·3	143·2	204·3	335·4
72	2·028	99·26	120·6	144·6	206·1	340·6
Methyl-α-bromocamphor-π-sulphonate in benzene						p = 2·761
10	0·8982	68·31	82·68	97·79	137·9	216·3
32	·8742	71·48	86·76	102·3	142·8	226·9
49	·8574	74·20	89·25	105·1	147·1	234·2
62·5	·8431	76·20	91·31	107·4	150·7	239·5
Methyl-α-bromocamphor-π-sulphonate in ethylene bromide						p = 2·527
12	2·161	89·71	109·0	129·5	180·0	284·1
33	2·120	90·93	111·0	131·7	183·1	289·7
51·5	2·082	92·41	112·8	133·5	186·0	294·2
81	2·020	94·61	114·9	136·2	189·5	300·9

Temp. °C	Density	$[\alpha]_{r_2}$	$[\alpha]_y$	$[\alpha]_g$	$[\alpha]_b$	$[\alpha]_v$
α-Bromocamphor-π-sulphonamide in pyridine $p = 1{\cdot}064$.						
14	0·9931	94·66	114·8	133·1	186·4	295·2
34	·9740	94·10	115·8	135·1	188·9	299·8
55	·9519	95·68	117·3	137·1	192·6	305·6
83	·9232	96·12	119·1	140·1	196·7	313·7

DISCUSSION.

The fundamental standpoint from which the present investigation has been conducted is that which has already been elaborated by Professor Patterson, more particularly in his work on the optical rotation of the tartaric esters, involving the assumptions that a chemical compound retains its individuality in solution and under the application of temperature change and further, that the rotatory powers of simple derivatives bear a simple and gradual relationship to that of the parent compound itself. Solvents, in producing changes in the rotation, are regarded as instrumental in disclosing phenomena characteristic of the active compound itself and otherwise capable of realisation given the necessary adjustment of applied forces. Thus, for example, the influence of temperature could it be applied over a sufficiently extensive range would, on this view, produce upon ethyl tartrate the rotational changes represented in the accompanying diagram, the various parts of which have been realised in practice by the use of solvents or by the formation of simple derivatives or by a combination of these two agencies (J.C.S.,



1916, 1139).

In the case of camphor and its derivatives complications are incurred, first by the formation of new asymmetric centres in many of its derivatives and perhaps not least of all by the complexity of the molecule itself. From the present investigation it appears that two groups of T-R curves (i.e., temperature-rotation curves) are to be distinguished, viz., (1) those for camphor and Reychler's acid in sulphuric acid together with those for camphorsulphonanhydramide in aniline and tetrachlorethane, where the rotations are negative and the rotation for violet light is least (in an absolute sense), and (2) those for camphor in organic solvents, Reychler's acid in water, its esters in organic solvents and αα dibromocamphor in alcohol, where the rotations are positive and the rotation for violet light greatest. Therefore for the rotation for violet in the first group to assume the position of the rotation for violet in the second group or vice versa, an area comparable with def of the diagram must be traversed. In practice, though only in the analogous case of the dispersion curves, such an area is encountered with camphor and with Reychler's acid in dilute sulphuric acid. With regard to the minima ab, lmn in the tartaric series nothing comparable has so far been found in the camphor series, but the T-R curves obtained with the esters of Reychler's acid correspond to the tartrate region hik and imply the existence of a maximum, which is perhaps realised in

$\alpha\alpha'$ dibromocamphor in alcohol. [The maxima obtained with the $\underline{\alpha}$ halogenated camphor derivatives are not considered because of the third asymmetric centre introduced here.]

It has been shown by Professor Patterson and his co-workers that in areas comparable with <u>cdef</u>, i.e., where the rotation is removed from a maximum or minimum value, certain close approximations may be made in correlating rotation data and that these approximations hold not only for individual active substances under different external conditions, but also for many of their simple derivatives. The approximations referred to constitute the characteristic diagram and since it is proposed to analyse the data of the present thesis from this standpoint, it will be necessary here briefly to review the situation with regard to these diagrams.

The characteristic diagram was really discovered by Darmois, who deduced it directly from Biot's rule for binary mixtures, while investigating the dispersion of mixed terebenthene essences. (Ann. de Chimie et Physique, 8^{e}S., <u>XXII</u>, 1911). Biot's rule may be written:-

$$[\alpha] = x[\alpha]_1 + (1 - x)\,[\alpha]_2$$

where $[\alpha]_1$, $[\alpha]_2$ represent the specific rotations of two substances A and B for a given wave length of light, and $[\alpha]$ the specific rotation for the same wave length of a mixture containing x gm. of A per gm. of the mixture. Now let the points A, B and C represent the points of intersection of any ordinate of wave length with the dispersion curves of the two parent substances and the mixture respectively. Then

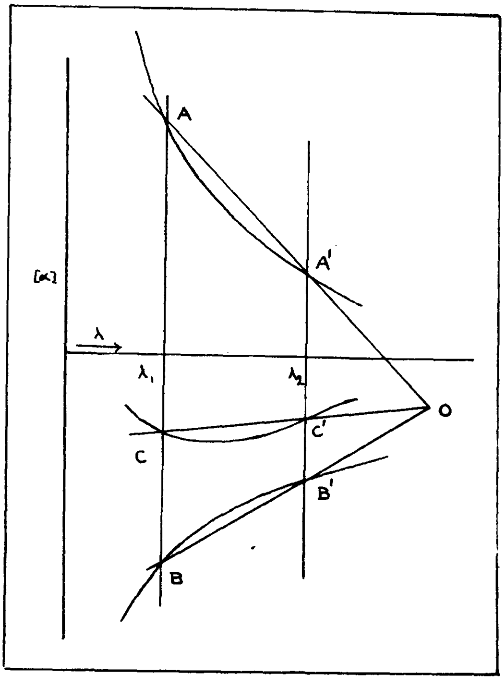
$$\frac{\overline{CA}}{\overline{CB}} = \frac{[\alpha]_1 - [\alpha]}{[\alpha]_2 - [\alpha]} = \frac{1 - x}{-x}$$

and similarly for any other ordinate A'C'B' :-

$$\frac{\overline{C'A'}}{\overline{C'B'}} = \frac{[\alpha']_1 - [\alpha']}{[\alpha']_2 - [\alpha']} = \frac{1 - x}{-x}$$

$$\therefore \quad \frac{\overline{CA}}{\overline{CB}} = \frac{\overline{C'A'}}{\overline{C'B'}}$$

i.e., the lines CC', AA', BB' are concurrent at some point O, and the dispersion curves for all mixtures of A and B cut these two ordinates in such a way as to provide a beam of lines concurrent at O. This beam of lines constitutes the Darmois diagram which has generally been constructed about the ordinates for yellow and violet light.



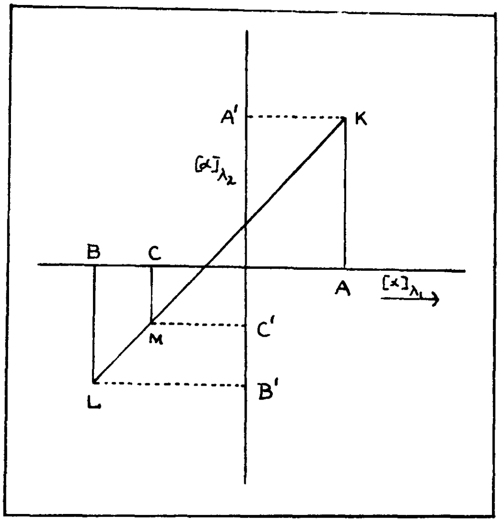
Armstrong and Walker (Proc. Roy. Soc., 1913, <u>88</u>, 392) constructed a diagram showing that, for an equilibrium of two active substances, the values of the specific rotation for one wave length, measured under different conditions, bears a linear relationship to the values for any other wave length measured under the same conditions. This is simply the Darmois theorem enunciated in a different form, for, plotting the different values of the specific rotation for one wave length A,C,B, against the corresponding values for the other wave length A',C',B', it follows from Armstrong and Walker's observation that the resulting points K, M, L lie on a straight line: whence, by geometry,

$$\frac{CA}{CB} = \frac{MK}{ML}$$

but $$\frac{MK}{ML} = \frac{C'A'}{C'B'}$$

$$\therefore \quad \frac{CA}{CB} = \frac{C'A'}{C'B'}$$

which is precisely the deduction made by Darmois.

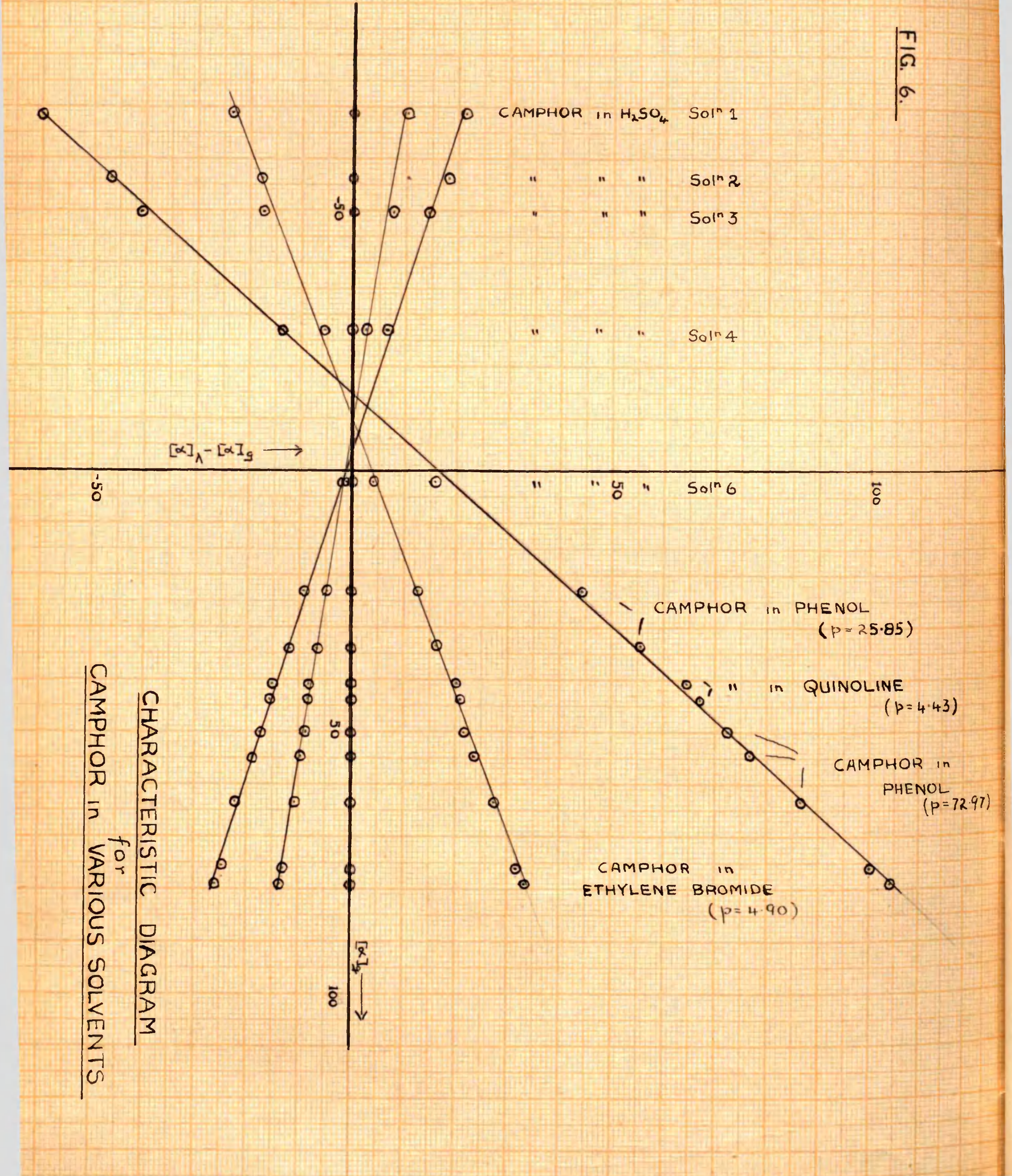


Now although the characteristic diagram has thus been developed from the assumed validity of Biot's binary mixture rule, it does not follow that the converse is necessarily true and that the construction of such a diagram from the rotation data of a compound is proof of the existence of that compound in two forms — e.g., theoretically, two intra molecular partial rotations could equally well be invoked to explain the phenomenon on the summation basis. Nevertheless, Malleman (Journ. de Phys. et le Radium, 1923, 18) expressly adopts this view and is followed by Lucas (Ann. de Phys., 1928, 381) who concludes from rather scanty data that, among other compounds, camphor in solution exists in two isomeric forms of different dispersion and opposite rotational sign. On the other hand Patterson (J.C.S., 1916, 1204 et seq.) and Bruhat (Trans. Far. Soc., 1930), arguing from totally different standpoints, conclude that the postulation of chemical heterogeneity of this type is inconsistent with experimental fact.

Patterson (J.C.S., 1916, 1176) has reduced the Armstrong-Walker diagram to a more compact form by plotting $[\alpha]_\lambda - [\alpha]_g$ against the values of $[\alpha]_g$ as reference axis, and in proceeding now to consider data for camphor and its derivatives with regard to this form of the diagram, it is only necessary to emphasise the fundamental identity of the characteristic diagrams at present in use, and conforming to the standpoint adopted and already expressed on page 49 to reject the view that these diagrams necessarily or even probably imply chemical heterogeneity.

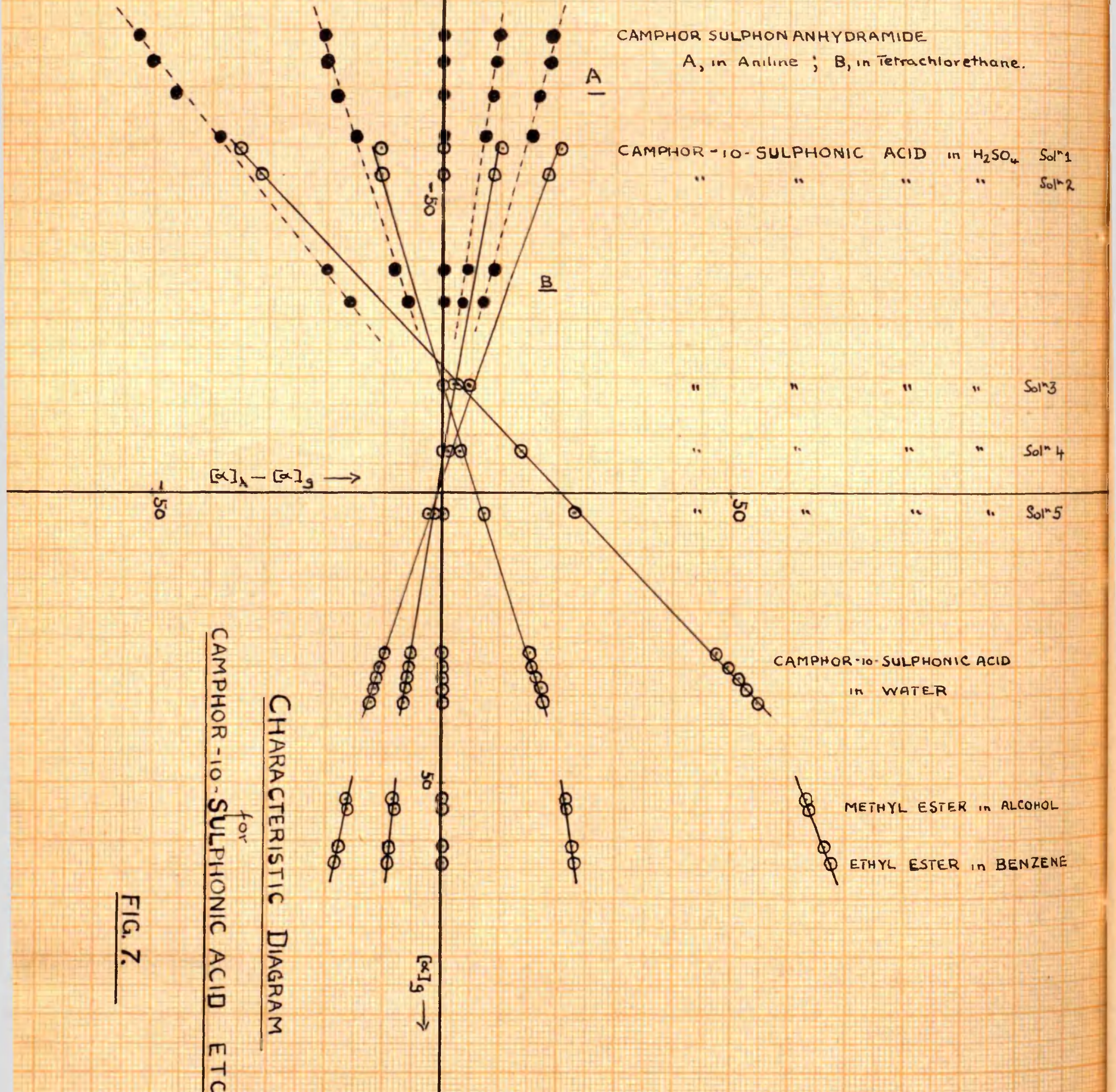
In Fig. 6 the rotation data for camphor have been fitted with a characteristic diagram of the type employed by Professor Patterson. In addition to the data for camphor in sulphuric acid (p. 24) the diagram includes rotation values of the compound obtained from a study of temperature and solvent influence, and which though not referred to previously in these pages, will be found in a paper by Patterson, Dunn, Buchanan and the present writer, recently submitted for publication in the J.C.S. Rotation data for camphoroxime in alcohol ($[\alpha]_g = -50{\cdot}09$) and in o-nitrotoluene ($[\alpha]_g = -65{\cdot}13$) and for oxymethylene camphor in chloroform ($[\alpha]_g = +229{\cdot}9$)

FIG. 6.



CHARACTERISTIC DIAGRAM for CAMPHOR in VARIOUS SOLVENTS also to be found in the above paper, lie closely on the diagram lines but have been omitted in order to avoid confusion and undesirable reduction of scale. It will be seen, however, that over a wide range of rotation the data lie with fair regularity upon the diagram lines and that these intersect over a considerable area in the negative region corresponding to the visible anomalousness found in that neighbourhood. The point of intersection of a given pair of lines is of interest in that this point being independent of solvent, concentration and temperature is characteristic of camphor and a suitable basis of reference for comparing rotations. Calculated from this point as zero, the dispersion ratio is constant for the two wave lengths of light corresponding to the pair of lines in question. From the diagram, the intersection of the lines for Hg_g and Hg_v appears to occur at $Hg_g = -15°$; i.e., at this value $[\alpha]_g$ becomes equal to $[\alpha]_v$.

The relationship between a compound and derivative with respect to the characteristic diagram does not appear to be a simple one, for though in many cases it has been found that the same diagram may be fitted to each, numerous other cases are known where this is impossible even when argument by analogy suggests the likelihood. The fact that in the neighbourhood of a maximum in temperature rotation curves the individual colours of light do not reach the turning value all at the same temperature, results in a deviation from the straight lines of the diagram and further, it is even



CHARACTERISTIC DIAGRAM
for
CAMPHOR-10-SULPHONIC ACID ETC.

FIG. 7.

indicated (Cf. Patterson, J.C.S., 1916, 1195) that each limb of the general T-R curve requires a diagram of its own. Derivatives, therefore, more effective than solvents in producing a pronounced shift of the observational region from one part of the general T-R curve to another, do not necessarily yield rotation data capable of accommodation on the diagram of the parent substance, but it is improbable that this is the complete explanation of the multiplication of diagrams sometimes found and indeed, when derivative formation involves the production of a new asymmetric centre or intimately affects existing centres as, for example, in reactions producing Walden Inversion, then obviously new factors are introduced.

The rotation data for camphor-10-sulphonic acid in aqueous solution lie fairly close to the lines of the camphor diagram and consequently, were no other data available, would be included in this diagram. The values obtained in sulphuric acid solution show quite plainly, however, that the diagrams for the two compounds are distinct. Fig. 7 contains the diagram for the sulphonic acid and it will be seen that whilst the various points lie in satisfactory fashion upon the lines drawn, the diagram as a whole in passing from camphor to camphor-10-sulphonic acid has been shifted slightly towards the negative region. Thus the region of anomalous dispersion is now found to extend further into the negative region than in the case of camphor, and intersection between the lines for green and blue light occurs now about -22° for Hg_g as contrasted with -15° in the case of camphor.

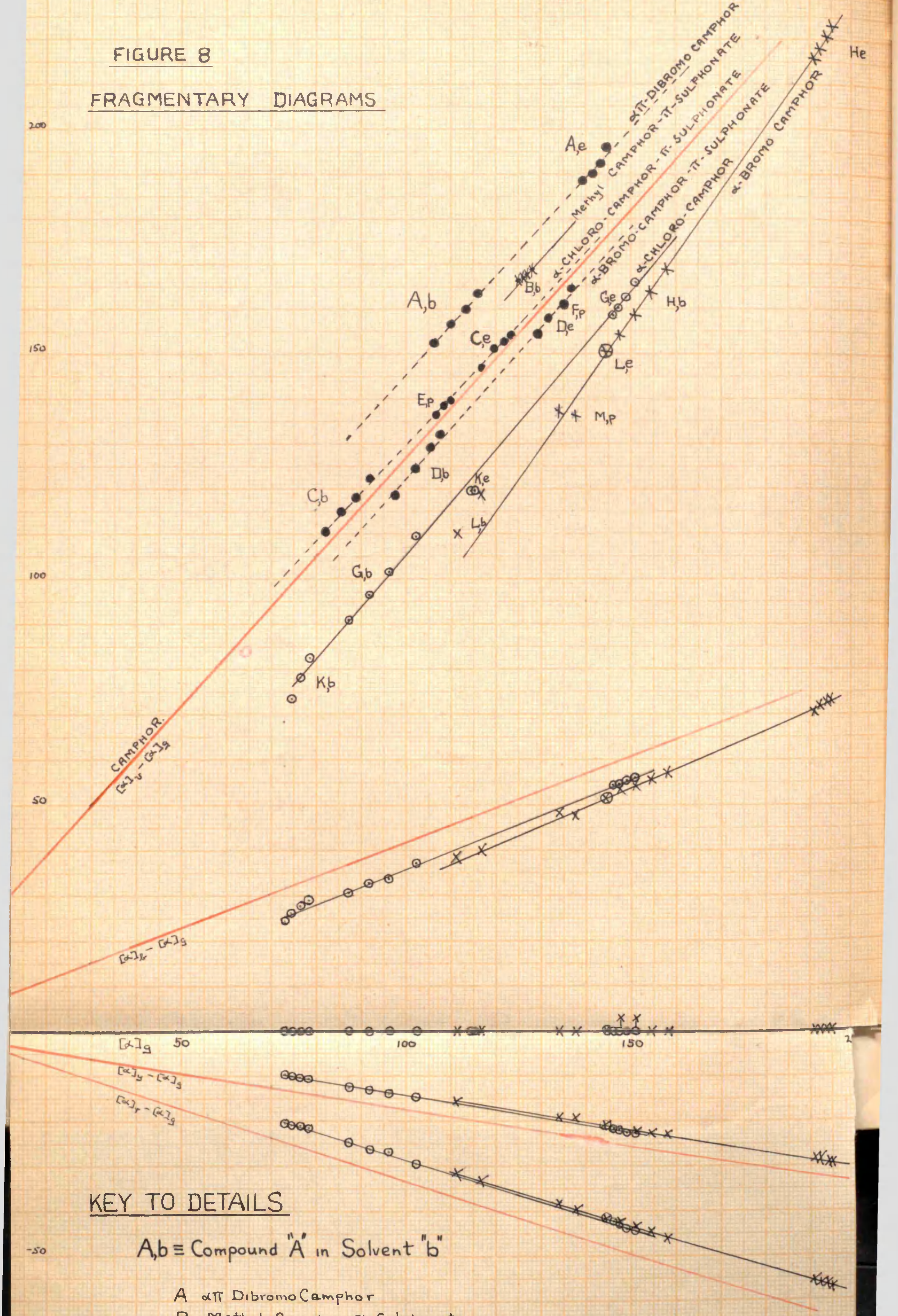
At this stage it may be pointed out that such a shift of characteristic diagrams in passing from one compound to another and implying an increase or decrease in positive rotation according as it occurs to the right or left respectively, cannot be predicted from consideration of the values of say $[\alpha]_g$ for the two compounds even if the solubilities allow of measurement at the same concentration and temperature in one solvent. It is impossible at the present time to say when two distinct molecular species are in a comparable state where their optical rotations are concerned and hence arises the necessity of studying the rotatory power of each over the widest range possible so that comparison may be based on general rather than on particular behaviour. The point in question receives ample illustration from Fig. 8 (see later).

In Fig. 7 there have also been included, to the left the data for camphorsulphonanhydramide and, to the right the data for the esters of camphor-10-sulphonic acid. As will be seen, each set requires its own series of lines, and whilst it is not altogether surprising that the anhydramide cannot be represented on the diagram of the parent acid in view of the structural changes involved in its formation, it is rather unexpected that the values of the esters show such a marked deviation. Repetition of the rotation measurements for the latter compounds confirmed in all essentials the values given in the T-R tables, so that the deviation from the diagram of the parent acid is perhaps to be explained in part at least from the fact that the rotations of these esters occupy a position on the descending limb of the T-R curve just beyond a maximum value, whilst the rotation values of the acid itself are situated on the opposite limb. The change, however, from strong polar characteristics in the acid to the covalent state in the esters may not be unimportant in this connection, but inferences cannot be drawn from a single example.

Since the characteristic diagram for camphor does not coincide with that for camphor-10-sulphonic acid which, in turn, is distinct from that of the esters, it is perhaps scarcely to be expected that, for example, the rotations for α-chlorocamphor and methyl α-chlorocamphor-10-sulphonate will be capable of representation on a single diagram, nor is it to be expected that these rotations will fall upon the diagram for camphor since the compounds contain a new asymmetric system. Moreover, unfortunately, as reference to the respective tables of solvent influence will show, the range of rotation available for study in the majority of cases is much restricted in comparison with that achieved with camphor and Reychler's acid. Consequently only a broad separation of the rotation data can be attempted, but if the diagrams on Figs. 6 and 7 show anything at all, they do show that for the same substance in

FIGURE 8

FRAGMENTARY DIAGRAMS



KEY TO DETAILS

A,b ≡ Compound "A" in Solvent "b"

A	απ Dibromo Camphor
B	Methyl Camphor-π-Sulphonate
C	Methyl α-chloro Camphor-π-Sulphonate
D	Methyl α bromo " " "
E	α Chloro Camphor-π-sulphonamide.
F	α Bromo " " " .
G	α Chloro Camphor.
H	Methyl α chloro Camphor-10-sulphonate
K	Ethyl α bromo " " "
M	α bromo Camphor-10 sulphonamide.

b = Benzene
e = Ethylene bromide
p = Pyridine.

different solvents the rotation values may be represented on a series of straight lines, and hence it is reasonable to suppose that extension of the line passing through two separate groups of points for (say) α chlorocamphor will represent the rotational behaviour of the compound under some undetermined conditions, provided always that the experimental points chosen do not lie in the neighbourhood of a maximum in the T-R curve.

With these considerations in view a number of fragmentary diagrams have been constructed in Fig. 8, the lines drawn referring particularly to the compound indicated as satisfying the proviso just mentioned, rather than to the points for other compounds which lie in the neighbourhood. Thus the set of lines marked "α bromocamphor" have been drawn through the points for this compound in benzene and in ethylene bromide, no attempt being made to alter the lines so as to accommodate more closely the points for the esters and amide of α bromocamphor-10-sulphonic acid which lie in the neighbourhood and which, like those of the corresponding α chloro compounds, belong to a rotational region at, or near, a maximum in the T-R curve (Cf. Figs. 3 and 4). The points for the π-derivatives do not belong to such a region (Cf. Fig. 5) and are therefore united here by their own respective lines. To avoid congestion of the diagram, only the lines for violet (i.e. $[\alpha]_v - [\alpha]_g$) have been drawn in the case of the π-derivatives, the lines for the other colours of light following the behaviour indicated in full for α chloro- and for α bromocamphor.

Treated in this way it will be seen that the mass of rotation data may be resolved into various groups according to the nature of the substitution changes wrought on the camphor molecule. [For comparison the diagram lines for camphor itself have been drawn in red in Fig. 8, though incidentally the scale does not yet allow the inclusion of the data for oxymethylene camphor which lie on the red lines beyond the right hand side of the figure]. The effect of these substitution changes is best seen in the lines for violet light where the differentiation is greatest. Thus with the introduction of a new asymmetric centre in passing from camphor to α chlorocamphor and derivatives of α chlorocamphor-10-sulphonic acid the rotation points have been moved towards the right, and in this sense the positive rotation of the compounds has been increased. A shift in the same direction and of greater magnitude is found in the corresponding α-brominated compounds indicating greater efficacy on the part of the bromine atom. On the other hand, as far as can be seen from the position of the points for methyl camphor-π-sulphonate, the formation of the new asymmetric centre here (C atom 7) has resulted in a shift of the rotation values towards the left of the camphor diagram and again, with the introduction of the α halogen atom, this shift has been practically nullified in the α chloro compounds and overtaken in the α bromo compounds which are situated to the right of the camphor lines. Further, the position of the line for α π dibromocamphor indicates that the bromine atom in the π-position exerts an even more powerful influence in producing a shift to the left than does the sulphonic grouping: the points for π bromocamphor itself would presumably lie beyond the line given for α π dibromocamphor. Unfortunately π bromocamphor is not among the compounds examined here, nor does the literature contain any record of its dispersion measurements, but in proceeding presently to consider some points of contact between this work and those carried out in the same field, reference will again be made to these π-derivatives.

To summarise the inferences from Fig. 8: the α bromine atom exceeds in power the α chlorine atom in increasing the dextro rotation of the substituted camphor molecule, whereas in the π-position it is probably most effective in producing the opposite result, substitution in this position increasing the laevorotation of the molecule. The results are all of a purely qualitative character, extrapolation to the reference line, where quantitative considerations might be attempted, being at present too extensive for accuracy.

As has already been stated in the introduction, the rotation dispersions of camphor and derivatives have been examined by Professor Lowry and his students from the point of view of the Drude equation. Camphor itself in benzene solution (J.C.S., 1925, 604) has been fitted with a two term equation, viz.:-

$$[\alpha] = \frac{29\cdot384}{\lambda^2 - 0\cdot0872} - \frac{20\cdot138}{\lambda^2 - 0\cdot05428}$$

The condition for anomalousness in an equation of this type is that the smaller dispersion constant be associated with the larger of the two rotation constants, and whilst the above equation fails to fulfil this condition, nevertheless the two terms are of opposite sign and it might be expected that if this were maintained under the impress of say different solvent circumstances, such alteration, particularly in the rotation constants, might be induced as to bring the dispersion curve into the truly anomalous class — the dispersion for camphor has indeed been described by Lowry as "quasi" or "potentially" anomalous. The complete anomalousness of camphor has now been demonstrated (Fig. 1) with aqueous sulphuric acid as solvent.

Similar remarks apply to camphor-10-sulphonic acid for which, in aqueous solution, the following Drude equation has been constructed (J.C.S., 1925, 1511):-

$$[\alpha] = \frac{22{\cdot}17}{\lambda^2 - 0{\cdot}08515} - \frac{18{\cdot}32}{\lambda^2 - 0{\cdot}04945}$$

Thus it will be seen that, although these two equations themselves yield perfectly normal dispersion curves, they do hint at an anomalousness which has actually been found: moreover the anomalousness occurs in the negative region in harmony with the association of the negative sign with the high frequency term in the equations.

The rotation dispersion of camphor sulphonanhydramide in acetone solution has been described (loc. cit., 1506) as conforming approximately to Biot's inverse square law. Now, in agreement with this conclusion, extrapolation of the characteristic diagram lines for this compound (Fig. 7) shows that they would intersect over a very small area, though this fact would suggest that the dispersion is more properly to be described as slightly anomalous.

Reference to Fig. 8 will show that extrapolation of the lines for α bromocamphor (or for α chlorocamphor) would lead to their intersection over a fairly wide area in the positive region corresponding with anomalousness in this region so far unattained experimentally. But the corresponding region has only now been reached for camphor and it is not too much to hope that in the future similar methods may disclose it for <u>α</u> halogenated camphors. Therefore, on the present view, just as the dispersion for camphor under all conditions is regarded as anomalous, since extrapolation of the rotational points for all conditions reveals this intersecting area (Fig. 6), so the dispersion for α bromocamphor (or α chlorocamphor) is regarded as anomalous for the same reason, and hence disagreement is expressed with the conclusion (loc. cit., 1268) that α bromocamphor (equation A) and α chlorocamphor (equation B) have normal complex dispersions.

$$[\alpha] = \frac{13\cdot276}{\lambda^2 - 0\cdot10855} + \frac{19\cdot53}{\lambda^2 - 0\cdot0562}\,; \qquad [\alpha] = \frac{12\cdot938}{\lambda^2 - 0\cdot0988} + \frac{7\cdot5189}{\lambda^2}$$

A. B.

It is not disputed that in the benzene solutions employed, the rotation values found fit these equations very well, but it is suggested that the inherent anomalousness of the dispersion is only masked by the distance separating these values from the true anomalous region and by the limits imposed upon the range of experimental observation in the ultra violet. The above equations do show, however, in the <u>α</u> halogenated camphors, the increase in positive rotation deduced from Fig. 8.

Cutter, Burgess and Lowry (ibid, 1268 - 1273) give dispersion measurements for several α' halogenated camphors. Now, since in the camphor molecule in so far as carbon atom 3 is concerned, α' halogens provide the optically isomeric forms of the α halogens and since it has been claimed that α halogens increase the positive rotation of the molecule, so it should result that α' halogens increase the negative rotation of the molecule, and on Fig. 8 the lines for the α' halogenated compounds should lie to the left of the red lines for camphor and to the left also of the lines for the corresponding α halogenated compounds. Unfortunately the data available are limited, consisting of but one point per wave length for three compounds, but in each case, as the following examples when tested will show, the various points fulfil the requirements of the prediction:-

α'-chlorocamphor $[\alpha]_g = +41$; $[\alpha]_v = +119{\cdot}1$
$\therefore [\alpha]_v - [\alpha]_g = +78{\cdot}1.$

α'-bromocamphor $[\alpha]_g = -47$; $[\alpha]_v = -49{\cdot}4$ (calculated)
$\therefore [\alpha]_v - [\alpha]_g = -2{\cdot}4$

$\alpha'\pi$-dibromocamphor $[\alpha]_g = +126{\cdot}6$; $[\alpha]_v = 323{\cdot}5$
$\therefore [\alpha]_v - [\alpha]_g = +196{\cdot}9.$

In one further particular the present view differs from that expressed by the above authors (J.C.S., 1925, 1265), viz. that the rotation of the π-derivatives is necessarily abnormal. As has been indicated on page 60, the rotation of these compounds as far as can be seen from the present work is quite consistent provided allowance is made for the new asymmetric system introduced here - a factor of which, strangely enough, Professor Lowry takes no account, expressedly at least, not even in discussing the symmetry of the substituted camphor molecule (J.C.S., 1925, 1509). Allowing for this factor and recognising that it contributes an increase in the negative rotation of the molecule, there is, for example, little apparent reason for considering it a matter of surprise that "the high frequency term is negative in *both* of the stereoisomeric $\alpha\pi$ and $\alpha'\pi$ dibromocamphors", the more especially if Professor Lowry is correct in regarding the high frequency term "as representing the sum of the partial rotations of the fixed asymmetric centres" in the camphor (or substituted camphor) molecule.

One further point of contact with recent work arises from the dispersion curves of camphor and camphor-10-sulphonic acid (Figs. 1 and 2), for these families of curves are in general shape and disposition just the opposite of the family for ethyl-d-tartrate (Patterson, J.C.S., 1916, 1201) and it is natural to inquire into the possibility of a cause or connection between them. Wood and Nicholas (J.C.S., 1928, 1071) have suggested such a possibility in pointing out that in all compounds which exhibit anomalous dispersion and to which the work of Clough (J.C.S., 1918, 526) and others has assigned a dextro configuration, the inflexions and maxima — criteria of anomalousness in dispersion curves — occur entirely in the positive region of rotation, whilst the curves cross the zero axis in such a way that $d\alpha/d\lambda$ is always positive. The corresponding laevo compounds have, therefore, points of inflexion and maxima in the negative region and $d\alpha/d\lambda$ negative where the curve crosses the axis. In advocating the adoption of these phenomena as criteria for relative configuration, the above authors further consider that in compounds possessed of more than one asymmetric centre, configuration is determined by the predominant centre in each molecule.

Since the characteristic diagram in showing the position of anomalousness*, realised experimentally or inferred by extrapolation, could obviously serve to determine relative configuration as defined by the above criteria, camphor on this view, together with camphor-10-sulphonic acid

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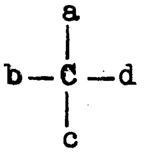
* The characteristic diagram may, of course, show that no anomalousness exists as in the case of mannitol and derivatives (Patterson and Todd, J.C.S., 1929, 2876), where the lines all intersect at the origin, i.e., $[\alpha]_g = 0$. The criteria in such cases do not apply.

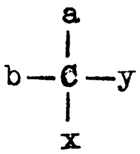
and by extrapolation, also the π-derivatives of camphor are to be regarded as laevo compounds, whilst α chloro- and α bromocamphor are predominantly dextro compounds (Figs. 6, 7 and 8). Indeed, considered from the point of view of the characteristic diagram, the observation of Wood and Nicholas is simply a reiteration and extension of the principle expressed by Pickard and Kenyon (Proc. Chem. Soc., 1913, 296), viz., "This method of plotting (in some cases at least) appears to afford a means by which a derivative differing in sign from that of the optically active parent substance can be properly designated "d" or "l" and also a means of determining whether a change in configuration has taken place in the formation of a derivative." The extension consists in applying the criterion to all active compounds without regard to their chemical lineage.

In considering whether or not this extension is justified, the meaning of the term "configuration" is involved, for if configuration refers to the relative disposition of atoms or groups in space around a central carbon atom according to the van 't Hoff scheme, then configurations are only comparable when at least three of the atoms or groups are the same in each of the systems to be compared. Thus to say that the systems



$$\begin{array}{c} a \\ | \\ b - C - d \\ | \\ c \end{array}$$

;



$$\begin{array}{c} a \\ | \\ b - C - y \\ | \\ x \end{array}$$

have similar or dissimilar configurations is meaningless since there is no adequate basis of comparison. Moreover, it is quite a legitimate objection that the rotation relationships established by Clough in systems a, b, c, d, C and a, b, c, x, C are too restricted to allow of any comprehensive generalisation.

Two experimental examples* may be quoted in illustration of the above points. The first (Levine and Marker, J. Biol. Chem., 1931, 77) shows that starting from two carboxy acids (A and B) which are mirror images except that one possesses a C_2H_5 group in place of C_3H_7 group, the same hydrocarbon (C) results from a series of reactions involving only the carboxy group indirectly attached to the asymmetric carbon and therefore not likely to be accompanied by Walden Inversion.

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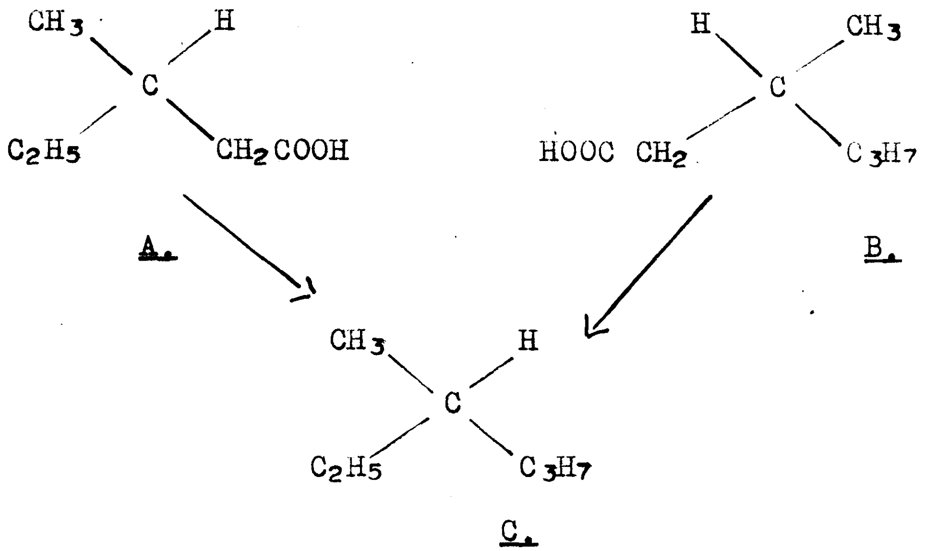
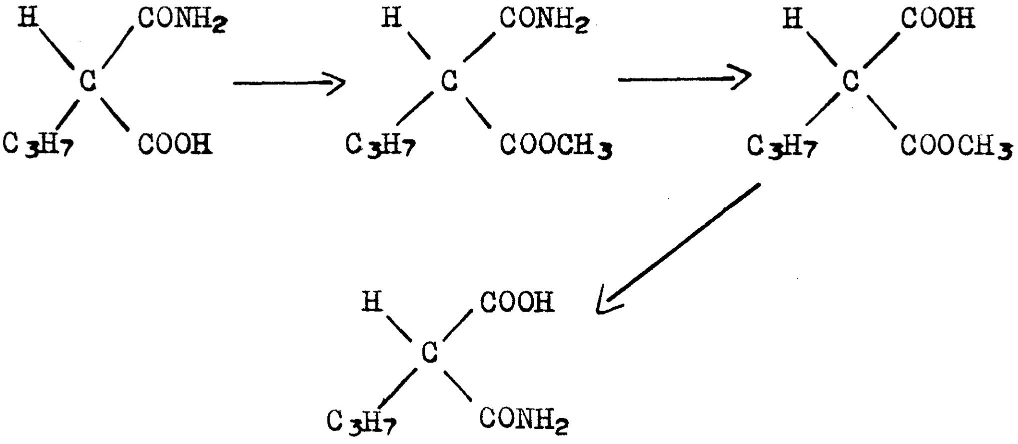
* I am indebted to Dr. C. Buchanan for these references.



Now, if A and B are to be considered as configuratively dissimilar, C on the same basis of comparison may have either the configuration of A or the configuration of B.

The second example (due to Fischer and Brauns, Cf. Cohen's <u>Organic Chemistry</u>, 5th Ed., Part II, p.205) may be quoted without further amplification:-

<u>d</u> Isopropyl malonaminic acid   <u>l</u> Isopropyl malonaminic acid



In fairness to Wood and Nicholas, however, it must be mentioned that they consider configuration to be in some way connected with molecular vibration, but as will be seen this involves a redefinition of the term which they neither express nor justify, and in any case their argument is based upon deductions made from the work of Clough. At present, therefore, without dismissing the possibility of a general relationship between configuration and rotational behaviour, there is an apparent need for care with regard to the definition of terms employed and for further research of a more extensive nature before the question can be definitely settled.

In concluding the account of this investigation in the camphor series, no claim is made to any degree of finality in any one department; certain inferences have been drawn and suggestions made where facts appeared to permit, but it is recognised that a still more extensive survey of the field is desirable. On the other hand, in the optical activity sections factors such as solvent and temperature, hitherto disregarded, have been taken into account and to some extent correlated, and incidentally the usefulness of concentrated and aqueous sulphuric acid in depressing the rotation of this class of compounds has received a proper emphasis. It is submitted, therefore, that a progressive step has been taken and that the increased information resulting may provide fresh starting points and directions to future research.