THE INFLUENCE OF POLAR SOLVENTS ON THE OPTICAL ROTATORY POWER OF SIMPLE sec-β-OCTYL DERIVATIVES.

By

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INTRODUCTION.

In his van't Hoff Memorial Lecture to the Chemical Society in 1913, Sir James Walker remarks that it is a constantly recurring phenomenon in the history of science to find a pioneer, capable, one might think, of any mental step, stopping short on the threshhold of some important discovery or generalisation. This peculiarity is illustrated in a striking fashion by the early history of stereochemistry.

Pasteur's valuable work on the tartaric acids and tartrates cannot be underestimated. He showed the nature of the asymmetry of the crystalline forms, but the essentially practical mind of the Frenchman could not picture an answer to the question, "Are the atoms of the dextro-rotatory acid grouped on the spirals of a dextro-gyrate helix or placed on the summits of an irregular tetrahedron?" Years elapsed and space formulae, as we know them, came into existence associated with the names of Kekulé, Paternò and Wislicenus. When the tetrahedral carbon atom had been accepted by scientists, van't Hoff and Le Bel, practically simultaneously, answered Pasteur's question. The great contribution of these investigators to stereochemistry was to define a condition under which asymmetry could appear, namely when at least one carbon atom in the molecule was attached to four different groups. Although for long afterwards all known pairs of enantiomorphous substances complied with this condition, it is surprising that van't Hoff never referred this activity solely to the presence of the asymmetric carbon atom but rather to the dissymmetry which it introduced into the molecule as a whole. That is, a dissymmetrical molecule would be optically active whether that state was caused by an asymmetric atom or not. The far reaching truth of this generalisation is now becoming daily more evident as numerous optically active compounds without asymmetric carbon atoms are being prepared.

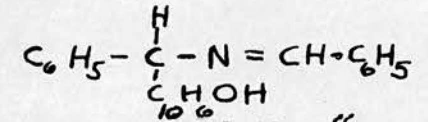
This principle being established, research naturally turned to the elucidation of the manner in which the rotatory power varied with the variation of the groups attached to the asymmetric atom. Foremost among the early theorists in this connection occur the names of Guye and Crum Brown. The former (Compt. rend., 1890 - 1896) suggested that the degree of asymmetry could be determined by the displacement of the centre of gravity of the regular tetrahedron from its planes of symmetry. Thus all that had to be considered was the mass of each group and the distance of its centre of gravity from the centre of the tetrahedron. Guye met with some success in his work on substituted amyl alcohols, but he, himself, soon discovered that the presence of two different groups of equal mass did not destroy optical activity as his theory demanded.

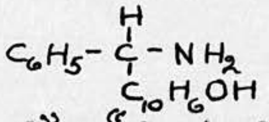
Although built on a less secure basis, in that it stipulated yet unknown quantities, Crum Brown's hypothesis (Proc. Roy. Soc. Edin., 1890, 17, 181), was more enduring. He suggested that, to each of the radicals about the asymmetric carbon atom, a function K could be ascribed, such that the product of the difference between each pair of K's would give the rotatory power. In his opinion the value of any given K would depend upon the composition and constitution of the radical. Crum Brown could not suggest any definite means of evaluating K, but his views are of interest in the light of modern theories of polarity.

A few more or less unconnected facts which obviously pointed to constitutional influences were known. Thus the presence of a double or triple bond or a ring structure usually increased the rotatory power. Also it had been discovered by Frankland (J.C.S., 1899, 75, 368) that in a homologous series of optically active compounds the value of the rotatory power sometimes undergoes a sudden change as the growing chain attached to the asymmetric atom reaches a length of five or six atoms. This was explained on the basis of Baeyer's Strain Theory as being caused by the tendency of the end of the chain to return to the neighbourhood of the asymmetric atom.

Our knowledge of this type of change has been considerably extended by the work of Kenyon and Pickard (J.C.S., 1912 onwards, see also Kenyon, Trans. Farad. Soc., 1930, 439) who showed that the maxima or minima may occur not only as the chain reaches 5 or 6 but also 10 or 11 carbon atoms in length, and that similar deviations sometimes occur when the whole molecule is made up of a chain containing this number of atoms.

However it was not until 1907 when Betti began his systematic researches that some definite progress began to be made in elucidating the relationship between the magnitude of the rotatory power and substituent influence. Lately, this worker has summarised his results in two papers (Gazz. Chim. Ital., 1927, 57, 814: Trans. Far. Soc., 1930, 26, 337). His most complete and convincing results were obtained with a series of Schiff's bases, of general formula I, obtained by condensing β-naphthol-phenyl-aminomethane, II, with benzaldehyde and substituted benzaldehydes.

I 
$C_6H_5-\underset{C_{10}H_6OH}{\overset{H}{C}}-N=CH\cdot C_6H_5$,

II 
$C_6H_5-\underset{C_{10}H_6OH}{\overset{H}{C}}-NH_2$

As a measure of the "constitutional" or "chemical" masses of the substituents he took the power each had to influence the dissociation of the carboxylic acids corresponding to the aldehydes, as determined by the dissociation constants of the acids. From an examination of over forty such compounds Betti has been able to establish a remarkable parallelism between the variation of the rotatory power and the dissociation constants, Compounds which have a higher positive rotation than the Schiff's base derived from benzaldehyde contain, in general, aldehydic residues corresponding to carboxylic acids with dissociation constants less than benzoic acid and vice versa. The nature of Betti's results has been emphasised (Rule, Trans. Far. Soc., 1930, 26, 324) by comparing the o- and p- substituted compounds with the corresponding acids in the following series. The agreement is particularly good among the para compounds.

Mono-ortho- substituted compounds.

$[M]_D$ $NO_2 < CH_3 < Cl < OH < OCH_3$

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

Mono-para- substituted compounds.

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

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

The scope of series such as the above is however not limited to problems in optical activity, but it has a wide application in general organic chemistry. Thus Olivier, (Rec. Trav. Chim., 1914, 33, 244) in a number of measurements of the velocities of Friedel-Crafts reactions between p-bromobenzene-sulphonyl chloride and substituted benzenes to form sulphones, obtained the series,

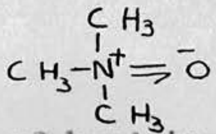
$$CH_3 > H > Br > Cl > NO_2$$

all these substituents being in the p-position. This author has also found (Rec. Trav. Chim., 1923, 42, 516, 775) that the rates of hydrolysis of p-substituted benzyl chlorides were in practically the same order

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

With only minor variations this series is repeated in the influence of the substituents on other properties, such as the dissociation constants of acids and bases (Flürscheim, J.C.S., 1909, <u>95</u>, 718) and the rate of hydrolysis of esters of substituted benzoic acids (Kellas, Zeit. Phys. Chem., 1897, <u>24</u>, 227). Robinson (Ann. Rep. Chem. Soc., 1922, 98) has called it a general polar series and the radicals composing it polar groups.

Until recent years very little was known as to what occurred in an organic molecule when polar groups were introduced. Rutherford, Bohr and Langmuir had given us atomic models which led to ideas of electro- and co-valencies in molecule formation, but it was in the sphere of inorganic chemistry that these conceptions were at first developed. In the latter state the bonding electrons are more or less equally shared by both atoms concerned in the combination, whereas in the former case, ions with equal and opposite electrical charges are formed by one or more electrons passing over completely from one atom or group of atoms to the other. Except where ions are known to be produced the atoms in an organic molecule were supposed to be held together by co-valencies and, while this is to a great extent true, later developments have shown that various intermediate stages may exist between a true co-valency and a true electro-valency. For example, the idea of the semi-polar double bond, as developed by Lowry and Sidgwick, stipulates that at a union one atom supplies both electrons constituting the linkage. Thus trimethylamine oxide is formulated,



$$CH_3-\overset{CH_3}{\underset{CH_3}{N^+}}\Rightarrow\overset{-}{O}$$

Further evidence of this type of bond is forthcoming from various sources, for example, parachor measurements (Sugden, The Parachor and Valency) and the resolution of sulphoxides (Harrison, Kenyon and Phillips, J.C.S., 1926, 2079).

It is now realised that when a co-valent linkage is made by substituting a polar group in a hydrocarbon molecule, the shared electrons are, in general, not equally shared but are attracted more strongly by one of the component parts of the resultant molecule. This part acquires a small negative charge, while the other acquires an equal positive charge. J.J.Thomson (Phil. Mag.,1923, 46, 497) has compared the introduction of a polar group into a hydrocarbon molecule to the insertion of an electrostatic doublet or dipole, which varies in strength and orientation with the nature of the substituent. Molecules containing such dipoles would, when placed in an electrostatic field, tend to orientate themselves with their dipoles opposing the field. Thomson therefore suggested that measurements of dielectric constants for long wavelengths would give an indication of the dipole strength, if corrections were made for the density and molecular weight of the substance. That this suggestion at least approximated to the truth was shown by Rule and Paterson,

(J. C. S., 1924, 125, 2186) who calculated a number of molecular inductive capacities for compounds of the types C_2H_5X and C_6H_5X, where X is a variable substituent. They found that in their power to increase the inductive capacity of both types of compounds the substituents fell in the order

$$NO_2 > CN > Cl > Br > CH_3 > H$$

which is once again an example of a polar series.

The whole theory of polar molecules has, within the last few years, been placed on a much sounder basis by the aid of a theory of dielectrics due to Debye (Physikal. Zeit., 1912, 13, 97: Polare Molekeln, Leipzig, 1929). It is now generally accepted that the dipole moment of a monosubstituted hydrocarbon is a true index of the polarity of the substituent atom or group. The dipole moment μ of a molecule may be defined as the charge on any one pole of the dipole, multiplied by the distance between the poles.

Debye developed his theory in the following manner. There are two main influences operative when polar molecules are placed in an electrostatic field. Firstly, an equilibrium will be set up between the above-noted tendency for the molecules to orientate themselves in opposition to the field and the tendency of thermal agitation to orient them equally in all directions. At equilibrium, a certain number of molecules, depending on their polarity, will be opposing the field.

Secondly, the external field will cause an appreciable distortion of the molecules, the electrons being attracted towards the positive side of the field and and the protons towards the negative side. This will lead to an induced polarization of the molecule as distinct from the permanent polarization due to the presence of polar groups.

The dielectric constant is a measure of the total change of the field strength due to the presence of the molecules. That is, it is a measure of the combined effects of orientation and distortion. According to Debye (Polare Molekeln) the electric moment or total polarization, P, per gram molecule is given by

$$P = \frac{\varepsilon - 1}{\varepsilon + 2} \cdot \frac{M}{\rho} \quad \text{------} (1)$$

$$= P_D + P_\mu \quad \text{-------} (2)$$

where ε is the dielectric constant,

M, the molecular weight of the dielectric,

ρ, the density of the dielectric,

P_D, the polarization due to distortion,

P_μ, the polarization due to orientation.

The next step is to evaluate P_μ. This unfortunately can not be done directly and P_μ is therefore usually given as the difference between P and P_D, both of which are amenable to direct measurement. The Lorenz-Lorentz equation

$$P_D = \frac{n^2 - 1}{n^2 + 2} \cdot \frac{M}{\rho} \quad \text{--------} (3)$$

where $\underline{n}$ is the refractive index of the dielectric, gives the value of the distortion term. Theoretically, far infra-red light should be employed in measuring n, in order to take account of both electronic and atomic distortions. The atomic distortion however is usually negligible as compared with the electronic distortion and therefore visible light, the refractive index of which is dependent on the latter phenomenon only, is used.

By making the appropriate determinations Debye was thus able to give a value to P_μ, the permanent polarization of the molecule. P_μ had yet to be connected with μ, the dipole moment of the molecule. A consideration of the conditions which limit the orientation of the polar molecules under the influence of a steady field enabled Debye to arrive at the following relationship,

$$P_\mu = \frac{4\pi N \mu^2}{9kT} \text{ ---------- } (4)$$

where N is Avogadro's number,

T, the absolute temperature, and

k, the Boltzmann constant.

The main effects considered in this equation were the influence of thermal agitation and dipole association. The latter phenomenon is one that is intimately connected with the work to be described in this thesis and so will be considered in some detail later. Polar molecules exert forces on each other when close together as in a liquid or highly compressed gas; they will therefore tend to arrange themselves in such a way as to minimise their external fields. This will apparently change their dipole moments. In order to obtain the true value of P_μ and hence μ, it is necessary to ensure that the dielectric constant measurements are made when each molecule is well separated from its neighbours and dipole association can not take place. Measurements in the vaporous state or in dilute solution in a non-polar solvent, such as benzene or hexane, are two available methods of which the latter is the most convenient and more generally applicable.

These methods have been used by Höjendahl (Thesis, Copenhagen, 1929), Errera (Leipziger Vorträge, 1929), C.P. Smyth (Chem. Rev., 549, 1929), J. Williams (Chem. Rev., 589, 1929), and many other investigators who have determined the dipole moments for a large number of compounds. From their results the most general conclusion is that dipole moments of monosubstituted hydrocarbons are to a great extent characteristic of the radical which brings about their existence and independent of the attached hydrocarbon residue. Thus nitro-paraffins and aromatic nitro-hydrocarbons have practically identical dipole moments although the hydrocarbon radicals are very different. Höjendahl (loc. cit.) has remarked on the sensibly constant dipole moment of homologues, while Debye points out that various simple aliphatic alcohols have the same dipole moments. From these observations it is reasonable to suppose that the electron shift which constitutes the dipole takes place only in the immediate neighbourhood of the substituent group. Since the measurements of dipole moments of monosubstituted hydrocarbons places the substituent radicals in the series,

$NO_2 > CN > CHO > \text{halogens} > OCH_3 > H > CH_3 > N(CH_3)_2 > NH_2$

it would seem that the general polar series represents a gradual transition from groups which attract electrons strongly to groups which repel electrons.

With this picture of the change which a polar group exerts on a molecule, the various regularities already noted in connection with reaction velocity, rate of hydrolysis and in particular Betti's investigations become explicable. As a further indication of the universality of this explanation one might cite a striking parallelism which has been shown by Rule (Trans. Far. Soc., 1930, 26, 325) to exist among the rotatory powers of *l*-menthyl and *l*-octyl esters of monosubstituted acetic acids, $XCH_2\ COOC_{10}H_{19}$ and $XCH_2\ COOC_8H_{17}$.

TABLE

X	μ x 10^{18} e.s.u.	Menthyl $[M]_D^{20}$	Octyl $[M]_D^{20}$
$N(CH_3)_2$	+1.4	-156.9	—
H	—	157.3	- 11.8(3)
CH_3	+0.4	160.2	- 13.0(3(
COOH	-0.9	160.2	—
OC_2H_5	—	160.6	—
OCH_3	-1.2	165	-16.3
OH	-1.7	165	—
Br	-1.5	169	-28.8
Cl	-1.5	171	-17.9
CN	-3.8	174	—

(1) Williams and Hojendahl (loc. cit.)

(2) Rule and Co-workers.

(3) Pickard and Kenyon, J.C.S., 1914, 105, 835.

Especially in the case of the menthyl esters the correspondence between the dipole moment series and the rotatory power series is remarkable. Assuming the validity of the theory of polarity as outlined above, Rule suggests (J.C.S., 1931, 674) the optical rotation of a dissymmetric compound is dependent on the magnitude and disposition of the dipoles within the molecule. Betti, on the other hand puts forward the hypothesis that the rotatory power depends upon the dipole moment of the molecule as a whole (Trans. Far. Soc., 1930, 26, 337).

The Influence of Polar Solvents on Optical Rotatory Power.

The observation of regularities when polar substituents are introduced into an optically active molecule, naturally led to investigations of the changes in rotatory power when the same optically active substance is dissolved in a series of related solvents, say monosubstituted benzenes.

Previous to this however, little or no definite progress had been attained in this direction despite a number of researches on the subject. In most cases the solvents used were too few in number or too varied in type to allow the observation of regularities.

Pickard and Kenyon (J.C.S., 1914, 105, 835) prepared a large number of esters of the type, CH_3 CHX COOR, where R is the optically active radical [illegible] and measured the rotatory powers in a number of solvents. Although these solvents were of diverse types, Pickard and Kenyon found that they fell into practically the same sequence in their effects on the rotation of many different esters. Generally, it was supposed that solvents affected the rotation by altering the degree of molecular association of the optically active molecules, but since esters are, as a rule, not associated to any great extent, the above authors suggested that the solvents may have had a specific effect on the carboxylic grouping which is common to all the substances examined. No general regularity that might lead to an explanation of the mechanism of solvent action was discovered, but the observation of the probable effect between the solvent and the ester grouping indicated the direction in which investigation should be pursued.

Rule and Mitchell (J.C.S., 1926 3202) were the first to employ a series of solvents derived from the same parent hydrocarbon, that is solvents which differed only in the substituent group present. They examined the effect of a series of substituted benzenes on five different d-sec-β-octyl acetates, $CH_2X\ COOH_8H_{17}$ (where X was respectively H, OCH_3, Cl, Br and I). The nature of their results is shown by the following table.

Molecular Rotations $[M]_D^{20}$ of d-octyl acetates in various 5% Solutions.

Solvent	Acetate	Methoxy Acetate	Chloro Acetate	Bromo Acetate	Iodo Acetate
Homog.	+11.8	+16.3	+17.9	+30.3	+41.1
$C_6H_5CH_3$	—	+ 0.8	—	+10.8	—
C_6H_6	- 1.4	- 1.0	+ 0.8	+10.1	+19.9
C_6H_5OEt	- 2.4	- 6.4	- 5.2	+ 4.9	+16.4
C_6H_5Cl	- 5.3	- 7.1	- 6.7	+ 2.5	+12.1
C_6H_5Br		- 7.0	- 8.8	+ 1.6	+ 9.1
C_6H_5I		-12.7	- 9.9	- 1.0	+ 2.9

Propionic ester, $[M]_D^{20}$ = 13.0° (homog). Pickard and Kenyon (J.C.S., 1914, 105, 831)

It will be noticed that the influence of substituents when present in the optically active acetate molecule is in the order,

$$I > Br > Cl > OME > Me > H.$$

and provided the same solvent is employed for all, the order of the substituents is practically independent of the nature of the solvent. When the solvent is changed by introducing a polar substituent into the molecule, as in C_6H_5X (where X is CH_3, halogens, etc.) The influence exerted by the substituent in the solvent on the dextro rotatory power of any single ester is in the order

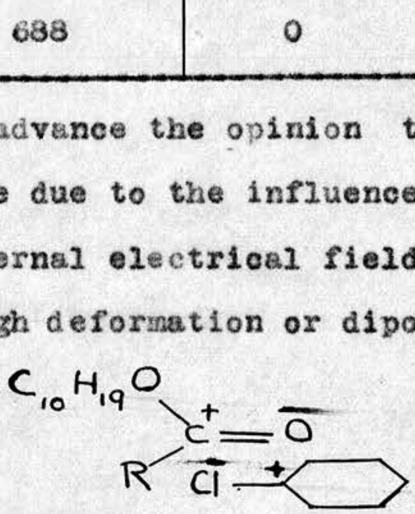
$$Me > H > OEt > Cl > Br > I$$

That is the changes produced by substitution in the solvent molecules are almost exactly the reverse of those produced by substitution in the optically active molecule. Thus in a later paper Rule (J. C. S., 1927, 58) suggested, that polar groups whether present in the asymmetric compound or in the solvent, also exert an influence on neighbouring molecules leading to corresponding changes in rotatory power.

The introduction of dipole moments gave a means of defining the polar nature of a solvent with much greater certainty than had hitherto been possible. It was not then surprising, in view of the previously noted conclusions, that Rule and McLean (J. C. S., 1931, 674) working with *l*-menthyl methyl naphthalate, which is extremely sensitive to change of solvent, should have arrived at more definite conclusions than previous investigators. They employed some fifty different solvents which may be, for the most part, placed in four classes as derivatives of methane, ethane, benzene and naphthalene respectively, and found that in each series as the dipole moment of the solvent increased, the rotatory power of the solution decreased. This is illustrated by the following table.

Solvent	$[M]^{20}_{5461}$	μ x 10^{18} e. s. u.
C_6H_5CN	-372	3.85
$C_6H_5NO_2$	423	3.98
C_6H_5CHO	432	2.75
o-$C_6H_4Cl_2$	433	2.24
C_6H_5Cl	463	1.62
C_6H_5I	465	1.50
C_6H_5Br	466	1.50
C_6H_5OMe	466	1.25
C_6H_6	543	0
$C_6H_5CH_3$	546	0
s-$C_6H_3(Me)_3$	583	0
Cyclohexane	688	0

These authors advance the opinion that the observed effects are due to the influence of the solvent dipole upon the internal electrical field of the solute, acting either through deformation or dipole association. For example



For example Rule and Hill (J.C.S., 1931, 2653) have observed similar variations in the rotation of d-sec-β-octyl hydrogen phthalate and d-sec-β octyl methyl phthalate in a series of related solvents. In both these recent papers by Rule and his co-workers, the regularities were more evident in the benzene solvents than in methane solvents, the explanation advanced being that in the latter case the methyl radical is so small that considerable differences in molecular volume and in physical shape are involved by the variations in X. Owing to the much larger volume and more rigid structure of the aromatic radicals these differences are of much less importance in the aromatic series.

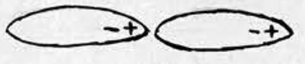
As Rule and McLean (loc. cit.) point out such a mechanism of solvent action is likely to be affected by factors other than the mere dipole strength of the solvent. Thus in the following table for -menthyl methyl naphthalate,

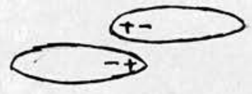
Solvent	$[M]^{20}_{5461}$
CH_3I	-336°
C_2H_5I	-383
C_6H_5I	-465
$C_{10}H_7Br$	-553
s-$C_6H_3(CH_3)_3$	-583

it will be seen that as the hydrocarbon residue attached to the same iodine atom increases in bulk, the rotation rises until it approximates to that given in a purely non-polar solvent. This effect in general is attributed to two causes. Firstly the diminished frequency with which the polar substituent in the larger molecule will come into the neighbourhood of the solute dipoles and secondly the screening of the solvent dipole by the bulky hydrocarbon residue, thus progressively hindering dipole association with the solute.

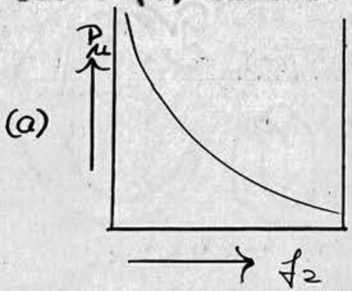
Association of Solvents.

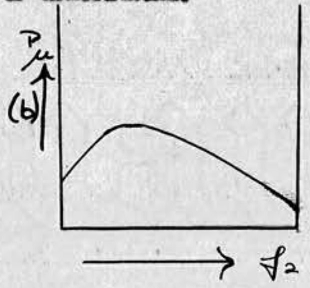
Another factor which is likely to interfere strongly with the observation of regularities in solvent action is molecular association of solvent molecules with themselves. The two most common ways in which this can take place may be illustrated diagrammatically as follows.

(1)


(2)


The dipole moment of a complex such as (1) would be more than twice that of a single molecule, while the dipole moment of two molecules associated in the manner (2) would be zero. (Smyth, Chem. Rev., 1929, 6, 549). Rule and McLean (loc. cit.) discuss this point and produce definite evidence that it is operative among the rotations observed by them. As has already been noted (p.) this difficulty was overcome in the measurements of dipole moments by diluting the associated polar substance with a non-polar medium such as benzene or hexane when it is progressively dissociated to the state of single molecules. In his measurements of dipole moments Debye showed that many substances have characteristic polarization-dilution curves. Thus nitrobenzene gave a curve of shape (a) when progressively diluted with benzene, while the ethyl alcohol polarization curve (b) exhibited a maximum.





In a compound, the polarization curve of which takes the form shown in (a) the molecules are associated so as to neutralise each others field (see (2)) and in (b) a mixture is supposed to exist, form (1) being more stable at low concentrations, and giving way to form (2) as the concentration increases.

By an analysis of the rotation curves obtained with ℓ-menthyl methyl naphthalate in mixtures of nitrobenzene and benzene, and ethyl alcohol and benzene, similar to Debye's analysis of his polarisation curves, Rule and McLean (loc. cit.) were able to show that to a great extent the rotation curves of the optically active substance in mixtures of solvents corresponded to the polarization curves of the solvent mixtures.

In the optical investigations already described, the compounds have been esters of complex structure such as menthyl methyl naphthalate or octyl hydrogen phthalate, in which one of the chief influences affecting the rotatory power is a spatial one propagated between the peri or ortho substituents. The present thesis deals with optically active derivatives of simple structure, with one exception all of the compounds examined are derived from sec-β-octane, and the majority of them contain only one polar substituent in the molecule. It was desired to determine whether similar solvent effects could be observed in these cases and if so, whether the direction of the changes could be related to those caused by the association of the optically active molecules with one another. It was also proposed to examine the change in the rotatory power of sec-β-octyl alcohol at different concentrations in benzene and hexane, in order to discover whether the rotation curve exhibited maxima or minima similar to those found for the polarization of many such alcohols under such conditions.

PREPARATIVE.

Resolution of sec. β-Octyl Hydrogen Phthalate and Preparation of d- and l-sec. β-Octyl Alcohol.

Racemic octyl hydrogen phthalate as supplied by Messrs. Boots was resolved by the method of Pickard and Kenyon (J. C. S., 1907, 2058: 1922, 2540). The brucine salt was formed in acetone and the separation of the diastereoisomerides accomplished in the same medium. Both salts were then treated with mineral acid and the enantiomorphous phthalates so obtained repeatedly crystallised (usually five times) from 90% acetic acid until the rotatory power attained the value $\alpha^{20}_{5461} = \pm 58.3^{\circ}$ (in ethyl alcohol, c = 5). These optimally pure phthalates were now hydrolysed by boiling with aqueous caustic potash. The alcohol was extracted with ether, the ethereal solution dried over anhydrous sodium sulphate and the alcohol distilled under reduced pressure. The observed boiling point was 71°/12 mm.

The most convenient quantity of phthalate to employ in one resolution was found to be 250 grams, from which approximately 60 grams of each of the pure phthalates and subsequently 28 grams each of the d- and - alcohols were obtained. Octyl hydrogen phthalate of a low activity was recovered from the mother-liquors and used in subsequent resolutions. The rotatory power of the alcohol varied within the limits $\alpha^{20}_{5461} = \pm 9.60^{\circ}$ to $\pm 9.67^{\circ}$ in a 1 dm. tube. Pickard and Kenyon quote on an average $\alpha^{20}_{5461} = 9.65^{\circ}$. With two exceptions all the optically active compounds described in this thesis were prepared from active octyl alcohol, and in most cases the yields obtainable were not very high. For this reason considerable quantities of the active alcohols were required as starting material, and it was found necessary to carry through the above procedure nine times in the course of the research.

Preparation of *d*-2-Chloro-octane.

There are several methods described in the literature for the preparation of this compound giving specimens with widely varying rotatory powers. Having regard to the yield and consistency of results, the method of McKenzie and Tudhope (J. Biol. Chem., 1924, 62, 551) was adopted. Thionyl chloride (32·5 grams) was added slowly to an ice-cold solution of *l*-octyl alcohol (26grams) in pure, dry pyridine (18 grams). A white crystalline solid separated and, by heating on the water-bath, this was decomposed with vigorous evolution of sulphur dioxide. Heating was continued for 3 hours, after which water was added and the mixture extracted with ether. The extract was washed thoroughly with hydrochloric acid and subsequently with dilute sodium bicarbonate solution followed by water. It was then dried over anhydrous sodium sulphate. After removing the solvent, a distillation under reduced pressure yielded 12 grams of colourless liquid, boiling at 57.5-58°/12 mm.

Several different samples were prepared with rotations varying from $\alpha^{20}_{5461} = +31.1^\circ$ to $\alpha^{20}_{5461} = +35.0^\circ$ in a 1 dm. tube. These values compare favourably with those obtained by other workers, as given below.

Levene and Mikeska (J. Biol. Chem. 1924, 59, 45)
$\alpha^{20}_{D} = 26.7^\circ$:

McKenzie and Tudhope (loc. cit.) $\alpha^{20}_{D} = 29.2^\circ$: and

Houssa, Kenyon and Phillips (J.C.S., 1929, 1704)
$\alpha^{15^\circ}_{D} = 31.0^\circ$

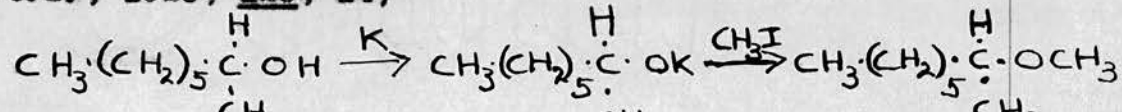
Preparation of d-2 Bromo-octane.

As in the previous preparation, the formation of the product involves an inversion of sign. To 32 grams of cooled ℓ-octyl alcohol, 75 grams of phosphorus tribromide were slowly added according to the instructions of Shriner and Young (J.A.C.S., 1930, 52, 3337), so that the temperature did not rise above 5°. The mixture was well stirred during the addition of the tribromide and after standing overnight, when it was allowed to rise to room temperature, it was heated on a water-bath for one hour. The liquid was then poured into 200 cc. of ice-cold water and the octyl bromide, which separated as an oil, was extracted with ether. After washing and drying, this extract yielded 36.5 grams (88.5% : quoted yield 85.3%) of d-2-bromo-octane, boiling at 72°/13 mm.

The rotatory power of bromo-octane so obtained was $\alpha^{20}_{5461} = +44.0^\circ$ in a 1 dm. tube. This is a more highly active product than that prepared by Shriner and Young, who quote $\alpha^{20}_{D} = 29.8^\circ$. Assuming a ratio $\alpha_{5461}/\alpha_{5893}$ of about 1.18 this value for α_D would correspond approximately to a value of $\alpha^{20}_{5461} = +35.2^\circ$. It was not possible to obtain a direct comparison with the value of Shriner and Young as no polarimeter for use with the D line was available.

Preparation of d-sec-β-Octyl Methyl Ether.

In the preparations noted above the complete hydroxyl group directly attached to the asymmetric carbon in sec-β-octyl alcohol is replaced by another radical. This change leads to an optical inversion and a product of variable rotatory power. The simple reaction giving the above ether (Kenyon and McNicol J. C. S., 1923, 123, 14)



$$CH_3\cdot(CH_2)_5\cdot\overset{H}{\underset{CH_3}{C}}\cdot OH \xrightarrow{K} CH_3\cdot(CH_2)_5\cdot\overset{H}{\underset{CH_3}{C}}\cdot OK \xrightarrow{CH_3I} CH_3\cdot(CH_2)_5\cdot\overset{H}{\underset{CH_3}{C}}\cdot OCH_3$$

indicates no detachment of the hydroxyl group, and there is no reversal in the sign of rotation. The variation in rotation noted below is therefore somewhat surprising considering the vigorous method adopted to free the substance from unchanged alcohol.

d-Octyl alcohol (25 grams) of $\alpha^{20}_{5461} = 19.64^\circ, \ell=2)$ was slowly added to metallic potassium (5gms) suspended in dry benzene (50 ccs.) The reaction was very slow and after heating for 9 hours about 0.5 grams potassium remained still undissolved. This was removed from the liquid and freshly distilled methyl iodide (18 gms) was slowly added, whereupon a copious white precipitate was immediately formed. The mixture was heated on a water-bath for 20 hours to complete the reaction. The potassium iodide was washed out with water and the dried benzene solution specially treated in order to remove unchanged alcohol. Preliminary experiments showed that a considerable quantity of unchanged alcohol remained mixed with the ether and that heating with phthalic anhydride as recommended by Kenyon and McNicol did not appear to remove it very effectively. Eventually the following procedure was adopted. The crude octyl ether, after removing benzene, was heated with one third of its weight of p-nitrobenzoyl chloride and one third of its volume of dry pyridine for 2 or 3 hours on a water-bath. After cooling, the mixture was treated with water and extracted with ether, the ethereal extract being washed with dilute acid. When all the pyridine had been removed by this means, the extract was washed with caustic soda solution and finally with water. It was then dried and distilled. The yield of ether boiling at 67°/40 mm. was poor (10 grams: 35.5%) The rotatory power of the product from several preparations varied between the limits $\alpha^{20}_{5461} = +7.36^\circ$ to $+6.14^\circ$ in a 1 dm. tube. The figure quoted by Kenyon and McNicol (loc. cit.) is $\alpha^{14}_{5461} = +7.14^\circ$, yield 50%.

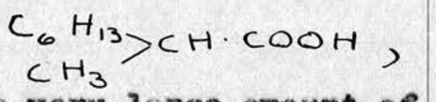
Preparation of *l*-2 Nitro-octane.

Shriner and Young (loc. cit.) also described the preparation of this compound. Finely ground silver nitrite (47 gms) was suspended in dry benzene (65 ccs.) and, with vigorous stirring, d-2-bromo-octane (36.5 grams) was slowly added. At no time did the temperature rise above 0° and after the addition of the bromide stirring was continued for three hours. During this time the mixture slowly acquired room-temperature and thereafter it was heated on a water-bath for six hours. The benzene solution was then removed by decantation and the solid residue washed twice with small quantities

25 cc. each time of benzene, the washings being added to the original benzene solution. This extract yielded 4 grams (13·4%) of nitro-octane of boiling point = 98-102°/18 mm. and rotation α^{20}_{5461} = -15·42° (ℓ= 1). A considerably larger quantity of octyl nitrite was also isolated. The poor yield obtained from the conversion of the bromide into the nitro-compound made it necessary to repeat this reaction to obtain sufficient material.

Shriner and Young (loc. cit.) quote a 15% yield. It was not possible to check the above rotation against their figure as they quote α^{25}_{D} = -10·8°, (absolute alcohol) which is useless for the purpose of comparison in the absence of any information regarding the concentration of the solution and the length of tube they employed.

Preparation of α-n-Butyl Propionic Acdi.

It was desired to investigate the optical properties of a carboxylic derivative of octane comparable with the alcohol, halides, nitro-compound and ether also under examination. Unfortunately the synthesis of sufficient quantities of the corresponding acid α-n-hexyl-propionic acid, 
$\begin{matrix} C_6H_{13} \\ CH_3 \end{matrix}\!>\!CH \cdot COOH$, would have required the use of a very large amount of n-hexyl iodide, which is a comparatively inaccessible compound. In the first instance, therefore, the next lower homologue was synthesised. This proved to form

alkaloidal salts having a poor power of recrystallisation, and could only be obtained in a partially active condition with the quantity available. The work with this acid is described below. (page)

Attention was next turned to α- n -butyl-propionic acid, $C_4H_9\cdot CH(CH_3)\cdot COOH$, which has been resolved by Levene and Bass (J. Biol. Chem., 1926, <u>70</u>, 211). This was prepared in the following stages.

(1) <u>Dimethyl Ester of n-Butyl-malonic Acid.</u>

Details of this stage in the preparation were obtained from "Organic Syntheses" (New York, 1924, Vol. IV, page 11). A solution of sodium ethoxide was prepared by dissolving 85 grams (1 mole) clean sodium in 950 cc. of absolute alcohol (newly dried by distilling from sodium). This solution was stirred and cooled to about 50°, after which 495 grams (1 mole) of dimethyl malonate were slowly added. To the mixture, 500 grams (1 mole) of freshly distilled n-butyl bromide were then gradually added. The reaction set in rapidly with the generation of considerable heat. The mixture was then boiled under reflux until neutral to litmus and thereafter as much alcohol as possible was distilled off on a steambath. One litre of water was added to the residue to dissolve out the sodium bromide which had been deposited and the whole shaken thoroughly. The upper layer of the dimethyl ester of n-butyl-malonic acid was separated and distilled under reduced pressure. It was collected over a range of 5°. Yield 430 grams.

(2) Dimethyl Ester of Methyl-n-butyl-malonic Acid.

In exactly the same way as above, the reaction was again carried out using methyl iodide instead of butyl bromide and n-butyl-malonic ester instead of malonic ester. As there is very little difference between the boiling points of these mono- and dialkylated malonic esters, separation by fractional distillation was not attempted. The yield was 480 grams of crude dialkylated ester.

(3) Methyl-n-butyl-malonic Acid.

The disubstituted malonic ester was hydrolysed by boiling under reflux for 10 hours with 2 molecular proportions of potassium hydroxide in aqueous alcohol (80% by volume). The alcohol was then distilled off and the residue taken up in water, from which the acid was precipitated by adding 20 per cent sulphuric acid. The resultant floculant mass was extracted with ether. At this point Levene and Bass recommended crystallisation but did not give experimental details. For this reason the method used by Rosetti (Bull. Soc. Chim., 1905, (3), 33, 688) involving solution in benzene and precipitation with petrol ether was employed. After three precipitations a clean substance of constant melting point (96°) was obtained. Yield 135 grams.

(4) α-n-Butyl-propionic Acid.

The methyl-n-butyl-malonic acid was heated to 180° in a flask fitted with an inclined air condenser. There was a brisk evolution of carbon dioxide and when this had ceased the resulting monobasic acid was distilled under reduced pressure. The yield was 80 grams boiling at 119°/22 mm.

Resolution of α-n-Butyl-propionic Acid.

The quinine salt of the acid was formed by adding 230 grams of alkaloid to 80 grams of the acid dissolved in 530 cc. of hot acetone. The quinine went into solution immediately and on cooling 132 grams of salt crystallised out. The mixed salts were separated by repeated crystallisation from acetone; it was noticeable that although the weight of salt decreased with successive crystallisations, the quantity of acetone required to dissolve it increased. After the 4th, 5th, and 6th recrystallisations, samples (3 gm.) of the salt were decomposed with 10 per cent sulphuric acid (15 cc.) and the free organic acid was extracted with ether. The extract was washed with dilute sulphuric acid and water, dried over anhydrous sodium sulphate and distilled in vacuo.

Solutions of the acid in benzene (c = 5) gave the following rotations:-

4th crystallisation, $[\alpha]^{20}_{5461} = 21{\cdot}1°$.

5th crystallisation, $[\alpha]^{20}_{5461} = 23{\cdot}5°$.

6th crystallisation, $[\alpha]^{20}_{5461}$ = 24·3°.

As there remained only 53 grams of salt at this stage, it was thought advisable to convert it to the acid as above in order to obtain sufficient material for the work proposed. Yield 12 grams of boiling point 116·5-117°/20 mm.

In ether (c = 5) the above acid gave a rotation of α^{20}_{5461} = 2·33°, which on the assumption of a ratio $\alpha_{5461}/\alpha_{5893}$ approximating to 1·18, gives a value of $[\alpha]^{20}_{5893}$ in the neighbourhood of 15·7°.* Levene and Bass quote $^{20}_{5893}$ = 19·6 in ether (c = 5·5). Hence the above resolution was not complete.

Preparation of α-n-Amyl-propionic Acid.

This compound was prepared in exactly the same way as described above for the n-butyl propionic acid.

The malonic synthesis was carried out using amyl bromide (265 grams) and sodium (40·8 grams). This yielded 278 grams of n-amyl-malonic ester of boiling point 140-145°/15 mm. The latter, on treatment with molecular quantities of methyl iodide and sodium gave 230 grams of methyl-n-amyl malonic ester, of boiling point 125-127°/12 mm. On hydrolysing the dialkyl malonic ester, 130 grams of methyl-amyl-

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* No polarimeter fitted for determining rotations with the D line was available at this time.

malonic acid were obtained, m.p. 98°. Finally on heating above its melting point the latter gave 65 grams of α-n-amyl-propionic acid, b.p. 124-126°/14 mm. The whole of this preparation was carried through once more using smaller quantitess, when a further 35 grams of acid were obtained.

Attempted Resolution of α-n-Amyl-propionic Acid.

(a) Attempted Resolution with Quinine.

To a solution of 8·5 grams of acid in 55 cc. of hot acetone was added 22 grams of quinine. The solution was cooled in ice and salt but nothing separated out. The solvent was then evaporated down in a desiccator, when a syrupy liquid remained, which eventually set to a glass. Attempts to recrystallise the latter from various solvents proved unsuccessful as it was either too soluble to be of any value for resolution or separated as an oil.

(b) Partial Resolution by means of Cinchonidine.

Test experiments were first carried out using small quantities. To a boiling solution of 5 grams of α-n-amyl-propionic acid in 50 cc. of acetone were added 10 grams of cinchonidine. Only about half of the alkaloid went into solution and when sufficient acetone was added to dissolve the remainder no salt separated out on cooling. Another attempt was then made in which, instead of adding more acetone the undissolved alkaloid was filtered off. On cooling the clear solution, a further quantity of white solid separated which on filtering and drying was found to be cinchonidine. The filtrate, when cooled in a freezing mixture, deposited successive crops of crystals. These were separated and dried. They were found to have melting points varying from 69° to 72° and were taken to be the cinchonidine salt of α-n-amyl-propionic acid.

To see if any resolution had taken place, the final filtrate from the crystals was evaporated to dryness, and the free acid liberated by adding dilute sulphuric acid. The organic acid was extracted with benzene. This solution was found to have a rotation $\alpha^{20}_{5461} = +0{\cdot}2^\circ (\ell = 2)$, whereas the cinchonidine is laevorotatory. The salt which had been filtered off was treated in the same way and the benzene solution found to have a negative rotation.

The main part of the racemic acid was thentaken and treated in the same manner. Cinchonidine (170 grams) was added to a solution of 85 grams α-n-amyl-propionic acid in 1200 cc. hot acetone. The alkaloid which remained undissolved was filtered off and, on cooling, 60 grams of salt were deposited. This melted sharply at 72°. The salt was again dissolved in acetone, but a further deposition of cinchonidine occurred when the solution was heated, and had to be filtered off. Decomposition of the salt was also evident from the small quantity which could be recovered. After two recrystallisations the weight of salt had been reduced to 10 grams. This was decomposed with 10 per cent sulphuric acid and the free organic acid extracted with ether. The ethereal extract was washed with dilute sulphuric acid and water, and then dried and distilled. The rotation of a benzene solution was $\alpha^{20}_{5461} = +16{\cdot}6^\circ$ (c = 4).

In agreement with the properties of other acids of this type, the rotatory power was unchanged after prolonged heating with excess of alkali. As has been shown by McKenzie and Smith (Ber., 1925, <u>58</u>, 894) such acids are comparatively readily racemised if one of the groups attached to the secondary carbon atom is an aromatic radical. It was therefore not possible to racemise the recovered acid of weak dextro-rotation for the purpose of utilising it in a further resolution. Owing to the difficulties involved in the resolution and the very small yield of active salt, this preparation was not further examined.

sec-β-Octyl Esters.

I am indebted to Dr. H. G. Rule for samples of the following octyl esters. The sec-β-octyl toluates were distilled before use but the sec-β-octyl methoxybenzoates were received in the pure condition. The rotations of these compounds were checked in the homogeneous state in a 1 dm. tube.

(1) *d*-sec-β-Octyl o-Toluate.

Found $\alpha_{5461}^{20} = +31{\cdot}16^\circ$. Rule, Hay, Numbers and Paterson (J.C.S., 1928, 184) quote $_{5461}^{20} = +31{\cdot}10^\circ$.

(2) *l*-sec-β-Octyl m-Toluate.

Found $\alpha_{5461}^{20} = -42{\cdot}63^\circ$. Rule and co-workers quote $\alpha_{5461}^{17\cdot6} = 43{\cdot}04^\circ$.

(3) *l*-sec-β-Octyl p-Toluate.

Found $\alpha_{5461}^{20} = -47{\cdot}13^\circ$. Rule and co-workers quote $\alpha_{5461}^{20} = 47{\cdot}25^\circ$.

(4) *l*-sec-β-Octyl o-Methoxy Benzoate.

Found $\alpha_{5461}^{20} = -14{\cdot}44^\circ$. Rule and Numbers (J.C.S., 1926, 2121) quote $\alpha_{5461}^{24\cdot4} = -14{\cdot}64^\circ$.

(5) *l*-sec-β-Octyl m-Methoxy Benzoate.

Found $\alpha_{5461}^{20} = -42{\cdot}13^\circ$. Rule and Numbers quote $\alpha_{5461}^{20} = -42{\cdot}05^\circ$.

(6) *l*-sec-β-Octyl p-Methoxy Benzoate.

Found $\alpha_{5461}^{19} = -51{\cdot}37^\circ$. Rule and Numbers quote $\alpha_{5461}^{21\cdot5} = -51{\cdot}12^\circ$.

SOLVENTS.

All solvents used were specially purified and benzaldehyde was always freshly treated immediately before it was required. The methods adopted for purification are described briefly in the following pages.

(1) Acetaldehyde. Aytoun, Scott and Co.'s acetaldehydr was dried over calcium chloride, boiled over succinic acid to remove traces of basic impurity and fractionated. B.p. 20·8°.

(2) Acetic Acid. Kahlbaum's 100% acetic acid was cooled until about two-thirds frozen; the liquid portion was decanted off and the crystalline mass fractionated. M.p. 16°; b.p. 118-118·2°.

(3) Acetone. B.D.H. "bisulphite purified" acetone was well dried over anhydrous calcium chloride and fractionated. B.p. 55-56°. The bottle was afterwards kept in a desiccator.

(4) Acetonitrile. Aytoun, Scott and Co.'s acetonitrile was dried over calcium chloride and fractionated, giving a colourless product, b.p. 80·7-81·4°.

(5) Acetophenone. Merck's acetophenone was partially crystallised and the crystalline portion, filtered off, dried and fractionated. M.p. 20°; b.p. 201·8-201·9°.

(6) Aniline. Kahlbaum's aniline "from sulphate" was dried and fractionated giving a colourless liquid of b.p. 182·9-183°.

(7) *Anisole.* B.D.H. anisole was washed with sodium hydroxide solution and water and then fractionated. It was colourless and gave no phenol reaction. B.p. 153·8°.

(8) *Benzaldehyde.* Kahlbaum's purified product was dried and fractionated, care being taken to expose to the air as little as possible. B.p. 179-179·2°.

(9) *Benzene.* B.D.H. "extra pure" benzene was partially frozen out and the solid mass removed, dried and fractionated. F.p. 5·5°; b.p. 80-80·1°.

(10) *Benzonitrile.* Aytoun, Scott and Co.'s product was dried and partially frozen out; the crystalline portion was fractionated under reduced pressure. It was obtained as a colourless liquid of f.p. -12·9°, and b.p. 82·5°/15 mm.

(11) *Bromobenzene.* B.D.H. bromobenzene was well washed with sodium carbonate solution and water, dried over calcium chloride and fractionated under reduced pressure. B.p. 50°/15 mm.

(12) *Carbon Disulphide.* Aytoun, Scott and Co.'s redistilled carbon disulphide was shaken with mercury to remove sulphur, dried over calcium chloride and repeatedly fractionated, b.p. 46-46·2°.

(13) *Carbon Tetrachloride.* The sample used had already been carefully purified. It was dried and fractionated. B.p. 131·6-131·8°.

(14) *Chlorobenzene.* The B.D.H. product was washed with sodium carbonate and water, dried over anhydrous calcium chloride and fractionated. B.p. 131·6-131·8°.

(15) Chloroform. Aytoun, Scott and Co.'s chloroform was shaken with concentrated sulphuric acid for $\frac{1}{4}$ hour to remove alcohol. It was then washed with sodium hydroxide solution and water, dried over anhydrous potassium carbonate and fractionated. B.p. 60·7-60·9°. This method is due to Hentzsh and Hoffmann, (Ber., 1911, **44**, 1777).

(16) Cyclohexane. B.D.H. cyclohexane was dried, partially frozen out, dried and fractionated. M.p. 4·1°; b.p. 80·1-80·3°.

(17) o-Dichlorobenzene. On cooling B.D.H. o-dichlorobenzene to -20°, a small amount of crystalline substance (probably p-dichlorobenzene) was deposited and rapidly filtered off at the pump. The liquid was then dried over calcium chloride and fractionated under reduced pressure, b.p. 60-61°/11 mm.

(18) Ethyl Alcohol. "Absolute" ethyl alcohol was refluxed over freshly prepared lime and then fractionated, b.p. 78°. The bottle was kept in a desiccator.

(19) Ethyl Ether. Macfarlan and Co.'s best quality anhydrous ether was dried with sodium wire and the fraction boiling over 34-36° collected.

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

(21) Iodobenzene. The B.D.H. product was washed with sodium carbonate solution and water, dried over calcium chloride and fractionated. It was obtained practically colourless, b.p. 75°/16 mm.

(22) Mesitylene. Merk's product was dried over calcium chloride and fractionated, b.p. 164-165°.

(23) Methyl Alchhol. "Absolute" methyl alcohol was purified according to the method of Bjerrum and Zichmeister. (Ber. 1923, 56, 897). The alcohol was allowed to stand in a reflux apparatus with clean dry magnesium, (10 grams to each litre). A vigorous reaction set in and the alcohol boiled. When all the metal had disppeared the mixture was refluxed for 4 hours and then distilled, (first and last fractions being rejected) in a current of dry air.

(24) Methylene Chloride. The B.D.H. product was washed with potassium hydroxide solution and water, dried over calcium chloride and fractionated, b.p. 41·8-42·2°.

(25) Methyl Iodide. Aytoun, Scott and Co.'s purified methyl iodide was washed with sodium carbonate solution and water, dried over calcium chloride and fractionated. B.p. 42·7-43·0°.

(26) Nitrobenzene. B.D.H. nitrobenzene was partially frozen out. The crystalline portion was separated, dried and fractionated under reduced pressure. F.p. 5·6-5·7°; b.p. 90-91°/15 mm.

(27) Nitromethane. The B.D.H. product was washed, dried over calcium chloride and fractionated. It was obtained colourless, b.p. 108-110·1°.

(28) Toluene. Aytoun, Scott and Co.'s "pure" toluene was dried with sodium wire and fractionated

using a long column.   B.p. 109·7-109·8°.

DETERMINATIONS OF OPTICAL ROTATORY POWER.

In the following pages are recorded the rotatory powers of the different octyl derivatives, when dissolved in solvents of varying polarity as determined from their dipole moments. The rotations are arranged in order of decreasing values of $[M]_{5461}$.

A polarimeter with an accuracy of ± 0.01° was used and in the majority of cases the solution was contained in a narrow-bore 2 dms. tube. In some cases where the observed rotations were very low, or showed very small differences, a tube of 4 dms. length was used, having a bore of 3-4 mm. The use of narrow-bore tubes was made necessary owing to the relatively small quantities of optically active products available. All the substances under examination, but especially the d-butyl-propionic acid and ℓ-2-nitro-octane, had to be recovered by vacuum distillation and their rotations checked many times during the investigations. The narrow-bore polarimeter tubes were not fitted with water jackets but the rotatory powers were determined in a constant-temperature room maintained at 20° (± 1°). Temperature changes had little effect on the rotations except in the case of d-2-chloro-octane and d-2-bromo-octane.

Where determinations were carried out over a range of concentrations varying from the homogeneous substances to a high dilution, the concentration is expressed in terms of the mole fraction (f) of the optically active substance present in the mixture.

DISCUSSION OF RESULTS.

TABLE I.

Rotatory Powers of ℓ-sec-β-Octyl Alcohol in Solvents.

In each case $t = 20°$ $\ell = 4$ dms.

(a) Methane Type.

Solvent	c gms/100 cc.	α^{20}_{5461}	$[M]^{20}_{5461}$	$\mu \times 10^{18}$ e.s.u.
CS_2	5·00	- 3·12°	-20·3°	0
CCl_4	5·00	2·99	19·4	0
C_6H_{14}	5·00	2·94	19·1	0
CH_3I	5·00	2·63	17·1	1·66
CH_3OH	5·00	2·61	17·0	1·64
CH_3COOH	5·00	2·55	16·6	0·75
Homogeneous		19·34	15·3	—
CH_3CN	5·00	2·28	14·8	3·05
$CHCl_3$	5·00	2·19	14·2	1·10
CH_2Cl_2	5·00	2·14	13·9	1·61

(b) Benzene Type.

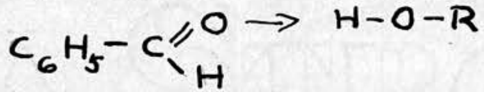
Solvent	c gms/100 cc.	α^{20}_{5461}	$[M]^{20}_{5461}$	$\mu \times 10^{18}$ e.s.u.
C_6H_5CHO	5·00	− 3·16°	−20·5°	2·75
$C_6H_5CH_3$	5·00	2·96	19·2	0·50
C_6H_6	5·00	2·95	19·2	0
$C_6H_5NH_2$	5·00	2·90	18·8	1·60
$C_6H_5COCH_3$	5·00	2·80	18·6	2·97
$C_6H_5NO_2$	5·00	2·80	18·2	3·90
$C_6H_5OCH_3$	5·00	2·78	18·1	1·25
C_6H_5Br	5·00	2·75	17·9	1·50
C_6H_5Cl	5·00	2·74	17·8	1·52
C_6H_5I	5·00	2·73	17·8	1·50
C_6H_5CN	5·00	2·66	17·3	3·85
Homogeneous		19·34	15·3	–

d_4^{20} = 0·822 (Pickard and Kenyon, J.C.S., 1922, 121, 2058).

l-sec-β-Octyl alcohol has already been examined polarimetrically in a number of solvents by Pickard and Kenyon (J.C.S., 1914, 105, 884), but in view of the regularities observed by Rule and his co-workers who employed series of related solvents, it was decided to extend the investigations of the former authors along similar lines. Although the variation of the molecular rotation with change of solvent is comparatively small in the case of octyl alcohol, a definite polar influence is evident. With two or three exceptions, there is a general tendency for solvents of low polarity to give high rotations and those of high polarity to give low rotations. Thus carbon disulphide, carbon tetrachloride and hexane in the methane series and toluene and benzene in the benzene series, all having a dipole moment approximating to zero, are found at the head of the lists, while the more polar solvents give lower values.

This is as would be predicted on the assumption of dipole association between optically active solute and solvent (Rule and McLean, loc. cit.). Non-polar solvents will split up the associated complexes of octyl alcohol to varying extents, depending upon a factor at present unknown, but otherwise will have little or no effect on the internal field of the optically active molecules. Polar solvents will also bring about the same change, but, in addition, the dipoles in the solvent molecules will be attracted to the hydroxylic dipoles, leading to association in the manner indicated in the introductory section. Such an association will lower the internal field of the optically active molecules and with the majority of simple monosubstituted compounds this may be expected to result in a lowering of the rotatory power.

As may be observed from the tables, a moderately good agreement with the polarity of the solvent is given with solvents derived from methane, in spite of the fact that a comparison is here made between a hydrocarbon and mono-, di-, tri- and tetrasubstituted derivatives. In the case of the aromatic solvents the differences in the observed values of α are smaller and experimental errors may account for some of the minor inversions found on comparing rotatory powers with dipole moments. The abnormal position of benzaldehyde, however, is very striking. Sidgwick (Electronic Theory of Valency, p. 148) points out that benzaldehyde may form a co-ordination compound with phenol or other hydroxylic compound, the aldehydic oxygen acting as donor atom in the linkage,



$$C_6H_5-C\overset{\displaystyle /\!\!/ O}{\underset{\displaystyle \diagdown H}{}} \rightarrow H-O-R$$

A definite chemical combination of this type would probably exert a stronger influence than dipolar association and, if it existed between benzaldehyde and octyl alcohol, the solution would be expected to exhibit an abnormal rotatory power. In this respect it is noteworthy that nitrobenzene, the oxygen atom of which can act in the same way, and acetophenone, which is related to benzaldehyde, also show rotations higher than might be expected. Since the ketonic group in acetophenone is more screened than that in benzaldehyde, it may be surmised that co-ordination will be more complete in the latter case, thus accounting for the more abnormal value for the rotation.

Further support for these conclusions regarding the mechanism of polar and non-polar solvent influence is provided by the following data referring to the changes in the rotatory power of octyl alcohol brought about on dilution with a non-polar medium. Alcohols in general show a great tendency to associate in the homogeneous state, and this association may be assumed to have much the same effect on the rotation as association with a polar solvent. In this manner the low position which the rotatory power of the homogeneous alcohol occupies in the tables is partly explained, although it is unexpectedly low in relation to the values obtained in aromatic solvents.

Table II.

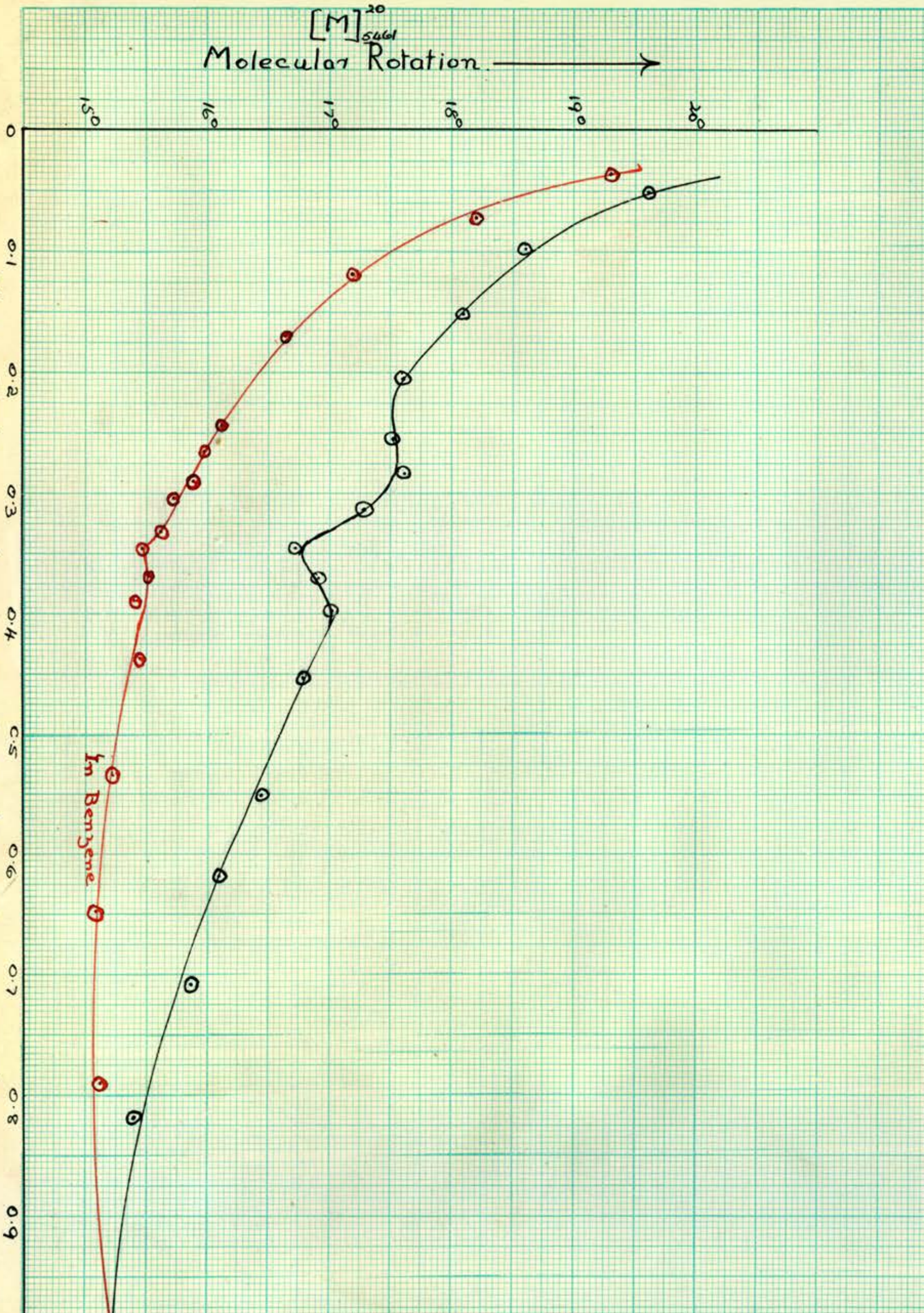
Rotatory Powers of d-sec-β-Octyl Alcohol in Solutions of varying Concentration.

In each case $t = 20°$ $l = 4$ dm

f = Mole fraction of d- -sec-octyl alcohol.

(a) In Hexane.

c gms/100 cc.	f	α^{20}_{5461}	$[M]^{20}_{5461}$
4·994	0·050	+ 3·01°	+19·6 °
10·00	0·099	5·72	18·6
15·07	0·151	8·41	18·1
20·00	0·203	10·83	17·60
23·38	0·253	12·62	17·54
27·03	0·283	14·66	17·62
30·00	0·313	15·09	17·29
33·02	0·345	17·0	16·73
35·00	0·372	18·21	16·91
37·28	0·399	19·91	17·02
42·05	0·453	21·72	16·79
50·01	0·551	25·32	16·45
55·01	0·618	27·24(5)	16·10
62·05	0·709	30·32	15·87
69·99	0·819	33·23	15·40
Homogeneous l = 2		19·20	15·24



Variation of the Molecular Rotation of d-sec.-β-Octyl Alcohol in Solution in Hexane and in Benzene.

(b) In Benzene. $\ell = 2$ dm

c gms/100 cc.	f	α^{20}_{5461}	$[M]^{20}_{5461}$
4·998	0·035	+ 1·48°	+19·3 °
9·994	0·072	2·79	18·2
15·99	0·119	4·23	17·2
22·01	0·170	5·64	16·65
30·01	0·224	7·44	16·12
32·27	0·266	7·93	15·97
34·76	0·292	8·49	15·87
36·78	0·308	8·89	15·71
38·61	0·331	9·28	15·62
39·97	0·346	9·51	15·46
41·87	0·368	10·01(5)	15·52
43·53	0·388	10·	15·40
47·56	0·436	11·30	15·44
55·30	0·532	12·93	15·20
62·42	0·647	14·49	15·09
71·18	0·789	16·54	15·13
Homogeneous		19·25	15·24

If the explanation of optical changes based on dipole association with the solvent is correct, it should be possible to trace the same effects on progressively dissociating the homogeneous alcohol by gradually increasing the dilution in a non-polar solvent such as hexane or benzene. Dissociation should be accompanied by a rise in rotation, since at high dilutions the optically active solute will exist largely in the form of single molecules and the full electrical effect of the hydroxyl group at the assymetric centre will then be realised.

The influence of dilution with hexane was first examined and was found to lead to a definite rise in rotation. Between the concentrations corresponding to mole fractions 0·2 and 0·5, however, a curious irregularity occurs, which appears to represent two maxima at the concentrations 0·28 and 0·4 respectively. On diluting with benzene a similar curve was obtained, and although the irregularity in this solvent was very small, it was situated at the same point as in the former case.

L. Lange (Zeit. Physik., 1925, 174) has determined the variation of the polarization of a number of aliphatic alcohols as they are dissociated by the addition of benzene.

The polarization curves constructed from these data show maxima, practically without exception, the position and magnitude of which vary in a regular manner from alcohol to alcohol. These inflections have been explained by Debye (Handbuch der Radiologie, Leipzig, 1925, *6*, 597) on the supposition that in such solutions an equilibrium occurs between the single molecules of alcohol and two types of alcohol complexes, one of which is less highly polarised than the individual molecule and the other more so. The less polar complex is supposed to be favoured at high concentrations, and on dilution this is replaced by the more polar type until finally the alcohol breaks down completely into single molecules. This affords a plausible explanation of the maxima frequently found in the polarization-dilution curves of alcohols. Although no polarization data are available for sec-β-octyl alcohol, there is thus reason to believe that the rotation-dilution graphs now obtained for this compound in benzene or hexane (p. =   ) also reflect the true nature of the polarization changes taking place in the alcohol as it is progressively diluted with the non-polar solvent. Arguing from the behaviour of the alcohol in the presence of polar solvents, it seems probable that the maxima in the rotation curves correspond to maximum values of the polarization.

Rule and McLean (loc. cit., and unpublished results) have measured the rotatory powers of *l*-menthyl methyl naphthalate when dissolved in alcohol-hydrocarbon mixtures such as were investigated by Lange, and have been able to show that the presence of maxima in the polarization of the alcohol leads to corresponding minima in the rotatory power. In these cases also a greater inflection was observed in hexane than in benzene, thus providing a further parallel with octyl alcohol.

TABLE III

Rotatory Powers of d-β-sec-Octyl Methyl Ether in Solvents.

In each case $t = 20^\circ$ $\ell = 2$ dms.

(a) **Methane Type.**

Solvent	c gms/100 cc.	α^{20}_{5461}	$[M]^{20}_{5461}$	$\mu \times 10^{18}$ e.s.u.
CCl_4	3·99	+ 0·97°	+17·5°	0
CS_2	4·00	0·95	16·9	0
C_6H_{14}	4·00	0·76	13·7	0
Homogeneous		14·73	13·1	–
CH_3I	3·99	0·66	11·9	1·66
CH_3OH	4·00	0·55	9·9	1·64
CH_3COOH	4·00	0·52	9·3(5)	0·75
CH_3CHO	4·01	0·52	9·3	2·71
CH_3CN	3·99	0·46	8·3	3·05
CH_2Cl_2	4·00	0·22	3·9(5)	1·61
$CHCl_3$	4·00	0·21	3·8	1·10
CH_3NO_2	4·01	- 0·02	- 0·35	3·78

(b) Benzene Type.

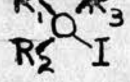
Solvent	gms/100 cc.	α^{20}_{5461}	$[M]^{20}_{5461}$	$\mu \times 10^{18}$ e.s.u.
C_6H_5I	4·00	+ 1·54°	+27·6°	1·50
C_6H_5Br	3·99	1·19	21·6	1·50
C_6H_6	3·99	1·11	20·0	0
C_6H_5Cl	4·00	1·07	19·2	1·52
$C_6H_5CH_3$	4·00	1·06	19·1	0·5
$C_6H_5OCH_3$	3·99	1·03	18·6	1·25
o-$C_6H_4Cl_2$	4·00	1·03	18·6	2·24
C_6H_5CHO	4·01	0·93	16·7	2·74
C_6H_5CN	4·01	0·86	15·4	3·85
Homogeneous		12·28	10·95	—
$C_6H_5NO_2$	4·01	0·60	10·5	3·90

d_4^{19} = 0·8076 (Kenyon and McNicol J.C.S., 1923, **123**, 14).

From the results of molecular weight measurements it is usually supposed that ethers have little tendency to exhibit molecular association. If we assume that the mechanism of solvent influence outlined in the case of octyl alcohol is valid also in this instance, it is somewhat surprising that the range of molecular rotations in the above tables is so wide. The ether linkage is not very highly polar, but it may be that although ether molecules show little tendency to associate with themselves they may do so to a greater extent with more highly polar molecules.

An examination of the tables shows that among aliphatic solvents there is a good agreement between rotatory power and polarity of solvent. As in the case of octyl alcohol, the non-polar liquids carbon tetrachloride, carbon disulphide and hexane give high rotations, while acetaldehyde, acetonitrile and nitromethane which are strongly polar, yield solutions of low activity. The inversion of sign in nitromethane is noteworthy.

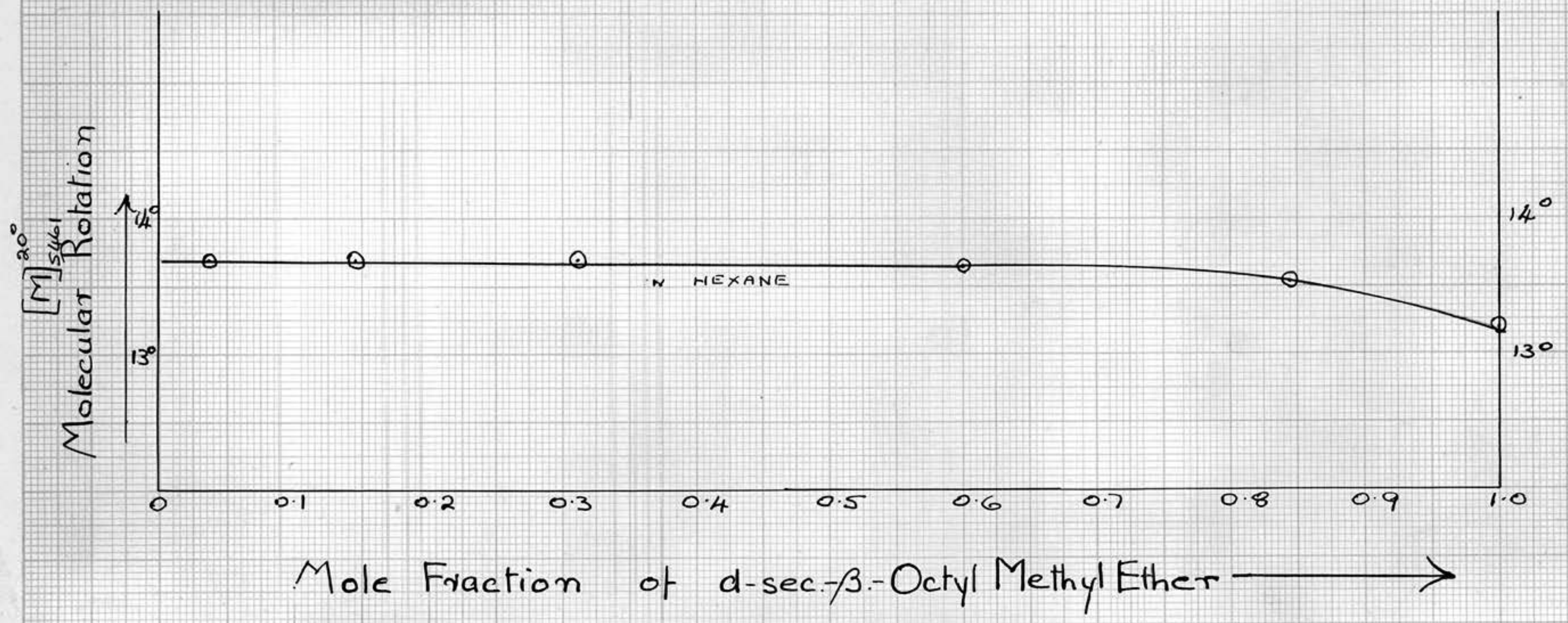
Among aromatic solvents the agreement would be equally good except for the displacement of the three halides, all of which give unusually high values. In this respect it will be observed that the iodo-compound is more abnormal than the bromo-, and this is more so than the chloro-compound. This arrangement is in the same order as that representing the magnitudes of the residual valencies of the halogen atoms. From these considerations it may be suggested that a tendency exists towards some kind of chemical union between the ether and the halides, such as that commonly assumed (Tschelinzeff, Ber., 1904, 37, 4534) in the first stage of the formation of a Grignard reagent.

$R_1\text{-}O\text{-}R_2 + R_3I \longrightarrow$ 

$$\begin{matrix}R_1 & & R_3\\ & O & \\ R_2 & & I\end{matrix}$$

It is hardly to be expected that a fundamental change

Variation of the Molecular Rotation of d-sec-β-Octyl Methyl Ether in Solution in Hexane.



of this nature would allow a solution of octyl ether in a halide to exhibit a normal rotation. A similar explanation would hold for methyl iodide, although the positions of the more highly substituted methylene chloride and chloroform cannot be explained in this way. It may be noted, however, that these last two solvents are displaced in the same manner when octyl alcohol is the optically active substance.

TABLE IV.

Rotatory Powers of d-sec-β-Octyl Methyl Ether in Hexane Solutions of varying Concentration.

In each case t = 20° l = 2 dms.

f = Mole fraction of d-sec-β-octyl methyl ether

c gms/100 cc.	f	α^{20}_{5461}	$[M]^{20}_{5461}$
4.002	0.036	+ 0.76	+13.7
15.44	0.146	2.94	13.7
30.66	0.310	5.82	13.7
53.70	0.601	10.18	13.65
69.36	0.845	13.04	13.53
Homogeneous	-	14.81	13.20

The polarization of diethyl ether as determined by Debye remains practically constant when the ether is diluted with benzene, the polarization-concentration diagram being a straight line. In a manner similar to that employed for the alcohols (p =), Rule and McLean (J.C.S., 1931, 674) obtained a diagram showing the change in the rotatory power of menthyl methyl naphthalate caused by ether when it was progressively diluted with benzene. This also takes the form of a straight line making a small angle with the horizontal axis. It is therefore not surprising that on diluting d-sec-β-octyl methyl ether with hexane, there is very little change in the molecular rotation. Judging from the rotation found for the benzene solution, (c = 4), dilution with this solvent produces a somewhat larger alteration. A difference in this direction is in agreement with the results of molecular weight determinations, which show that benzene is more effective in separating the molecules of an associated solute than are saturated aliphatic hydrocarbons. Apparently the proximity of the weakly polar ether molecules to one another has quite a definite influence on the rotatory power although they may not undergo association to any great extent. The actual direction of the optical change with increasing concentration corresponds to that which would be expected from the influence of an added polar solvent, both leading to a diminished rotation.

TABLE V.

Rotatory Powers of d-2-Chloro-octane in Solvents.

In each case t = 20° l = 2 dms.

(a) Methane Type.

Solvent	gms/100 cc.	α^{20}_{5461}	$[M]^{20}_{5461}$	$\mu \times 10^{18}$ e.s.u.
CH_3CN	4.99	+ 3.88	+57.7	3.05
CH_3OH	4.95	3.79	56.8	1.64
CH_3NO_2	5.04	3.79	55.9	3.78
CH_3COOH	5.00	3.71	55.0	0.75
C_6H_{14}	4.97	3.67(5)	54.8	0
Cyclohexane	5.04	3.66	54.0	0
Homogeneous	—	62.36	53.5	—
CH_2Cl_2	5.04	3.61(5)	53.3	1.61
$CHCl_3$	5.01	3.55(5)	52.7	1.10
CCl_4	5.01	3.55	52.6	0
CH_3I	4.99	3.36(5)	50.1	1.66
CS_2	4.97	3.23(5)	48.1	0

(b) Benzene Type.

C_6H_5CN	5.01	+ 3.70(5)	55.0	3.85
Homogeneous	—	62.36	53.5	—
$C_6H_5NO_2$	4.99	3.55	52.8	3.90
C_6H_5CHO	5.01	3.48	51.6	2.74
o-$C_6H_4Cl_2$	5.00	3.35	49.6	2.24
C_6H_5Cl	4.98	3.29	49.1	1.52
C_6H_5Br	4.98	3.23(5)	48.3	1.50
$C_6H_5OCH_3$	4.99	3.20	47.6	1.25
$C_6H_5CH_3$	4.98	3.10	46.2	0.5
C_6H_6	4.97	3.08(5)	46.1	0
C_6H_5I	4.99	3.09(5)	46.0	1.50

d = 0.866 McKenzie and Tudhope, (J. Biol. Chem., 1924, 62, 551)

Among aliphatic solvents there appears to be a tendency for the strongly polar solvents, e. g. acetonitrile and nitromethane to yield solutions of the highest rotatory power, and for the less polar and non-polar media such as chloroform, carbon tetrachloride and carbon disulphide to give lower values. The polar influence is however, irregular and the hydrocarbons hexane and cyclohexane occupy positions in the middle of the table.

A more definite relationship may be noted among the aromatic solvents, for which the agreement is excellent, apart from a small displacement of iodobenzene.

A striking point about chloro-octane is that it differs completely from other octyl derivatives previously discussed, in that the presence of highly polar solvents raises the rotatory power instead of diminishing it. The direction of this change may have a bearing on the question as to whether the dextrorotatory halide is directly related to the d- or the *l*-alcohol, a problem which has been examined by a number of investigators, including Levene (J. Biol. Chem., 1924, <u>59</u>, 473) and in considerable detail by Kenyon and his co-workers (Houssa, Kenyon and Phillips, J. C. S., 1929, 1700: Kenyon, Tipscomb and Phillips, J. C. S., 1930, 415: Houssa and Phillips, J. C. S., 1932, 108). This point will be referred to again in the conclusion of this thesis. An almost identical solvent effect is found in the case of d-bromo-octane, as may be seen from the following table.

TABLE VI

Rotatory Powers of d-2-Bromo-octane in Solvents.

In each case $t = 20^\circ$ $\ell = 4$ dms.

(a) Methane Type

Solvent	c gms/100 cc.	α^{20}_{5461}	$[M]^{20}_{5461}$	$\mu \times 10^{18}$ e.s.u.
CH_3CN	5.00	+ 8.92	+85.8	3.05
CH_3OH	5.02	8.85	85.0	1.64
CH_3NO_2	4.99	8.59	82.9	3.78
CH_3COOH	5.00	8.58	82.7	1.4
C_6H_{14}	5.02	8.38	80.5	0
Homogeneous	($\ell = 2$)	88.93	78.7	—
Cyclohexane	5.00	8.0	77.3	0
$CHCl_3$	5.00	8.02	77.3	1.10
CCl_4	5.00	7.96	76.7	0
CH_3I	4.99	7.72	74.4(5)	1.66
CS_2	5.00	7.54	72.7(5)	0

d = 1.090 (Pickard and Kenyon, J.C.S., 1911, 99, 69).

(b) Benzene Type l= 2 dms.

Solvent	c gms/100 cc.	α^{20}_{5461}	$[M]^{20}_{5461}$	$\mu \times 10^{18}$ e.s.u.
Homogeneous		+88.93	+78.7	–
C_6H_5CN	5.00	4.08	78.7	3.85
$C_6H_5NO_2$	4.99	4.02	77.6	3.90
C_6H_5CHO	5.01	3.96	76.2	2.74
o-$C_6H_4Cl_2$	5.01	3.80	73.1	2.24
C_6H_5Cl	5.00	3.77	72.8	1.52
C_6H_5Br	5.02	3.72	71.5	1.50
$C_6H_5OCH_3$	4.99	3.69(5)	71.45	1.25
$C_6H_5CH_3$	5.00	3.62	69.8	0.5
C_6H_6	5.01	3.61	69.5	0
C_6H_5I	4.99	3.60	69.5	1.50
s-$C_6H_3(CH_3)_3$	4.98	3.58	69.3	0

d_4^{20} = 1.090 (Pickard and Kenyon, J.C.S., 1911, 99, 69).

The arrangement in the foregoing tables differs little from that given under chloro-octane. The influence of aromatic solvents is in excellent agreement with their polar properties, and non-polar solvents again give rotations of the lowest magnitudes. In this case an additional solvent, mesitylene, was examined, and gave a slightly lower value than benzene or iodobenzene.

TABLE VII

Rotatory Powers of d-2-Chloro-octane in Solutions of varying Concentrations.

In each case t = 20° l = 2 dms.

f = Mole fraction of d-2-chloro-octane.

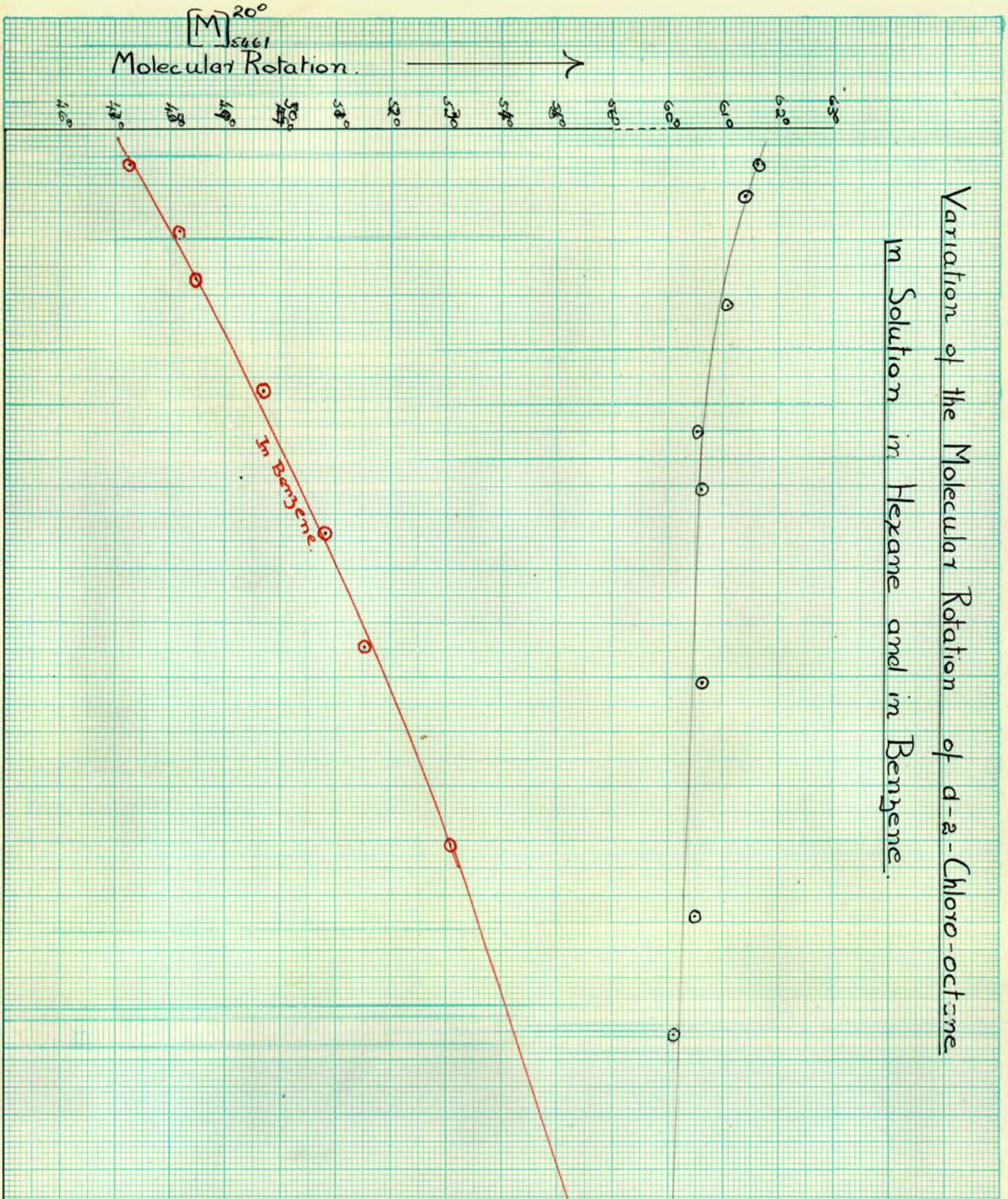
(a) In Hexane.

c gms/100 cc.	f	α^{20}_{5461}	$[M]^{20}_{5461}$
3.542	0.030	+ 2.94	+61.6
6.922	0.059	5.72	61.4
13.00	0.159	14.80	61.07
26.55	0.242	21.64	60.51
34.85	0.326	28.44	60.60
45.43	0.444	37.11(5)	60.66
50.87	0.505	41.45	60.63
67.03	0.717	51.94	60.50
75.80	0.829	61.35	60.10
Homogeneous	—	70.00	60.04

(b) In Benzene.

5.090	0.031	+ 3.24	+47.3
12.75	0.083	8.28	48.2
19.99	0.135	13.06	48.49
33.14	0.242	22.19	49.71
46.09	0.369	31.55	50.82
55.00	0.473	38.19	51.55
67.86	0.652	48.54	53.10
Homogeneous		64.57	55.38

d = 0.886 MacKenzie and Tudhope (J. Biol. Chem., 1924, 62, 551)


Variation of the Molecular Rotation of d-2-Chloro-octane
in Solution in Hexane and in Benzene.
$[M]^{20°}_{5461}$
Molecular Rotation.
Mole Fraction of d-2-Chloro-octane
In Benzene.
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
46°
47°
48°
49°
50°
51°
52°
53°
54°
55°
56°
60°
61°
62°
63°

As was stated on page , these dilution measurements were made in a 4 dms. tube, which was unjacketed and had a narrow bore. The operations, except that of weighing, were all carried out in a constant-temperature room maintained at 20° (± 1°). The octyl halides, however, are very sensitive to temperature changes and for this reason the points on the graph representing the dilution of chloro-octane with hexane do not lie quite evenly on the smoothed curve. There appears to be no doubt that a decreasing concentration in hexane results in a very small rise, amounting to only about 2° on the molecular rotation, whereas a much more definite change in the opposite direction is produced by the use of benzene. If we assume that the latter change is the normal one, it may be concluded that an increasing degree of association in this solvent leads to a rise in rotatory power, i.e. to a change in the same sense as that brought about by association with other polar molecules. The maximum range of rotation observed in each of these last two cases amounts to about nine degrees.

With reference to the unexpected direction of these optical changes, it is of interest to note that Smyth and Rogers (Rog. C. S., 1930, 52, 2227) have examined the polarization of n-heptyl bromide in heptane, and find it to be represented by a smooth curve which slowly but steadily falls as the concentration is increased. This is the usual behaviour of simple polar molecules, and does not suggest any reason for the observed optical properties.

l-2-Nitro-octane.

Owing to the very small yields obtained of the nitro-compound it was decided to examine the change in rotatory power on dilution with hexane and benzene respectively and thereafter to investigate the influence of as many other solvents as was possible with the material available. The compound had to be recovered several times and there remained only sufficient material to examine three solutions.

TABLE VIII

Rotatory Powers of l-2-Nitro-octane in Solutions of varying Concentration.

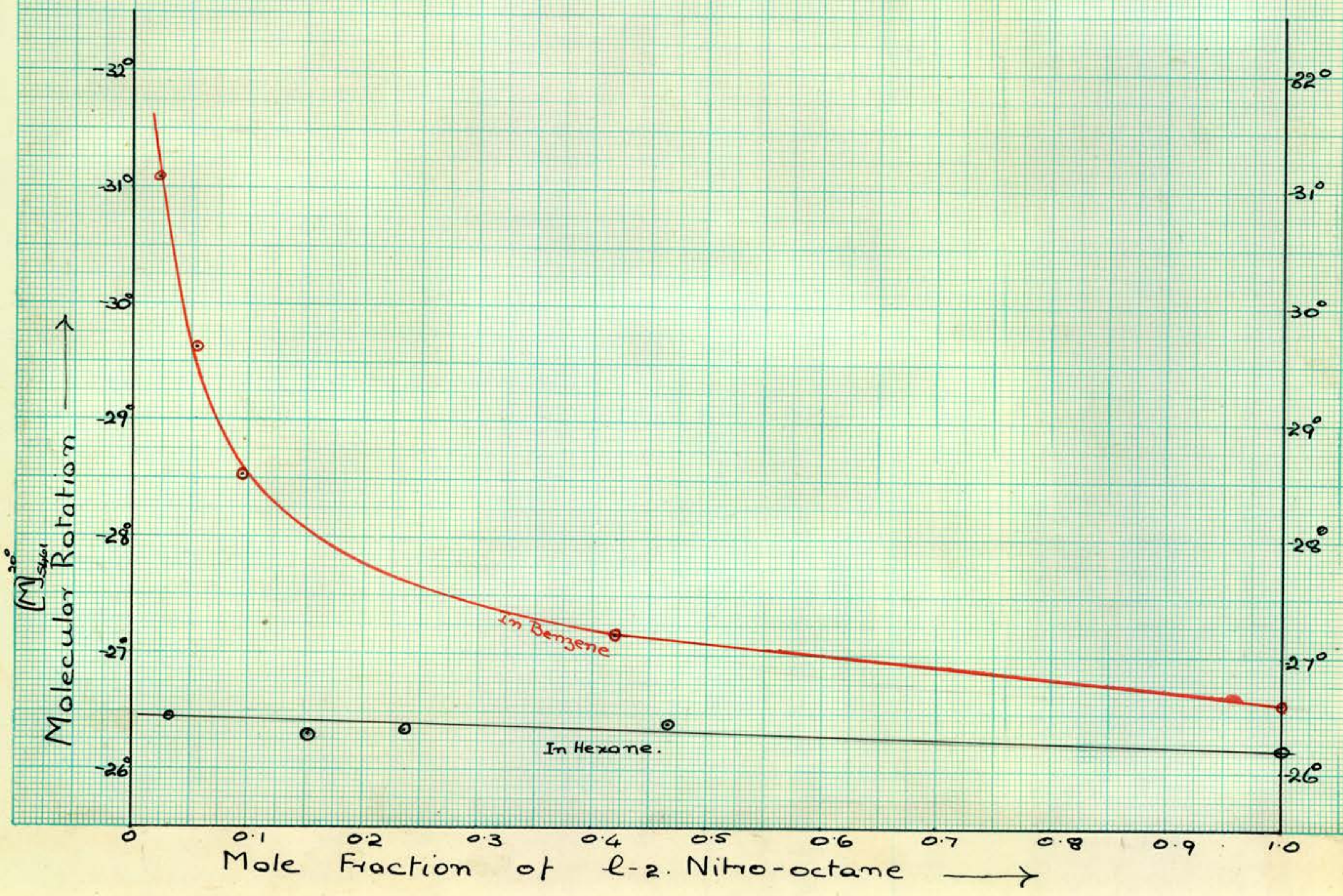
In each case $t = 20^\circ$ $l = 2$ dms.

f = Mole fraction of l-2-nitro-octane.

(a) In Hexane.

gms/100 cc.	f	α^{20}_{5461}	$[M]^{20}_{5461}$
3.994	0.033	- 1.33	-26.45
17.98	0.152	5.95	26.30
27.27	0.237	9.03	26.33
50.07	0.467	16.63	26.40
Homogeneous		30.38	26.18

Variation of the Molecular Rotation of l-2-Nitro-octane in Solution in Hexane and in Benzene.



(b) In Benzene.

c gms/100 cc.	f	α^{20}_{5461}	$[M]^{20}_{5461}$
3.998	0.023	- 1.56	-31.08
9.346	0.055	3.48	29.61
15.80	0.095	5.67	28.53
53.71	0.420	18.35	27.16
Homogeneous	–	30.83	26.58

The curves obtained by plotting the values of the rotatory powers in hexane and in benzene against the mole fraction of *l*-2-nitro-octane present in solution are very different in shape. Nitro-compounds are known to dissociate in such a manner as to reduce the polarization, but once again hexane does not appear able to break up the complexes to any appreciable extent even in dilute solution. Although it cannot be said whether complete dissociation is attained, benzene certainly does tend to dissociate the aggregates into single molecules, the change being accompanied by a rapid rise in rotation in dilute solutions. It appears that a fairly large proportion of benzene is required before much dissociation is perceptible, but once that stage has been reached the aggregates break down with great rapidity. From the polarization experiments of Debye, and the rotation experiments of Rule and McLean, very similar graphs have been deduced for the dilution of nitrobenzene with benzene. (fig. page).

TABLE IX

Rotatory Power of l-2-Nitro-octane in a few Typical Solvents.

In each case $t = 20^{\circ}$ $l = 2$ dms.

Solvent	c gms/100 cc.	α^{20}_{5461}	$[M]^{20}_{5461}$	$\mu \times 10^{18}$ e.s.u.
$C_6H_5OCH_3$	4.01	- 1.79	-35.5	1.25
C_6H_5Cl	4.01	1.59	31.5	1.52
C_6H_6	3.99	1.56	31.1	0
$C_6H_5NO_2$	4.00	1.37	27.2	3.90
C_6H_{14}	3.99	1.35	26.9	0
Homogeneous	—	30.85	26.7	—

d^{20}_{20} = .9224 (Shriner and Young, J.A.C.S., 1930, <u>52</u>, 3336).

These results which at first sight seem very irregular, may be explained in terms of the varying degrees of association of the nitro-octane molecules with one another and with the solute. From the dilution curve for benzene (page =) it may be deduced that the rotatory power of nitro-octane, in the form of single molecules is considerably greater than 30-40°. In the homogeneous state this value is lowered by electrical association between the highly polar nitro-groups. As is to be expected, little change is produced by the addition of nitro-benzene, the polarity of which is very similar to that of the active solute. In this medium association will take place between solute and solvent, but this evidently has the same effect on the rotation as association between the active molecules. An excess of a weakly polar solvent like anisole may be expected to dissociate the nitro-octane complexes more or less completely, but will not allow the rotation to rise to its maximum value, owing to the depressive influence of association between the nitro-group and the methoxy-group in the anisole molecule. An excess of chloro-benzene operates in the same way, but being relatively more polar than anisole the depression in this case is greater and the observed rotation lower. On this view benzene and to a still more noticeable degree hexane fail to effect complete disruption of the solute complexes, indicating that the individual molecules of nitro-octane should exhibit a very high rotatory power. These considerations are further supported by molecular weight determinations which have been recorded in the literature for nitro-derivatives dissolved in various solvents, e. g. nitroethane in 3% solution in cyclohexane shows a molecular weight of 136 instead of 75 as required by the formula (Marscarelli and Benati, Gazzetta, 1911, 41a, 642) while nitropropane in 4% solution in benzene shows a molecular weight of 94 instead of 89 (Auwers Zeit. phys. Chem., 1893, 12, 689).

d-α-n-Butyl propionic Acid.

It is well known that carboxylic acids exhibit the phenomenon of molecular association to a remarkable extent. Even in dilute solution in non-polar solvents and in the vaporous state at ordinary pressure this association persists. For example, Auwers (loc. cit.) found that the measured molecular weight of n-caprylic acid in a 2% benzene solution was 247 instead of 144 as required by the formula. Again from polarization measurements of acetic acid (K. A. Wolf and co-workers, Phys. Zeit., 1930, **31**, 227) in very dilute solution in non-polar solvents, the calculated value of the dipole moments is 0.74 $\times 10^{-18}$, whereas the same measurements when made in dilute ether solution gave $\mu = 1.4 \times 10^{-18}$ e.s.u. (Smyth and Rogers, J.A.C.S., 1930, **52**, 1824). The value of the dipole moment of acetic acid from polarization measurements in the vapour state at very low pressures is also 1.4 (Zahn. unpublished) hence the probability is that this is the true value for the unassociated molecule. It may have been considerations such as these which led Levene to conclude that optically active carboxylic acids exhibit their maximum rotations in ether solution. In order to test this point it was decided to carry out solution measurements in ether as well as in hexane and benzene. The results of these experiments led to a further extension in which the remainder of the acid was diluted with acetone.

TABLE X

Rotatory Powers of d-α-n-Butyl-propionic Acid in Solutions of varying Concentration.

In each case $t = 20^\circ$ $\ell = 2$ dms.

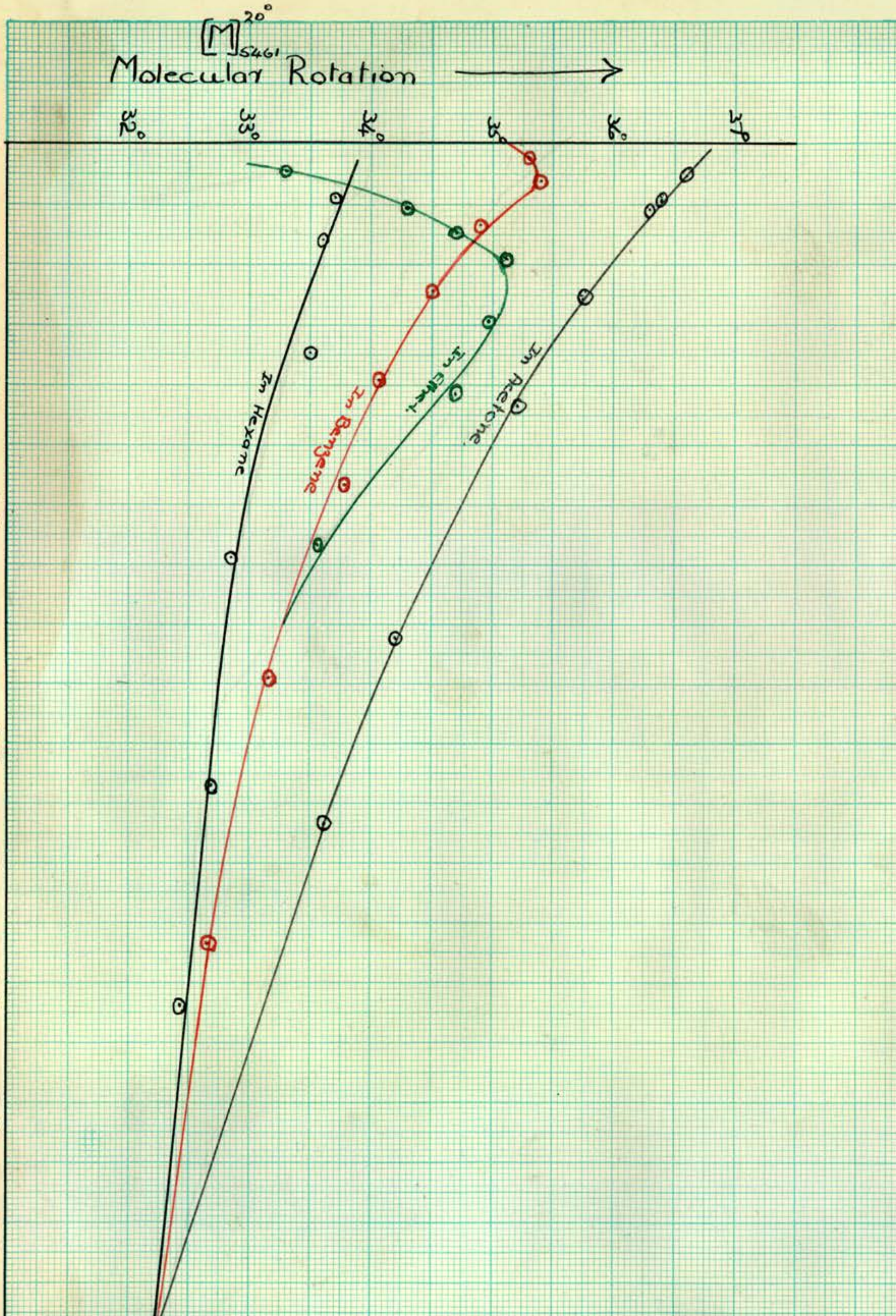
f = Mole fraction of α-n-butyl-propionic acid.

(a) In Hexane.

c gms/100 cc.	f	α^{20}_{5461}	$[M]^{20}_{5461}$
5.000	0.045	+ 2.34	+33.7
8.892	0.079	4.15	33.6
18.79	0.173	8.73	33.5
35.97	0.344	16.42	32.85
53.87	0.536	24.46	32.69
69.51	0.719	31.32	32.44
Homogeneous		40.87	32.17

(b) In Benzene.

2.098	0.013	+ 1.03	+35.3
4.948	0.031	2.43	35.4
10.55	0.068	5.12	34.9
18.07	0.122	8.67	34.5
27.65	0.196	13.09	34.07
37.64	0.283	17.66	33.78
53.70	0.447	24.72	33.15
71.20	0.667	32.29	32.65
Homogeneous	—	40.87	32.14



Variation of the Molecular Rotation of d-α-n-Butyl-propionic Acid in Solution in Hexane, Benzene, Ether and Acetone.

(c) In Ether.

c gms/100 cc.	f	α^{20}_{5461}	$[M]^{20}_{5461}$
5.004	0.023	+ 2.33	+33.3
11.16	0.053	5.31	34.3
14.59	0.072	7.04	34.7
18.02	0.094	8.79	35.1
27.25	0.147	13.23	34.96
35.94	0.207	17.33	34.70
50.62	0.334	23.59	33.56
Homogeneous	–	40.87	32.15

(d) In Acetone.

4.928	0.026	+ 2.50(5)	+36.6
8.992	0.048	4.54	36.4
10.30	0.055	5.19	36.3
22.65	0.132	11.25	35.75
34.46	0.217	16.85	35.21
55.09	0.412	26.18	34.21
67.42	0.566	31.48	33.61
Homogeneous	–	40.87	32.15

d^{20}_{4} = .915.

The diagrams obtained by plotting the experimental data in the usual way justify expectations to a certain extent, but some unexpected points arise.

Thus with hexane as solvent, the curve is almost a straight line, rising slightly at high dilution. There is evidently very little breaking down of the association complexes in this case. In benzene solution the dissociation appears to be rather more pronounced and the rotation apparently reaches a maximum value at great dilution. (The experimental error at this stage is large but the positions of the points were verified by repetition). It is doubtful however if this maximum value corresponds to the rotatory power of the individual acid molecules, since under these conditions the molecular weight determinations still give about double the normal figure. From the general shape of the curves one may conclude, however, that the rotation of the acid is lower in the associated state. On diluting with ether the rotation varies in almost exactly the same way as for benzene over the greater part of the scale, and then rises to a maximum, after which it falls rapidly. The increased values observed down to 0·1 mole fraction appear to be due to the greater dissociating power of the medium as compared with hexane or benzene, resulting in a gradual disruption of the acid-acid complexes and replacement by acid-ether complexes of a higher rotation. Judging from the normal molecular weights given by carboxylic acids up to moderate concentration in ether solution (cf. Turner, Molecular Association, p. 130) it must be assumed that this replacement is nearly complete, although no explanation can be given for the sudden fall below 0.1 mole fraction. The strongly polar solvent acetone gives a smooth curve which lies above those of hexane, benzene and ether. This may be a normal effect, in which case the solvents on the whole fall into the order of their polarities. On the other hand it might have been expected that a highly polar solvent would depress the rotation as compared with ether. In the case of octyl alcohol dissolved in benzaldehyde (p. =) an abnormally high rotation was observed, which it is suggested is caused by co-ordination between the keto- and hydroxy-groupings. A similar co-ordination between acetone and the hydroxyl group of the acid might be expected a highly active solution in the present example. Without further evidence it is difficult to draw more definite conclusions from these results.

ESTERS.

TABLE

TABLE XI

Rotatory Powers of sec-β-Octyl Toluates in Benzene Solvents.

In each case $t = 20^\circ$ $l = 2$ dms.

(a) d-Octyl-o-toluate.

Solvent	c gms/100 cc.	α^{20}_{5461}	$[M]^{20}_{5461}$	$\mu \times 10^{18}$ e.s.u.
Cyclohexane	4.01	+ 2.74	+84.9	0
Homogeneous	(l = 1)	31.16	81.2	–
s-$C_6H_3(CH_3)_3$	4.03	2.49	76.5	0
C_6H_6	4.00	2.29	71.1	0
$C_6H_5CH_3$	4.02	2.31	71.0	0.5
$C_6H_5OCH_3$	4.05	2.27	69.7	1.25
$C_6H_5NO_2$	4.01	2.07	63.9	3.90
C_6H_5Cl	3.98	1.96	61.0	1.52
C_6H_5Br	3.99	1.93	60.0	1.50
o-$C_6H_4Cl_2$	4.00	1.84(5)	57.2	2.24
C_6H_5CN	4.01	1.83(5)	56.8	3.85
C_6H_5CHO	4.00	1.82	56.4	2.74
C_6H_5I	4.01	1.72	54.5	1.50

$d_4^{20} = 0.9522$ (Rule, Hay, Numbers and Paterson, J. C. S., 1928, 176).

(b) ℓ-Octyl-m-toluate.

Solvent	c gms/100 cc.	α^{20}_{5461}	$[M]^{20}_{5461}$	$\mu \times 10^{18}$ e.s.u.
Homogeneous	(ℓ = 1)	-42.63	-111.4	[illegible]
$C_6H_5OCH_3$	4.00	3.45	106.9	1.25
Cyclohexane	3.99	3.35	104.1	0
$C_6H_5CH_3$	4.00	3.27	101.5	0.5
$C_6H_5NO_2$	4.00	3.16	97.9	3.90
C_6H_6	4.00	3.09	95.8	0
C_6H_5Cl	4.01	3.00	92.7	1.52
C_6H_5Br	3.98	2.95	91.9	1.50
C_6H_5CHO	3.99	2.90	90.1	2.74
C_6H_5CN	4.00	2.87	89.0	3.85
C_6H_5I	4.00	2.87	89.0	1.50
o-$C_6H_4Cl_2$	4.01	2.85	88.1	2.24

d_4^{20} = 0.9492 Rule Hay, Numbers and Paterson (loc. cit.).

(c) ℓ-Octyl-p-toluate.

Homogeneous		-94.36	-122.5	-
$C_6H_5OCH_3$	4.03	3.85	118.3	1.25
s-$C_6H_5CH_3$	4.01	3.76	116.2	0.5
s-$C_6H_3(CH_3)_3$	4.02	3.76	115.8	0
Cyclohexane	4.04	3.77	114.7	0
C_6H_6	4.00	3.58	111.9	0
C_6H_5Cl	3.99	3.37	104.7	1.52
C_6H_5Br	4.02	3.39	104.5	1.50
C_6H_5I	4.00	3.30	102.4	1.50
C_6H_5CHO	4.00	3.26	101.3	1.74
C_6H_5CN	3.99	3.20	99.3	3.85
$C_6H_5NO_2$	4.02	3.18	98.9	3.90
o- $C_6H_4Cl_2$	4.02	3.17	97.7	2.24

d_4^{20} = 0.9492 Rule Hay, Numbers and Paterson (loc. cit.).

TABLE XII

Rotatory Powers of β-sec-Octyl-methoxy Benzoates in Benzene Solvents.

In each case $t = 20^\circ$ $\ell = 2$ dms.

(a) -Octyl-o-methoxy benzoate.

Solvent	C gms/100 cc.	α^{20}_{5461}	$[M]^{20}_{5461}$	$\mu \times 10^{18}$ e.s.u.
Homogeneous	–	-28.88	-38.2	–
$C_6H_5CH_3$	3.99	1.04	34.4	0.5
$C_6H_5OCH_3$	4.00	0.97	32.0	1.25
C_6H_6	4.02	0.90	29.6	0
C_6H_5Cl	4.00	0.79	26.1	1.52
C_6H_5Br	4.02	0.75	24.8	1.50
$C_6H_5NO_2$	4.02	0.67	22.0	3.90
C_6H_5CN	4.00	0.64	21.1	3.85
o-$C_6H_4Cl_2$	4.00	0.59	19.1	2.24
C_6H_5I	4.02	0.57	18.7	1.50
C_6H_5CHO	4.01	0.55	18.1	2.74

$d_4^{20} = 1.000$ (Rule and Numbers J. C. S., 1926, 2116).

(b) <u>l-Octyl-m-methoxy benzoate.</u>

Solvent	c gms/100 cc.	α^{20}_{5471}	$[M]^{20}_{5461}$	$\mu \times 10^{18}$ e.s.u.
Homogeneous	(l = 1)	-42.15	-111.4	–
$C_6H_5OCH_3$	4.01	3.17	104.4	1.25
Cyclohexane	4.01	3.08	101.5	0
$C_6H_5CH_3$	3.99	2.98	98.4	0.5
$C_6H_5NO_2$	4.00	2.78	92.0	3.90
C_6H_6	4.00	2.77	91.4	0
C_6H_5Cl	3.99	2.72	90.0	1.52
C_6H_5Br	3.99	2.69	89.0	1.50
C_6H_5CHO	4.00	2.68	88.4	2.74
C_6H_5CN	4.00	2.67	88.1	3.85
o-$C_6H_4Cl_2$	4.00	2.66	87.8	2.24
C_6H_5I	4.00	2.53	83.5	1.50

$d_4^{20.4}$ = 0.9939. Rule and Numbers (loc. cit.).

(c) <u>l-Octyl-p-methoxy benzoate.</u>

Homogeneous	(l = 1)	-51.37	-136.4	–
$C_6H_5OCH_3$	3.99	4.06	134.2	1.25
$C_6H_5CH_3$	4.00	3.91	128.9	0.5
s-$C_6H_3(CH_3)_3$	4.01	3.87	129.2	0.5
C_6H_6	4.00	3.80	125.5	0
Cyclohezane	4.00	3.78	124.9	0
C_6H_5Br	4.00	3.55	117.1	1.50
C_6H_5Cl	4.00	3.55	117.0	1.52
C_6H_5I	4.02	3.53	116.0	1.50
C_6H_5CHO	4.00	3.44	113.4	2.74
C_6H_5CN	4.00	3.39	111.9	3.85
$C_6H_5NO_2$	3.99	3.33	110.3	3.90
o-$C_6H_4Cl_2$	4.00	3.23	107.0	2.24

d_4 = 0.9940 (Rule and Numbers loc. cit.).

These esters were examined in order to determine whether the solvent influences were of a regular nature, and if so, the direction in which they moved. As there was only a limited quantity of each ester available, the determinations were confined to the benzene series of solvents, as being likely to yield more definite results.

In every case there is a general tendency for solvents of low polarity to head the list with the highest values of the rotatory power. Strongly polar liquids in the same way tend to occupy positions at the bottom of the tables. Among the ortho and meta isomerides in particular, there are a number of minor displacements, anisole and nitrobenzene usually giving higher values than correspond to their polar character and iodobenzene in general giving a lower value. The agreement is better in the para series, although anisole again behaves somewhat abnormally. The maximum range of the observed rotations does not differ materially on passing from the ortho to the meta and para derivatives, probably because in neither of the esters under examination does the ortho substituent possess a high polarity.

CONCLUSION AND SUMMARY.

The present work extends the investigations of Rule and McLean to include examples of simple optically active compounds related to sec-β-octyl alcohol, most of which contain only one definitely polar group in the molecule. Among the substances studied are the hydroxy, methoxy, chloro-and bromo-derivatives, the nitro-compound, and a carboxylic acid (not directly related to octyl alcohol). In addition, the behaviour of the more complex o-, m- and p- methoxy benzoic and o-, m- and p-toluic esters has been examined.

In practically every case the evidence shows that, when series of related solvents are compared, there is a well marked tendency for the rotatory powers of the solutions to arrange themselves in the order of the dipole moments of the solvents employed. Except for the octyl halides, the highest values of the molecular rotations were observed in non-polar liquids or those of low polarity. In the majority of examples the regularity of the agreement is disturbed by minor displacements. For example, iodobenzene frequently gives abnormal values, which may be traced to the high residual valency of the iodine atom. In the case of octyl alcohol the rotatory powers in benzaldehyde and nitrobenzene occupied an unexpectedly high position in the table, probably because these solvents become co-ordinated with the hydroxylic solute. Again, the irregularities observed in the case of nitro-octane may be explained on the basis of varying degree of association of the strongly polar nitro-compound with itself or with a polar solvent. It is obvious that a regular polar influence of the kind under examination can only be readily discerned provided (a) that optically active solute is itself more or less completely dissociated in the solvents under consideration, and (b) that the process of dipole-association between solute and solvent is not disturbed by a more intimate type of chemical union.

It is interesting to note that the rotatory power of octyl alcohol on continuous dilution with hexane exhibits maxima and minima similar to those which have been observed by Lange in the polarization of alcohols (e.g. isoamyl alcohol) when they are treated in the same way. Dilution experiments were also carried out with octyl ether, chloro-octane, nitro-octane and α-n-butyl-propionic acid. These compounds all gave regular curves except the acid when dissolved in ether, for which a maximum was found.

In all these cases the direction of the optical change with increasing concentration in benzene of hexane confirmed the conclusions drawn from the behaviour of polar solvents. The results indicate that a modification in the same sense is produced by association, irrespective of whether this occurs between the molecules of the active solute, or between the solute and an added polar solvent.

The octyl halides differed in a surprising way from the remaining octyl derivatives, as their rotatory powers were found to rise, either with increasing concentration in benzene or with increasing polarity of the solvent. It is interesting to consider whether these facts throw any light on the family relationships existing between the halides and the alcohol from which they are prepared. Levene has concluded that the dextrorotatory alcohol, is genetically related to the laevorotatory halide. and bases his reasoning on the supposed similarity of the following polar changes, both of which he states bring about an inversion of sign.

$$-SH \rightarrow -SO_3H \; ; \; -OH \rightarrow -Cl.$$

No Walden inversion can take place in the first of these, and therefore it is assumed that none occurs during the second.

Kenyon and his co-workers have made a detailed examination of the conditions under which the dextro-alcohol may be converted into the d- and ℓ-halides respectively, as a result of which they conclude that the d-alcohol is spatially related to the d-halide.

In considering the changes undergone by the octyl derivatives, we may assume for the moment that the alcohol is related to the halide of opposite sign. It will then be found that on comparing the various derivatives prepared from the dextrorotatory alcohol, the direction of the change is in every case towards a diminishing dextrorotation (or, what amounts to the same thing an increasing laevorotation) as the polarity of the solvent becomes greater. Two compounds situated on the border line between dextro- and laevo-rotations are d-octyl methyl ether, which is laevorotatory in nitromethane solution, and d-octylacetate (examined by Pickard and Kenyon, J.C.S., 1914, **105**, 881: and Rule and Mitchell, J.C.S., 1926, **129**, 3202) which is laevorotatory in all the aromatic solvents employed. The latter compound is regarded by Pickard and Kenyon as belonging to the d-series but resembles the halides in yielding more laevorotatory solutions in aromatic solvents of high polarity. In the corresponding case of d-amyl alcohol there is no possibility of a Walden inversion, and there is a similar change of the sign of rotation on passing from the alcohol to its halides and to the acetate. No solvent influence has yet been determined for the amyl derivatives, but it is possible that anexamination of the halides might be of assistance in solving this problem.

On this assumption that the laevo-halide belongs to the d-series the various simple derivatives under examination fall into the following order as regards the magnitudes of their rotatory powers: - nitro-octane, octyl alcohol, octyl methyl ether, chloro-octane, bromo-octane. This sequence of groups

$$NO_2 > OH > OMe > Cl > Br.$$

does not however correspond very closely to the polar order, since the nitro group is the strongest electronegative substituent and the methoxyl group the weakest.

Although it appears that the evidence in this thesis dealing with solvent influence lends some support to the view that d-octyl alcohol is spatially related to the laevorotatory halides, it must be concluded that our knowledge of polar influences is at present too undeveloped to allow a definite decision to be made.

In conclusion, I wish to state my indebtedness to Dr. H. G. Rule and to express my thanks for much valuable advice and helpful criticism during the course of this investigation.