THE INFLUENCE OF SUBSTITUENTS AND SOLVENTS ON THE OPTICAL ROTATORY POWER OF THE l-MENTHYL ETHERS.

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CONTENTS.

INTRODUCTION.

In the year 1890, two eminent chemists, Crum Brown and Guye, each advanced a theory of Optical Activity. Crum Brown held the view that the degree of activity of an optically active compound was dependent on the differences between the four groups attached to the asymmetric carbon atom. He assumed a constant, K , characteristic of each group, supposedly capable of numerical representation, and a function of its composition, constitution, and temperature. (Proc. Roy. Soc. Edin. 1890, 181).

The rotatory power was supposed to depend on the asymmetry of the molecule, as calculated from the values of k for the four radicals. This theory had much to commend it, but the determination of k has, so far, been found to be impracticable.

Guye, (Compt. rend. 1890, 110, 74 et seq.), on the other hand, attacked the problem from a more mechanical point of view. He suggested that the activity was proportional to the degree of asymmetry of/

of the molecule, as determined by the displacement of the centre of gravity of the regular tetrahedron from its six planes of symmetry. As an approximation, Guye calculated the asymmetry of the molecule from the differences of the masses of the four radicals.

This theory was applied successfully to the compounds first examined, but it collapsed completely when groups of different constitution, or structure, were linked to the asymmetric atom, especially when these were of equal mass.

Thus of the two theories, Crum Brown's was the more far-reaching; for he considered the constitution, as well as the composition, of the four groups concerned. One of the simplest methods of varying the constitution of a compound, is to replace one, or more, hydrogen atoms by substituent groups. During recent years, a number of studies have been carried out, with a view to determining the influence of substituents on various properties of compounds.

Flürscheim, (J.C.S., 1909, 95, 718), investigated the reactivity of substituted acids and bases, and arranged the substituents in the order of their influence. In the case of the acids, X-R-COOH /

X-R-COOH, where R is any radical, and X, the substituent therein, Flürscheim concluded that, for the same solvent, the dissociation constant, and hence the reactivity, depends on two factors.
(1) The dissociation constant is proportional to the force with which the negative electron adheres to the acidic radical. The force depends on the polar nature of the acidic radical, which,in turn, depends on the polar nature of the substituent. The more negative this is, the greater the force becomes. An influence of this kind is called the "Polar Factor".

(2) The dissociation constant is inversely proportional to the force of linkage of the hydrogen atom to the acidic radical. This depends on the affinity that the atom, to which the hydrogen atom is linked, can place at the disposal of the latter. Such a force is variable, and depends on the forces with which the substituents are linked to the molecule and on their position therein. This is called the "Quantitative Factor". A similar line of argument is applied to bases.

From the values which he obtained for the dissociation constants, Flürscheim compiled a series giving/

giving the order of their influences.

Olivier (Rec. Trav. Chim., 1914, 33, 244) investigated the effect of substituents in the benzene derivatives C_6H_5X , by determining the velocity of their Friedel-Crafts reaction with para-bromobenzene sulphonyl chloride. He also determined the velocity constant for the parallel reaction where X, the variable substituent, was in the para position in the benzene sulphonyl chloride molecule. For both reactions the following order held:-

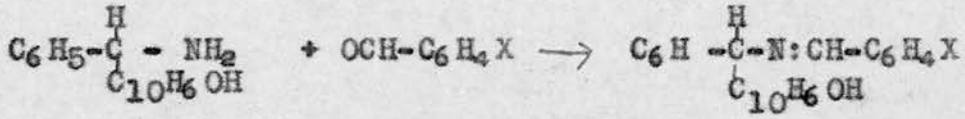
$$CH_3 > H > I > Br > Cl > NO_2$$

In the case of the nitro-substituted acid chloride, the meta-isomer was used, but Olivier maintained that, if the para-isomer had been employed, the order would not have been changed. He noted, however, that whenever the variable substituent was in the acid chloride ring, the changes in the velocity constant were much smaller; that is, the influence was weaker.

To approach closer to the subject of this thesis, Betti, in 1909, initiated a classic research correlating the influence of substituents on the optical/

optical rotatory power of a substance, with their influence on acidic strength. (For summary, see Gazz. Chim. Ital., 1923, 53, 424).

Betti prepared a series of Schiff's bases, formed by the condensation of the amine, d-naphthol benzylamine, with a large number of substituted benzaldehydes,



and compared the optical rotation of the bases with the dissociation constants of the substituted benzoic acids, derived from the aldehydes employed.

The observed rotatory powers, $[M]_D$, (in benzene solution), varied from +2676° to -991°, and when these were arranged in order of magnitude, they gave a series which corresponded approximately to that of the dissociation constants of the derived benzoic acids.

Table I /

Table I.

$[M]_D$	Aldehyde employed	k x 10^{18} for Acid
+2676°	p-dimethylaminobenzoic	1 (?)
+1507	veratric	3.6
+1220	vanillic	3.0
+1154	anisic	3.2
+1049	p-hydroxybenzoic	2.9
+ 894	o-methoxybenzoic	8.2
+ 746	cuminic	5.
+ 691	p-toluic	5.1
+ 589	protocatechuic	3.3
+ 504	m-toluic	5.1
+ 373	benzoic	6.
+ 363	m-hydroxybenzoic	8.7
+ 282	p-chlorobenzoic	9.3
+ 256	m-chlorobenzoic	15.5
+ 207	p-nitrobenzoic	39.6
+ 168	m-nitrobenzoic	34.5
- 85.7	salicylic	102.
- 128	o-chlorobenzoic	132.
- 326	o-toluic	12.0
- 766	5-nitrosalicylic	890.
- 991	o-nitrobenzoic	616.

Betti and his co-workers obtained similar, but less complete, results by using the active bases, α-naphthyl benzylamine, and α-anisyl ethylamine.

Rule (Trans. Far. Soc., 1930, 26, 324) analyses the above table, and notes that among the mono-substituted ortho compounds, the substituents influence the rotatory power, and the dissociation constant thus:-

$[M]_D$ $NO_2 < CH_3 < Cl \leq OH \leq H \leq OCH_3$

k $NO_2 > Cl > OH > CH_3 > OCH_3 > H$

and in the para-compounds:-

$[M]_D$ $NO_2 < Cl < H < CH_3 < (OH.OCH_3) < N(CH_3)_2$

k $NO_2 > Cl > H > CH_3 > (OCH_3.OH) > N(CH_3)_2$

Rule (loc. cit.) observes that a more marked agreement is noticeable in the para series than in the ortho. This, he suggests, is possibly due to disturbances in the case of the ortho derivatives, arising from the proximity, in space, of the substituent to the asymmetric carbon atom.

The latter suggestion is disputed by Betti, who emphasises the fairly close parallel between the optical rotatory powers of the compounds and the dissociation constants of the derived acids.

Recently/

Recently much work has been done on the electrical state of organic molecules. The idea of dipoles is not a new one, for in 1912 Debye first introduced the theory, and suggested a method of evaluation. In the modern view, the introduction of a polar substituent into a symmetrical hydrocarbon molecule is equivalent to the insertion of an electrical doublet, or dipole. This may be of variable intensity, and, according to the nature of the substituent, may have its positive, or negative end towards the hydrocarbon chain to which it is attached.

Thomson (Phil. Mag. 46, 497) suggested that the relative magnitudes of these doublets could be determined, irrespective of sign, by comparing the molecular inductive capacities, for long wave lengths, of the compounds R-X, where R is a hydrocarbon radical, and X the polar substituent.

This led Rule to calculate the effect of various polar substituents on the inductive capacities of substituted hydrocarbons (J.C.S. 1924, 125, 2156). It was found that, on being corrected for molecular weight and density, the inductive capacities, for long wave lengths, of liquids of the series C_2H_5X, fell into the following order:

NO_2 /

NO_2 > CN > $COCH_3$ > OH > CHO > Cl > Br > I > Alkyl

and for the corresponding benzene series:

NO_2 > CN > $COCH_3$ > CHO > Cl > Br > C_2H_5 > CH_3 > H

Rule and Paterson investigated the rate of ester formation from substituted benzoic anhydrides, and found the velocities to fall into the following series:

NO_2 > Cl > ($H.OCH_3$) > CH_3

Finally they summarised these and a number of other results as follows.

Table II - see following page.

These results, they point out, indicate the existence of a similar substituent influence in a wide range of chemical and physical properties.

Debye (Polar Molecules, Chem. Catalog Co.,1929) describes a method of calculating the actual dipole moment/

Table II.

Molecular Inductive Capacities:- (i)

C_2H_5X: $NO_2 > CN > COCH_3 > OH > CHO > Cl > Br > I > Alkyl$

C_6H_5X: $NO_2 > CN > COCH_3 > CHO > Cl > Br > C_2H_5 > CH_3 > H$

Rate of hydrolysis of substituted benzoic esters:- (ii)

$NO_2 < Halogens < H < CH_3$

Rate of esterification of substituted benzoic acids:-

No catalyst $NO_2 > Cl > H > CH_3$ (iii)

HCl as catalyst $NO_2 < Cl < CH_3 < H$ (iv)

Rate of sulphone formation:- (v)

$NO_2 < Halogens < H < CH_3$

Rate of hydrolysis of substituted benzyl chlorides:- (vi)

$NO_2 < COOH < Halogens < H < CH_3$

Rate of ester formation from substituted benzoic anhydrides:- (vii)

$NO_2 > Cl > (H, OCH_3) > CH_3$

(i) Rule. loc. cit. quoted from Landolt-Bornstein's 'Tabellen'.

(ii) Kellas. Zeit. phys. Ch., 1897, 24, 227.

(iii) Michael and Oechslin. Ber., 1909, 42, 317.

(iv) Kellas. loc. cit.

(v) Olivier. v. ante.

(vi) Olivier. Rec. Trav. Chim., 1923, 42, 516, 775.

(vii) Rule and Paterson. loc. cit.

moment of a compound, from data referring to its dielectric constant, and refractive index. This method has been used by Lange (Zeit. Physik., 1925, 33, 169), Smyth (J. Am. C.S., 1925-27), Errera (Physik. Zeit., 1926, 27, 764), Williams and his co-workers (J. Am. C.S. 1927-28) and Höjendahl (Thesis, Copenhagen, 1928).

These workers have amassed a large amount of data, which indicates that the dipole moment is characteristic of the substituent group, rather than of the molecule as an entity. The values which they obtain lie, in general, in a series parallel to those found for the various properties mentioned above.

The series is usually known as the General Polar Series. One thus realises that the question of the dipole moment of a group, if it may so be called, is a very fundamental one.

The question of correlating the electrical state of an optically active molecule, with its rotatory power, has been the subject of the researches of Rule and his co-workers.

Rule maintains that the rotatory power of

a/

a compound is governed by the arrangement and nature of the polar groups present in the molecule, and depends mainly on the dipole values of these groups.

This hypothesis, put forward first in 1924 (J.C.S., 1924, 125, 1121) is, in a sense, a modification of that of Crum Brown. Rule suggested that "the rotatory power of a molecule was a function of the (dipole) moments of the four groups attached to the asymmetric atom, and that the influence of a substituent on the optical rotation would, therefore, depend in sign and magnitude upon the polarity of the substituent". (Trans. Far. Soc. 1930, 26, 323).

When one considers the rotatory powers of derivatives of optically active alcohols, two distinct effects, due to the substituents, are noticeable. It has been shown that, for esters of the straight chain aliphatic acids, the influence of various polar substituents arranges them according to the General Polar Series. Rule and Smith (J.C.S., 1925, 127, 2188) examined the rotatory powers of l-menthyl esters of the type $X\text{-}CH_2\text{-}COOC_{10}H_{19}$, where X is the variable substituent. For these compounds, the authors represented the influence of the substituents as follows:-

$$CN > Cl > Br > OH > OCH_3 > CH_3 > COOH > H$$

This/

This series, they point out, is closely analogous to the General Polar Series.

Rule and Mitchell (J.C.S., 1926, 129, 3202) investigated the corresponding sec. β-octyl esters. They found that in this series the arrangement is very similar, the order of influence being as follows:-

$$I > Br > Cl > C_2H_5 > OCH_3 > CH_3 > H$$

The acidities of the substituted acids give the arrangement:-

$$Cl > Br > I > OCH_3 > H > CH_3$$

A similar effect is found with the sec.β octyl para-substituted benzoates. Rule, Hay, Numbers and Paterson (J.C.S., 1928, 131, 178), on arranging the rotatory powers of these compounds, in the order of their magnitude obtained

$$NO_2 > COOH > OCH_3 > Cl > CH_3 > H$$

In this series the general polar influence of the groups is also apparent.

The second type of substituent effect is noticeable when the optically active esters of various ortho-substituted aromatic acids are considered. In this case the groups do not follow the general polar series completely. In the subjoined table the values for the rotatory powers

of the l-menthyl esters of ortho-substituted benzoic acids are those of Cohen (J.C.S. 1914, 105, 1892), while those of the sec. β octyl esters, are due to Rule and co-workers (J.C.S., 1926, 127, 553, 2116; 1928, 131, 178; 1929, 133, 401, 2274).

Table III.

$[M]_D^{20}$ for homogeneous l-menthyl and sec.β-octyl esters of the acids, $X\text{-}C_6H_4COOH$.

Substituent X	l-Menthyl ester	sec.β-octyl ester
NO_2	-381°	-122°
COOH	-332	- 90 to 117
OH	-279	-78.2
H	-239	-77.8
CH_3	-231	-68.1
I	-231	-44.3
Br	-205	-49.2
Cl	-195	-47.1
OCH_3	-148	-33.0
$N(CH_3)_2$	-200	-28.1
NH_2	-261	-23.0

Thus we see that the influence of ortho substutuents on the rotatory power is identical for both l-menthyl and sec.β octyl esters, except for/

for the small displacement of iodine with respect to bromine and chlorine. The amino and dimethylamino groups are also somewhat displaced in the l-menthyl series.

On comparing this series with the general polar series obtained for the substituted acetic esters, one notices certain points of similarity. The most polar groups still retain the same relative positions, but the intermediate groups, hydrogen and methyl, are strongly displaced. Methoxyl and the halogens are reversed, the rotation falling below the level of the unsubstituted compound. A further interesting point is that the series can, on the whole, be divided into two parts, for substituents which direct into the meta position lie in one section, and those which direct ortho-para, in the other (Rule, J.C.S. 1924, 125, 1122).

Rule, Bretscher and Spence (J.C.S., 1929, 131, 2516) have investigated a number of l-menthyl esters of ortho- and peri-substituted naphthoic acids. They obtained the following figures:-

Table IV /

Table IV.

$[M]^{20}_{5461}$ of l-menthyl naphthoates (in benzene).

1-Naphthoates		2-Naphthoates		Peri-Naphthoates	
Unsubs.	-319°	[Unsubs. $[M]_D$ -288°]		8-NO_2	-841° *
2-CH_3	-99.6	1-OCH_3	-268	8-Cl	-172
2-OCH_3	+45.3	3-Cl	-278	8-OCH_3	-157
-	-	3-OCH_3	-206	-	-

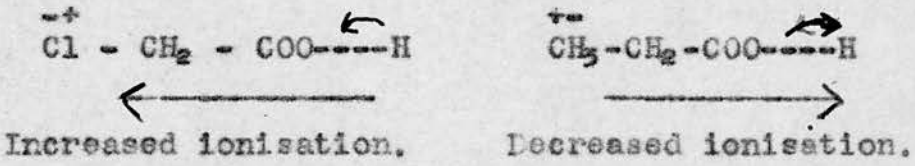
Thus those substituents which have been examined fall into an order similar to that for the ortho-substituted benzoic esters, and agree with their directive powers in benzene substitution. So great is the combined effect of the ortho-para-directive methoxy group and the adjoining hydrocarbon linking, (also o-p-directive) in the case of the 2-methoxy 1-naphthoate, that the sign of the rotation is reversed.

This divergence from the General Polar Series constitutes the second type of effect, and it has been suggested that the differences observed are, in some way connected with the peculiar arrangement of/

* Tschugaeff, Ch. Z. (II) 1902, 1238.

of the ortho substituent with respect to the asymmetric radical.

Now if an electrical doublet be situated at one end of a hydrocarbon chain, it will exert a field on adjacent parts of the molecule. Thus, according to whether the positive end, or the negative end, is attached to the chain, there is a tendency for it to attract, or repel, electrons. This will alter the properties of the chain, and it will have the effect, in the substituted aliphatic acids, of a change in the degree of ionisation.



In optical activity, these electrical changes will be expected to have corresponding effects on the rotatory power. It has already been shown for the optically active esters of substituted acetic acids, that the more electronegative the substituent, the higher is the rotatory power. Withdrawing electrons from the vicinity of the asymmetric atom thus gives an increase in rotation, while the reverse holds for the effect of electropositive groups, such as the dimethylamino.

Influence/

Influence of Ionisation.

In the foregoing pages it has been shown to what extent the presence of dipoles in the molecule may influence the physical and chemical properties. Accordingly it is to be expected that the introduction of a free positive or negative charge would lead to changes of a similar or even greater magnitude.

In benzene substitution, for example, the presence of an ionic charge on a substituent in the molecule has a great influence on the course of further substitution. (Flürscheim, Chem. and Ind., 1926, 45, 43; also Ingold and Robertson, J.C.S. 1926, 127, 1655). Normally, aniline substitutes in the ortho and para positions but if the amino group be ionised, as in the sulphate, the main product is the meta-substituted isomer.

When the sodium salt of an acid is formed, the carboxyl group is ionised, and the presence of the negative charge results in an electron shift. Bjerrum (Zeit. physik. Chem., 1923, 106, 240), has calculated that this electron shift is of the same order of magnitude, but of opposite sign, as that occurring when a carboxyl, or hydroxyl/

hydroxyl group is introduced into the hydrocarbon chain of an organic acid.

Taking this fact as a primary assumption, Rule predicted (J.C.S., 1927, 129, 54) that in a compound containing an asymmetric atom linked to three comparatively non-polar radicals and one strongly polar amino or carboxyl group, the result of ionisation would be to reverse the original effect of the polar substituent upon the rotatory power. The direction of the change in rotation from $\overset{+-}{C}OOH$ to $\overset{\ominus}{C}OO$ should be the same as that from $\overset{\oplus}{N}H_3$ to $\overset{-+}{N}H_2$, where the circled signs indicate a free ionic charge.

Thus if the introduction of a carboxyl group into an asymmetric molecule raises the rotatory power, ionisation of that carboxyl group will tend to lower the rotation. Conversely, if the introduction of a basic group lowers the rotation, the values will rise on ionisation. An example of this change is seen in the behaviour of the following d-amyl derivatives.

$C_2H_5-CH(CH_3)-CH_2-\overset{-+}{N}H_2$ ⟵ Free amine $[M]_D = -5.2°$

$C_2H_5-CH(CH_3)-CH_2-\overset{+-}{C}OOH$ ⟶ Acid $[M]_D = +10.5°$

$C_2H_5-CH(CH_3)-CH_2-\overset{\oplus}{N}H_3\,\overset{\ominus}{Cl}$ ⟶ Amine Hydrochloride $[M]_D = +11.7°$

$C_2H_5-CH(CH_3)-CH_2-\overset{\ominus}{C}OO\overset{\oplus}{Na}$ ⟵ Salt: probably low positive rotation.

The value for the salt is not obtainable, but the result has been derived by analogy from the rotation of its lower homologue, valeric acid.

Marked changes of this nature in the rotatory power often occur on the ionisation of optically active acids and bases. When lactic or methoxy-succinic acids are converted into their sodium salts, the sign of the rotation is actually reversed. This also occurs in the case of salt formation from the bases, d-menthylamine, d-amylamine and nicotine.

An excellent example of the alteration of sign on ionisation is afforded by the variation of the rotatory power of active amino acids in alkaline, neutral and acid solutions. In neutral solution, only slight ionisation occurs; in acid solution, the electropositive $\overset{-+}{NH_2}$ group is changed to the complex $\overset{-+\oplus}{NH_3}$, with a positive charge; while in alkaline solution, the electronegative COOH group is almost entirely changed to the negatively charged $\overset{+-\ominus}{COO}$ complex.

Table/

Table V.

Alkaline solution	Neutral solution	Acid solution.
$H_2N-\overset{a}{\underset{b}{C}}-COO^-$	$H_3\overset{+}{N}-\overset{a}{\underset{b}{C}}-COO^-$ or $H_2N-\overset{a}{\underset{b}{C}}-COOH$ Hybrid Ions	$H_3\overset{+}{N}-\overset{a}{\underset{b}{C}}-COOH$
d-aspartic acid		
+ 1 mol NH_3		+ 1 mol HCl
$[\alpha] = -9.02°$	+ 4.36°	+ 30.0°
l-asparagine		
+ 1 mol NaOH		+ 1 mol HCl
$[\alpha] = -8.64°$	- 5.30°	+ 24.6°

From these results it may be seen that the changes observed agree with the theory, for on ionisation of the COOH group, a reverse change is obtained to that caused by ionisation of the NH_2 group.

Solvent/

Solvent Influence.

Hitherto, very little definite information has been gained concerning the influence of solvents on the rotatory power of an optically active compound. In 1926 Rule and Mitchell noticed certain regularities in the variation of the rotatory power of substituted sec. β-octyl acetates in different solvents. They found (J.C.S. 1926, 127, 3202) that the molecular rotations of the sec. β-octyl esters of methoxy, chloro, bromo and iodoacetic acids gave a similar order of influence for a range of solvents.

On analysis of the results only one definite regularity was discovered. It was found that in the case of the solvents derived from benzene, the relative depressions due to the entry of different substituents into the benzene molecule was given by:-

$$CH_3 < H < OC_2H_5 < Cl < Br < I$$

and this held for all five esters.

The authors noted that this order was almost exactly the reverse of that representing the increase in rotatory power brought about by the substituents when introduced into the molecule

of/

of sec. β-octyl acetate, viz.

$$H < CH_3 < OCH_3 < Cl < Br < I.$$

They suggested that, if the relationship between rotatory power and solvent influence were to be investigated, success would only result if a series of similar solvents were employed, where the character of the molecule undergoes no violent change in passing from member to member. The benzene series mentioned above is of this simple type.

Subsequent to this, several interesting effects of solvents on the rotatory power were noticed by Rule, Bretscher and Spence. In studying the rotatory powers of the substituted menthyl naphthoates, they obtained the following results:-

Table VI /

Table VI.

$[M]^{20}_{5461}$ of substituted menthyl naphthoates (c =5)

Solvent	8-OCH_3 1-COOM	8-NO_2* 1-COOM	2-OCH_3 1-COOM	1-OH 2-COOM	3-OCH_3 2-COOM
C_6H_6	-157°	-841°	+28.9°	-384°	-206°
CS_2	-137	-644	-16.3	-	-191
$(CH_3)_2CO$	-	-	-62.2	-	-
$CHCl_3$	-181	-389	-76.2	-342	-139
C_2H_5OH	-184.5	-806	-	-316	-
ref.	a	a	b	a	a

*This ester was not in a pure state.

References: a - J.C.S., 1929, 133, 2516.

b - J.C.S., 1928, 131, 1493.

The authors concluded that whether the peri or ortho substituent raised or lowered the rotation of the parent ester, the effect tended to be observed to the maximum extent in solvents of low dielectric constant.

Thus it will be seen that this particular field is one which is almost entirely untouched, and which affords a possible opportunity for obtaining further insight into the state of the molecule giving rise to optical activity.

The present thesis deals with an attempt to extend the investigations on substituent influence to compounds of the ether type. The derivatives selected were l-menthyl ethers of the general formula, $C_{10}H_{19}$-O-CH_2X, and also the corresponding phenyl ethers, $C_{10}H_{19}$-O-C_6H_4X, containing substituents in the benzene nucleus.

Further observations were made with a view to examining solvent influence on the rotatory powers of these compounds.

DISCUSSION OF RESULTS.

Discussion of Results.

It has been shown in the Introduction that the insertion of an electronegative group into the acidic radical of an optically active ester normally has the effect of increasing the rotation. This change has been discussed with special reference to the l-menthyl and sec.β-octyl esters of substituted acetic acids, and of p-substituted benzoic acids. The effect of a nitro-group in the ortho-position always leads to an increased rotatory power of the benzoic esters.

a). Ethers of Type $C_{10}H_{19}-O-CH_2X$

Relatively few ethers of menthol have been described hitherto, but in the subjoined table are given a number of rotatory powers for previously known compounds, together with other values obtained in the present research.

Table VII.

Rotations of Ethers $C_{10}H_{19}-O-CH_2X$

X	H *	CH_3 *	C_2H_5 *	C_3H_5 * (Allyl)	$CONH_2$ †
$[M]_D$	-163°	-179°	-183°	-193°	-194°
k x10^{-5} for XCH_2CO_2H	1.8	1.4	1.5	2.1	---

X	$COOCH_3$	C_6H_5 *	$COOC_3H_7$ *	COOH	Cl *
$[M]_D$	-233°	-233°	-234°	-280°	-353°
k x10^{-5} for XCH_2CO_2H	45.1	5.3	45.1	161	155

The rotations refer to the homogeneous ethers at 20°, with the exception of the ether marked †, which was in 5% solution in benzene. Values for ethers marked ※ are from Beilstein's 'Lexicon'. Dissociation constants are from Landolt-Börnstein's 'Tabellen'.

In this series, the order of influence of the groups on the rotatory powers is in approximate agreement with their general polar effect, as deduced from the dissociation constants of the corresponding substituted acetic acids. Hence, in the case of the ethers, as in that of the esters, the general polar influence is the governing factor. It will be noticed that those acidities which can be obtained, run approximately parallel to the molecular rotations. No values can be quoted for the acids $HOOC-CH_2-CONH_2$, $HOOC-CH_2-COOCH_3$ and $HOOC-CH_2-COOC_3H_7$, the value shown in the table for the two latter being that for ethyl hydrogen malonate.

In so far as the rotatory powers in the homogeneous state are concerned, it may be noted that the values fall into the series:-

$CONH_2$ † < $COOCH_3$ < $COOC_3H_7$ < COOH

† In C_6H_6 (c=5)

This arrangement indicates, that when the polar effect of the electronegative carboxyl group is weakened by the introduction of the weakly electropositive alkyl groups, the rotation is lowered. The presence/

presence of the strongly electropositive amino group in the amide still further lowers the rotation.

Table VIII.

Ethers, $C_{10}H_{19}-O-CH_2X$

X	$CONH_2$	$COOCH_3$	$COOC_3H_7$	COOH
$[M]_D$	-194°	-233°	-234°	-280°

Nevertheless, caution must be exercised in interpreting the influence of complex groups of this type. The relative order is, for example, altered when the compounds are examined in solution.

One strongly disturbing factor is the tendency of the carboxylic acid and the amide to undergo association, a tendency which will vary strongly with the solvent. In alcoholic solution, the solvent may become co-ordinated with the carboxyl and amido groups.

It will also be seen that the rotatory power of the benzyl ether is abnormally high in comparison with the dissociation constant of the phenyl substituted acetic acid. This is in keeping with the usual exaltation in optical properties due to the presence of an unsaturated grouping. The same influence is visible to a lesser extent in the value quoted for the allyl compound.

b). Secondary Effect of Ionisation.

An identical effect to that quoted in the Introduction for the ionisation of optically active acids and bases and of acidic and basic esters of optically active alcohols, is found among the optically active ethers as may be seen from the following table:-

Table IX.

X	COONa	COOH	COOH	COOH	COOH	$CONH_2$	$CONH_2$	$CONH_2$
Solvent	C_2H_5OH	C_2H_5OH	C_6H_6	$C_2H_5OH + 4HCl$	Homog.	C_2H_5OH	$C_2H_5OH + 2HCl$	C_6H_6
$[M]_{5461}^{20°}$	-180°	-231°	-239°	-241°	-332°	-243.6°	-245.0°	-230°

Here the influence of ionisation upon the acid in ethyl alcoholic solution is to lower the rotation. This is in agreement with the polar changes involved, since the presence of a negative electrical charge will tend to reverse the normal effect on the asymmetric radical due to the positive pole of the carboxyl group

$$\overset{+-}{-COOH} \longrightarrow \overset{+-\ominus}{-COO}$$

Solution in a non-polar solvent such as benzene raises the rotation above the value in alcohol, while the repression of ionisation in alcohol containing four molecules of hydrogen chloride per molecule of acid, raises it still further. The last change is thus a reversal of that discussed above for the conversion of the acid into/

into the sodium salt. The very high value for the homogeneous acid is probably partly due to molecular association.

In the case of the amide, the rotatory power was also determined in alcohol containing two molecular proportions of hydrogen chloride, in the expectation that salt formation might become evident in a small rise in rotation. It is well known that the basic properties of the group $CONH_2$ are extremely weak. Nevertheless, a very small rise could be confirmed, which was greater than the order of experimental error involved in the determination.

It is interesting to compare the fall in rotation of the above carboxy-compound on ionisation, with that recorded by Rule and Harrower, (J. C. S., 1930,2319.), for the corresponding change for l-menthyl hydrogen malonate. The figures are quoted for alcoholic solution (c ≒ 5) and for the line λ =5461.

Table X.

Acid	Acid $[M]^{20^\circ}_{5461}$	Salt $[M]^{20^\circ}_{5461}$	Δ
$C_{10}H_{19}$-O-OC-CH_2-COOH	-193°	-185°	8
$C_{10}H_{19}$-O-CH_2-COOH	-231°	-180°	51

Hence, in agreement with theory, the result of moving the carboxyl group one atom nearer the asymmetric complex is to increase greatly the magnitude of the change on ionisation.

c). Ethers of the Type, $C_{10}H_{19}-O-C_6H_5$.

The substituted phenyl l-menthyl ethers are not strictly comparable with the aliphatic derivatives discussed above and are therefore discussed separately. Including the compounds of this type described in the experimental section of this thesis only four representatives are known, viz., the benzyl, phenyl, picryl and 2:4-dinitrophenyl ethers. In spite of numerous attempts under varying conditions it was not found possible to prepare the 2:6-dinitrophenyl ether or any of the mononitro compounds. Since the halides corresponding to l-menthol are not available it was necessary to use sodium or potassium menthoxide as the starting material in all these preparations, and in the case of the halogenated benzenes containing only one nitro group it appeared that the activation of the halogen was relatively small. Consequently, other by-reactions were favoured, especially the formation of azoxy compounds.

The rotatory powers are summarised in the following table:-

Table XI.

Aromatic l-Menthyl Ethers of the Type, $C_{10}H_{19}-O-X$

X	*$CH_2C_6H_5$	C_6H_5	$C_6H_3(NO_2)_2$	$C_6H_2(NO_2)_3$
$[M]_D$	-233°	-301°	-149°	-1082°
	Homog. in C_6H_6 (c=5)	in C_6H_6 (c=5)	in C_6H_6 (c=5)	

* Tschugaeff, (J. Russ, Phys.Chem.Soc. 34, 611.).

Although a rotation is quoted for the 2:4-dinitrophenyl ether, the value cannot be used in estimating the effect of the substituent group, as this ether differs from the other compounds in exhibiting a strongly anomalous dispersion. This peculiarity is discussed in more detail later.

A comparison of the benzyl and phenyl ethers shows that as was to be expected the increased rotatory power caused by the introduction of the phenyl group rises still further when the phenyl group is moved nearer to the menthyl complex. In agreement with the exaltation caused by the introduction of electronegative groups into the aliphatic ethers, it is found that the powerfully electronegative picryl radical produces an enormous rise in rotation. Thus the molecular rotation of the phenyl ether, -301°, becomes -1082° in the s-trinitro derivative. A similar remarkable influence of the picryl group has been observed by Peacock, (Proc. C.S., 1914, 30, 275.), in the case of cinchonine, ([M] D +165°, in acetone) and picryl cinchonine ([M]D -1968°, in acetone).

These results therefore lead to the conclusion, that, as in the case of the esters, the influence of substituents on the rotatory power of l-menthyl ethers largely depends on the polarity of the substituent. The higher the electronegative polarity of the group introduced, the higher is the rotatory power/

power of the ether. The comparison holds for aliphatic, as well as for aromatic esters and ethers, although the evidence for aromatic ethers depends only on the properties of the picryl compound. Whether the introduction of chlorine or methoxyl into the ortho position in the phenyl nucleus will bring about a diminution in rotation, as has been observed in the ortho substituted benzoates, has yet to be determined.

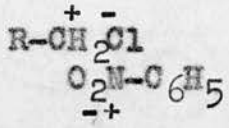
d). Influence of Solvents.

If an electronegative substituent be introduced into the acid radical of an ester of l-menthol or β-octanol, or into the second hydrocarbon residue in an l-menthyl ether, the general effect is a rise in the rotatory power. We may discuss in more detail the manner in which the rotatory power may be affected by the presence of solvents.

For the present purpose the mutual influence of solvent upon solute can be regarded from two points of view, viz:, (a) the changes due to the variable polarity of the solvent and (b) those caused by the variable polar substituents in the solute.

According to Debye the presence of a dipole in a compound will lead to dipole association, the positive end of one dipole being attracted by the negative/

negative end of a second (and vice versa), as represented in the following diagram:-



This association will diminish the internal electrical field exerted by each of the polar substituents on the organic radical to which they are united. Thus if the chloro compound in the above diagram is an optically active substance, it is to be expected that dipole association with a polar solvent will tend to neutralise the characteristic effect of the chlorine substituent on the rotatory power.

This effect should be more marked for solvents of high polarity, less for solvents of lower polarity and should produce least change in solvents of zero polarity. Thus, for an active compound in which the rotation has been raised to a high value by an electronegative substituent, the rotation should be highest in non-polar solvents such as benzene, where no neutralisation of charge occurs; and lowest in highly polar solvents such as nitrobenzene, where the maximum neutralisation occurs.

Further, the more polar the substituent or substituents in the optically active compound, the greater is the influence on the optical rotatory power and the greater will be the changes undergone in/

in the presence of solvents. And, in the limiting case of an optically active substance with no polar substituent, the same rotations may be expected in all solvents whether of low or of high polarity.

These generalisations may be applied to the ethers which are the subject of this thesis, although in view of our almost negligible knowledge of solvent action in connection with optical activity, it appears certain that other as yet undetermined factors also enter into the problem.

Both of the above effects may be illustrated by the values obtained for the rotatory powers of l-menthyl picryl ether and l-menthyl methyl ether in various solvents. In the following tables the solvents are arranged in order of decreasing dipole moments.

Table XII.

Table XII.

Solvent Action on l-Menthyl Picryl and Methyl Ethers.

Solvent.	$[M]_{5461}^{20}$ Picryl Ether.	$[M]_{5461}^{20}$ Methyl Ether.	$\mu x 10^{18}$
CH_3CN	-1075	-197.3	3.94
CH_3NO_2	-1100	-191.3	3.78
CH_3OH	-1139	-198.7	1.64
CH_3Cl	-1403	-191.0	1.61
CH_3I	-1420	-190.3	1.60
$CHBr_3$	(-1597)	-188.2	1.30
$CHCl_3$	-1527	-189.3	1.10
CH_3COOH	-1248	-198.9	~~0.74~~ 1.4
CS_2	-1597	-216.0	0
CCl_4	-1541	-195.1	0
C_6H_{14}	(-1489)	-194.6	0
$C_6H_5NO_2$	-1306	-189.3	3.90
C_6H_5CN	-1222	-192.7	3.85
C_6H_5CHO	-1277	-193.2	2.75
C_6H_5Br	-1417	-191.5	1.56
C_6H_5I	-1472	-195.3	1.25
$C_6H_5OCH_3$	-1361	-196.8	1.16
$C_6H_5CH_3$	-1384	-192.3	0.40
C_6H_6	-1384	-195.0	0
$(C_6H_5NH)_2$	-	(-173.5)	(1.51)

In the case of the picryl ether containing strongly polar groups, a marked change is observed on passing from polar to non-polar solvents. Thus the rotation rises steadily from -1075° in acetonitrile to reach maximum values of -1597° and -1541° in carbon disulphide and carbon tetrachloride, both of zero dipole moment. A high value is also obtained in bromoform. The variations are somewhat smaller in aromatic solvents although here again the lowest rotatory powers are observed for the three most polar liquids examined, namely nitrobenzene, benzonitrile and benzaldehyde.

The molecular rotation of the methyl ether only undergoes relatively small variations with change of solvent. If we except aniline which appears to form a highly coloured complex with the solute, the maximum observed range only amounts to 7.5 degrees for the aromatic solvents employed, and to 28 degrees for the aliphatic compounds. In neither case is there any sign of a relationship between the polarity of the solvents and the change in rotation.

The results obtained for the l-menthyl phenyl ether are summarised in Table XIII.

Table XIII.

Solvent Action on *l*-Menthyl Phenyl Ether.

c = 1%; l = 1 dm.; t = 20°. $\alpha \doteq 1.5°$

Solvent	$[M]_{5461}^{20}$	$\mu \times 10^{18}$
$C_6H_5NO_2$	- 302°	3.90
C_6H_5CN	- 316°	3.85
C_6H_5CHO	- 348°	2.75
C_6H_5Br	- 344°	1.56
$C_6H_5NH_2$	- 367°	1.51
C_6H_5I	- 348°	1.25
$C_6H_5OCH_3$	- 334°	1.16
$C_6H_5CH_3$	- 336°	0.40
C_6H_6	- 353°	0
CH_3CN	- 350°	3.94
CH_3OH	- 370°	1.64
CH_2Cl_2	- 371°	1.61
CH_3I	- 359°	1.60
$CHCl_3$	- 338°	1.10
CH_3COOH	- 371°	0.74
CS_2	- 368°	0
CCl_4	- 328°	0
C_6H_{14}	- 348°	0

In this case the variations in molecular rotation are also small, although somewhat greater than those recorded for the methyl ether. The rotatory powers in the benzene solvents give evidence of a polar influence, the lowest values being again exhibited in the two most polar liquids, nitrobenzene and benzonitrile. No regularities can be traced among the aliphatic solvents.

The dispersion of the 2:4-dinitrophenyl ether has already been shown to be anomalous. This compound cannot therefore be discussed in connection with the ethers showing normal dispersion, but is treated in detail in the section on dispersion.

It may therefore be concluded that solvent influences among the l-menthyl ethers under discussion lends some support to the theoretical views expressed on page 37, although the predicted agreements are subject to a number of exceptions.

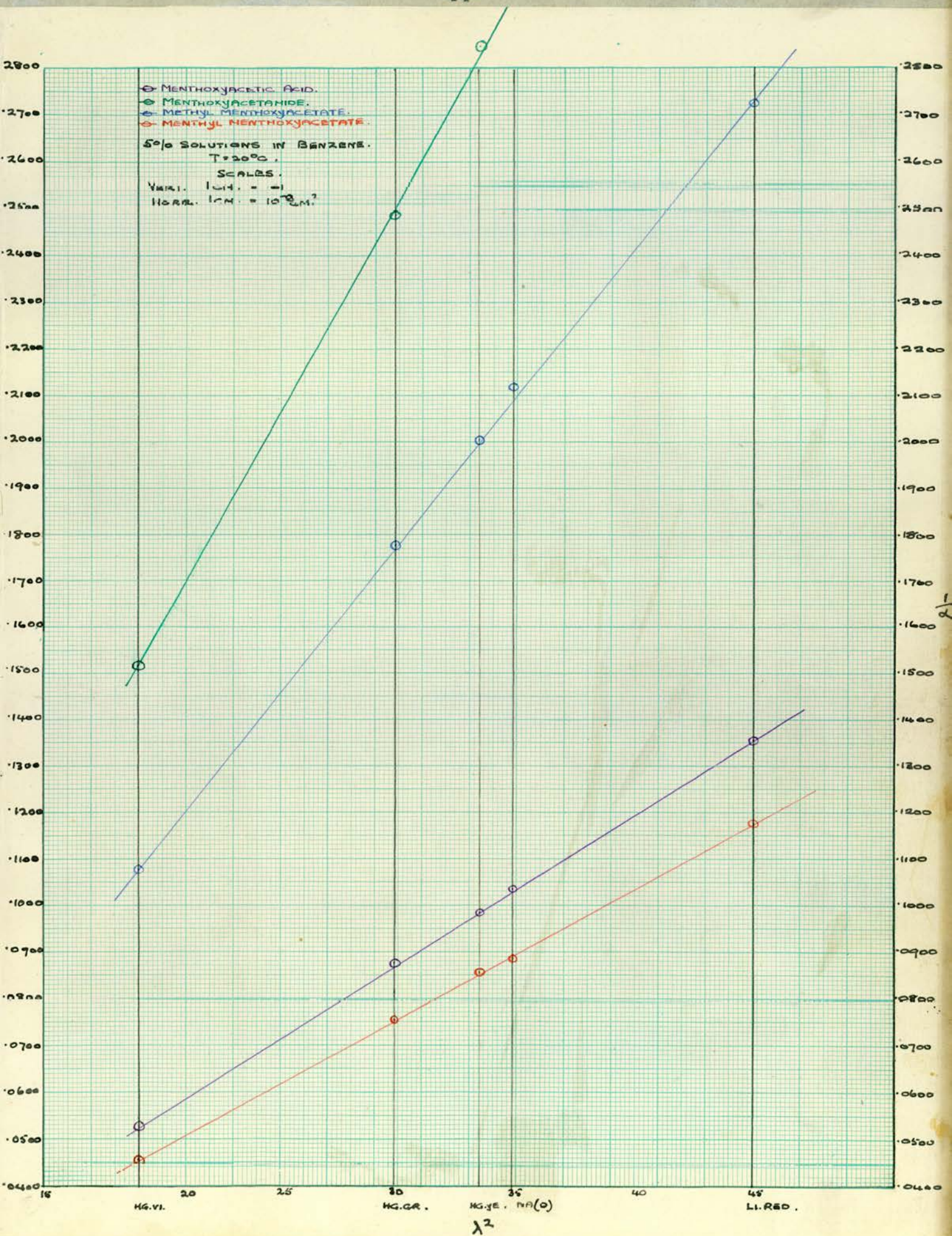
Dispersion.

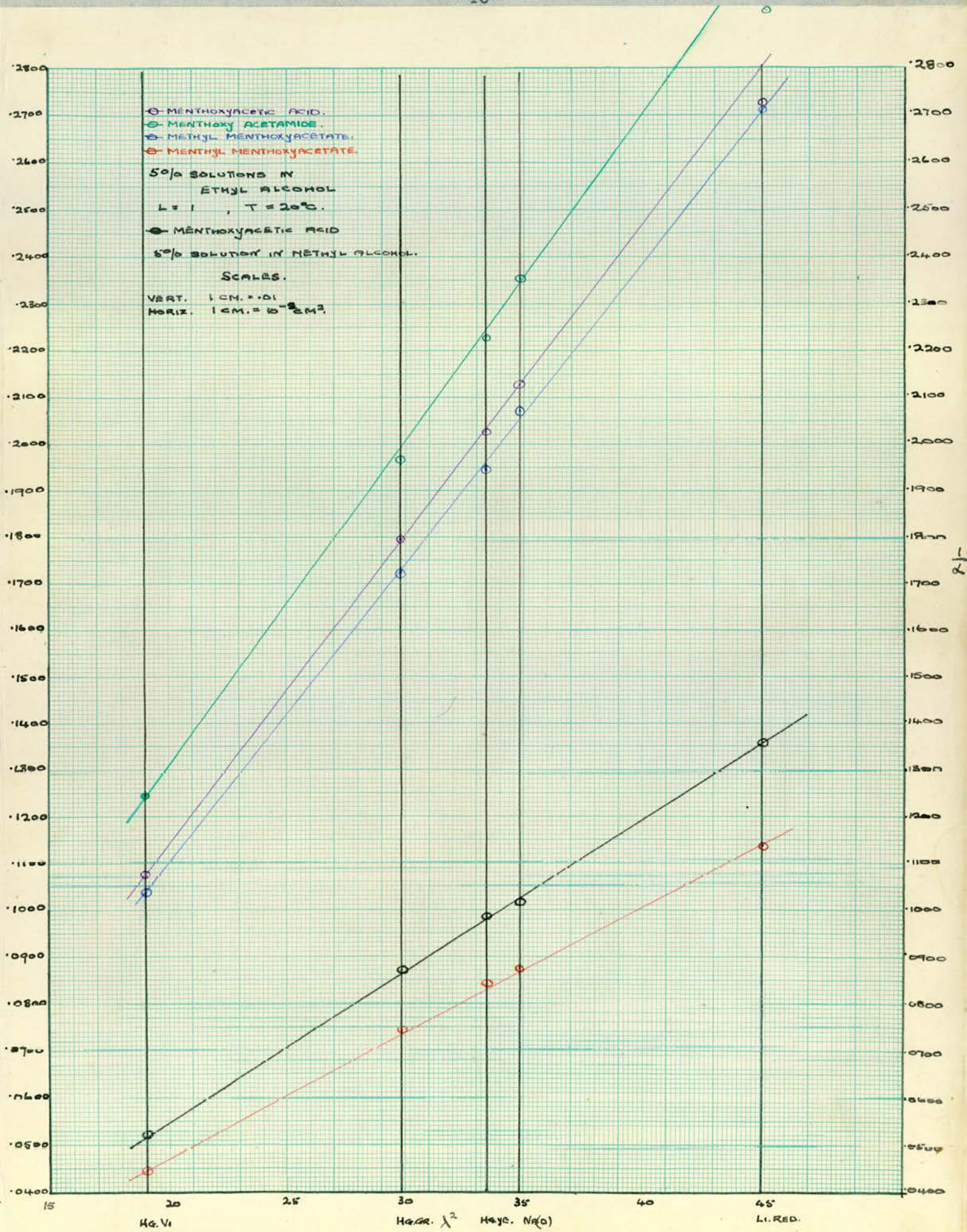
The dispersion of l-menthoxyacetic acid and its derivatives was found to be normal and simple in all solvents in which the compounds were examined, as is shown by the graphs herewith.

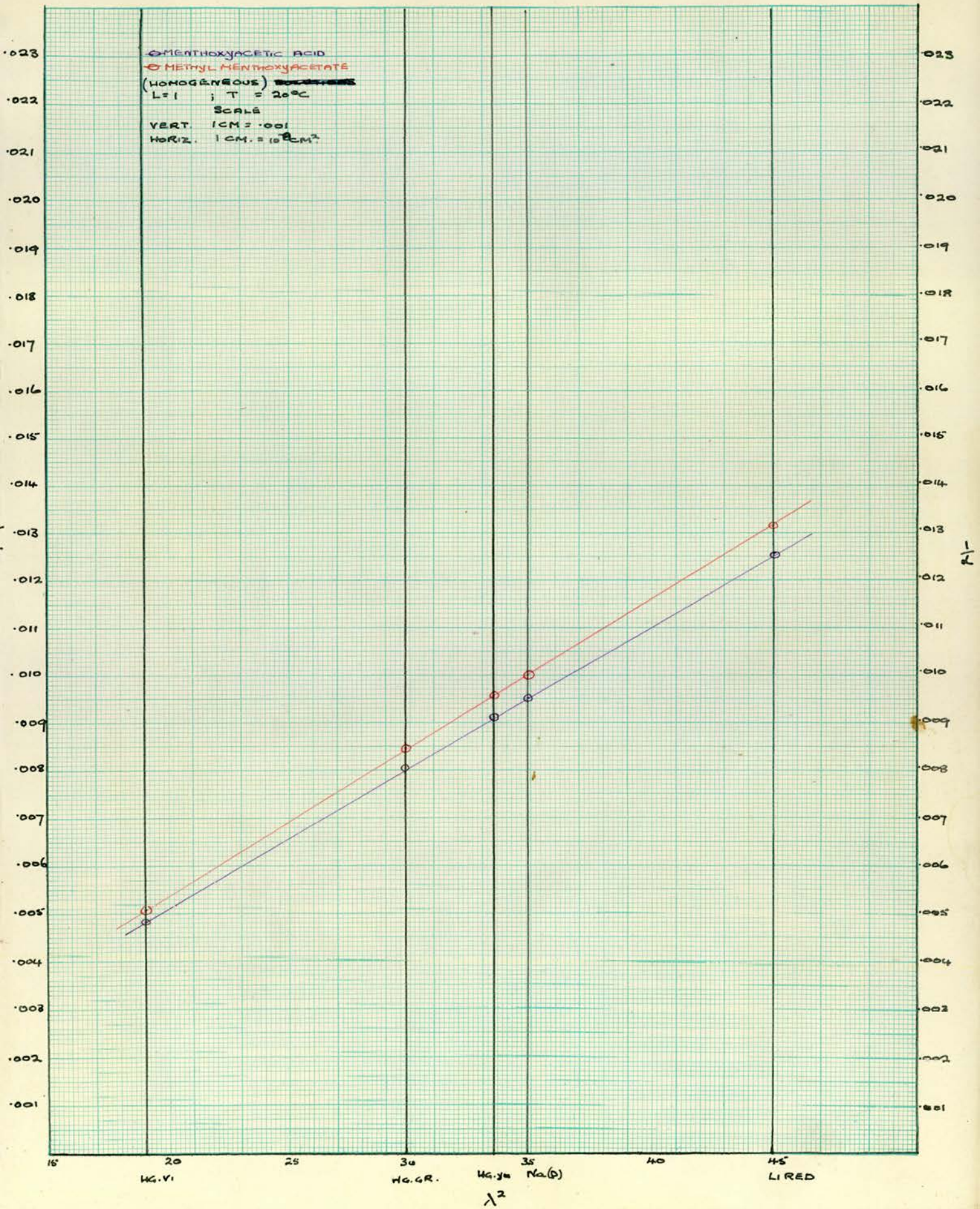
l-Menthyl picryl ether was examined in benzene and in acetone and was also found to exhibit simple dispersion, as was the case with l-menthyl phenyl ether, and l-menthyl methyl ether.

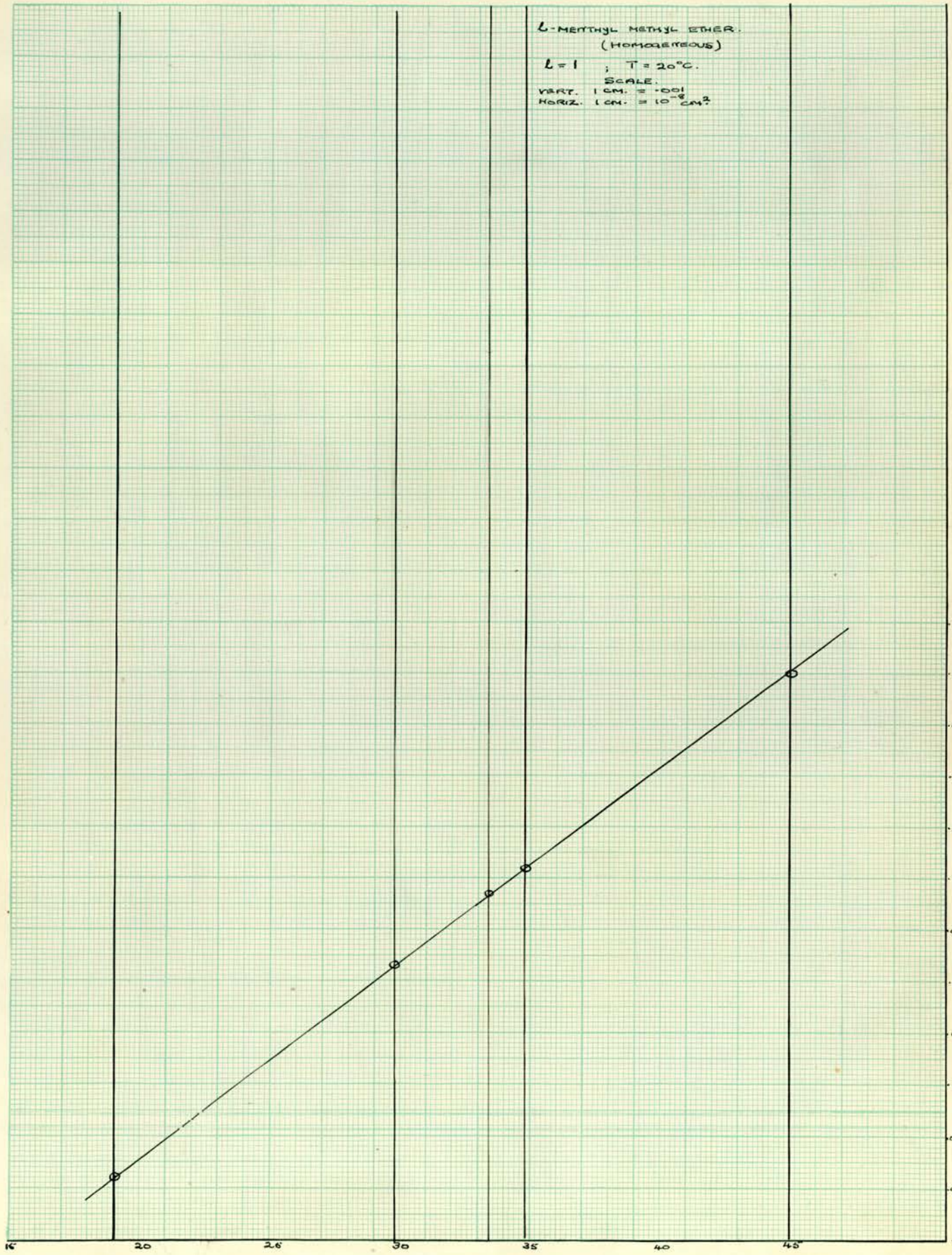
On the other hand, when the dispersion of l-menthyl 2:4-dinitrophenyl ether was examined in benzene, it was found to be highly anomalous. For example, the molecular rotation of this ether for λ =5461 was found to be - 155°, while for λ =4359 it was + 70°. In alcohol and in acetone solutions, the dispersion was still anomalous, but the rotations for the violet line had now become negative in sign. Accordingly an extended examination of the dispersion was made for two series of solvents, derived from benzene and methane respectively. In the case of the benzene solvents the combined effect of the trace of colour in most of the solvents, together with the yellow colour of the ether made it impossible to obtain values for λ 4359. The values for the rotatory powers are repeated in the following summary, which clearly shows the gradual change from anomalous to normal dispersion as the polarity of the solvent is increased.

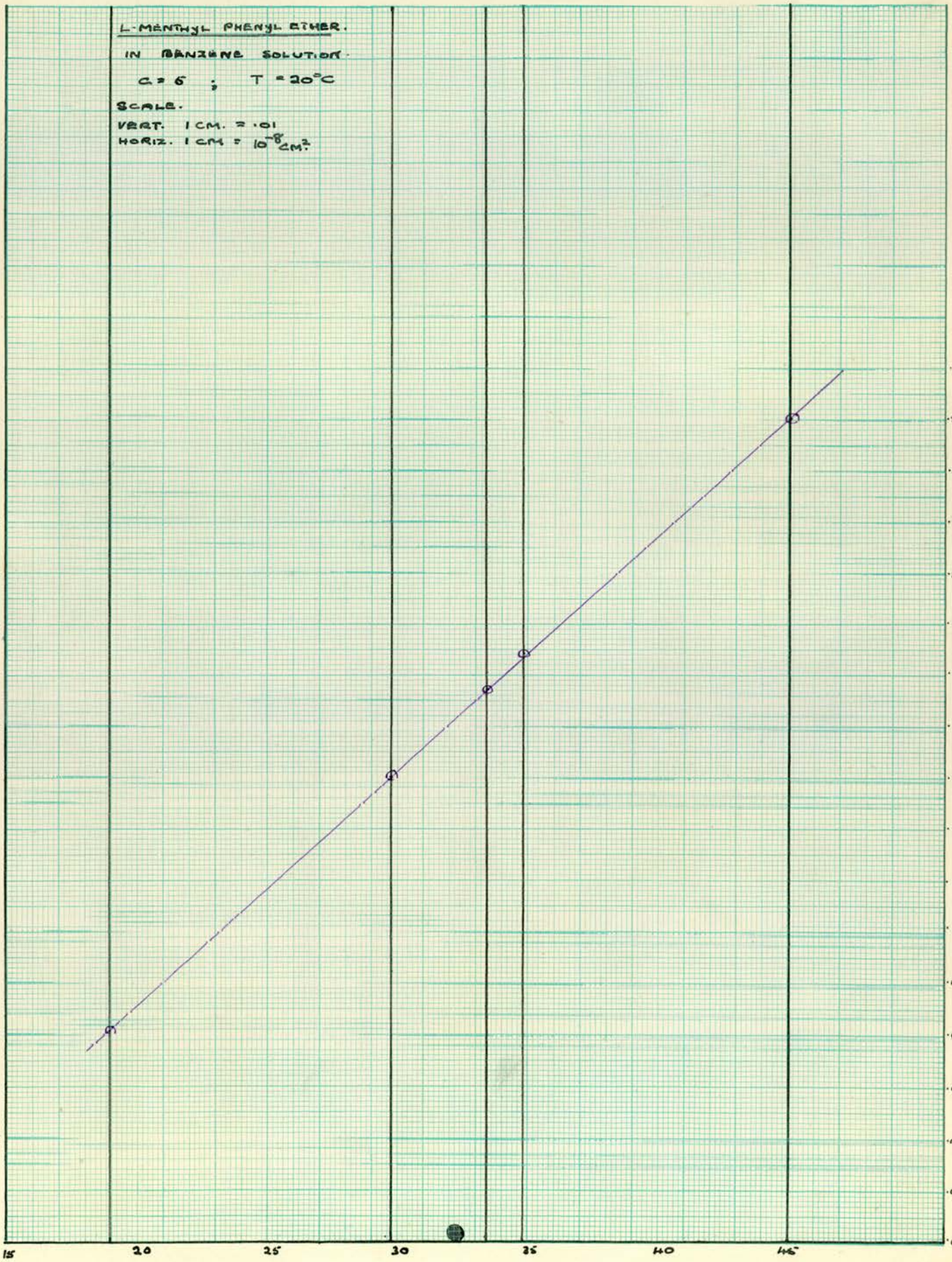
Table XIV./


MENTHOXYACETIC ACID.
MENTHOXYACETANIDE.
METHYL MENTHOXYACETATE.
MENTHYL MENTHOXYACETATE.
5% SOLUTIONS IN BENZENE.
T = 20°C.
SCALES.
VERT. 1cm. = -1
HORIZ. 1cm. = 10^8 cm.^2
2800
2700
2600
2500
2400
2300
2200
2100
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
0900
0800
0700
0600
0500
0400
1/λ
16
20
25
30
35
40
45
HG.VI.
HG.GR.
HG.YE. NA(D)
LI.RED.
λ^2


MENTHOXYACETIC ACID.
MENTHOXY ACETAMIDE.
METHYL MENTHOXYACETATE.
MENTHYL MENTHOXYACETATE.
5% SOLUTIONS IN ETHYL ALCOHOL
L = 1 , T = 20°C.
MENTHOXYACETIC ACID
5% SOLUTION IN METHYL ALCOHOL.
SCALES.
VERT. 1 CM. = .01
HORIZ. 1 CM. = 10⁻⁸ CM².
·2800
·2700
·2600
·2500
·2400
·2300
·2200
·2100
·2000
·1900
·1800
·1700
·1600
·1500
·1400
·1300
·1200
·1100
·1000
·0900
·0800
·0700
·0600
·0500
·0400
15
20
25
30
35
40
45
Hg. Vi
Hg. Gr. λ²
Hg. Ye. Na(D)
Li. Red.
1/α


⊖MENTHOXYACETIC ACID
⊖METHYL MENTHOXYACETATE
(HOMOGENEOUS)
L=1 ; T = 20°C
SCALE
VERT. 1CM = ·001
HORIZ. 1 CM. = 10 CM²
·023
·022
·021
·020
·019
·018
·017
·016
·015
·014
·013
·012
·011
·010
·009
·008
·007
·006
·005
·004
·003
·002
·001
1/ρ
16
20
25
30
35
40
45
HG.VI
HG.GR.
HG.yw
Na(D)
LI RED
λ²


l-MENTHYL METHYL ETHER.
(HOMOGENEOUS)
l = 1 ; T = 20°C.
SCALE.
VERT. 1 CM. = ·001
HORIZ. 1 CM. = 10^{-8} CM^2
·0170
·0160
·0150
·0140
·0130
·0120
·0110
·0100
·0090
·0080
·0070
·0060
·0050
$\frac{1}{\lambda^2}$
15
20
25
30
35
40
45
HG. VI.
HG. QR.
λ^2 HGYE. NA(D)
LI. RED.


L-MENTHYL PHENYL ETHER.
IN BENZENE SOLUTION.
c = 6 ; T = 20°C
SCALE.
VERT. 1 CM. = ·01
HORIZ. 1 CM = 10⁻⁸ CM²
·2100
·2000
·1900
·1800
·1700
·1600
·1500
·1400
·1300
·1200
·1100
·1000
·0900
·0800
·0700
·0600
·0500
·0400
15
20
25
30
35
40
45
HG.VI
HGGR.
YE
nm(o)
LIRED.
λ²

L-MENTHYL PICRYL ETHER (IMPURE)

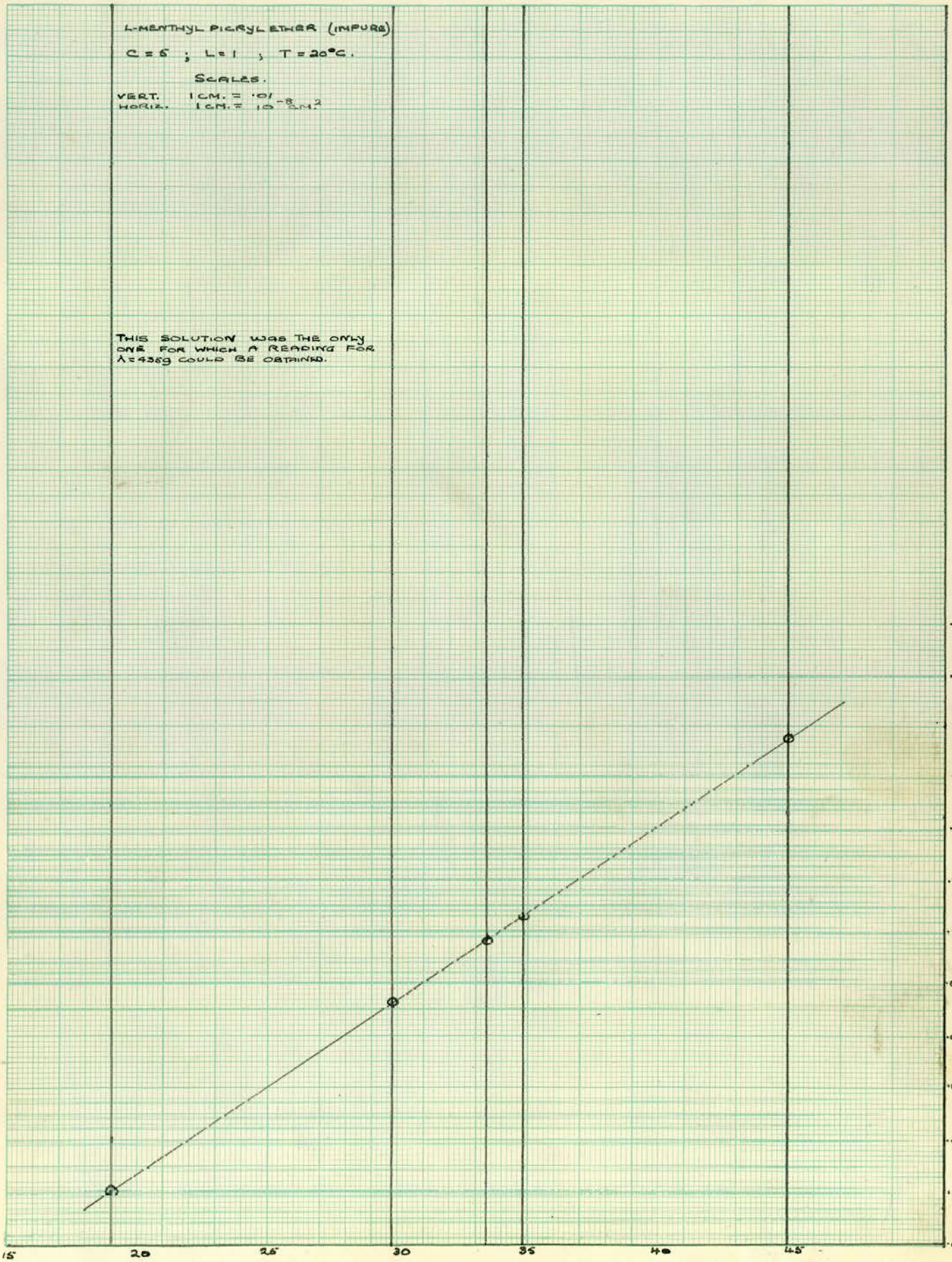
C = 5 ; L = 1 ; T = 20°C.

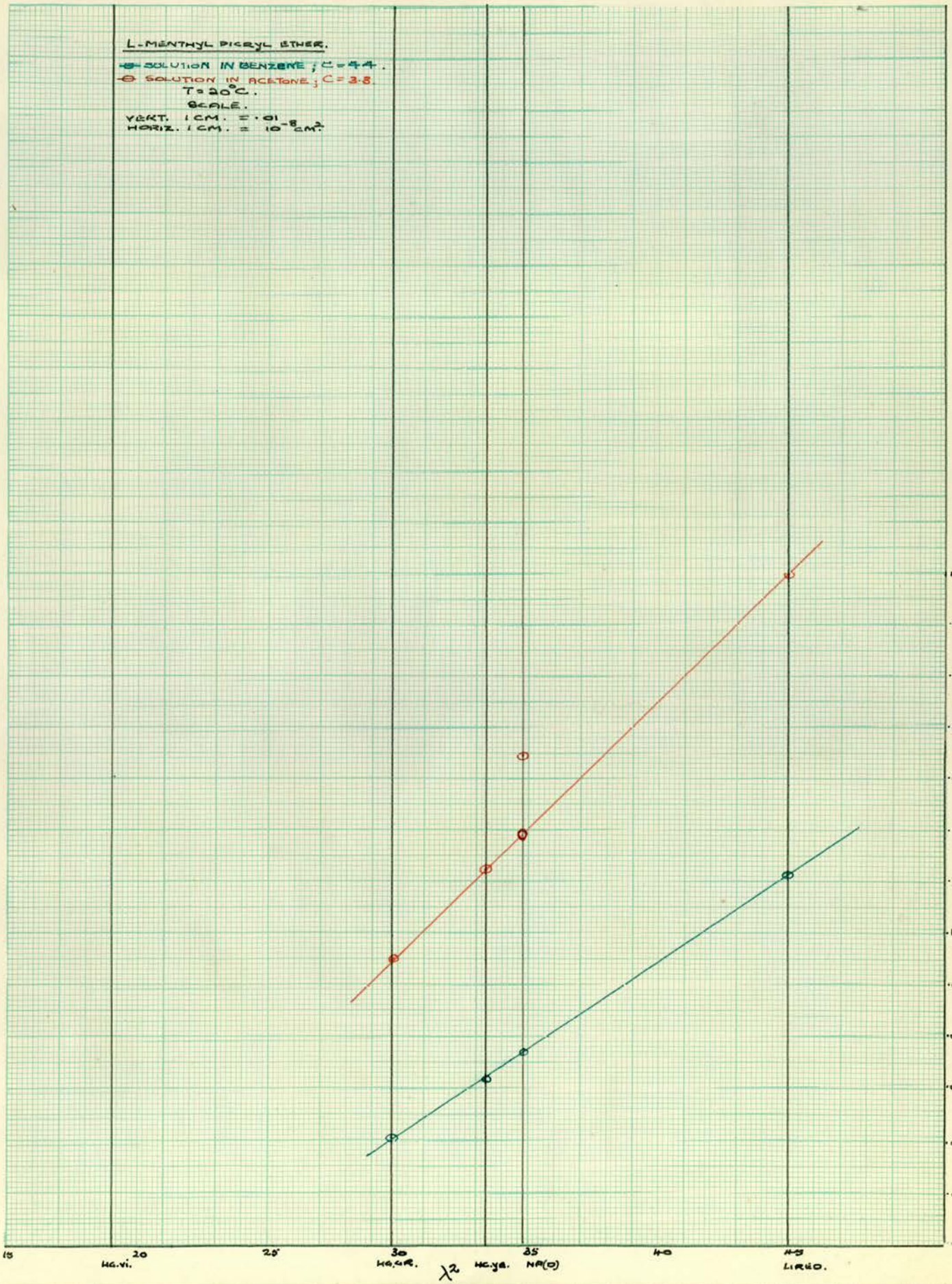
SCALES.

VERT. 1 CM. = ·01

HORIZ. 1 CM. = 10^{-8} SQ.CM.

THIS SOLUTION WAS THE ONLY ONE FOR WHICH A READING FOR λ = 4358 COULD BE OBTAINED.




L-MENTHYL PICRYL ETHER.
⊕ SOLUTION IN BENZENE; C = 4·4.
⊖ SOLUTION IN ACETONE; C = 3·8.
T = 20°C.
SCALE.
VERT. 1 CM. = ·01
HORIZ. 1 CM. = 10^{-8} CM.^{2}
1/λ
λ²
HG.vi.
HG.viR.
HG.yB.
NA(D)
LIREO.

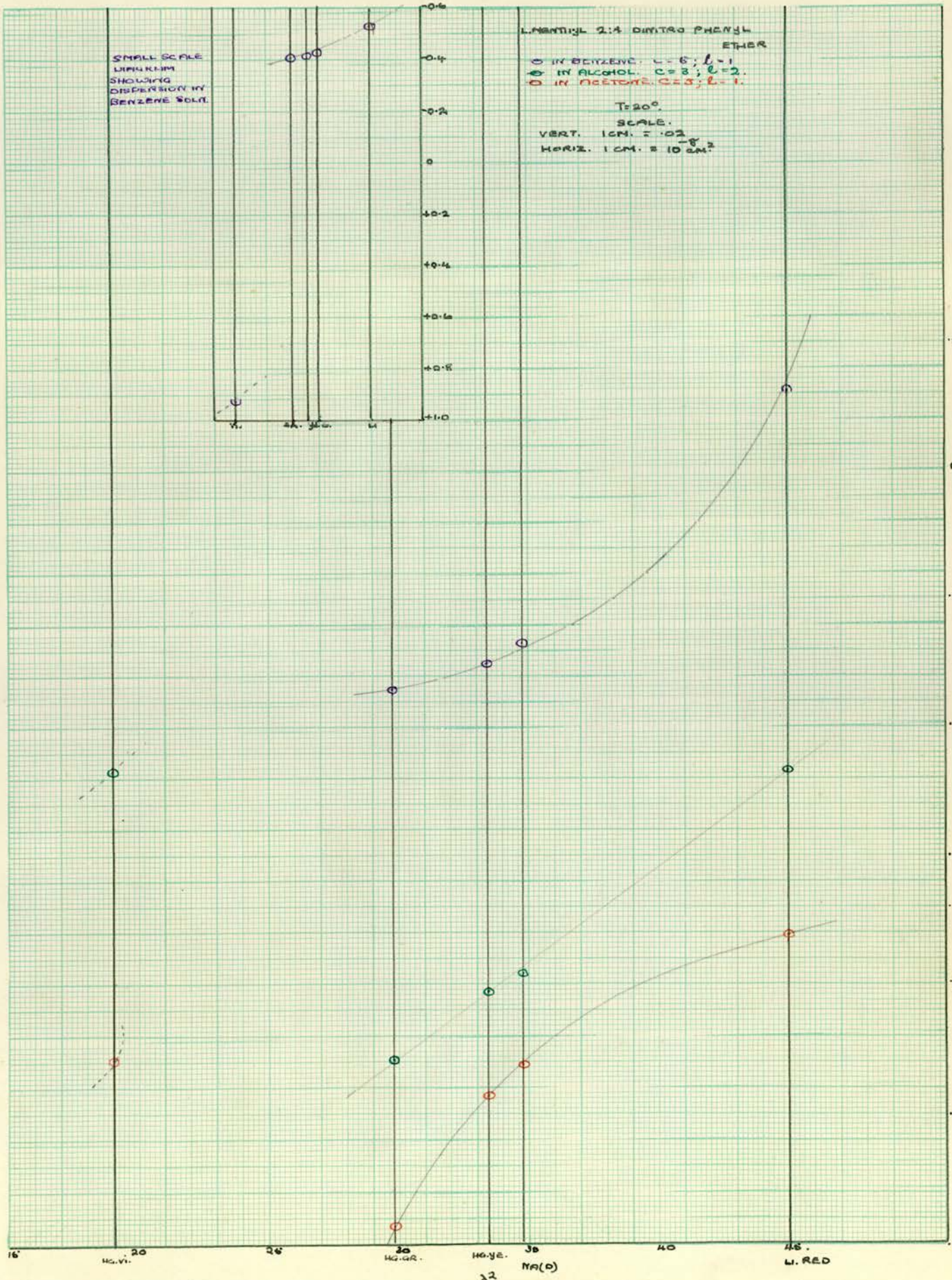

SMALL SCALE DISPERSION SHOWING DISPERSION IN BENZENE SOLN.
L-MENTHYL 2:4 DINITRO PHENYL ETHER
IN BENZENE. C = 6 ; l = 1
IN ALCOHOL. C = 3 ; l = 2.
IN ACETONE. C = 3 ; l = 1.
T = 20°.
SCALE.
VERT. 1 CM. = ·02
HORIZ. 1 CM. = 10 $\frac{-8}{cm^2}$
+0·6
+0·4
+0·2
0
+0·2
+0·4
+0·6
+0·8
+1·0
·55
·50
·45
·40
·35
·30
·25
·20
16
20
24
30
36
40
46
HG. VI.
HG. GR.
HG. YE.
NA(D)
LI. RED
λ^2

Table XIV.

Solvent Action on l-Menthyl 2:4-Dinitrophenyl Ether.

Solvent	λ =4358	4940	5461	5780	$\mu \times 10^{18}$
$C_6H_5NO_2$	-	-236.7	-220.6	-209.2	3.90
C_6H_5CN	-	-249.6	-241.5	-233.4	3.85
C_6H_5CHO		-264.0	-233.4	-223.8	2.75
C_6H_5Br	(+53.13)	-135.2	-151.3	-146.5	1.56
C_6H_5I	-	-125.7° ~~-156.1~~	-161.0	-156.2	1.25
$C_6H_5OCH_3$	-	-161.0	-165.8	-153.0	1.16
$C_6H_5CH_3$	(+67.6)	-112.7	-133.7	-128.8	0.40
C_6H_6	(+80.5)	-109.5	-136.9	-132.0	0
CH_3CN	(-365.5)	-359.0	-301.0	-276.9	3.94
CH_3OH	(-209.2)	-273.6	-264.0	-238.3	1.64
CH_2Cl_2	(-209.2)	-299.4	-264.0	-246.3	1.61
CH_3I	(-241.5)	-204.5	-206.1	-188.4	1.60
$CHCl_3$	(-289.8)	-293.0	-259.2	-241.5	1.10
CH_3COOH	(-72.4)	-297.9	-272.0	-249.6	0.74
C_6H_{14}	-28.98	-154.5	-193.2	-173.9	0 *
CS_2	(-38.6)	-132.0	-159.3	-153.0	0
CCl_4	+27.36	-144.9	-162.6	-154.5	0

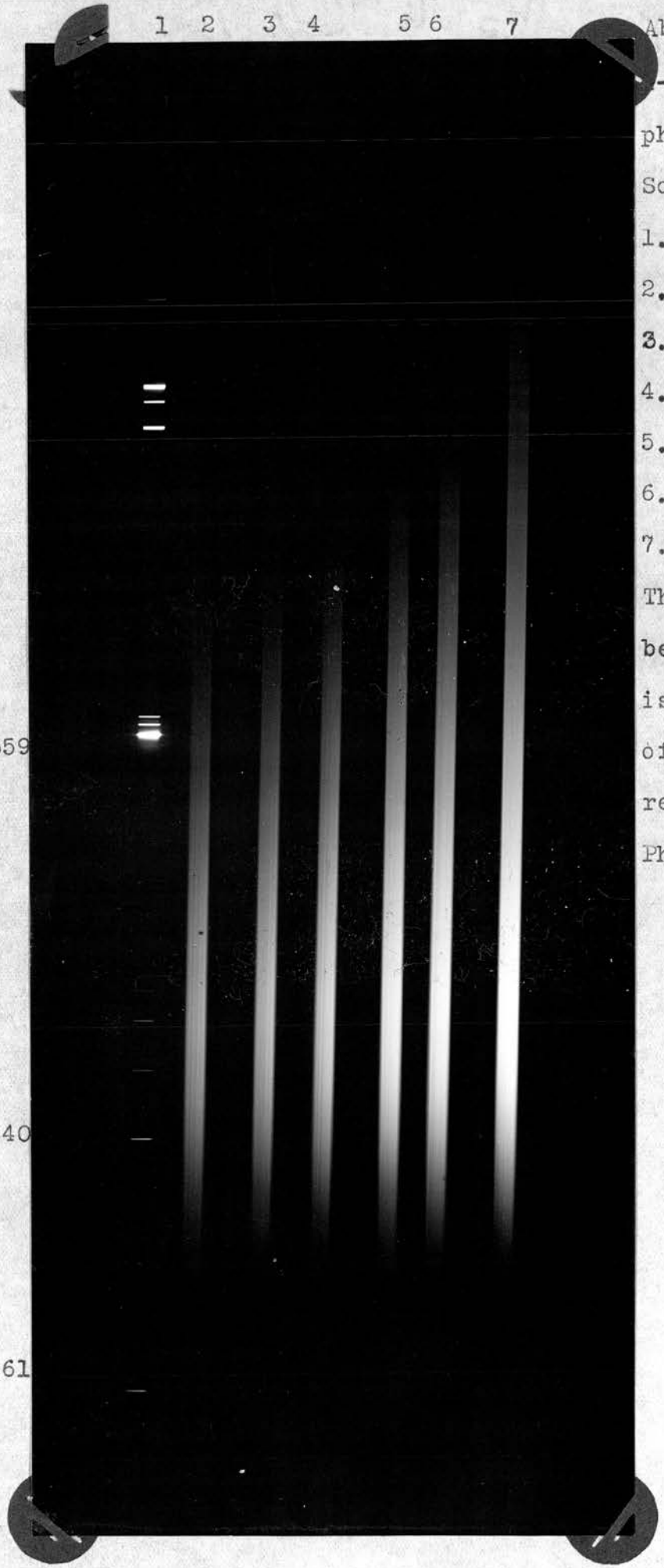
* $c = 1/2\%$ $l = 2$ dm.

Bracketed values are approximate, owing to partial absorption.

The usual causes of anomalous dispersion are (i) the presence of an absorption band in the spectrum of the compound in the region of the wavelength employed for the determination of the rotatory power; (ii) the presence of two centres of asymmetry having opposite signs of rotation and different dispersion ratios and (iii) a low rotatory power lying in the neighbourhood of the zero axis.

In the case of the 2:4-dinitrophenyl ether the last cause appears to be absent as the molecular rotation of the compound is comparatively high.

In order to examine the second possibility, the absorption spectrum of the compound in acetone was determined. Although the rotatory power is anomalous under these conditions, there is no evidence of any definite absorption band over the range of wavelength employed (up to the neighbourhood of λ =4359). If the anomaly had been associated with the presence of an absorption band, it would also have been expected to be even more pronounced in the trinitrophenyl ether, which, however, actually exhibits normal and simple dispersion.



Absorption Spectra of -Menthyl 2:4-Dinitrophenyl Ether. Acetone Solution, 2 %.

1. Hg lamp control.
2. 4 cm. solution
3. 3 cm. "
4. 2 cm. "
5. 1 cm. "
6. ½ cm. "
7. Control, 1 cm Aceton

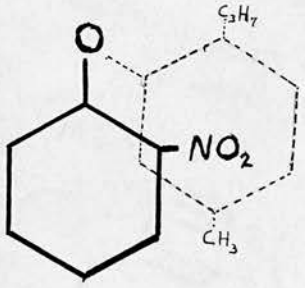
The weakness of the bands between 5461 and 4940 is due to the inactivity of the plate in this region. See next Photograph.

Absorption Spectra of l-Menthyl 2:4-Dinitrophenyl Ether, 2 % solution in acetone.(Panchromatic Plate)

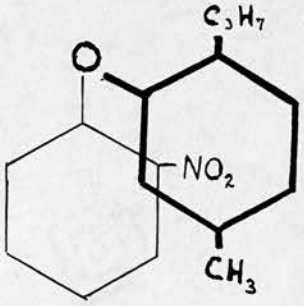
1. 4.5 cm. solution, Hg lamp.
2. 0.5 cm. solution, Hg lamp.
3. Hg lamp control.
4. 0.5 cm. solution, Tungsten lamp.
5. 1.5 cm. solution, " "
6. 3.0 cm. solution, " "
7. 4.5 cm. solution, " "
8. Control, 1 cm. acetone.

There remains the first suggestion that the anomaly is due to the existence of an additional centre of asymmetry. This is not at all improbable in view of the recent discovery of optical isomerism in derivatives of diphenyl and other similar compounds, in which the blocking of free rotation round a bond permits the occurrence of enantiomorphous forms in substances which were formerly thought to be symmetrical.

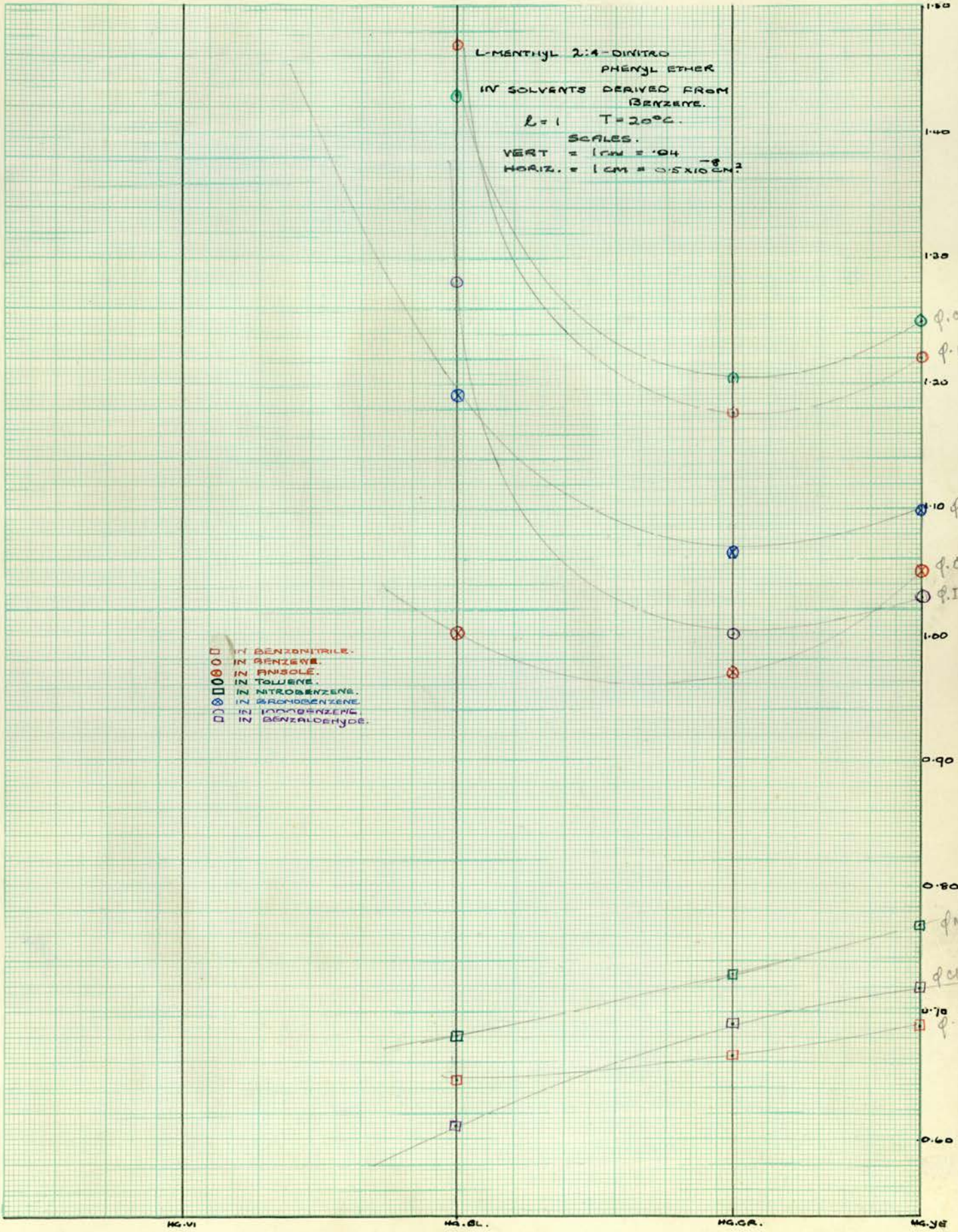
Now, the investigation of dipole moments has lead Debye to conclude that the oxygen bonds in ethers form an angle with one another, probably similar in magnitude to that subtended by carbon bonds. In this case it is possible that the l-menthyl 2:4-dinitrophenyl ether may exist as an equilibrium mixture of two mirror image forms, especially if the nitro group in the ortho position exerts an electrical attraction on the menthyl complex.

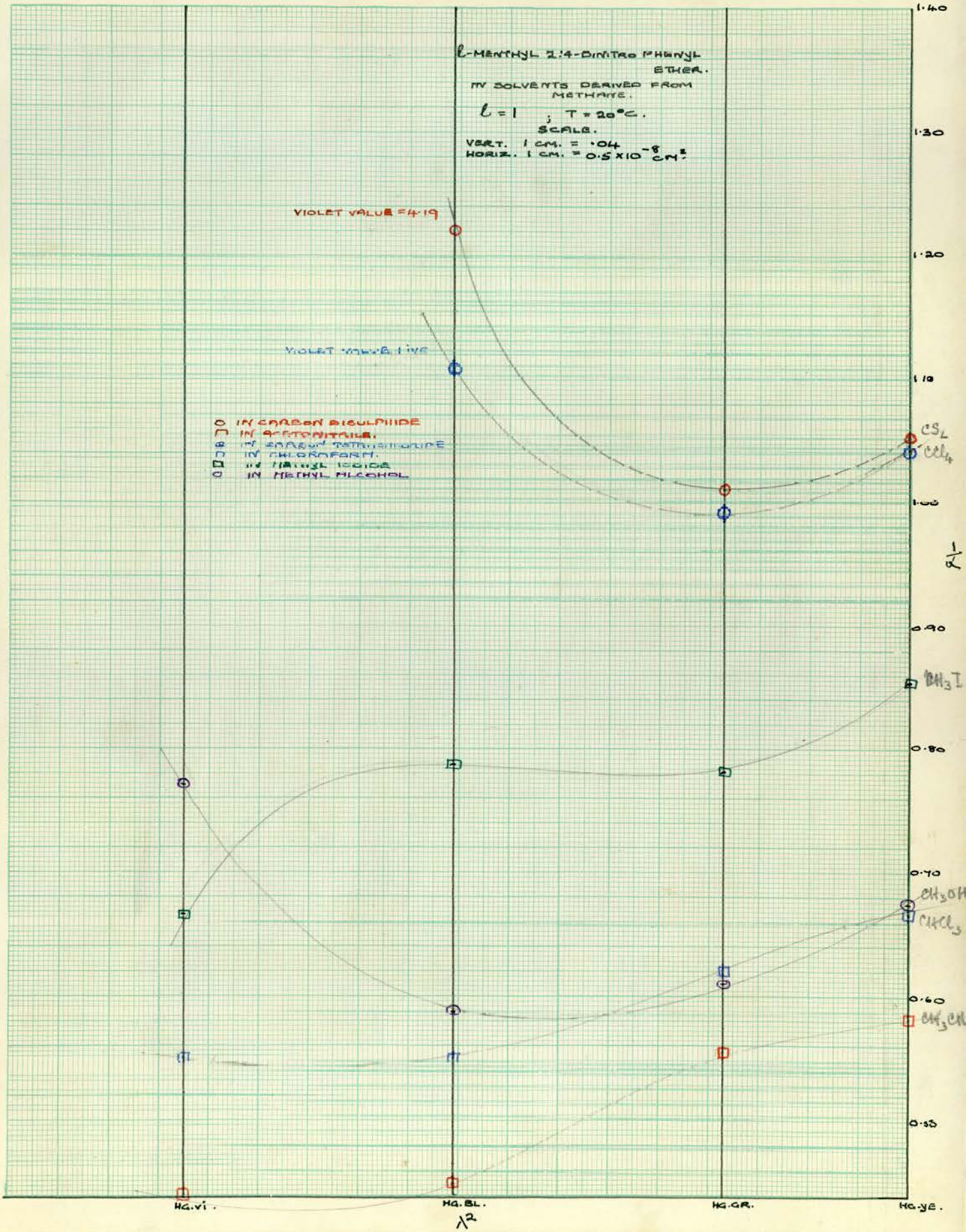


Menthyl radical behind nitro group.



Menthyl radical in front of nitro group.

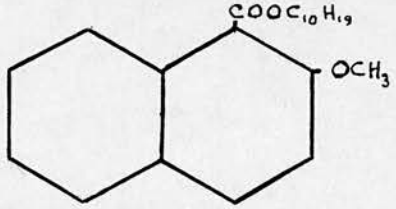

L-MENTHYL 2:4-DINITRO PHENYL ETHER
IN SOLVENTS DERIVED FROM BENZENE.
ℓ = 1 T = 20°C.
SCALES.
VERT = 1 CM = ·04
HORIZ. = 1 CM = 0·5 X 10⁻⁸ CM²
IN BENZONITRILE.
IN BENZENE.
IN ANISOLE.
IN TOLUENE.
IN NITROBENZENE.
IN BROMOBENZENE.
IN IODOBENZENE.
IN BENZALDEHYDE.
1·50
1·40
1·30
1·20
1·10
1·00
0·90
0·80
0·70
0·60
HG.VI
HG.BL.
HG.GR.
HG.YEL
λ²


l-MENTHYL 2:4-DINITRO PHENYL ETHER.
IN SOLVENTS DERIVED FROM METHANE.
l = 1 ; T = 20°C.
SCALE.
VERT. 1 CM. = ·04
HORIZ. 1 CM. = 0·5 X 10⁻⁸ CM²
VIOLET VALUE = 4·19
VIOLET VALUE 1 IVE
IN CARBON BISULPHIDE
IN ACETONITRILE.
IN CARBON TETRACHLORIDE
IN CHLOROFORM.
IN METHYL IODIDE
IN METHYL ALCOHOL
CS₂
CCl₄
CH₃I
CH₃OH
CH₂Cl₂
CH₃CN
1·40
1·30
1·20
1·10
1·00
0·90
0·80
0·70
0·60
0·50
1/λ
Hg.vi.
Hg.BL.
Hg.GR.
Hg.ye.
λ²

In the latter event the ether will exist in the form of a mixture of unequal amounts of the l-menthyl-l-isomeride and the l-menthyl-d-isomeride, of which the latter will probably possess anomalous dispersion (cf. l-menthyl d-camphorsulphonate).

The anomaly would be most evident in solvents of low polarity (benzene and carbon disulphide) since the electrostatic attraction which has been assumed to exist between the menthyl radical and the nitro group would then be at its maximum. In solvents of high polarity the field exerted by the strongly polar nitro group will be reduced by dipole association with the solvent, largely releasing the menthyl group from its sphere of influence and again allowing free rotation around the C - O bond. The above assumption also accounts for the observed reversal of the usual effect of polar solvents, since a non-polar medium increases the anomaly and thus lowers the apparent rotatory power.

In this connection it is of interest that anomalous dispersion has previously been observed in l-menthyl 2-methoxy 1-naphthoate



by Bretscher, Rule and Spence, (J.C.S., 1928, 1493.)

and in the l-menthyl ester of benzene o-nitrosulphonic acid by Gordon Smith (Thesis, Edinburgh, 1930),

to/

to both of which a similar explanation may be applied.

In conclusion, the writer wishes to express his gratitude to Dr. H. G. Rule for his generous interest and helpful advice during the progress of this work.

Summary.

(i). The influence of polar substituents on optical rotatory powers of l-menthyl derivatives has been extended to include the l-menthyl ethers of both aliphatic and aromatic types.

(ii). The effect of ionisation on the rotatory power of ethers containing acidic, and probably also basic, substituents is in agreement with prediction.

(iii). Improved methods are described for the preparation of l-menthoxyacetic acid, l-menthyl methyl ether, and potassium and sodium menthoxides.

(iv). In some cases the influence of solvents on the rotatory power of the l-menthyl ethers is in agreement with the polarity of the solvent, highly polar solvents tending to reverse the characteristic effect of the substituents in the optically active molecule. In other cases the solvent changes are small and show no regularity.

(v). l-Menthyl 2:4-dinitrophenyl ether is found to be definitely anomalous in solvents of low polarity but its dispersion becomes normal, although complex in solvents of high polarity. This change is discussed in connection with the properties of other ortho-substituted benzoic derivatives.

EXPERIMENTAL

The menthol used in this investigation was B.D.H. "recrystallised menthol", and had a rotatory power $[\alpha]_D = -49.75^{\circ}$ in alcoholic solution (c = 10).

The criterion of optical purity was a constant rotational value, obtained by recrystallisation in the case of the solid compounds, and fractionation in the case of the liquids.

l-Menthyl Methyl Ether.

This preparation was first attempted, using a modification of Lander's method for the ethyl ether, (J.C.S., 1901, 77, 731). Menthol, 50 gm., was mixed in a flask under a reflux condenser with fresh, dry, silver oxide, 100 gm., and methyl iodide, 130 gm. No action occurred at first, so the flask was warmed. Reaction set in, and the mixture boiled of its own accord for about an hour. When the ebullition had ceased, the mixture was heated for eight hours on the water-bath. The silver oxide was filtered off, and washed thoroughly with ether; the ether was then distilled off from the extract, and the product fractionated. The portion boiling at 190-200° was collected separately and its rotatory power determined. Tschugaeff (Beilstein, VI, p. 31) quotes for *l*-menthyl methyl ether, $[\alpha]_D = -95.67°$, $D^4_{20} = 0.8607$, but the above preparation only gave $[\alpha]_D = -50°$. The mixture was therefore remethylated.

After six methylations the $[\alpha]_D$ had only risen to -65°, and the yield had dropped to 15 gm., since in each fractionation only the portion boiling at/

at 193-200° was retained. Accordingly, a second preparation was carried out, and after six methylations the rotation value had reached the same figure. The two yields were then combined, and given a further six methylations, which only increased the $[\alpha]_D$, by small changes, to -70°, the last rise being very small indeed.

The difficulty obviously lies in the separation of the unchanged menthol from the other, by distillation; other methods were therefore attempted. The yield was heated with sodium and methyl iodide, but the sodium failed to react, and no change in rotation was found. The mixture was next steam-distilled, until about one-third of its volume had passed over, when the remainder was separated from the water and dried. The rotation was found to have risen to -75°. Evidently this process resulted in a partial removal of menthol, although insufficient for the purpose.

Lastly the mixture was heated with excess para nitrobenzoyl chloride, and pyridine, for five hours on the water-bath. Ether was added to the mixture, and the ethereal solution washed with dilute hydrochloric acid, dilute sodium hydroxide/

hydroxide, and finally with water. The ethereal layer was separated, dried, and the ether removed. When the residue was fractionated, a portion was obtained which boiled steadily at 195°. Its specific rotation was -85.41°. This portion was re-fractionated carefully, and divided into two practically equal parts, which boiled sharply at 193° and 197° respectively. The lower fraction (b.p. 193°) had $[\alpha]_D$ = -79.7°, and the higher boiling portion -89.4°; this latter only amounted to 3 gm.

A third preparation was commenced with the modifications that the mixture was stirred, and that the product from the evaporation of the ethereal extract was not fractionated. This latter was to avoid losses in fractionation. After four methylations the yield was fractionated, but the portions showed so little change from menthol, that the method was abandoned.

Now, Tschugaeff's method of preparation, as quoted in Beilstein (loc. cit.) was to treat sodium menthoxide with methyl iodide. Owing to the inaccessibility of his original paper, experimental details were unknown, but it was decided to attempt the/

the method using sodium menthoxide as free as possible from menthol. Accordingly, Beckmann's method (J. für Prak. (II), 55, 16) was employed. An equimolar mixture of sodium and menthol was heated at 200° (maximum) in an atmosphere of hydrogen, which had been carefully purified and dried. For this purpose the hydrogen was passed successively through wash-bottles containing acid permanganate, silver nitrate, and alkaline permanganate solutions, two sulphuric acid bubblers, and soda-lime and calcium chloride tubes. An all-glass apparatus with ground glass joints was used. The inlet tube for the hydrogen fitted closely into the tubule of the flask, and the thermometer was placed inside the inlet tube, which dipped under the surface of the molten menthol. A long outlet was attached to the tubule of the receiving flask, and a calcium chloride tube was fitted to the end of this outlet to prevent back-diffusion of moisture. In this way, 47 gm. of menthol were treated with 7 gm. of sodium, and the mixture kept at a maximum temperature of 200° for two and a half hours. Although at the conclusion of this time, about 1.5 gm. of sodium still remained undissolved, the mixture had formed a viscous mass of sodium menthoxide. To minimise the risk of isomerisation, the heating was stopped at this stage/

stage. A rapid stream of hydrogen was next blown through, which carried over most of the excess menthol.

The flask was next cooled in ice, the condenser reversed, and 140 gm. of methyl iodide added. A vigorous action ensued, the mixture boiling steadily, even when cooled in ice, and a copious precipitation occurred. The mixture was then heated on the water-bath for four hours, after which ether was added to the pasty product. (Excess of sodium had previously been removed by the addition of methyl alcohol). The mixture was filtered, the ether removed, and the residue fractionated. Two fractions were obtained:-

B.P. 195-198°, $[\alpha]_D$ = -70.16° $[\alpha]_D$ = -81.5°, 20 gm.

B.P. 198-210°, $[\alpha]_D$ = -66.40° ———— 12 gm.

A solid residue (methoxide, etc.) remained in the flask.

As these fractions were of close rotational value, they were combined and treated with excess para-nitrobenzoyl chloride and pyridine. The mixture was heated on the water-bath for three hours, and then worked up as before. Two fractions/

fractions were obtained:- b.p. 195-200° α_D = -75.74°, 200-205° α_D = -76.73° $[\alpha]_D$ = -89.15°. A further preparation was subsequently carried out.

In this case the reaction mixture was allowed to stand overnight in the cold, and was then refluxed for six hours. The sodium was filtered off with the sodium iodide, thus avoiding the formation of a solid residue. This, when fractionated in vacuo, gave three portions:-

b.p. 68-75° / 11 mm.	$[\alpha]_D$ = -70.85°	5 gm.
75-85°	$[\alpha]_D$ = -76.21°	22 gm.
85-95°	$[\alpha]_D$ = -63.57°	10 gm.

The fraction, b.p. 75-85°, was treated with para-nitrobenzoyl chloride and pyridine, and heated on the water-bath for eight hours. It was then worked up as before, and on distillation under 10 mm. pressure gave three portions:-

b.p. 73-80° / 10 mm.	$[\alpha]_D$ = -79.28°	15 gm.
80-81°	$[\alpha]_D$ = -82.50°	9 gm.
81-85°	———————	2 gm.

For the second fraction $[\alpha]_D$ was found to be -95.85°, which represents optical purity as obtained by/

by Tschugaeff.

The first fraction and other fractions of the same order of purity were mixed together, and treated with the acid chloride as before. This yielded, on fractionation, 2 gm. which were of sufficiently high rotation to be mixed with the optically pure product from the previous fractionation.

Rotation values were determined for this, the final product, which showed that l-menthyl methyl ether has normal dispersion. For this product, $[\alpha]_D$ was found to be -95.17°.

A study of the influence of solvents on the optical rotatory power of this compound was carried out.

l-Menthyl Methyl Ether. Homogeneous, 20°.

$D_{20} = 0.8607.$

λ	6708	5893	5780	5461	4358
α_λ	-62.69°	-81.91°	-85.69°	-97.01°	-161.23°
$\frac{1}{\alpha_\lambda}$	.0160	.0122	.0117	.0103	.0062
$[\alpha]_\lambda$	-72.88°	-95.17°	-99.56°	-112.6°	-187.3°
$[M]_\lambda$	-123.9°	-161.7°	-169.2°	-191.5°	-318.3°

Solvent Action on *l*-Menthyl Methyl Ether.
l = 4 dm. c = 5%.

Solvent	$[M]_{5461}^{20}$	Dipole Moment $\mu \times 10^{18}$	
CH_3CN	-197.3°	3.94	
CH_3NO_2	-191.3°	3.78	
CH_3OH	-198.7°	1.64	
CH_2Cl_2	-191.0°	1.61	
CH_3I	-190.3°	1.60	
$CHBr_3$	-188.2°	1.30	$\alpha_{gi} = 24°$
$CHCl_3$	-189.3°	1.10	
CH_3COOH	-198.9°	0.74	
CS_2	-216.0°	0	
CCl_4	-195.1°	0	
C_6H_{14}	-194.6°	0	
C_7H_{16}	-192.4°	0	
$CH_3OH + HCl$	-195.8°	?	
$C_6H_5NO_2$	-189.3°	3.90	
C_6H_5CN	-192.7°	3.85	
C_6H_5CHO	-193.2°	2.75	
C_6H_5Br	-191.5°	1.56	
$C_6H_5NH_2$	-173.5°	1.51	Red colour, ? complex
C_6H_5I	-195.3°	1.25	
$C_6H_5OCH_3$	-196.8°	1.16	
$C_6H_5CH_3$	-192.3°	0.40	
C_6H_6	-195.0°	0	
Homogeneous	-191.5°	?	

Preparation of *l*-Menthoxyacetic Acid and its Derivatives.

(a) *l*-Menthoxyacetic acid.

The preparation of this ether-acid was carried out according to the instructions of Frankland and O'Sullivan (J.C.S., 1911, 99, 2329), using chloracetic acid and sodium menthoxide, but with the following modifications. The syrup obtained from the ethereal extract on evaporation did not crystallise, and it was therefore fractionated in vacuo. Chloracetic acid distilled at 83-85° under 10 mm. pressure, and the menthoxyacetic acid at 162-168°. The product was a yellow syrup, for which $[M]_D$ was found to be -195.8°, in methyl alcohol (c = 5). (Frankland, loc. cit., finds $[M]_D$ = -198.8°, after six recrystallisations from ether). On re-fractionation, the portion boiling at 163-164° / 10 mm. was taken, and was found to be optically pure. The present writer suggests that this is a much simpler method of purification than that of Frankland and O'Sullivan. Yield 44 gm.

Weights of components used?

The/

The rotatory power of the acid was measured in methyl and ethyl alcohols, and in ethyl alcohol containing hydrogen chloride, and also in the homogeneous state at 20°. The observed values are given in the tables herewith.

(b) Sodium *l*-Menthoxyacetate.

A solution of the sodium salt of this acid in ethyl alcohol, was prepared by titration of a weighed quantity of the acid with a standard solution of sodium ethoxide, and making up to 10 ml. with ethyl alcohol. This solution gave $[M]_{5461}$ = -180.4°, while that of the free acid in ethyl alcoholic solution was -230.9°.

(c) *l*-Menthoxyacetyl Chloride.

Menthoxyacetic acid (20 gm.) was treated with thionyl chloride (35 gm.) in a flask with a ground-in air condenser fitted with a calcium chloride tube. A violent reaction ensued, which may have been increased by traces of water in the recovered acid, necessitating cooling in ice. After the reaction had slowed down, the mixture was/

was heated for an hour at 50°, on a water-bath, until all action ceased. The excess thionyl chloride was then removed under diminished pressure at 50°, and the acid chloride used in this form. Yield, 22 gm.

(d) *l*-Menthoxyacetamide.

Of the above yield of acid chloride, 7 gm. were dissolved in dry benzene, and dry ammonia gas introduced through a tube just above the liquid surface. When no more heat was evolved on shaking, more benzene was added and the gas lead removed. Any ammonium chloride etc. was filtered at the pump, and the solution concentrated and allowed to crystallise. Yield of crude amide, 7 gm.

The amide was recrystallised from petrol ether (b.p. 60-80°) until constant rotation was found in five per cent. ethyl alcoholic solution. It then gave $[M]_D = -203.4°$, and $[M]_{5461} = -243.6°$. The rotation of this compound was also determined in benzene (c = 5), $[M]_{5461} = -229.6°$.

A solution of l-menthoxyacetamide (c = 5) was made in ethyl alcohol containing two molecules of hydrogen chloride for each molecule of amide, but no appreciable change in rotation was obtained, hence/

hence little, if any, ionisation of the $-CONH_2$ group can have occurred. ($[M]_{5461}$ = -245.0°).

l-Menthoxyacetamide (m.p. 93°) forms white needles, extremely soluble in alcohol, ether, acetone, carbon tetrachloride and methyl alcohol. It is also soluble in benzene and petrol ether, but is insoluble in water.

This compound was analysed for nitrogen by Ter Meulen's catalytic hydrogenation method, and gave N = 6.50%, $C_{12}H_{23}O_2N$ requires N = 6.57%.

(e) Methyl *l*-Menthoxyacetate.

The remaining 15 gm. of the acid chloride were added to excess methyl alcohol, and refluxed for four hours. Water was added, and the ester extracted with ether. This extract was washed with sodium hydroxide, then with water, and finally dried. The ether was removed, and the ester fractionated in vacuo. It boiled at 131° under 8 mm. pressure. After four fractionations the ester was obtained optically pure, and had a rotation, in the homogeneous state, $[M]^{20}_{5461}$ = -275.6°, D_{20} = 0.9804. Yield, crude ester, 9 gm; pure ester, 4 gm. Rotations were also taken of the ester in ethyl alcohol/

alcohol and in benzene (c = 5).

This compound was analysed by combustion for carbon and hydrogen and gave: C = 68.32%, H = 10.62%. $C_{13}H_{24}O_3$ requires C = 68.42, H = 10.53%.

(f) *l*-Menthyl *l*-Menthoxyacetate.

l-Menthoxyacetyl chloride was prepared as above, from 15 gm. of l-menthoxyacetic acid. On this occasion the acid was dry, and the action was slower, requiring heat to allow it to proceed.

To the acid chloride was added menthol (1.5 molecules) and the mixture heated for three hours, corresponding to one and a half hours after the cessation of evolution of hydrogen chloride. Ether was then added, and the ethereal extract washed and dried over calcium chloride. After removing the ether, the resulting syrup was heated in vacuo to 185°, below which temperature all menthol and menthoxyacetic acid distilled over. Yield, 20 gm.

The product remaining in the flask was recrystallised twice from methyl alcohol, in which it is sparingly soluble, and its rotation taken (c = 5). Yield, 17 gm.

As the ester so obtained still had a yellowish colour/

colour, it was decolorised in methyl alcoholic solution, with animal charcoal. This gave a yield of white prisms, which were found to be optically pure, m.p. 58.5°. Yield, 15 gm.

Rotations were taken in benzene (c = 5), which gave $[M]_{5461} = -468.1°$, and also in ethyl alcohol (c = 5). The values are given in the subjoined tables.

This compound was analysed for carbon and hydrogen by combustion and gave C = 74.99%, H = 11.41%. $C_{22}H_{40}O_3$ requires C = 75.01%, H = 11.37%.

λ =	6708	5893	5780	5461	4358	
	l-Menthoxyacetic acid, homogeneous 20°. (l=1)					(M.W. 214.2)
α	-79.72°	-105.26°	-109.82	-124.50°	-207.32°	D_{20} = .8030
$\frac{1}{\alpha}$	.01254	.00950	.00911	.00803	.00482	
$[\alpha]_\lambda$	-64.01°	-84.55°	-88.18°	-99.95°	.258.1°	
$[M]_\lambda$	-212.4°	-280.8°	-292.7°	-331,7°	-552.5°	
	l-Menthoxyacetic acid, 5% soln. ethyl alcohol. (l=1)					
α	-3.67°	-4.70.	-4.93°	-5.57°	-9.28°	c = 5.165
$\frac{1}{\alpha}$	.2725	.2128	.2028	.1795	.1078	
$[\alpha]_\lambda$	-71.08°	-91.01°	-95.45°	-107.8°	-179.9°	
$[M]_\lambda$	-152.1°	-194.7°	-204.3°	-230.9°	-384.5°	
	l-Menthoxyacetic acid, 5% soln. methyl alcohol. (l=2)					
α	-7.36°	-9.81°	-10.16°	-11.49°	-19.10°	c = 5.285
$\frac{1}{\alpha}$	.1359	.1019	.0984	.0870	.0524	
$[\alpha]_\lambda$	-72.91°	-92.85°	-96.10°	-108.6°	-180.7°	
$[M]_\lambda$	-149.0°	-198.6°	-205.6°	-232.6°	-386.7%	
	l-Menthoxyacetic acid, 5% soln. benzene. (l=2)					
α	-7.40°	-9.66°	-10.14°	-11.45°	-18.91°	c = 5.135
$\frac{1}{\alpha}$	.1351	.1035	.0986	.0873	.0529	
$[\alpha]_\lambda$	-72.06°	-94.08°	-98.74°	-111.5°	-184.2°	
$[M]_\lambda$	-154.2°	-201.3°	-211.3°	-238.6°	-394.1°	

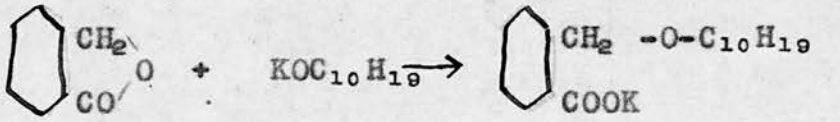
λ = 5461 only	*l*-Menthoxyacetic acid	Sodium *l*-Menthoxyacetate	(l=1)
	5% alcohol - HCl	5% soln. alcohol.	
α	-6.01°	-4.40°	
$[\alpha]_\lambda$	-112.7°	-84.29°	
$[M]_\lambda$	-241.1°	-180.4°	
	c = 5.335	c = 5.220	

λ =	6708	5893	5780	5461	4358	
	l-Menthoxyacetamide 5% soln. ethyl alcohol. (M.W. 213.2)					
α	-3.42°	-4.25°	-4.49°	-5.09°	(8.03°)	c = 4.45
$\frac{1}{\alpha}$	.2924	.2353	.2227	.1965	(.1245)	
$[\alpha]_\lambda$	-76.85°	-99.12	-100.9°	-114.4°	(-180.4°)	
$[M]_\lambda$	-163.7°	-203.4°	-214.9°	-243.6°	(-384.5°)	
	l-Menthoxyacetamide 5% soln. benzene.					
α	-2.64°	-3.39°	-3.53°	-4.02°	(-6.59°)	c = 3.73
$\frac{1}{\alpha}$	.3788	.2950	.2833	.2588	(.1517)	
$[\alpha]_\lambda$	-70.80°	-90.91°	-94.60°	-107.7°	(-176.7°)	
$[M]_\lambda$	-150.8°	-193.6°	-201.6°	-229.6°	(-376.3°)	
	Methyl *l*-Menthoxyacetate 5% ethyl alcohol. (M.W. 228.2)					
α	-3.69°	-4.83°	-5.14°	-5.81°	-9.64°	c = 5.115
$\frac{1}{\alpha}$	.2710	.2070	.1946	.1721	.1037	
$[\alpha]_\lambda$	-72.14°	-94.43°	-100.5°	-113.6°	-188.5°	
$[M]_\lambda$	-164.4°	-215.3°	-229.2°	-259.0°	~~-341.4°~~ -429.7°	
	Methyl *l*-Menthoxyacetate 5% benzene.					
α	-3.67°	-4.72°	-4.99°	-5.62°	-9.28°	c = 5.020
$\frac{1}{\alpha}$	.2725	.2119	.2009	.1779	.1078	
$[\alpha]_\lambda$	-73.11°	-94.01°	-99.40°	-111.9°	-184.8°	
$[M]_\lambda$	-166.6°	-214.3°	-226.7°	-255.2°	-421.4°	
	Methyl *l*-Menthoxyacetate, Homogeneous 20°.					
α	-76.25°	-100.04°	-104.53°	-118.54°	-197.10°	D_{20} = .9804
$\frac{1}{\alpha}$	.01311	.01000	.00957	.00844	.00507	
$[\alpha]_\lambda$	-77.78°	-102.0°	-106.6°	-120.9°	-201.0°	
$[M]_\lambda$	-177.3°	-232.6°	-243.0°	-275.6°	-458.3°	

λ =	6708	5893	5780	5461	4358	
(l=2)	<u>l-Menthyl l-Menthoxyacetate 5% ethyl alcohol.</u>					(M.W. 352.4)
α	-8.79°	-11.46°	-11.89°	-13.47°	-22.42°	c = 5.000
$\frac{1}{\alpha}$	.1138	.0873	.0841	.0742	.0446	
$[\alpha]_\lambda$	-87.90°	-114.6°	-118.9°	-134.7°	-224.2°	
$[M]_\lambda$	-309.4°	-403.3°	-418.6°	-474.2°	~~-807.4°~~ -789.1°	
(l=2)	<u>l-Menthyl l-Menthoxyacetate 5% benzene.</u>					
α	-8.48°	-11.29°	-11.74°	-13.30°	-22.01°	c = 5.000
$\frac{1}{\alpha}$	.1179	.0886	.0852	.0752	.0454	
$[\alpha]_\lambda$	-84.80°	-112.9°	-117.4°	-133.0°	-220.1°	
$[M]_\lambda$	-298.5°	-397.3°	-413.2°	-468.1°	-774.7°	

In the above table those values in brackets are approximate, owing to absorption.

Attempted Preparation of o-Menthoxymethyl Benzoic Acid.



The phthalide used in this preparation was obtained from phthalimide by Reissert's method of reduction with sodium hydroxide and zinc dust. (Ber., 1913, 46, 1489).

A solution of phthalide, 3 gm., in toluene was added to a toluene solution of potassium menthoxide, obtained from 0.87 gm. of potassium. The mixture was boiled gently until a sample, to which water had been added, only showed a faintly alkaline reaction. Water was then added, and the mixture shaken. The clear aqueous layer was separated off, acidified, and the resulting emulsion extracted with ether. The ethereal solution was dried over calcium chloride, and the ether removed. There remained a small quantity of a thick, sticky liquid, which, on drying in vacuo, formed a resinous mass.

The preparation was repeated on a larger scale/

scale, using 18 gm. of phthalide, and gave a similar resinous yield. When a sample of this was treated with benzene and ether, small crystals were formed, and the total yield was then treated with this mixture. By varying the proportions of the solvents, until an optimum mixture was reached, whitish yellow crystals were obtained, m.p. 155°. These were soluble in alcohol and very soluble in acetone. A five per cent. solution of this acid in alcohol showed no activity. As a check, a five per cent. solution of the sodium salt in alcohol was prepared, which also showed no trace of activity, and it was concluded that this was not the required acid.

The mother liquors from which the foregoing substance was deposited were treated with sodium hydroxide solution and the purified sodium salt so obtained was acidified. The emulsion was extracted with ether and the ethereal solution dried. On evaporation of the ether an acid was obtained as a resinous solid. This was also found to be inactive. It was therefore assumed that the reaction had taken place in a direction other than that indicated by the above equation and the preparation was accordingly abandoned.

Attempted Preparation of o- and p-Nitrobenzyl l-Menthyl Ethers.

Although it was known that the nitrobenzyl halides readily pass into stilbenes in the presence of alkali, the preparation of the l-menthyl ether from p-nitrobenzyl bromide was attempted in the hope that a small amount might be isolated. Two methods were employed. The first was the interaction of potassium menthoxide (from .39 gm. of potassium) in solution in excess menthol, with p-nitrobenzyl bromide. This, on heating, gave a highly coloured yield, which, when treated with benzene, separated into two portions. The first, which was insoluble in benzene, but soluble in alcohol, formed a brown powder melting above 200°. This was found to be optically inactive, and was probably 4:4'dinitro-stilbene. The second fraction, in solution in the benzene, was separated from the excess menthol present by fractionation in vacuo. Menthol distilled at 95° under 12 mm. pressure, while the second product sublimed at140-145° as a brilliant red solid. It was inactive, and was taken to be an/

an azoxy-compound. The small residue in the flask was carbonaceous.

The second method used was heating a mixture of 7.8 gm. menthol, 2.8 gm. potassium hydroxide, 3 ml. water, 23 ml. absolute alcohol and 10.8 gm. p-nitrobenzyl bromide, gently for two hours. Very little action occurred, and on working up the resulting mixture, only the starting materials, together with traces of stilbenes and other inactive highly coloured products were obtained.

Similar highly coloured inactive products, together with much tar, were obtained from the ortho-isomer by both methods.

Purification of Solvents.

(1) Nitromethane:-

The B.D.H. product was washed, dried over calcium chloride, and fractionated. It was obtained colourless, b.p. 100.8 - 101.1°.

(2) Acetonitrile:-

Aytoun, Scott and Company's acetonitrile was dried over calcium chloride and fractionated, giving a colourless product, b.p. 80.7 - 81.4°.

(3) Methyl Iodide:-

Aytoun, Scott and Company's purified methyl iodide was washed with sodium carbonate solution, dried over calcium chloride, and fractionated, b.p. 42.7 - 43.0°.

(4) Methylene Chloride:-

The B.D.H. product was washed with potassium hydroxide solution, dried over calcium chloride and fractionated, b.p. 41.8 - 42.2°.

(5) Acetone.

B.D.H. "bisulphite purified" acetone was well dried over calcium chloride and fractionated, b.p. 55-56°.

(6) /

(6) Methyl Alcohol:-

A sample of "absolute" methyl alcohol was freed from acetone, refluxed over freshly prepared quick-lime and fractionated, b.p. 63.7 - 63.8°.

(7) Acetic Acid:-

Kahlbaum's 100% acid was cooled until about two-thirds frozen; the liquid was decanted off and the crystalline mass fractionated, m.p. 16°, b.p. 118-118.2°.

(8) Chloroform:-

A good sample was washed, dried and fractionated to constant boiling point, b.p. 61-61.1°.

(9) Bromoform:-

B.D.H. bromoform (sp.gr. 2.85 - 2.90) was washed, dried and fractionated, b.p. 147-147.4°.

(10) Carbon Disulphide:-

Aytoun, Scott and Company's redistilled carbon disulphide was shaken with mercury, dried and fractionated, b.p. 46-46.2°.

(11) Carbon Tetrachloride:-

The sample used had already been carefully purified. It was dried and fractionated, b.p. 77.6 - 77.8°.

(12) Hexane:-

B.D.H. hexane ("free from aromatic hydro-carbons") was dried and fractionated, b.p. 67-69°.

(13) /

(13) Ethyl Alcohol:-

"Absolute" ethyl alcohol was refluxed over freshly prepared lime and then fractionated, b.p. 77.8° under 749 mm. pressure.

(14) Benzonitrile:-

Aytoun, Scott and Company's product was dried and partially frozen out; the crystalline product was fractionated under reduced pressure, and was obtained as a colourless liquid, m.p. -12.9°, b.p. 82.5° under 15 mm. pressure.

(15) Nitrobenzene:-

B.D.H. nitrobenzene was fractionated and the portion boiling over 190.0 - 190.4° was partially frozen out. The crystalline portion was melted, dried and fractionated under reduced pressure, m.p. 5.6 - 5.7°, b.p. 90-91° under 15 mm. pressure.

(16) Benzaldehyde:-

Kahlbaum's purified product was washed with sodium carbonate solution, dried and fractionated, care being taken to expose as little to the air as possible, and to use it within two hours of fractionation, b.p. 179-179.2°.

(17) Aniline:-

Kahlbaum's aniline "from sulphate" was dried and fractionated, giving a colourless liquid of b.p. 182.9 - 183°.

(18) /

(18) Anisole:-

B.D.H. anisole was dried and fractionated and was obtained colourless and gave no phenol reaction, b.p. 153.8°.

(19) Bromobenzene:-

This was prepared in the laboratory. It was well washed with sodium carbonate solution and water, dried over calcium chloride and fractionated, b.p. 154.8 - 155.2°.

(20) Iodobenzene:-

This was also prepared in the laboratory and was treated in the same way as the bromo compound. It was obtained almost colourless, b.p. 187.8 -188.1°.

(21) Benzene:-

B.D.H. "extra pure" benzene was partially frozen out and fractionated, m.p. 5.5°, b.p. 80-80.1°.

(22) Toluene:-

Aytoun, Scott and Company's "pure" toluene was dried over metallic sodium wire and fractionated, b.p. 109.7 - 109.8°.

l-Menthyl Picryl Ether.

The picryl chloride used in the following preparationswas prepared by the method of Jackson and Gazzolo (J. Am. C.S., 1900, 23, 384). Sodium (0.19 gm.) was dissolved in excess of menthol in toluene solution, picryl chloride (2 gm.) in toluene added, and the mixture heated on the water-bath for eight hours. After cooling, it was extracted with ether, and the ethereal extract washed with water, followed by dilute sulphuric acid, and dilute sodium hydroxide. Finally, it was washed again with water. By this means most of the intense red colour of the solution was removed. The ethereal layer was dried over calcium chloride, and the solvent evaporated. The solid thus obtained was dried in vacuo, and recrystallised from ligroin. Small yellow needles were deposited (m.p. 66-68°) and the mother-liquor on concentration gave plates (m.p. 110-111°).

The above preparation was repeated, using potassium menthoxide, from 4.19 gm. of potassium, instead of the sodium compound, since potassium menthoxide is more rapidly formed. Picryl chloride/

chloride (26 gm.) was added to the toluene solution of potassium menthoxide thus obtained, and the same procedure followed. Four crops of crystals were deposited, (1) m.p. 66-69°, 4 gm.; (2) m.p. 38-42°, 16.5 gm.; (3) m.p. 34-36°, 4.5 gm.; (4) residues, 3 gm. A five per cent. solution of the first crop in benzene gave a rotation $[a]_{5461} = -21.25°$.

Owing to the low activity and low melting point, it was supposed that this was not the actual ether, but probably a complex of the solvent with picryl chloride, or picric acid, contaminated with menthol.

As the above method was not successful, the instructions of Jackson and Boos (Am. Ch. J. 1898, 20, 449) were followed in the hope of isolating the complex composed of one molecule of the ether with one molecule of sodium menthoxide. A solution of sodium menthoxide in benzene was prepared and a solution of picryl chloride in the same solvent added to it. Sufficient menthoxide was provided to give two molecules of menthoxide for each molecule of picryl chloride.

$$C_6H_2(NO_2)_3Cl + 2\ NaOC_{10}H_{19} \rightarrow C_6H_2(NO_2)_3\text{-}O\text{-}C_{10}H_{19}, NaOC_{10}H_{19} + NaCl$$

complex

$$C_6H_2(NO_2)_3\text{-}O\text{-}C_{10}H_{19}, NaOC_{10}H_{19} + HCl \rightarrow C_6H_2(NO_2)_3\text{-}O\text{-}C_{10}H_{19} + C_{10}H_{19}OH + NaCl$$

The/

The mixture was stirred vigorously, and a considerable amount of heat was evolved, while a deep red colour developed throughout the solution. Only a few deep red crystals could be removed by filtration, and these on drying, and trituration with hydrochloric acid, gave the ether as a yellow crystalline solid. This was recrystallised from ligroin, and melted at 132°. A solution in benzene, (c = 5), gave $[\alpha]_{5461} = -381.9°$. The original benzene solution was therefore treated with dilute hydrochloric acid, and concentrated to a small bulk. On cooling, the residue solidified. The solid was warmed, to melt the menthol present, and the latter decanted off, leaving a small yield of yellow needles similar to those obtained from the complex.

The method of Jackson and Boos (loc. cit.) was repeated on a larger scale, using potassium menthoxide, prepared from 1.7 gm. of potassium and excess of menthol in toluene solution, to which was added gradually picryl chloride dissolved in hot toluene. A black mass formed, with the evolution of much heat, some of the toluene being driven off. The mixture was filtered, and the precipitate washed thoroughly with benzene, when it formed a dark crimson mass, which, on drying, became/

became a bright crimson. Yield 12 gm. The melting point of this complex was above 140°, the exact temperature not being observed on account of the risk of explosion.

The complex was placed in a mortar and ground gently with dilute hydrochloric acid, when its colour changed slowly to orange. The colour change was much slower with the potassium complex than with the sodium, indicating that the complex derived from potassium menthoxide is more stable to acid than that derived from the corresponding sodium compound.

Difficulty was encountered at this stage, as the menthol liberated formed a layer around the unchanged complex, rendering the mass sticky, and stopping the reaction. A little ethyl ether was added, which allowed the reaction to proceed, the picryl ether being obtained as a yellow solid. Yield 3 gm.

A repetition of the preparation, using 18 gm. of picryl chloride, gave 21 gm. of the dried complex. The combined yields (about 7 gm.) were recrystallised from petrol ether (b.p. 80-100°), and gave an orange coloured crystalline product which adhered to glass. It was dissolved in the/

the minimum amount of hot benzene, and the cloudy solution so obtained was precipitated by the addition of petrol ether. A brown by-product was filtered off, and the clear yellow liquors concentrated until crystallisation set in. In this manner, a yellow solid was obtained, which, on drying in vacuo gave $[\alpha]_{5461} = -276.8°$, in benzene (c = 5). On recrystallisation from petrol ether, (b.p. 80-100°), the rotation rose slowly, until after several repetitions it reached $[\alpha]_D = -291.0°$. Subsequent recrystallisations gave $[\alpha]_D = -296.2°$, and -294.7°. (The D-line was employed, as a mercury arc lamp was not available at this stage). It was assumed that this represented optical purity, the molecular rotation for the D-line being -1082°, and for the mercury green line, -1391°.

On each recrystallisation the ether was obtained in the form of very pale yellow crystals. On drying the crystals and exposing them to light they darkened, and on solution in benzene or petrol ether, a small amount of a brown, insoluble powder was obtained. The latter was soluble in alcohol or acetone, but not in benzene or petrol ether/

ether. As the solutions of this substance in acetone or alcohol had a very intense red colour, it was not found possible to obtain readings for it in the polarimeter.

A steady fall in the yield resulted and a similar change seems to proceed in solution, as solutions darken quite appreciably on standing. When the ether was kept in the dark during the process of drying, less discoloration occurred, and the compound so obtained was used for the final determinations of rotatory power. Hence it appears that the decomposition proceeds in the presence of light.

A sample of the ether was placed between two surfaces of glass, and exposed to the action of sunlight. After a preliminary rapid darkening, the action seemed to proceed more slowly. On removing the covering glass a strong smell of menthone was perceptible, and the whole layer was found to be viscous. Hence it would appear that menthone and possibly menthol, together with the brown powder insoluble in benzene are formed from l-menthyl picryl/

picryl ether by the action of light. Owing to the difficulty in obtaining reasonably large quantities of this ether, this reaction was not further investigated.

Rotatory powers were observed for five per cent. solutions in benzene and in acetone. The rotation tables are subjoined.

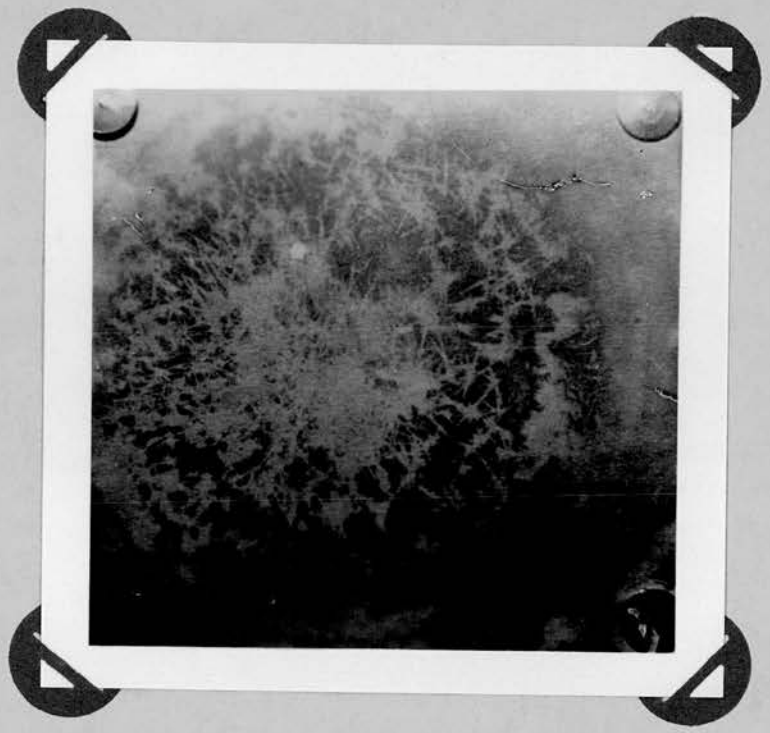
The compound was analysed for nitrogen by Ter Meulen's method of catalytic hydrogenation, and gave the value N = 11.24%. $C_{16}H_{21}O_7N_3$ requires N = 11.44%.

l-Menthyl picryl ether separates in yellow plates from benzene or acetone, in clusters of needles, tending towards prisms from ligroin and the petrol ethers, or in some cases long plates. These are probably hexagonal prisms. Some photographs of crystals are shown which are of blue-prints taken directly, using the crystals as the negative. Another print is shown of some abnormally shaped crystals deposited slowly from petrol ether solution on standing at room temperature.

l-Menthyl picryl ether is moderately soluble in petrol ether or alcohol, and easily soluble in acetone, benzene and chloroform. It melts at 133° and explodes violently at 150°.

The influence of solvents on the rotatory powers of this compound was examined, the tables of these values being subjoined.

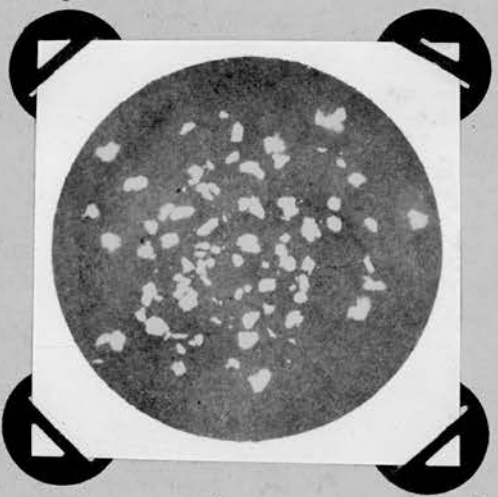
Abnormal oval crystals, from weak solution in petrol ether (b.p. 60 - 80°), on evaporation of solvent at room temperature.



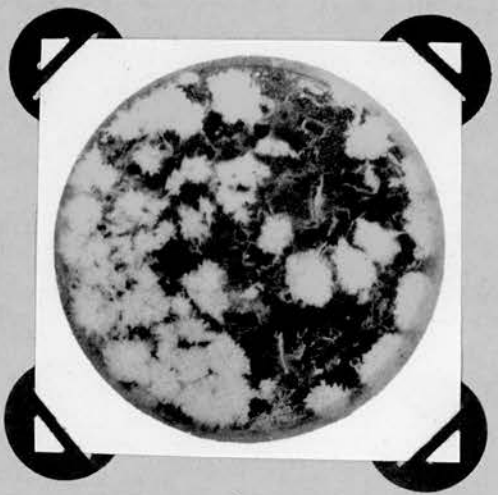
Normal crystals, from concentrated solution in hot benzene, on cooling.

Normal crystals from dilute solution in benzene by evaporation of solvent at room temperature.

From Acetone, by evaporation of solvent, at room temperature.



From Petrol Ether, (b.p. 80-100°), at room temperature.



From Petrol Ether, (b.p. 80 - 100°), hot saturated solution, on cooling.

λ =	6708	5893	5780	5461	4358

l-Menthyl picryl ether, 4.40% soln. in benzene. (M.W. 364·2)

α	-9.00	-12.98	-13.90	-16.68	-
$\frac{1}{\alpha}$	.1111	.0770	.0719	.0600	-
$[\alpha]$	-204.5	-295.0	-315.9	-379.0	-
[M]	-751	-1082	-1160	-1391	-

No reading could be obtained for λ = 4358 as owing to the yellow colour of the solution, total absorption occurred.

l-Menthyl picryl ether, 3.34% soln. in acetone.

α	-5.89	8.44 ~~-8.44~~	-8.92	-10.53	-
$\frac{1}{\alpha}$	.1698	·1185 ~~.1344~~	.1121	.0950	-
$[\alpha]$	-176.6	-252.4 ~~-283~~.0	-267.4	-315.6	-
[M]	-648.0	-924.4 ~~-818.7~~	-981.5	-1158	-

As above, no reading could be obtained for λ = 4358, owing to absorption.

Solvent Action on *l*-Menthyl Picryl Ether.

$\lambda = 5461$, c = 1%. *l* = 1 dm. t = 20°.

Solvent	$[M]^{20}_{5461}$	Dipole Moment $\mu \times 10^{18}$	Conc. % soln.
CH_3CN	-1075°	3.94	1
CH_3NO_2	-1100°	3.78	1
CH_3OH	-1139°	1.64	0.5
CH_2Cl_2	-1403°	1.61	1
CH_3I	-1420°	1.60	1
$CHBr_3$	-1597°	1.30	1
$CHCl_3$	-1527°	1.10	1
CH_3COOH	-1248°	~~0.74~~ 1.4	1
CS_2	-1597°	0	1
CCl_4	-1541°	0	1
C_6H_{14}	(-1489°)	0	0.25
$C_6H_5NO_2$	-1306°	3.90	1
C_6H_5CN	-1222°	3.85	1
C_6H_5CHO	-1277°	2.75	1
C_6H_5Br	-1417°	1.56	1
$C_6H_5NH_2$	Intense red colour, total absorption		
C_6H_5I	-1472°	1.25	1
$C_6H_5OCH_3$	-1361°	1.16	1
$C_6H_5CH_3$	-1384°	0.40	1
C_6H_6	-1384°	0	1

l-Menthyl 2:4: Dinitrophenyl Ether.

As a trial preparation, 2 gm. of potassium were dissolved in 40 gm. of molten menthol at 100°, forming potassium menthoxide. To this was added 5 gm. of 1:2:4:chlorodinitrobenzene, and the mixture shaken. A brown precipitate was deposited, and the product was then heated on the water-bath for two hours. It was cooled, treated with ether and the precipitated potassium chloride filtered off. The ethereal filtrate was washed with water, dried, and the solvent evaporated. Excess of menthol was sublimed off, but the residue consisted almost entirely of tar, and was unworkable.

The preparation was repeated, using two molecules of potassium menthoxide per molecule of the chlorodinitrobenzene, in order to see whether a complex could be isolated, as in the case of the picryl ether (q.v.). The solutions were mixed hot, with stirring. Again a dark product was formed, with the precipitation of a solid which proved to be potassium chloride. The highly coloured mother-liquors were evaporated down, and left to crystallise for several days. The menthol/

menthol was washed out with petrol ether, small pale yellow needles being left behind. These seemed to be soluble in menthol, and to crystallise out therefrom, as at an earlier stage, all of the solid dissolved in petrol ether. Yield of crude ether 2 gm.

The preparation was repeated, using 20 gm. of chlorodinitrobenzene, and two molecular proportions of menthoxide in benzene solution. On this occasion the solutions were mixed cold. A thick brown precipitate of potassium chloride was formed, leaving pale yellow mother-liquors, which were concentrated and allowed to crystallise for a week. On extracting the crystalline product in the cold with petrol ether (b.p. 40-60°), 8 gm. of yellow needles were obtained, m.p. 88°. The product was recrystallised from petrol ether (b.p. 60-80°), from which it crystallised in pale yellow fibrous tufts of needles. These were ground up and dried in vacuo, for three to four days, before the rotations were taken in benzene solution (c = 5). A desiccator painted black with Negroline was used for drying this ether, as in the presence of light it/

it turns brown, probably owing to decomposition as in the case of the l-menthyl picryl ether. In benzene, c = 5, this compound shows anomalous dispersion, the rotation for λ = 4358 being dextrorotatory ($[M]_{5461}$ -154.5°; $[M]_{4358}$ + 77.8°)

The ether was analysed for nitrogen by Ter Meulen's method, and gave N = 8.65%; $C_{16}H_{22}N_2O$ requires N = 8.70%.

The dispersion of the compound was examined in five per cent. solutions in benzene and in acetone, and in 2.3 per cent. solution in alcohol, owing to its sparing solubility in that solvent.

The influence of solvents on the rotatory powers of this compound was also examined.

l-Menthyl 2:4:Dinitrophenyl Ether, in benzene 5% soln.(M.W. 322.2).

λ =	6708	5893	5780	5461	4358
α	-1.88°	-2.31°	-2.35°	-2.41°	+1.08°
$1/\alpha$	-.5319	-.4329	-.4255	-.4149	+.9259
$[\alpha]_\lambda$	-37.60°	-46.20°	-47.00°	-48.20°	+21.60°
$[M]_\lambda$	-121.1°	-148.9°	-151.4°	-155.2°	+69.55°

l-Menthyl 2:4:Dinitrophenyl Ether,in acetone 5% soln.

α	-3.14°	-3.72°	-3.89°	-4.21°	-3.70°
$1/\alpha$	.3185	.2688	.2571	.2068	.2703
$[\alpha]_\lambda$	-62.80°	-74.40°	-77.80°	-84.20°	-74.00°
$[M]_\lambda$	-202.2°	-239.5°	-250.5°	-271.1°	-238.3°

l-Menthyl 2:4: Dinitrophenyl Ether, in ethyl alcohol.

c = 2.34%, *l* = 2 dm.

α	-2.68°	-3.29°	-3.36°	-3.68°	-2.69°
$1/\alpha$	.3732	.3040	.2977	.2717	.3717
$[\alpha]_\lambda$	-57.38°	-70.46°	-71.94°	-78.79°	-57.61°
$[M]_\lambda$	-184.8°	-226.9°	-231.7°	-253.8°	-185.5°

Solvent Action on ℓ-Menthyl 2:4:Dinitrophenyl Ether.

c = 2% l = 1 dm. t = 20°

Solvent	Molecular Rotations λ =4358	4940	5461	5780	μ x 10^{18}
$C_6H_5NO_2$	-	-236.7°	-220.6°	-209.2°	3.90
C_6H_5CN	-	-249.6	-241.5	-233.4	3.85
C_6H_5CHO	-	-246.0	-233.4	-223.8	2.75
C_6H_5Br	(+53.1)	-135.2	-151.3	-146.5	1.56
C_6H_5I	-	~~-158.1~~ 125.7	-161.0	-156.2	1.25
$C_6H_5OCH_3$	-	-161.0	-165.8	-153.0	1.16
$C_6H_5CH_3$	(+67.6)	-112.7	-133.7	-128.8	0.40
C_6H_6	(+80.5)	-109.5	-136.9	-132.0	0
CH_3CN	(-365.5)	-359.0	-301.0	-276.9	3.94
CH_3OH	(-209.2)	-273.6	-264.0	-238.3	1.64
CH_2Cl_2	(-209.2)	-299.4	-264.0	-246.3	1.61
CH_3I	(-241.5)	-204.5	-206.1	-188.4	1.60
$CHCl_3$	(-289.8)	-293.0	-259.2	-241.5	1.10
CH_3COOH	(- 72.44)	-297.9	-272.0	-249.6	0.74
C_6H_{14}	- 28.98	-154.5	-193.2	-173.9	0 *
CS_2	(-38.64)	-132.0	-159.3	-153.0	0
CCl_4	+27.36	-144.9	-162.6	-154.5	0

* c = ½% l = 2 dm.

Bracketed values are approximate, owing to partial absorption.

Solvent Action on 2:4:Dinitrophenyl *l*-Menthyl Ether.

l = 1 dm. c = 2%. t = 20°.

Solvent	λ = 4358		4940		5461		5780	
	α	$\frac{1}{\alpha}$	α	$\frac{1}{\alpha}$	α	$\frac{1}{\alpha}$	α	$\frac{1}{\alpha}$
$C_6H_5NO_2$			-1.47	.6803	-1.37	.7300	-1.30	.7693
C_6H_5CN			-1.55	.6452	-1.50	.6667	-1.45	.6896
C_6H_5CHO			-1.64	.6098	-1.45	.6896	-1.39	.7194
C_6H_5Br	(+.33	3.03)	-0.84	1.191	-0.94	1.064	-0.91	1.099
C_6H_5I			-0.78	1.282	-1.00	1.00	-0.97	1.030
$C_6H_5OCH_3$			-1.00	1.00	-1.03	.9709	-0.95	1.053
$C_6H_5CH_3$	(+.42	2.38)	-0.70	1.429	-0.83	1.205	-0.80	1.250
C_6H_6	(+.50	2.00)	-0.68	1.471	-0.85	1.177	-0.82	1.220
CH_3CN	(-2.27	.441)	-2.23	.4484	-1.87	.5348	-1.72	.5815
CH_3OH	(-1.30	.769)	-1.70	.5883	-1.64	.6098	-1.48	.6756
CH_2Cl_2	(-1.30	.769)	-1.86	.5376	-1.64	.6098	-1.53	.6536
CH_3I	(-1.50	.667)	-1.27	.7874	-1.28	.7812	-1.17	.8547
$CHCl_3$	(-1.80	.555	-1.82	.5494	-1.61	.6212	-1.50	.6667
CH_3COOH	(-.45	2.22)	-1.85	.5405	-1.69	.5917	-1.55	.6452
CS_2	(-.24	4.17)	-0.82	1.220	-0.99	1.010	-0.95	1.053
CCl_4	+.17	5.88	-0.90	1.111	-1.01	.9902	-0.96	1.042
C_6H_{14}	-.09	11.1	-0.48	2.084	-0.60	1.667	-0.54	1.852 ẋ

ẋ $c = 1/2\%$ $l = 2$ dm.

Bracketed values are approximate, owing to partial absorption.

l-Menthyl Phenyl Ether.

Potassium menthoxide was prepared from potassium (7.8 gm.) and menthol (100 gm.), keeping the temperature of the menthol at 100° by means of a water-bath. To this, 40 gm. of iodobenzene were added, the mixture kept at 100° for eighteen hours, and subsequently heated in an oil-bath at 180° for six hours. At the end of this time, the action appeared to have ceased, as no more potassium iodide was depositing. The product was then transferred to a distilling flask, and distilled in vacuo.

The fraction boiling up to 100° under 12 mm. pressure was taken to be menthol and menthene, etc., as most of it distilled at 95-97°. A second portion then came over, the temperature rising slowly to 140° and remaining fairly steady. This portion was re-distilled in vacuo, and separated sharply into two fractions, the lower boiling steadily at 97° under 12 mm., and the higher uniformly at 144°.

The yield of the latter only amounted to 5 gm., and gave $[\alpha]_{5461} = -130.4°$. (c = 5, in benzene). The ether was then recrystallised from/

from alcohol, 95 per cent., and the product (3 gm.) was dried in vacuo. This, when dissolved in benzene (c = 5) gave $[\alpha]_{5461} = -149.6°$. On further recrystallisation, the rotation rose to the constant value -154.0°, which was taken to represent optical purity. This corresponded to a molecular rotation of -357.3°. (λ = 5461). Yield 2 gm.

l-Menthyl phenyl ether forms colourless needles, m.p. 49.5°, b.p. 144° under 12 mm. pressure. It is freely soluble in benzene, ether and acetone, less soluble in alcohol and petrol ether, and insoluble in water.

The compound was analysed for carbon and hydrogen by combustion, and gave C = 82.69% ; H = 10.38%; $C_{10}H_{24}O$ requires C = 82.76% ; H = 10.35%.

The effect of solvents on the rotation of this ether was investigated, the results being given in the table herewith.

l-Menthyl Phenyl Ether. 5% solution in benzene, *l* = 1 , t = 20°. (M.W. 232.2).

λ	6708	5893	5780	5461	4358
α	-5.00°	-6.49°	-6.80°	-7.69°	-12.38°
1/α	.2000	.1541	.1471	.1300	.0808
$[\alpha]_\lambda$	-100.0°	-129.8°	-136.0°	-153.8°	-247.6°
$[M]_\lambda$	-232.0°	-301.1°	-315.5°	-356.8°	-574.4°

Solvent Action on *l*-Menthyl Phenyl Ether.

c = 1% ; l = 1 dm.; t = 20°.

Solvent	$[M]^{20}_{5461}$	$\mu \times 10^{18}$
$C_6H_5NO_2$	- 302°	3.90
C_6H_5CN	- 316°	3.85
C_6H_5CHO	- 348°	2.75
C_6H_5Br	- 344°	1.56
$C_6H_5NH_2$	- 367°	1.51
C_6H_5I	- 348°	1.25
$C_6H_5OCH_3$	- 334°	1.16
$C_6H_5CH_3$	- 336°	0.40
C_6H_6	- 353°	0
CH_3CN	- 350°	3.94
CH_3OH	- 370°	1.64
CH_2Cl_2	- 371°	1.61
CH_3I	- 359°	1.60
$CHCl_3$	- 338°	1.10
CH_3COOH	- 371°	0.74
CS_2	- 368°	0
CCl_4	- 328°	0
C_6H_{14}	- 348°	0

Attempted Preparation of 2:6:Dinitrophenyl Menthyl Ether.

As 1-chloro-2:6-dinitrobenzene is not quoted in any lists issued by chemical manufacturers, the writer communicated with six of the largest firms with a view to having it prepared, but without success. One firm, however, referred to Messrs Hickson of Castleford, who had a crude mixture which was stated to contain 2:6- and 2:4-dinitrochlorobenzenes. Messrs Hickson kindly sent a kilogram to the present writer, and it was this crude eutectic mixture which was used in the hope that the 2:6-ether would be formed in sufficient quantity for isolation.

Accordingly, two molecular proportions of the crude mixed isomers (which melted at about 30°) were allowed to interact at 120° with one proportion of potassium menthoxide in the homogeneous state. A very deep red colour developed, which could not be removed by purification, hence no rotatory powers could be observed for any of the products.

The reaction was next attempted in toluene solution at 110°, but again a strong colour developed.

The/

The third attempt was made in benzene solution when a copious dark red precipitate was deposited. This suggested complex formation as in the case of the picryl ether (q.v.). The precipitate was shaken with dilute hydrochloric acid and a little petrol ether (b.p. 40-60°), leaving a yellowish viscous mass. When this was extracted with hot petrol ether (b.p. 80-100°) the solution deposited pale yellow crystals on cooling. These were found to be optically inactive, and were soluble in alkali; they were therefore taken to be a nitrophenol, which was borne out by the fact that the original mixed isomers produced a strong irritant action on the skin. The filtrate from the precipitate was evaporated and allowed to crystallise, but the resulting mass was of such a dark colour as to be useless for polarimetric observations.

In the final preparation the crude chloro-nitro compound was purified by treatment with alkali, and recrystallisation from benzene. This purified product was then allowed to interact with potassium menthoxide at about 50°. The object of working at this low temperature was to minimise the formation of azoxy-compounds. Unfortunately, the only product which could be isolated by the

usual/

usual means was the 2:4-dinitro-ether (v. ante). Thus as it was not known for certain if the mixture obtained from Messrs Hickson actually contains any 1-chloro-2:6-dinitrobenzene, the preparation was abandoned.

Attempted Preparations of o- and p-Nitrophenyl *l*-Menthyl Ethers.

Numerous attempts were made to prepare these ethers, but with no success. Preparations were carried out under various conditions, as follows:-

(a) Potassium menthoxide was prepared from 3.9 gm. of potassium and excess menthol at 170°, and the mixture was then treated with 25 gm. of p-iodonitrobenzene. A very violent reaction ensued, and after this had subsided, the product was kept at 150° for two hours. The mixture was quite black, and on treatment with petrol ether (following the method used for the 2:4-dinitrophenyl ether) gave a black insoluble tarry residue, which on extraction with petrol ether (b.p. 80-100°) yielded only p-iodonitrobenzene. The portion soluble in petrol ether (b.p. 40-60°) was fractionated in vacuo, and gave menthol, and a little p-iodonitrobenzene.

o-Iodonitrobenzene, under the same conditions, reacted strongly, but gave a very dark brown syrup which could not be obtained crystalline. On distillation this was separated into unchanged o-iodonitrobenzene, and a tarry residue, which could/

could not be further purified.

(b) The preparations were repeated, working at 120°, but as before, only the starting materials and tarry products were obtained.

(c) In toluene solution at its boiling point, 110°, less reaction seemed to occur, and the starting materials, with tarry syrups were again obtained.

(d) The reactions were carried out in benzene solution at its boiling point, 85°, with the same results.

(e) As it was thought that the presence of excess menthol was perhaps preventing a separation of the ether, if formed, potassium menthoxide was prepared free from menthol by Beckmann's method (v. ante). This was allowed to react in two portions in boiling benzene solution, with the two isomers. As before, only dark strongly coloured products were obtained, together with menthol and the starting materials. Since large amounts of menthol were recovered, it showed that the reactions were proceeding along lines other than those desired.

(f) /

(f) It seemed that some of the intense red colour of the residues was due to iodine or iodine compounds, and the chloro-compounds were therefore used instead of the iodo. The reactions were first carried out in benzene solution in the cold, and the mixtures were then heated at 85° for two hours. Halide was found in the precipitates insoluble in benzene, and a considerable crop of needles was obtained from the para-compound. The product, however, proved inactive; it melted at 155°, and was probably 4:4'-dichloroazoxybenzene (m.p. 155°). The ortho-isomer gave a brown tarry syrup which could not be entirely freed from menthol.

(g) As Beckmann's method of preparing sodium menthoxide involves a prolonged heating, (about three hours) at high temperatures (200°) which may tend to the isomerisation of the menthol, a modified procedure was worked out which offers certain advantages.

Improved Method of Preparation of Sodium and Potassium Menthoxides.

Four or five molecular proportions of menthol were placed in a distilling flask, the side tube of which was stoppered, the neck being fitted with a long/

long air condenser. The flask was heated to 150° in an oil-bath, and one molecular proportion of the metal, cut into small pieces, was gradually added through the air condenser. In this way 7.8 gm. of potassium may be dissolved in about thirty-five minutes. The apparatus was then rearranged as for a distillation under diminished pressure, and the excess of menthol distilled over at low pressure in a current of hydrogen. The menthol passed over rapidly, and the residue in the flask suddenly solidified. It was assumed that the bulk of the menthol had then been removed, and this was shown to be correct by subsequently weighing the distilled menthol. The distillation with the oil-bath at 150-160° took three-quarters of an hour, which means that the reaction was carried out about fifty degrees lower, and in half the time of Beckmann's method. With practice this might be improved upon.

The product was used for a final attempt by allowing it to cool, adding the ortho-compound dissolved in dry benzene and shaking vigorously. After standing in the cold for three hours, the mixture was warmed at 70° for three hours, by the end of which no more solid was being deposited. On working up the product, the bulk of the menthol was/

was recovered, together with a syrup of very intense colour, which was found to be inactive.

These preparations were then abandoned, as the p-nitrochlorobenzene formed 4:4'-dichloroazoxybenzene, and the ortho-isomer, highly coloured inactive by-products.