

INDEX

	Page
General Introduction.	1 - 12.
Scope of present investigation, I and II.	13.
I. Spiro-spiro-cyclic Derivatives of Diphenyl.	
Discussion of configuration-	14 - 45.
7 membered ring compounds.	14 - 19.
9 membered ring compounds.	20 - 26.
STEREOCHEMICAL STUDIES IN THE DIPHENYL SERIES.	
<u> II. Spiro-spiro-cyclic Derivatives of Diphenyl.</u>	
7 membered ring compounds.	27 - 33.
9 membered ring compounds.	34 - 45.
Conclusion.	46 - 49.
Discussion of Synthetic Schemes.	50 - 45.
Thesis presented by Dorothy E. Cook for the	
degree of Doctor of Philosophy, in the Faculty	
of Science, in the University of London.	
Discussion of Polar Effects.	46 - 51.
Discussion of Polar Effects.	52 - 55.
Discussion of meta- and para- substituents.	56 - 58.
2-(2-methoxy-1'-methylethyl)-4'-ethoxyphenyl bromide-trimethylammonium iodide-	
Attempted optical resolution.	59 - 63.
2-(2-methoxy-1'-methylethyl)-4'-ethoxyphenyl bromide-trimethylammonium iodide-	
Ease of resolution of salts.	64 - 65.
Conclusion.	66.
References.	67 - 127.
References.	68.
References.	69 - 132.

ProQuest Number: 10097908

All rights reserved

INFORMATION TO ALL USERS

The quality of this reproduction is dependent upon the quality of the copy submitted.

In the unlikely event that the author did not send a complete manuscript and there are missing pages, these will be noted. Also, if material had to be removed, a note will indicate the deletion.



ProQuest 10097908

Published by ProQuest LLC(2016). Copyright of the Dissertation is held by the Author.

All rights reserved.

This work is protected against unauthorized copying under Title 17, United States Code.
Microform Edition © ProQuest LLC.

ProQuest LLC
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106-1346

I N D E X.

	Page
General Introduction.	1 - 12.
Lines of present investigation, <u>I</u> and <u>II</u> .	13.
<u>I</u> Hetero-spiro-cyclo Derivatives of Diphenyl.	
Discussion of configuration-	14 - 45.
7 membered ring compounds.	14 - 19.
9 membered ring compounds.	23 - 26.
Types chosen, their investigation and its results-	
7 membered ring compounds.	20 - 22.
9 membered ring compounds.	27 - 28.
Conclusion.	29.
Discussion of Synthetic Schemes.	30 - 45.
<u>II</u> Influence of Polar Effects on the Optical Stability of 2:2'-Disubstituted Diphenyls.	46 - 63.
General Discussion of Polar Effects.	46 - 51.
Influence of meta- and para- substituents.	52 - 55.
5-Ethoxy-2-(2'-dimethylamino-4'-ethoxyphenyl) phenyl-trimethylammonium iodide-	
Attempted optical resolution.	56 - 58.
2-(2'-Dimethylaminophenyl) phenyltrimethylammoniumiodide-	
Rates of racemisation of salts.	59 - 62.
Conclusion.	63
Experimental.	65 -129.
Index to Experiments.	64
Summary.	131 -132.

The asymmetry is comparable to that of the allene derivatives

$\begin{matrix} A & & X \\ & \diagdown & / \\ & C=C=C & \\ & / & \diagdown \\ P & & Q \end{matrix}$, the essential condition being the attachment
 to a central carbon of two different groups, the essential condition being the attachment

STEREOCHEMICAL STUDIES IN THE DIPHENYL SERIES.

unlike groups, the term "group" in the diphenyl series being taken to include 2- and 3- (or 5- and 6-) substituents.

i.e. for asymmetry:-

(1) A and/or B must be sufficiently large not to pass X or Y so that they cannot become coplanar and (2) A and B must be different from each other as must X and Y although A may be the same as X and/or B as Y. Alternatively A and B and/or X and Y may be alike provided the asymmetry is complete or a 5 substituent in the ring. (see examples 6, 13, 19 and 20 below). Of the numerous derivatives of diphenyl which have been shown to be capable of resolution, the following may be taken as representatives:-

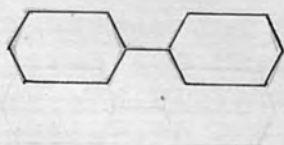


Fig. I.

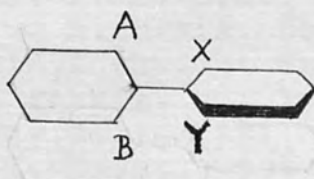


Fig. II.

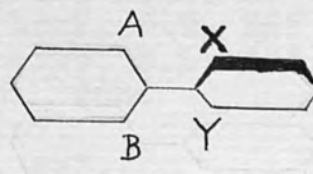
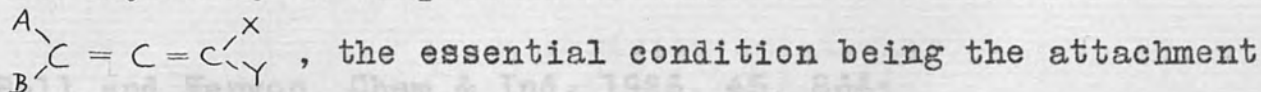


Fig. III.

References for Part I.

For formulation of the theory of restricted rotation see:-

The asymmetry is comparable to that of the allene derivatives



to a centre of dissymmetry of two non-coplanar pairs of

unlike groups, the term "group" in the diphenyl series

being taken to include 2-and3- (or 5-and6-) substituents.

i.e. for asymmetry:-

(1) A and/or B must be sufficiently large not to pass X

or Y so that they cannot become coplanar, and

(2) A and B must be different from each other, as must X

and Y, although A may be the same as X and/or B as Y.

Alternatively, A and B and/or X and Y may be alike

provided the asymmetry is completed by a 3-substituent in

the ring, (see examples 6, 15, 19 and 20 below).

Of the numerous derivatives of diphenyl which have been

shown to be capable of resolution, the following may be

taken as representatives:-

- Williams and Weissberger, J.Am. Soc., 1928, 50, 2332;
 Z.physik. Chem., 1929, B.3, 367.
 Weissberger and Sangewald, Z.physik. Chem., 1929, B.3, 237.
 Williams and Fogelberg, Physik. B., 1930, 31, 365.
 Clark and Fickett, J.Amer.Soc., 1931, 53, 167.
 Mengstenberg and Mark, J. Krist., 1929, 70, 265.

Reference for Page I.

For formulation of the theory of restricted rotation see:-

- Bell and Kenyon, Chem & Ind. 1926, 45, 864;
 J.C.S., 1926, 3045.
 W. H. Mills, Chem & Ind. 1926, 45, 883, 905;
 Solvay-Vortrag, Brussel, 1931, S.47.
 Le Fèvre and Turner, Chem. & Ind. 1926, 45, 831;
 J.C.S., 1926, 2476.

For agreement see:-

- Meisenheimer and Höring, Ber. 1927, 60, 1425.
 Kuhn and Albrecht, Annalen, 1927, 455, 272.
 Mascarelli, III, Congr. Nazionale Chim. pura applicata.
 Firenze e Toscana, 1929, 249.
 Stanley and Adams, J.Am.Soc., 1930, 52, 1200.

For additional evidence see also:-

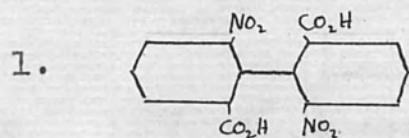
- Dennett and Turner, J.C.S., 1926, 478.
 Christie, Holderness and Kenner, J.C.S., 1926, 671.
 Kuhn and Zumstein, Ber., 1926, 59, 488.
 Ferriss and Turner, J.C.S., 1920, 117, 1140.
 E. E. Turner, J.C.S., 1917, 1; ibid. 1915, 1495.

For confirmation by physical evidence see:-

- Williams and Weissberger, J.Am. Soc., 1928, 50, 2332;
 Z.physik. Chem., 1929, B.3, 367.
 Weissberger and Sangewald, Z.physik. Chem., 1929, B.5, 237.
 Williams and Fogelberg, Physik. Z., 1930, 31, 363.
 Clark and Pickett, J.Amer.Soc., 1931, 53, 167.
 Hengstenberg and Mark, Z. Krist., 1929, 70, 285.

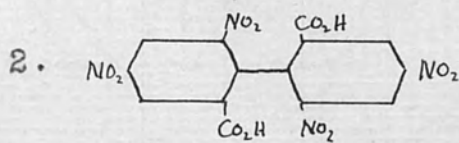


Mayer and Adams,
 J.Am. Soc., 1929, 51, 820.

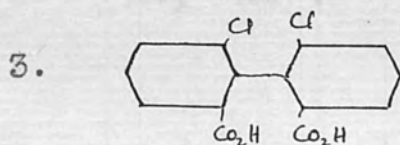
Group I. Restriction due to four substituent ortho-groups.

Christie and Kenner,
J.C.S., 1922, 614.

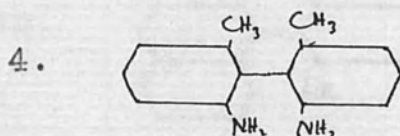
Stanley and Adams, J.C.S., 1929, 48, 1333.



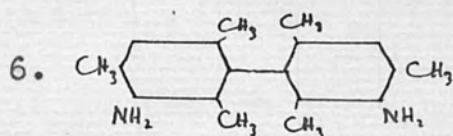
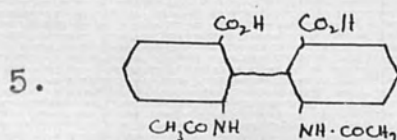
Kleiderer and Adams,
J. Am. Soc., 1931, 53, 1573.



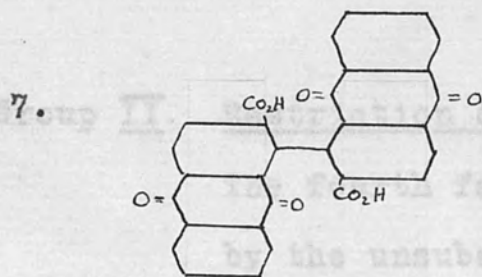
Christie, James and Kenner,
J.C.S. 1923, 1948.



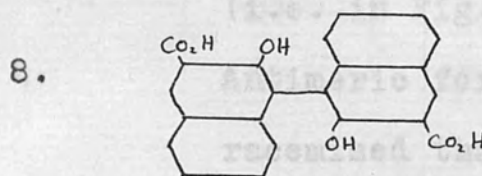
Meisenheimer and Horing,
Ber., 1927, 60, 1425.



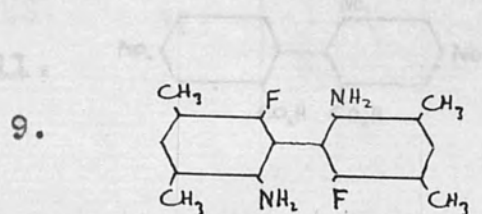
Moyer and Adams,
J. Am. Soc., 1929, 51, 630.



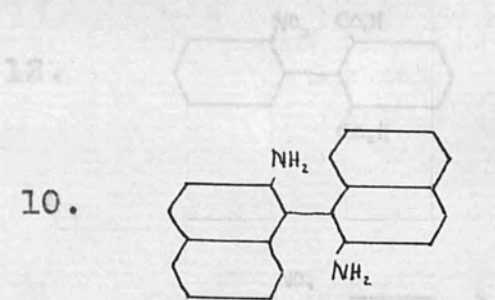
Kuhn and Albrecht,
Annalen, 1928, 91, 464.



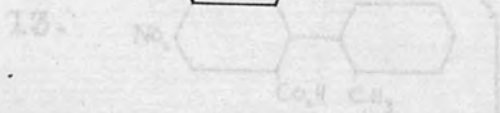
Stanley and Adams, Rec.trav.chim.
1929, 48, 1035.



Christie and Kenner,
J.O.S., 1925, 779
Kleiderer and Adams,
J.Am. Soc., 1931, 53, 1575.



Bell and Kenyon,
Chem and Ind. 1926, 45, 864.



Lesalle and Turner,
J.O.S., 1930, 1753; *ibid.* 1931, 1186.



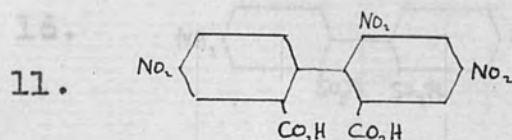
Stearn and Adams,
J.Am. Soc., 1931, 53, 2070.

Group II. Restriction due to three substituent ortho groups.

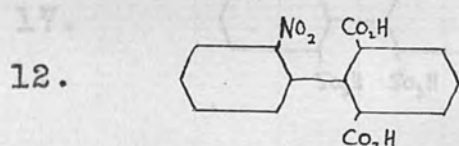
The fourth factor in heterogeneity is introduced by the unsubstituted ortho hydrogen atom.

Group III. (i.e. in Fig. II, A = H.).

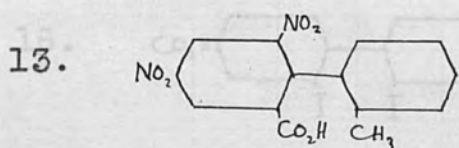
Antimeric forms are, on the whole, more readily racemised than in Group I.



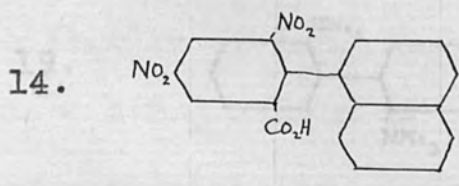
Christie and Kenner,
J.C.S., 1923, 779.



Bell and Kenyon,
Chem and Ind. 1926, 45, 864.

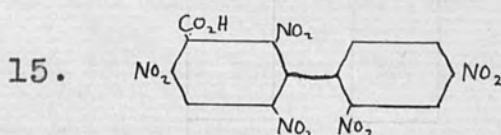


Lesslie and Turner,
J.C.S. 1930, 1758; *ibid.* 1931, 1188.



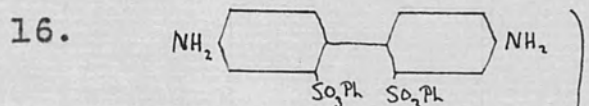
Shaw and Turner,
J.C.S., 1933, 135.

The NO_2 group can pass the o-hydrogen atom but being different from H it introduces asymmetry.

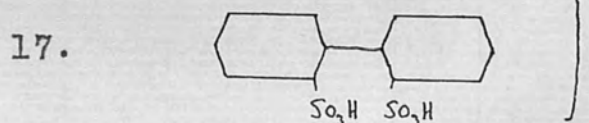


Stearn and Adams,
J.Am. Soc., 1931, 52, 2070.

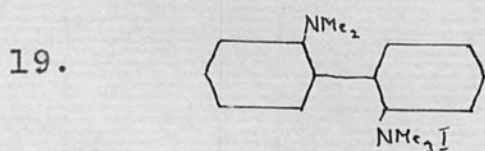
Group III. Restriction due to two substituent ortho groups.
(i.e. $A = X = H$ in Fig. II).



Lesslie and Turner,
J.C.S., 1932, 2021, 2394.



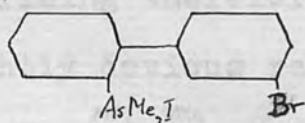
Searle and Adams,
J.Amer.Soc., 1933, 55, 1649.



Shaw and Turner,
J.C.S., 1933, 135.
The NMe_2 group can pass the
o-Hydrogen atom, but being different
from $NMe_3 \cdot I$ it introduces
asymmetry.

20. Group IV. Restriction due to one substituent ortho group

Apart from example 19, only one derivative in this class has been resolved:-

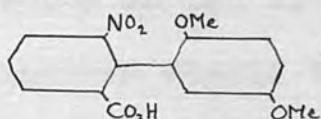


Lesslie and Turner, J.C.S. 1933, 1588.

Comparing this molecule with Fig. II, B-AsMe₃I, A = X = H, and although Y = H it is precluded from identity with X by the 3-substituent bromine.

It has been a matter of particular interest to determine the size of the ortho substituents which, in the limit, will just prevent rotation. Stanley and Adams (J. Am. Soc., 1930, 52, 1200) considered that a collision area or "overlap" of 0.39 \AA was necessary for the complete stability of isomers, and gave the general equation $d_s - 2.9 \geq 0.39 \text{ \AA}$ as the condition for resolvability with non-racemisation, where d_s is the sum, in Angström units, of the diameters of the two substituent ortho groups, and 2.9 (\AA) is twice the value taken for the diameter of an aromatic carbon atom. The calculation was necessarily an

empirical one, and since the derivatives of diphenyl which had then been resolved mostly had $-\text{NO}_2$ or $-\text{CO}_2\text{H}$ as ortho substituents very few data were available. It is not surprising therefore that more recent work has given slightly devious results (e.g. the ready racemisation of



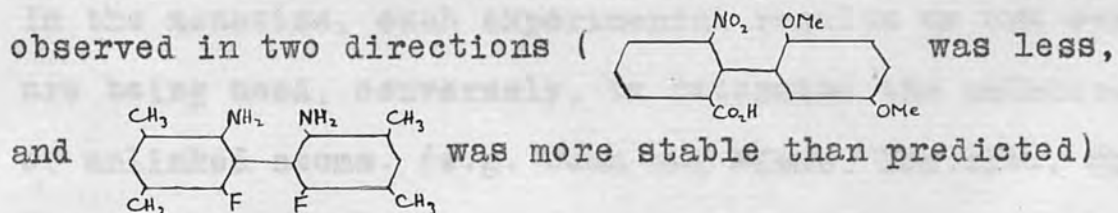
observed by Yuan and Adams,

(J.Amer.Soc. 1932, 2966). Especially notable is the resolution of 2:2'-difluoro - 6:6'-diamino- 3:5:3':5'-tetramethyl-diphenyl (Kleiderer and Adams, J.Amer. Soc. 1931, 53, 1575). Calculation shows that there is no overlap either between two ortho-substituent nitrogen atoms or between a nitrogen atom and a fluorine atom. Adams explains this apparent deviation by attributing some volume effect to the hydrogen atoms of the amino group, and states (Kleiderer and Adams, J.Amer.Soc., 1933, 55, 4219) that the short half-life period (60 mins. in boiling absolute alcohol) is exactly what they had predicted from their calculations in which due allowance had been made for hydrogen.

Sidgwick, (Annual Reports --- of the Chemical Society, 1922, p.69) however, holds the view that the hydrogen atoms are turned out of the way of the fluorine atom, and attributes the discrepancy to forces of electrical origin. Sidgwick considers that the mutual electrostatic repulsion between

ortho groups (as between unlinked atoms in general) creates an outer sphere of influence or "envelope" round each group, inside which the boundaries of other atoms cannot penetrate, so that the effective volumes (of the groups) are mutually increased. The value 0.5 \AA is given for the probable thickness of the envelope, but on this basis many diphenyl derivatives should be optically active which so far have resisted all attempts to resolve them, e.g. diphenic acid. The matter has been discussed by Shaw and Turner (J.C.S. 1933, 135). These authors also hold the view that electrical effects are responsible, to some extent at least, for the restriction of rotation. They point out that the numerical data generally used in calculating collision effects between (unlinked) ortho groups is not strictly applicable, being obtained from measurements of internuclear distances between linked atoms either in the solid (from X-ray crystal analysis) or in the vapour (from electron diffraction patterns) state. It is interesting to note that "electrical effects" were among the factors considered by Le Fèvre and Turner (loc.cit) in their original survey of the possible causes of molecular asymmetry in this series, and whether the electrostatic repulsion between approaching ortho-groups be regarded as maintaining the angular separation of the diphenyl rings directly, or whether it acts by increasing the volume of the ortho groups, the result is the same. The fact that

deviations from the Stanley-Adams equation have been observed in two directions (



suggests that the cause is an external one and may be connected with the opposite polar effects of $\leftarrow\text{OMe}$ and $\rightarrow\text{F}$.

In conclusion it may be said that there is reason to believe that the internuclear distances between contiguous unlinked atoms is definitely greater than between linked atoms, to which numerical calculations apply, the increase probably being due to the electrostatic repulsion between electrons whose magnetic moments are already paired within the molecule (see further discussion p.46 below). It seems reasonable to assume therefore, that polar effects are a potential factor in the restriction of rotation of the 2:2' - disubstituted diphenyl molecule, although they may be the deciding factor only in limiting cases. 2:2'-difluoro-6:6' - diamino - 3:5:3':5' - tetramethyl diphenyl may be a limiting case, calculation from X-ray data allows nitrogen and fluorine just to pass, and fluorine is highly polar. The synthesis of such compounds, having small, but highly polar, univalent atoms as ortho substituents, presents considerable difficulties, and until these have been overcome and more experimental evidence is available it is impossible to decide how far the restriction

is due to mechanical effects and how far to polar ones. In the meantime, such experimental results as are available are being used, conversely, to determine the relative sizes of unlinked atoms. (e.g. Yuan and Adams, loc.cit., Shaw and Turner, loc.cit.).

The present work has dealt with the mechanical and with the electrical aspect of diphenyl dynamics.

I. In the first place, an attempt has been made to synthesise a compound in which the asymmetric configuration of the diphenyl molecule is maintained, not by the mutual impedance of 2:2'-substituents, but by a spirocyclic chain forming a mechanical bridge across the 2:2'-positions.

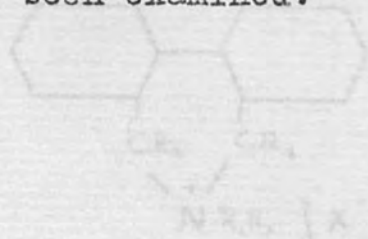
II. In the second place, the effect of a polar substituent in the 4:4'-positions on the rate of racemisation of a 2:2'-disubstituted derivative of diphenyl has been examined.

The present work has dealt with the mechanical and with the electrical aspect of diphenyl dynamics.

In all the compounds of the diphenyl series which have so far been resolved, the asymmetry has been attributable to the restriction of rotation by ortho

I. In the first place, an attempt has been made to synthesise a compound in which the asymmetric configuration of the diphenyl molecule is maintained, not by the mutual impedance of 2:2'-substituents, but by a spirocyclic chain forming a mechanical bridge across the 2:2'-positions. This chain may be regarded as acting in two ways. It will anchor the ortho positions near together in space, and so restrict rotation of the nuclei, and it will also, by virtue of its own size, keep the planes of the rings apart, so that a rigid, stable structure will be set up.

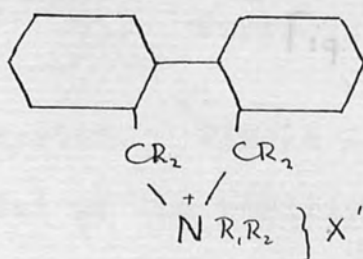
II. In the second place, the effect of a polar substituent in the 4:4'- positions on the rate of racemisation of a 2:2'- disubstituted derivative of diphenyl has been examined.

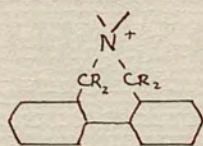
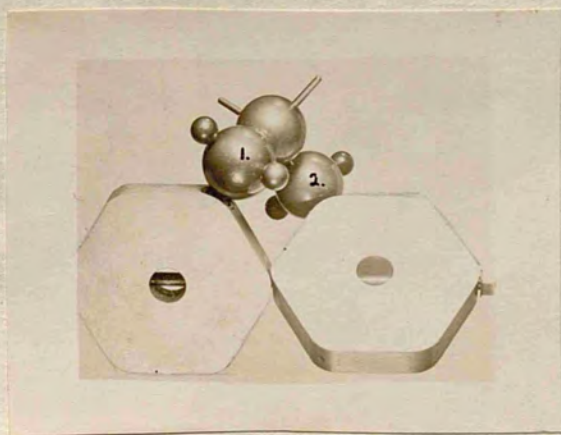


I. HETERO-SPIRO-CYCLO DERIVATIVES OF DIPHENYL.

In all the compounds of the diphenyl series which have so far been resolved, the asymmetry has been attributable to the restriction of rotation by ortho substituents. In the present work an attempt has been made to synthesise a diphenyl derivative in which rotation is restricted by a chain bridging the 2:2' positions. This chain may be regarded as acting in two ways: it will anchor the ortho positions near together in space, and so restrict rotation of the nuclei, and it will also, by virtue of its own size, keep the planes of the rings apart, so that a rigid, stable structure will be set up.

Fig. IV is a spatial representation of the skeleton structure of a compound of the type:-





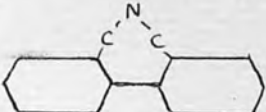
For the sake of clearness the model is shown
with hydrogen as R-substituents.

Fig. IV.

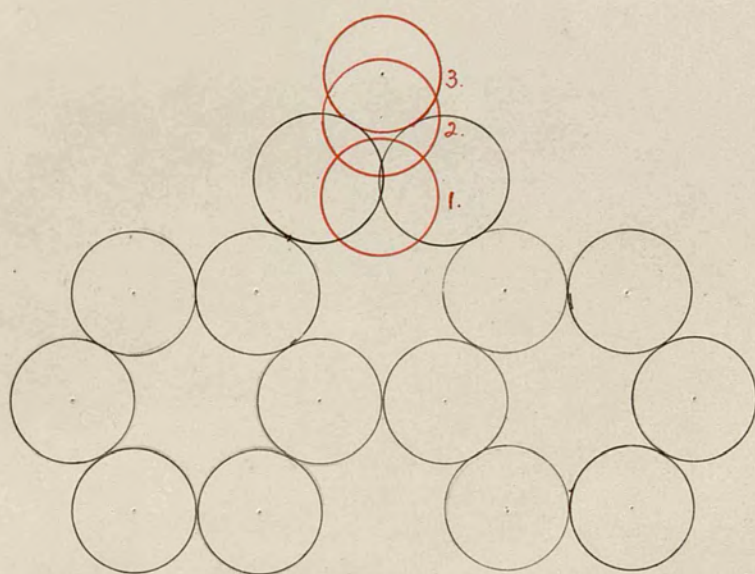
The linked aliphatic carbon atoms 1 and 2, being slightly larger than aromatic carbon atoms, which would just touch in such circumstances, (0.77\AA radius as against 0.725\AA), will slightly overlap each other, but this overlap is not sufficient of itself to cause molecular asymmetry. The incidence of the nitrogen atom, as it were, stabilises the aplanar position of the rings and at the same time introduces asymmetry.

The optical stability of the isomers will depend upon the relation between the rigidity of the spiro-cyclo chain and the momentum of the rotating molecule. If the spiro chain loses its rigidity, e.g. by distention of valency angles, to the rotating molecule, the entire configuration becomes coplanar and asymmetry disappears. If, however, the rigidity of the chain is sufficiently great to withstand the tendency to rotation of the molecule, buckling of the spiro-chain will occur, with stabilisation of isomers.

The condition for instability of the isomers is represented in Fig. V, which is a coplanar representation

of  . Consider the angular strain in the

spiro-cyclo system. Circle 1, Fig. V, represents what may be regarded as the position of the nitrogen atom before strain has been distributed, or the position of nitrogen



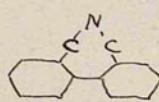
The Spatial Arrangement of .

Fig. V.

relative to individual carbon atoms when the rings are non-coplanar, the centre of circle 1 being the point of intersection, in the plane of the rings, of the lines representing the directions of the free carbon valencies. From the figure, which is drawn approximately to scale, (atomic dimensions as determined by X-ray crystal analysis (Pauling) can here be applied with some certainty) the angle between the two nitrogen valencies concerned is then about 200° , giving a strain of about 90° . To relieve this, we may imagine the nitrogen atom moved up to a position as indicated by circle 2, the strain then being shared by the two carbon atoms, i.e. the spiro chain is buckled. There is still not room for the nitrogen atom, and further adjustments must be imagined until nitrogen can occupy a position represented by circle 3. This position represents the symmetrical configuration, or the arrangement at the moment of racemisation. The valency angle of nitrogen is then contracted (strain is about -50°) while the valency angle of each carbon atom is distended (strain is about $+70^\circ$.) This imaginary configuration must, therefore, be unstable, and must give rise to a position of equilibrium such as that indicated by circle 2, i.e. the configuration cannot be coplanar.

A three-dimensional model of the molecule, of which Fig. IV is a photograph, shows that, as the phenyl rings

rotate, the apex angle which the free valencies of carbon atoms 1 and 2 make with each other decreases, and at the point where this angle is $109\frac{1}{2}^{\circ}$, the length from the angular apex to the surface of the carbon atoms is almost equal to the radius of a nitrogen atom, i.e. there will be very little strain in the 7-membered ring. An independent 7-membered heterocyclic ring system is strainless, but the identity of four of the carbon atoms with those already fused in the 1:1':2:2' portions of the diphenyl molecule may suppress the appropriate buckling and so account for the slight strain which seems to be present in the model. The model itself is a perfectly rigid structure.

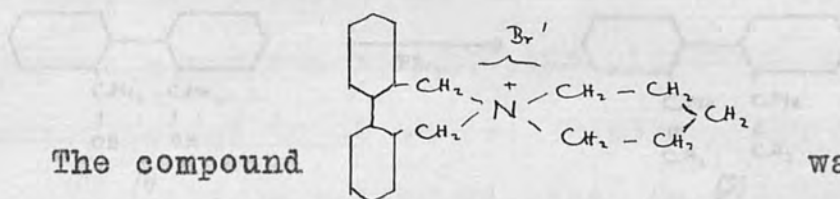
It seemed reasonable to infer, therefore, that structure IV would be

- (1) stable, and
- (2) asymmetric: a mirror in the plane of the paper of Fig. IV would reflect the antimeric configuration, in which the nitrogen is in front of carbon atom 1 and behind carbon atom 2.

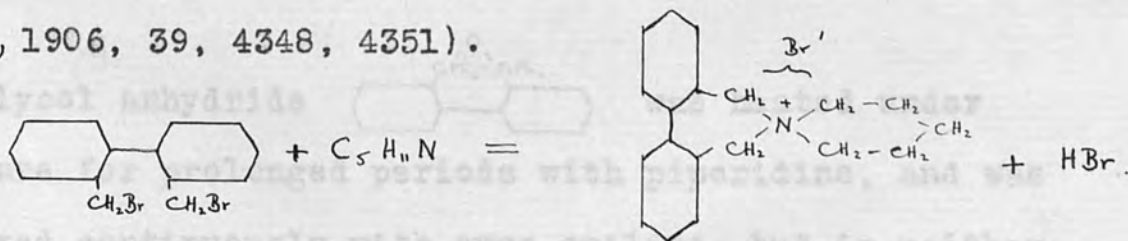
pressures, except in extremely small quantities.

Compounds of the type  (where R=H, CH₃

and C₂H₅) however, were readily obtained, and attempts to prepare their spiro derivatives led to some interesting results. The action of phosphorus tribromide on the tetramethyl glycol was that of dehydration, leading to a hydrocarbon to which formula (2) has been assigned:-



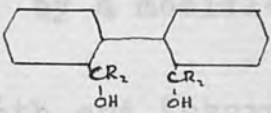
chosen as being of the type suitable for investigation, since it appeared to have the double advantage of possessing an ionised bromine atom, on which to perform resolution experiments, and of being easily prepared from 4:4'-dibromo-2:2'-ditolyl, by condensation with piperidine:- (cf. von Braun's experiments on the condensation of piperidine with pentamethylene dibromide (Ber., 1906, 39, 4348, 4351).

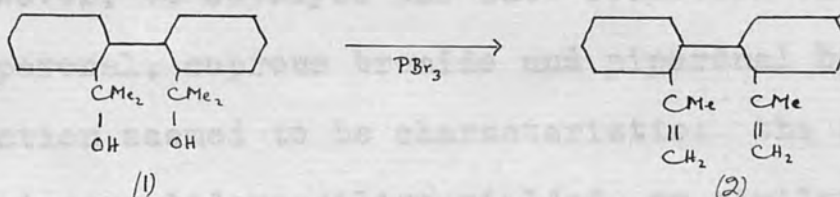


Contrary to expectations, 2:2'-ditolyl was not found to be obtainable by a series of simple reactions at ordinary

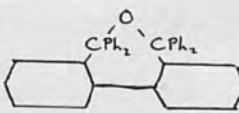
supplementary investigations were carried out simultaneously

pressures, except in extremely small quantities.

Compounds of the type  (where R=CH₃ and C₆H₅) however, were readily obtained, and attempts to prepare their halogen derivatives led to some interesting results. The action of phosphorus tribromide on the tetramethyl glycol was that of dehydration, forming a hydrocarbon to which formula (2) has been assigned:-

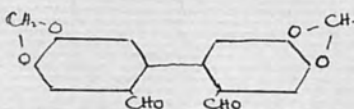


Even more remarkable was the result that dry hydrogen chloride gas had a similar action, and the same hydrocarbon (2) was formed. The halogen derivatives of the tetraphenyl glycol were found to be so excessively reactive that they could not be isolated in a condition sufficiently specific for the final condensation with piperidine.

The glycol anhydride  was heated under pressure for prolonged periods with piperidine, and was refluxed continuously with pure aniline, but in neither case did any reaction occur.

Subsidiary investigations were carried out simultaneously

on 6-bromopiperonal, with the object of preparing the

dialdehyde  by a modified Ullmann reaction

with copper bronze. (cf. Späth and Kahover, Ber., 1924, 67, 1511).

The isolation of this compound would open a fertile field for general investigation, apart from the fact that it was a

feasible preparative method in the present scheme. The

action of copper bronze in an atmosphere of carbon dioxide was, however, to catalyse the auto-reduction of the

bromopiperonal, cuprous bromide and piperonal being formed.

The reaction seemed to be characteristic: the derivative

6-bromopiperonylideneaniline yielded, on similar treatment,

piperonylideneaniline. Its skeleton structure



shows that the 6-membered ring is not only

strainless, but, having a greater degree of freedom than

the 7-membered ring, it is flexible and capable of

adapting to various positions. Fig. VI (iii)

represents the ring position, and since the occurrence is

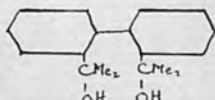
probably more frequent than that of any other it may

be called the axial configuration. The chain may swing

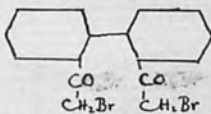
downwards to the left, as viewed in the Fig., through

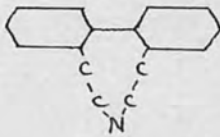
position (2) to position (3), and can similarly swing

upwards to the right to corresponding positions (2') and (3')

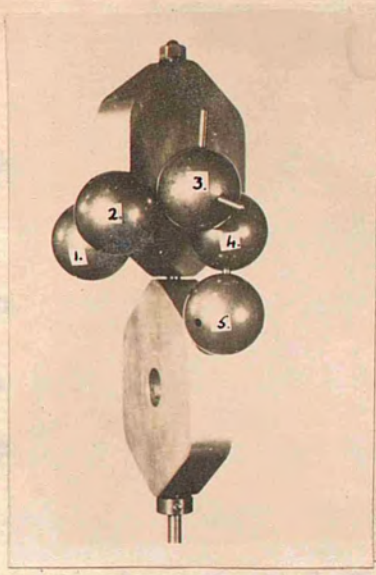
The possibility that 2:2'-diacetyldiphenyl (used in the synthesis of  above) may, by analogy

with acetophenone, undergo smooth w-bromination to

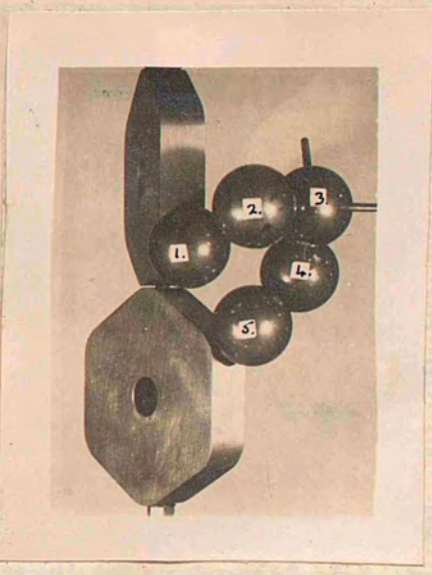
give  suggested the study of 9-membered spiro-cyclo derivatives.

The 9-membered spiro-cyclo ring would produce the same stereochemical effect as the 7-membered ring, and the same reasoning as to possible stability and asymmetry applies. A model of the skeleton structure 

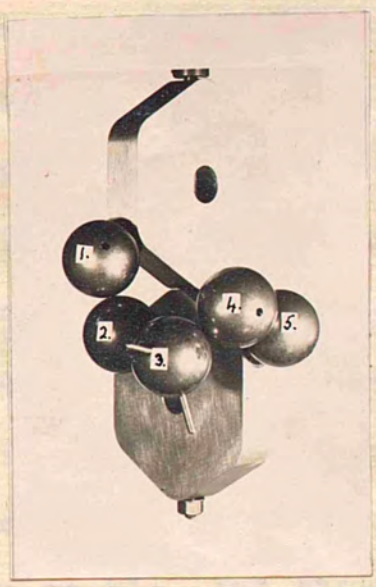
shows that the 9-membered ring is not only strainless, but, having a greater degree of freedom than the 7-membered ring, it is flexible and capable of oscillating between ~~the~~ two positions. Fig. VI (1) represents the mean position, and since its occurrence is probably twice more frequent than that of any other it may be called the normal configuration. The chain can swing downwards to the left, as viewed in the Fig., through position (2) to position (3), and can similarly swing upwards to the right to corresponding positions (2') and (3')



(2')



(3')



(1).

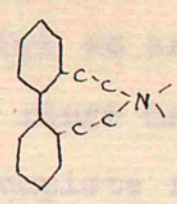
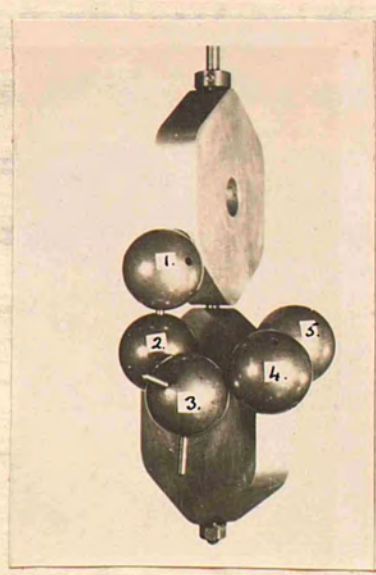
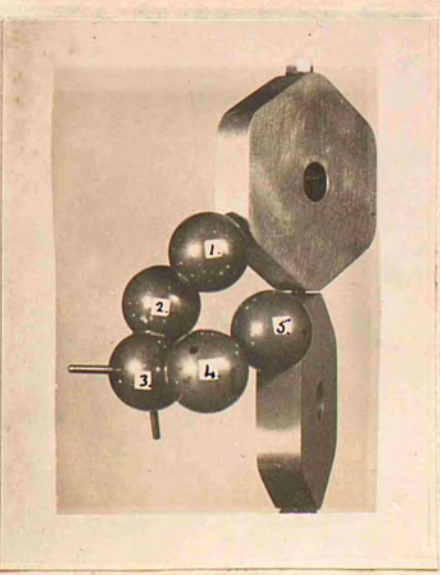


Fig. VI.



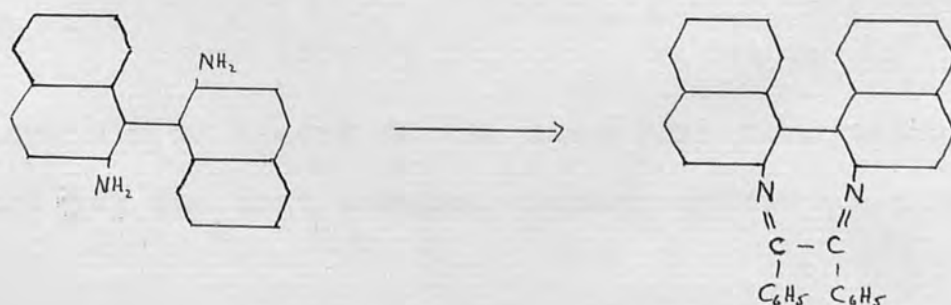
(2).



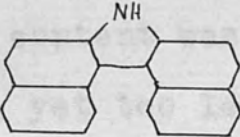
(3).

on the other side of the molecule. The extreme positions (3) and (3') represent identical configurations, no interconversion of forms is involved. Position (3) does, however, represent the arrangement prior to interconversion, and from it the process (of racemisation) can be pictured; the two carbon atoms 1 and 5 must pass each other and the spiro-cyclo ring must undergo distortion to the effect of being turned inside out. One complete oscillation of the spiro-cyclo chain allows one of the diphenyl rings to rotate relatively to the other through an angle of about 60° . The momentum acquired by the rings may accelerate any impetus in the direction of a complete rotation, so that the 9-membered ring compound may be expected to be more easily racemised than the 7-membered one.

The model indicates that the 9-membered ring compound would be stable, and this surmise is supported by the fact that an 8-membered-spiro-cyclo derivative has been made and found to be optically stable. Kuhn and Goldfinger, (Annalen, 1929, 470, 183) prepared the benzil derivative of their optically active diamine:-



and found that it retained the optical activity. The obstacle effect of ortho substituents is still active in this derivative, and their observation is not relevant to the point at issue, except that it shows that the spiro cyclo chain is sufficiently stable to carry two phenyl nuclei, and that its configuration is non-coplanar. (cf. the condensation of the active diamine to form an

inactive anil:-  which has, by inference, a coplanar configuration.

The bromination was complicated by replacement reactions of the type described by Robinson, Ger and Williams, (J.C.S. 1917, 909, 945). These authors find that bromine in acetic acid solution may first replace an enol group and then brominate in the usual way. Applying this to the action on diacetyl diphenyl there is the possibility of the following reactions:



The presence of traces of the hexabromo-derivative would account for the high bromine content of the product.

Direct chlorination of 2:2'-diacetyl diphenyl gave a product of indefinite m.p. and visibly consisting of two crystalline forms, which could not be separated by fractional crystallisation.

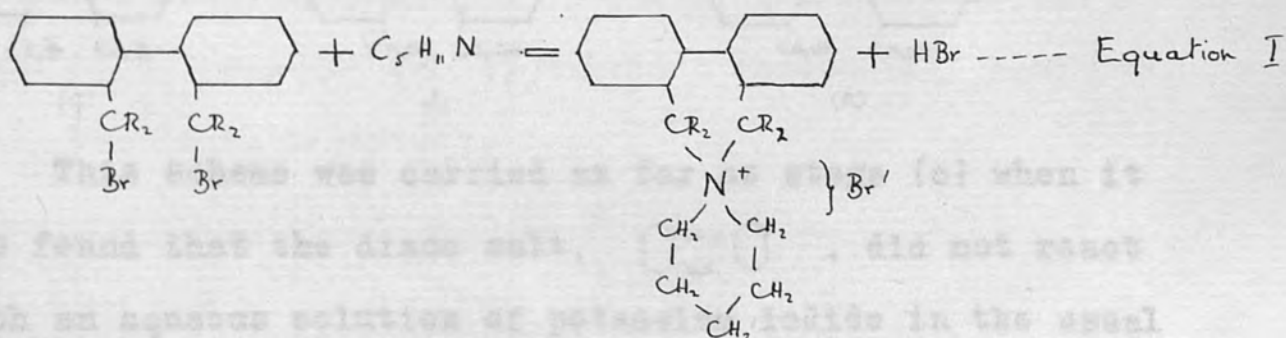
Time did not allow these complications to be investigated and in view of them experiments had to be abandoned. The synthesis of a spiro-cyclo derivative has not been completed. It may be said that various methods of attack have been explored, and the results do not indicate that further work along the same lines would be successful. It seems that the spiro-cyclo system is not easy to form, and there appears to be need for a great deal of exploratory work in order to determine the properties peculiar to reactive 2:2'-substituents themselves in the diphenyl molecule, and possibly to deduce a general reaction for the synthesis of spiro-cyclo compounds before their detailed structure can be elucidated stereochemically.

Thus, although these investigations have achieved some measure of success and have led to some interesting results, especially in the ditolylene glycol series, the synthesis of a spiro-cyclo derivative has not been completed. It may be said that various methods of attack have been explored, and the results do not indicate that further work along the same lines would be successful. It seems that the spiro-cyclo system is not easy to form, and there appears to be need for a great deal of exploratory work in order to determine the properties peculiar to reactive 2:2'-substituents themselves in the diphenyl molecule, and possibly to deduce a general reaction for the synthesis of spiro-cyclo compounds before their detailed structure can be elucidated stereochemically.

with copper powder in a sealed tube at 210°C for 8 hours.
 In the present series of experiments it was desired to
 eliminate such a tube work as much as possible, and a
 SCHEMES FOR THE SYNTHESIS OF HETERO-SPIRO-CYCLO DERIVATIVES
 OF DIPHENYL.

A. 7-MEMBERED SPIRO-CYCLO RING COMPOUNDS.

It was anticipated that these could be prepared from
 halogen derivatives of 2:2'-ditolyl, or its analogues,
 by interaction with a secondary base, e.g. piperidine:-



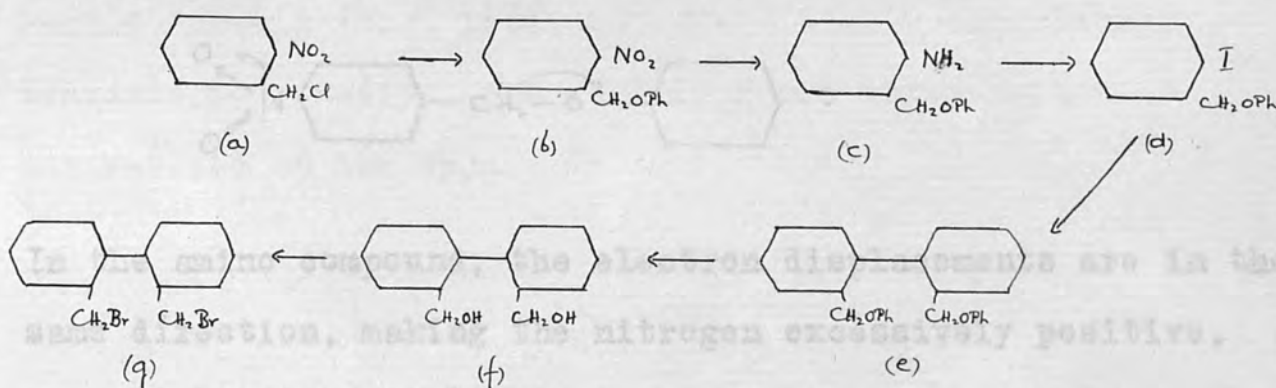
1. 2:2'-Ditolyl Derivatives.

(R=H in Equation I).

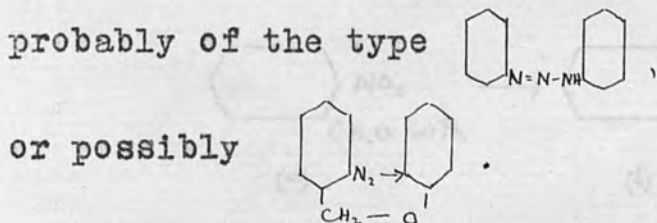
Kenner and Turner (J.C.S. 1911, 2101) prepared
 w:w'-dibromo-2:2'-ditolyl by the direct bromination of
 ditolyl, which they obtained by heating o-iodotoluene

with copper bronze in a sealed tube at 210° for 8 hours. In the present series of experiments it was desired to eliminate sealed tube work as much as possible, and a series of simple, straightforward reactions which would give good yields of dibromo-ditolyl seemed preferable. Several such schemes were planned, five of these have been investigated.

I From o-nitrobenzyl phenyl ether:-

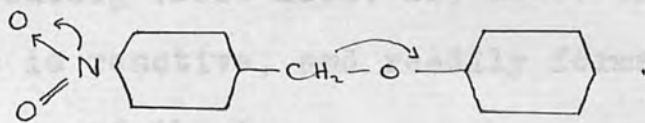


This scheme was carried as far as stage (c) when it was found that the diazo salt, c1ccc(cc1)C[N+]#N[O-], did not react with an aqueous solution of potassium iodide in the usual way, but formed instead a highly-coloured compound,

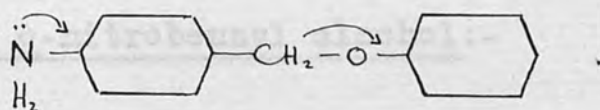


Reactions with corresponding p compounds were also studied

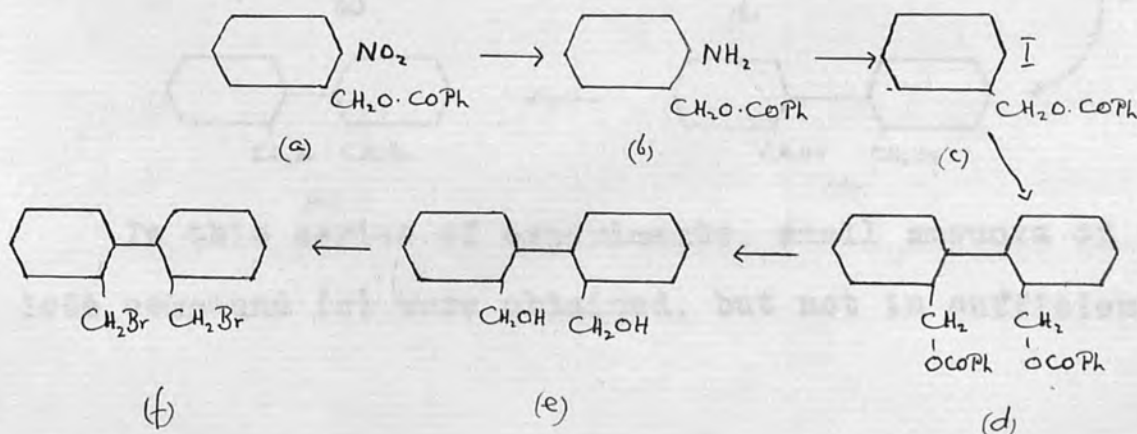
in order to obtain experience of the reactions involved. *p*-Aminobenzyl phenyl ether proved difficult to isolate on account of its extreme reactivity and light-sensitiveness. Kumpf & Fische (Annalen, 1862, 224, 106, 153) commented on its excessive reactivity and concluded that attempts to reduce *p*-nitrobenzyl phenyl ether were futile. An explanation does not seem to be forthcoming in terms of electronic effects. In the nitro ether there are opposing electron displacements which, being situated at opposite ends of the molecule, may be capable of balance:-



In the amino compound, the electron displacements are in the same direction, making the nitrogen excessively positive, i.e. stable to oxidation:-

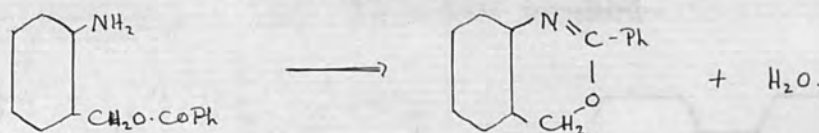


II From *o*-nitrobenzyl benzoate:-

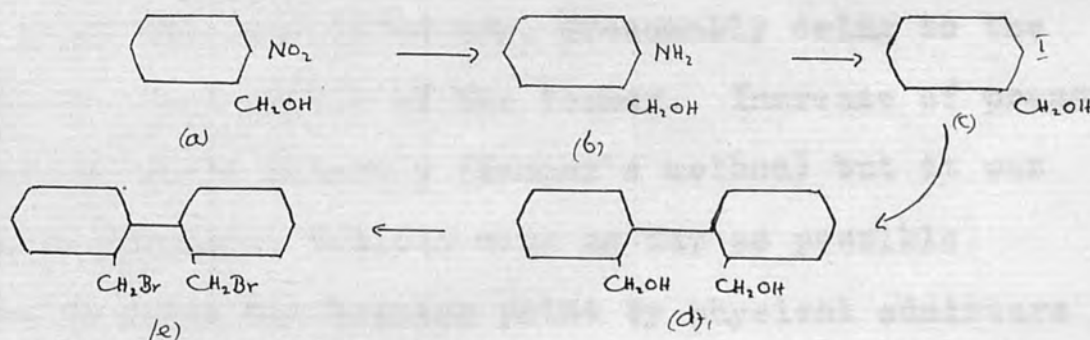


At stage (b) it was anticipated theoretically that the presence of the carbonyl (-CO-) link might have some deactivating effect on the lability of the phenyl nucleus, and that the diazo salt should, in consequence, be sufficiently stable to form the iodo derivative (c). In practice it was found that a coloured precipitate was again formed, and no iodo compound could be detected among the products of reaction.

This result is in agreement with the observation made by Paal & Bodewig (Ber. 1892, 25, 2965) that *o*-aminobenzyl benzoate is reactive, and readily forms intra-molecular derivatives of the type:-



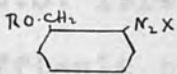
III From *o*-nitrobenzyl alcohol:-



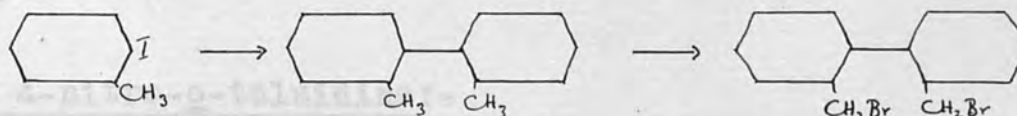
In this series of experiments, small amounts of the iodo compound (c) were obtained, but not in sufficiently

good yield to justify adoption of the scheme unmodified. Reissert & Cr amer, (Ber., 1928, 61B, 2555) have stated that the diazonium chloride of o aminobenzyl alcohol is extremely labile and decomposes completely in HCl solution in 1 hour at 0°.

The replacement of Phenyl by hydrogen produced an effect in the right direction, and although this result seemed to indicate the direction in which further attempts should be made to reduce the lability of the system

 , these had to be postponed owing to dermatitic properties of chemicals used, the workers being in danger of becoming super-sensitised.

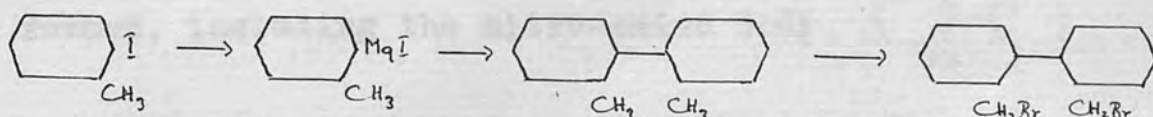
IV From o-iodotoluene (a) Ullmann method.

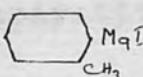


Under ordinary conditions the conversion of o iodotoluene into ditolyl was unsatisfactory, presumably owing to the low boiling point (204°) of the former. Increase of pressure improved the yield slightly (Kenner's method) but it was desired to eliminate tedious work as far as possible. Attempts to raise the boiling point by physical admixture with a non-reacting, easily recoverable substance of high

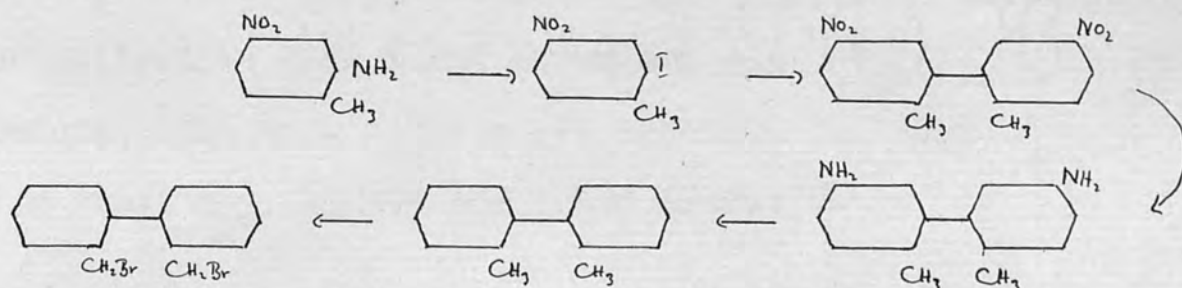
boiling point (e.g. dinitrobenzene, naphthalene) did not give good results.

(b) Grignard method.



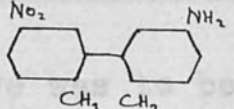
The Grignard compound  reacted only incompletely with chromic chloride (Bennett & Turner J.C.S. 1914, 105, 1057) and the product was consequently difficult to work up. Similar results were obtained by treating the Grignard reagent with cupric chloride (Turner & Krizewsky (J.C.S. 1919, 559)). This scheme has so far been used only for the preparation of small quantities of ditolyl.

V. From 4-nitro-*o*-toluidine:-

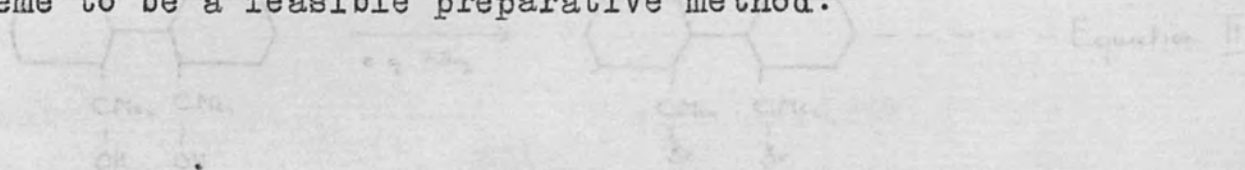


This scheme was devised as an attempt to obviate the difficulty (compare IVa) of preparing 2:2'-ditolyl directly by the Ullmann method. 2-iodo-4-nitrotoluene boils above 250° , and the conversion into 5:5'-dinitroditolyl was found

to proceed satisfactorily at 210-220°. Reduction of the dinitro-ditolyl was effected in two attempts made, and 5:5'-diamino-2:2'-ditolyl isolated. Other products were

also formed, including the nitro-amino body, ,


and the yield of pure base was not sufficient for the scheme to be a feasible preparative method.



With a view to deciding the best method of preparation of the glycol itself, the action of methyl magnesium iodide



was first investigated. From the acid chloride, (i) a semi-crystalline product was obtained which, by fractional crystallisation from light petroleum b.p. 80-100°, gave two products. The more soluble (A) crystallised in prisms and had a final m.p. of 138-139°, and proved to be the

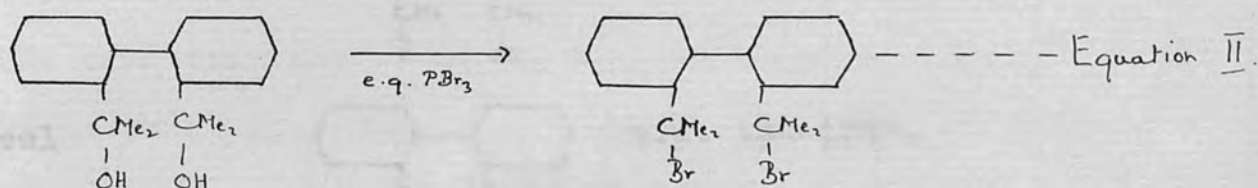
glycol ; the less soluble (B) crystallised in needles, melted at 164-165° and was identified as the

alcohol-ketone .

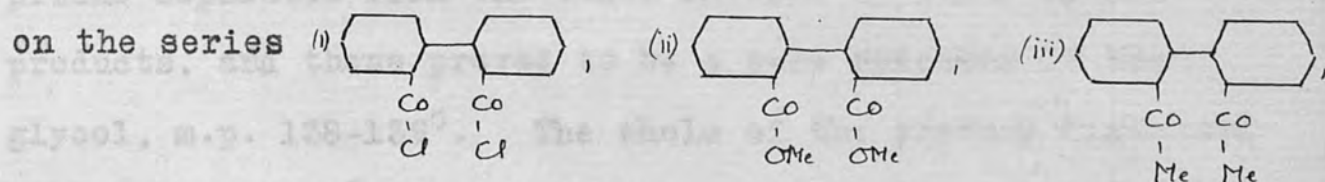
2. w:w'-Tetramethyl-2:2'-ditolyl Derivatives.

(R=CH₃ in Equation I)

In this series the halogen derivative was to be prepared from the glycol:-



With a view to deciding the best method of preparation of the glycol itself, the action of methyl magnesium iodide on the series

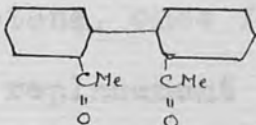
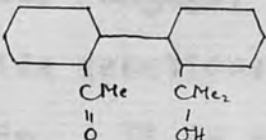
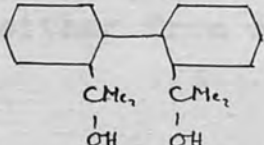


was first investigated. From the acid chloride, (i) a semi-crystalline product was obtained which, by fractional crystallisation from light petroleum b.p. 80-100°, gave two products. The more soluble (A) crystallised in prisms and had a final m.p. of 138-139°, and proved to be the

glycol ; the less soluble (B) crystallised in needles, melted at 164-165° and was identified as the

alcohol-ketone

The melting points in this series show a curious irregularity which is worthy of note:-

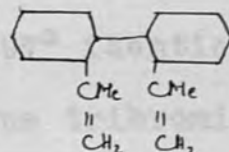
diacetyl diphenyl		m.p. 93-94°. (Zincke and Tropp, Annalen 1908, 362, 305, give m.p. 83°).
alcohol-ketone		m.p. 164-165°.
glycol		m.p. 138-139°.

In the reaction with diacetyl diphenyl (iii) large colourless prisms separated from the ether extract of the Grignard products, and these proved to be a pure specimen of the glycol, m.p. 138-139°. The whole of the product dissolved readily in 60-80° light petroleum, and no trace of the alcohol-ketone could be detected. The reaction was clean and straightforward, and was afterwards used for the preparation of large quantities of the glycol, giving a 60% yield of pure product. From the ester, dimethyl diphenate (ii) a fairly pure specimen of the glycol was obtained if the ether extract was previously washed with caustic soda. This washing removed a bye-product, probably the lactone, which was present in considerable amount. The final yield of glycol was 45% of the theoretical.

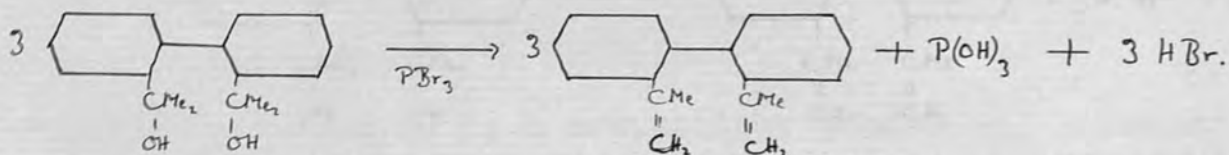
The alcohol-ketone obtained from the dichloride of diphenic

acid was not readily converted into the glycol. After refluxing with a large excess of Grignard reagent for six hours only a 10% conversion occurred. It must be inferred that the alcohol-ketone, once formed, is extremely stable, and the incomplete replacement in the original reaction ($\text{ClCO} \cdot \text{C}_6\text{H}_4 - \text{C}_6\text{H}_4 \cdot \text{COCl} + \text{CH}_3\text{MgI}$) is not due to an inhibiting effect or to any side reactions connected with the presence of the acid chloride. It is curious that no alcohol-ketone could be obtained either from diacetyl diphenyl or from dimethyl diphenate.

Phosphorus tribromide had an immediate action on the glycol, which was complete in five minutes at 40° . The product crystallised from light petroleum b.p. $40-60^\circ$ in rectangular prisms, m.p. $96-97^\circ$. It contained neither halogen nor oxygen and was given the formula



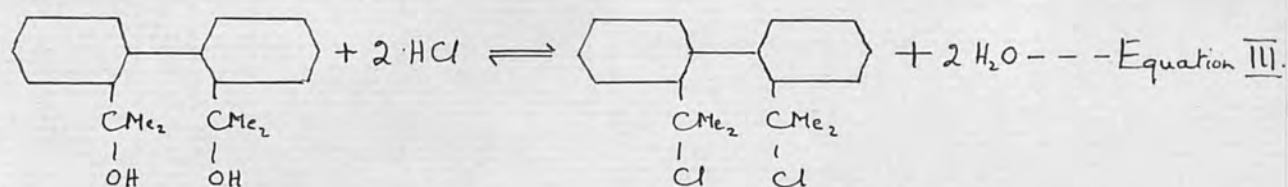
Equation II therefore takes the corrected form:-



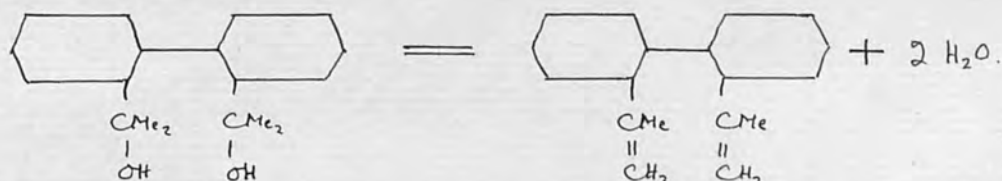
A mixture of phosphorus tribromide and pentabromide had the same effect as the tribromide alone.

Phosphorus tribromide in chloroform solution gave back the glycol.

Pure, dry hydrogen chloride gas was passed carefully over the molten glycol (150°), precautions being taken to exclude all moisture from the apparatus and to remove any water formed from the reaction mixture. The establishment of an equilibrium

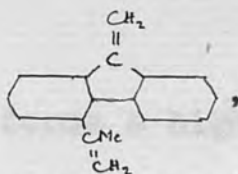


was assumed, and the gas was passed for three or four hours in an attempt to displace the equilibrium as far to the right as possible. The HCl gas was swept out by a current of nitrogen, and the product extracted with dry, boiling light petroleum, b.p. 80-100°. Concentration of the solution followed by precipitation with dry, light petroleum, b.p. 40-60°, gave prisms, m.p. 96-97° identical with those obtained by the action of phosphorus tribromide. Equation III therefore becomes:-



Corresponding experiments were carried out on the alcohol-ketone. Phosphorus tribromide reacted immediately, but the product was hydrolysed during ether-extraction, and the alcohol-ketone was recovered. Dehydration analagous

to that of the glycol would give



, but this

could hardly be expected to undergo hydrolysis with wet ether. More probably a halogen derivative was formed.

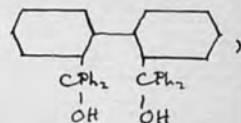
Dry hydrogen chloride gas gave a product which could only be crystallised from alcohol/conc. HCl. It then melted at 64-65°, but contained only 4% of chlorine.

3. w:w'-Tetraphenyl-2:2'-ditolyl Derivatives.

(R=C₆H₅ in Equation I)

Experiments parallel to those in the tetramethyl

series were carried out with the tetraphenyl glycol,

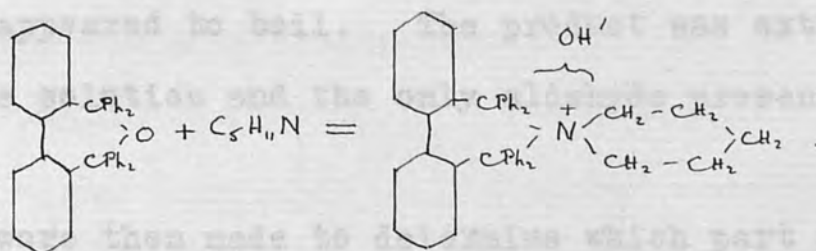


which had been prepared by Tschitschibabin and Ssergejeff (Ber., 1926, 59, 654).

Phosphorus tribromide reacted with the glycol to give a solid product, stable to ice-water. This dried as white, hygroscopic granules, which contained bromine. On attempting to obtain it in a crystalline condition, however, hydrolysis invariably occurred. For example, it dissolved sparingly in A.R. acetone, but after two minutes standing in air it dissolved readily, and removal of the solvent left the glycol. This behaviour can only be accounted for by assuming that the bromo-derivative (1) is almost completely

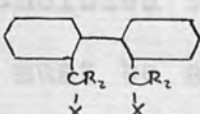
insoluble in water at 0° , and (2) forms a highly hygroscopic solution in most of the common solvents. As a side-track experiment, the crude product was refluxed with pure, dry dimethyl aniline in dry benzene solution. On cooling, no crystals separated and no solid material could be obtained from the solution.

The tetraphenyl glycol melts at 252° , so the effect of dry hydrogen chloride on the molten material was not investigated. In acetic acid solution at 170° , no reaction occurred. Its proneness to attack by phosphorus tribromide led to speculation on the possibility of the glycol reacting directly, in the form of its anhydride, with piperidine:-



After heating under pressure at 120° for six hours, however, no change was observed, 2.3 g. of glycol anhydride being recovered from 2.5 g. of starting material.

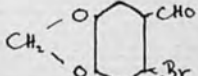
It was apparent that the isolation of halogen

derivatives of the type  required specialised technique, and time did not allow further investigation.

Experiments on 6-Bromopiperonal.

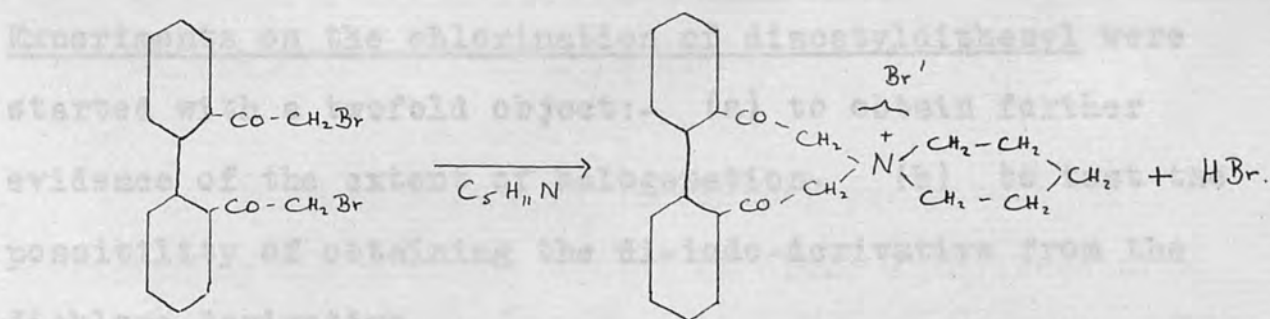
Späth and Kahover (Ber., 1924, 67, 1511) obtained 6-phenylpiperonal by the action of copper bronze on iodobenzene and 6-bromopiperonal. A corresponding process could not be traced in the action of copper bronze, in an atmosphere of carbon dioxide, on 6-bromopiperonal alone. At 220° no reaction occurred, the bromopiperonal being recovered unchanged. At 240° there was indication of some reaction, a deposit of cuprous bromide collected on the surface, and after five minutes (bath at 240°) the temperature rose rapidly to 280°, the whole mixture blackened and appeared to boil. The product was extracted with bisulphite solution and the only aldehyde present was piperonal.

Attempts were then made to determine which part of the molecule was responsible for the anomalous behaviour. Protection of the aldehyde group did not affect the result, 6-bromopiperonylideneaniline yielded, under similar conditions piperonylideneaniline. The diacetate of bromopiperonal could not be made by the usual methods, a compound having acetic acid of crystallisation being always formed. It was concluded that auto-reduction in the presence of copper bronze must be a property induced in the

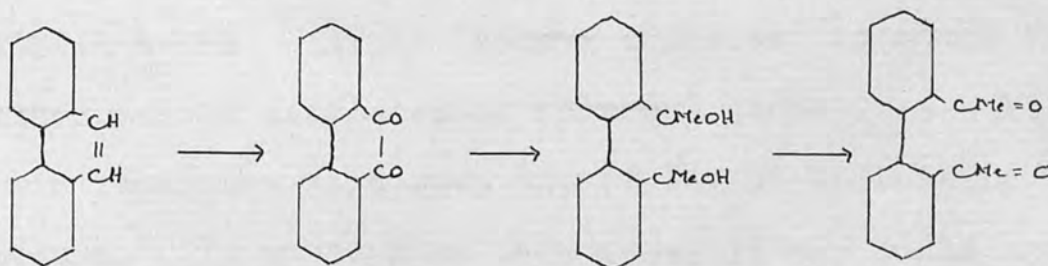
system  by the methylene oxide grouping.

It was inferred that the reaction was complicated by
 B. DIPHENYL DERIVATIVES HAVING A 9-MEMBERED SPIRO-CYCLO RING.

These are theoretically obtainable from
 w:w'-dibromo-2:2'-diacetyldiphenyl:-



It was intended (by analogy with the preparation of
 phenacyl bromide) to obtain the dibromo-derivative by the
 direct bromination of diacetyldiphenyl, which was
 conveniently prepared from phenanthrene:-



The product obtained had melting point $93-94^{\circ}$ (Zincke & Tropp
 gave melting point of diacetyldiphenyl 83° , Annalen 1908,
362, 305). The melting point of the bis-phenylhydrazone
 agreed with that given in the literature. On bromination,
 the diacetyldiphenyl gave a crystalline compound of constant
 melting point which analysis showed to have a higher bromine
 content than that required by the dibromo-derivative.

It was inferred that the reaction was complicated by "replacement" of the enol group and that several higher bromo-derivatives were probably present. (cf. Robinson, Orr & Williams, J.C.S., 1917, 909, 946).

IV. THE INFLUENCE OF TERNARY EFFECTS ON THE OPTICAL STABILITY

Experiments on the chlorination of diacetyldiphenyl were started with a twofold object:- (a) to obtain further evidence of the extent of halogenation. (b) to test the possibility of obtaining the di-iodo-derivative from the dichloro-derivative.

The product obtained was a mixture of chloro-derivatives.

general, unlinked atoms, whether in different molecules or in different parts of the same molecule, exert a more effective electrostatic repulsion upon each other than do linked atoms. If by "atomic diameter" is meant the internuclear distances of (linked) atoms in a solid compound, this repulsion will have the effect of increasing the atomic volume. It would have been ideal if one could have defined "atomic diameter" as the internuclear distance of unlinked homogeneous atoms less the minimum interatomic distance, but combined atoms were the first to be measured and the term has been applied to them. Measurements of intermolecular distances have been made in the solid state by S. B. Hendricks, (J. Amer. Soc., 1928, 48, 3027; Chem. Reviews, 1930, No. 4) and in the vapour state by Wierl (Physik. Z., 1930, 31, 368, 1026;

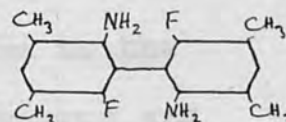
II. THE INFLUENCE OF POLAR EFFECTS ON THE OPTICAL STABILITY
OF 2:2'-DISUBSTITUTED DIPHENYLS.

The importance of electrical properties in determining the obstacle effect of ortho substituents in the diphenyl molecule has already been mentioned (p 9 above).

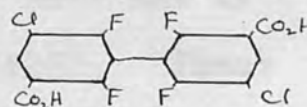
The study of other compounds has shown that, in general, unlinked atoms, whether in different molecules or in different parts of the same molecule, exert a more effective electrostatic repulsion upon each other than do linked atoms. If by "atomic diameter" is meant the internuclear distances of (linked) atoms in a solid compound, this repulsion will have the effect of increasing the atomic volume. It would have been ideal if one could have defined "atomic diameter" as the internuclear distance of unlinked homogeneous atoms less the minimum interatomic distance, but combined atoms were the first to be measured and the term has been applied to them. Measurements of intermolecular distances have been made in the solid state by S. B. Hendricks, (J.Amer.Soc., 1928, 48, 3007; Chem. Reviews, 1930, No.4) and in the vapour state by Wierl (Physik. 2., 1930, 31, 366, 1028;

Ann. Physik, 1931, 8, 521). The results, as interpreted by N. V. Sidgwick (George Fisher Baker Non-Resident Lectureship in Chemistry, Cornell University, Vol. II p.232) indicate that the increase in diameter due to electrical repulsion - the difference between internuclear distances for linked and unlinked atoms - may be of the order of 1 \AA° . This value is an average one and therefore approximate. In applying calculations to the diphenyl molecule, allowance must be made for the fact that ortho substituents are not comparable to "unlinked" atoms, being indirectly attached through a system which tends to force their approach: their effective volumes must lie somewhere between the limits set for linked and unlinked atoms. This would be in agreement with the limits set by experimental

results (e.g. the linked values indicate that



should not be resolvable, and it is (loc.cit.); the unlinked values are said to indicate that



should be resolvable, and it is not. (Kleiderer & Adams, J. Amer. Soc., 1933, 53, 4219).

Applying the results to constituent parts of the same molecule Sidgwick has cited the Thorpe-Ingold effect as evidence of interatomic repulsion. For example, the Cl-Cl distance in carbon tetrachloride, where all forces

are evenly distributed, is $2.99 \pm 0.03 \text{ \AA}$, whereas in methylene chloride it is $3.23 \pm 0.1 \text{ \AA}$. Sidgwick attributes this separation of the chlorine atoms to their mutual electrostatic repulsion. It may also be due to the greater size of the chlorine atoms: the separation certainly tends towards a more even distribution of mass about the central carbon atom. Also, there must be an equal repulsion between the unscreened positive hydrogen nuclei, but, assuming the law of inverse squares, this could not be so effective owing to the smaller size of hydrogen. It would seem then, that mass rather than polarity is the fundamental determinant in this case. In the case of diphenyl, this would mean that electrical properties are only effective on large atoms and again emphasises the fact that they must be studied for limiting types.

General evidence which is more applicable to the diphenyl molecule has been obtained by Weissberger and Sängewald (Z. physik, Chem., 1931, B 12, 399) and by Hassel and Naeshagen (ibid. 1931, B 14, 232). These authors have measured the dipole moments of hydrobenzoin and isohydrobenzoin, $\text{C}_6\text{H}_5 \cdot \text{CHOH} \cdot \text{CHOH} \cdot \text{C}_6\text{H}_5$. For completely free rotation about the C - C bond the two forms should have the same moment. The results showed a difference of 25%, and although the authors do not claim that any quantitative statement is possible, they infer that the electrical forces

do, in some degree, restrict the free rotation.

Corroborative evidence has been obtained by K. L. Wolf (Trans. Faraday Soc., 1930, 26, 315) for the diethyl esters of dextro- and meso-tartaric acids, the dipole moments of which differ by 18%. These results may be taken as evidence for believing that electrical forces do exist between different parts of the same molecule, and that they are operative when steric effects are absent.

Meyer (Z. physik. Chem., 1930, B.8, 27) has studied the results of dipole moment measurements quantitatively, and has calculated that, if the dipoles are separated by a distance which is less than twice the diameter of a linked carbon atom, then the intramolecular potential is greater than the energy of thermal agitation and rotation is

prevented. An extreme example is the carboxyl group, $-\text{C} \begin{array}{l} \text{=} \text{O} \\ \diagdown \\ \text{OH} \end{array}$, which is so polar that the hydrogen is held in the position of minimum moment up to a temperature of 20,000°.

In applying these general considerations to the diphenyl molecule there are many allowances to be made. Ortho substituents can never be of the nature to exert such a force upon each other as -OH does, for example, upon >CO. Moreover it is not only the rotation of the groups themselves which must be prevented but that of the whole diphenyl system, the moment of inertia of which must be considerable. As Senior

has pointed out in another connection (J.Amer.Soc., 1933, 50, 4704) the asymmetry of diphenyl derivatives has no connection with any pre-established set of ideas, so that while comparisons may indicate the various possibilities, no accurate conclusions can be drawn from them.

It follows then, that comparison with compounds in general suggests that electrical forces exist between approaching ortho substituents, and provides broad limits for the extent of their effect. Finer limits can be set only by resolution experiments on limiting types. Given that the electrical forces are operative, it still remains to decide whether they will act by causing deflection of the valency bonds, as suggested by Stanley & Adams, (J.Amer.Soc. 1930, 50, 1200), and so decreasing optical stability, or whether they will add to the volume of the groups and so increase the obstacle effect. Some information as to the ease of deflection of the valency bonds as compared with the degree of restricted rotation may have been forthcoming from the successful resolution of a 2:2'-spiro-cyclo derivative, and it was hoped that some correlation may have been possible.

As the effects due to polarity are small and vary with the nature of each group it is not easy to detect them experimentally. No definite conclusions can be drawn from the results of X-ray analysis of crystals of active,

as compared with inactive, diphenyls (e.g. Clark & Pickett J.Amer.Soc., 1931, 53, 167). The problem is further complicated by the fact that no clear distinction can be made between polar effects and volume effects, the effect measured, even by resolution experiments, is always the resultant of both.

It is known to be relayed across the molecule and any differences observed between the optical stability of substituted and unsubstituted antimers can be taken as the effect of the induced polarity of the ortho groups. This is a most convenient method of investigation, since, by selecting a substance which had stable but resolvable antimeric forms and synthesizing a corresponding substituted derivative, many accurate measurements can be made which offer a mass of material for direct comparison. Moreover, complications due to differences in mass or size are eliminated and electrical effects can be observed directly.

The first work in this connection was done by Euhn and Albrecht (Annalen, 455, 272; *ibid.*, 455, 321), who observed that the isomers of the para di-substituted

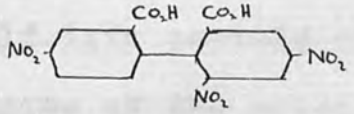
nitrodiphenic acid,  had a half-value

period nearly three times that of the meta mono-substituted

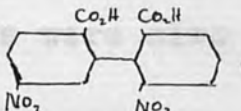
acid . The actual values were 59 mins. and

In the present work the electrical effect has been studied through the allied effect of *p*-substituents on the optical stability of antimeric forms. Polar effects are known to be relayed across the molecule and any differences observed between the optical stability of substituted and unsubstituted antimers can be taken as the effect of the induced polarity of the ortho groups. This is a most convenient method of investigation, since, by selecting a substance which has stable but racemisable antimeric forms and synthesising a corresponding substituted derivative, many accurate measurements can be made which offer a mass of material for direct comparison. Moreover, complications due to differences in mass or size are eliminated and electrical effects can be observed directly.

The first work in this connection was done by Kuhn and Albrecht (*Annalen*, 455, 272; *ibid.*, 458, 221), who observed that the isomers of the para di-substituted

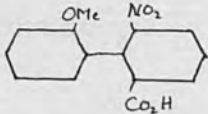
nitrodiphenic acid,  had a half-value

period nearly three times that of the meta mono-substituted

acid . The actual values were 50 mins. and

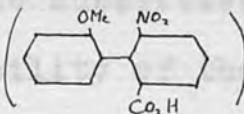
18 mins. respectively, and corresponding values for the energy of activation were 22,400 and 26,000 cal.

Kuhn attributed the effect to the difference between the masses of the two compounds, and considered the two para nitro groups as increasing the moment of inertia of the molecule and so reducing its rate of oscillation. More recent work by Adams and co-workers has shown that the effect is, however, an electrical one. Yuan and Adams (J.Amer.Soc., 1932, 54, 4434) observed, for example, that chlorine and bromine have almost the same effect on the

rate of racemisation of the compound  , when

substituted in the 5' position (para to the methoxy group).

As the masses of chlorine and bromine are sufficiently different, in comparison with the mass of a nitro group, for the effect to be measureable, the cause must lie in the similar electrical properties of the halogens. Yuan and Adams studied the effect of the series of 5'-substituents -OMe, -CH₃, -Cl, -Br, -NO₂ on the rate of racemisation

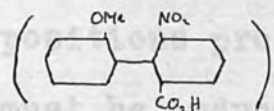
of the compound mentioned,  , and found that

the values for the half-life periods of the isomers were in the order of the polarity of the substituent groups, the most polar groups having the most stabilising effect. The values were also compared with the dipole moments of the

correspondingly substituted anisoles:- (No data are available for the dipole moments of active diphenyls and would not be significant owing to their complicated structure).

5' Substituent	Half-value Period of acid in alcohol.	Dipole moment of 5-substituted anisole.
H	10.8	1.8
CH ₃	11.5	1.2
Cl	31.0	2.24
Br	32.0	2.24
NO ₂	35.4	4.3

The comparison suggests that there is some relationship between the obstacle effect of the ortho groups and the electrical properties of the molecule. Chien and Adams (J.Amer.Soc., 1934, 56, 1787) have given support to this evidence by finding that the substituents have the same relative effect on the stability of the same compound



when substituted in the 3'-position (ortho to the methoxy group). The 3'-substituted compounds are much more optically stable than the corresponding

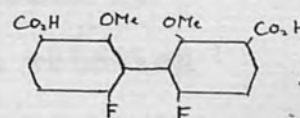
5'-substituted compounds:-

Substituent effect on Half-value Period of acid in alcohol.

examined by synthesis 3'-position. 5'-position.

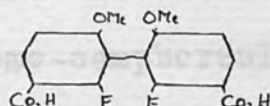
Substituent	3'-position.	5'-position.
OMe	98.1 mins.	10.8 mins.
CH ₃	331.9	11.5
Cl	771.3	31.0
Br	827.0	32.0
NO ₂	1905.2	35.4

Similarly, the 3:3'-dicarboxy derivative,



seemed to be more optically stable (its active brucine salt was isolated by Stoughton and Adams, (J.Amer.Soc. 1932, 54, 4436) than the corresponding 5:5'-dicarboxy

derivative,

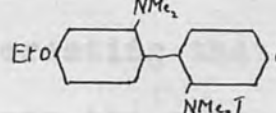
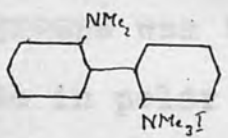


, which could not be resolved.

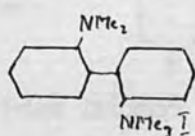
These results seem to prove conclusively that the effects observed are not due to any difference in the masses of the molecules, nor directly to the electrical character of the substituents themselves, since the same group in different positions produces different effects. Electrical effects must be induced in the ortho substituents by the molecule as a whole.

which has a half-value period of 316 mins. at 20°C. (see p. 110)

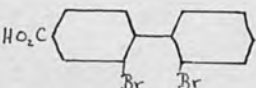
The effect of 4:4'-substituents has now been

examined by synthesising  for comparison with  resolved by Shaw & Turner (loc.cit.)

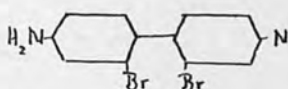
The d.dl-camphorsulphonate and the d.dl- α -bromocamphor sulphonate of the 4:4'-diethoxy derivative, have been prepared and crystallisation experiments have been carried out in two solvents, but although some heterogeneity was indicated no separation into optical antipodes could be observed. The greatest differences in specific rotation observed were between $[\alpha]_{5791}^{20} + 16.3^{\circ}$ and $[\alpha]_{5791}^{20} + 19.0^{\circ}$, (a difference of 0.12° between observed angles) for the camphorsulphonate, of which fourteen specimens were examined, and between $[\alpha]_{5791}^{20} + 52.0^{\circ}$ and $[\alpha]_{5791}^{20} + 47.8^{\circ}$ for the bromo-camphorsulphonate. This may mean that the d- and l- forms have almost identical solubilities, in both solvents, or it may mean that the isomers are optically unstable, the more soluble always being converted into the less soluble form during the process of crystallisation. The latter alternative would imply that the para ethoxy groups have a very marked effect on the optical stability

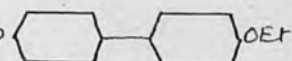
of the compound , the camphorsulphonate of which has a half-value period of 310 mins. at 90° . (see p.121)

The only other observation of the effect of para substituents on the unsubstituted molecule is that of Kuhn and Albrecht (*loc.cit.*), and it is interesting that the effect of para nitro groups was to increase the optical stability. \leftarrow OEt is opposite in polar effect to \rightarrow NO₂, and this may account for the possible instability. Searle and Adams (*J.Amer.Soc.*1934, 56, 2112) have recently shown that on the 2:2'-dibromo-diphenyl, p-substituted \rightarrow CO₂H and \leftarrow NH₂ have sufficiently different effects to decide between resolvability and

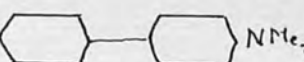
non-resolution. The compound  gave active

brucine salts which showed mutarotation, but both the camphorsulphonate and the bromocamphorsulphonate of the

compound  showed constant rotation.

The dipole moment of 4:4'-diethoxydiphenyl, 

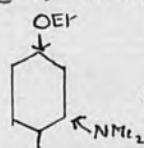
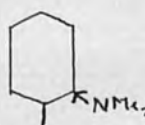
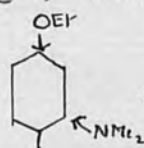
is given as 1.9, and that of 4:4'-tetramethyldiaminodiphenyl,

 as 1.25. (Williams and Weissberger,

J.Amer.Soc., 1928, 50, 2332; *Z. physik. Chem.*, 1929, B3, 367)

If the potentials of the ETO and NMe₂ can be regarded as of

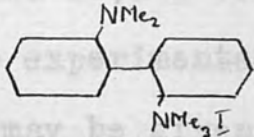
opposite sign, then

 and  would have a greater dipole than  and might be expected to be more optically

stable. (*cf.* Yuan and Adams, *loc.cit.*).

It is unfortunate that while there is no information as to the relative solubilities of antimeric forms the significance of these results cannot be assessed.

The measurements of the rates of racemisation at three temperatures, 65°, 80°, and 95°, allowed the energy of activation to be calculated. For the β -iodide, the values were 11,400 and 10,200 cal. The difference, 1,200, is the

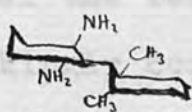
Primarily to provide material for comparison, the rate of racemisation of the unsubstituted 2:2'-disubstituted derivative,  was investigated. Measurements were made with the d.d-camphorsulphonate in five solvents at 90°, water, alcohol, acetone, acetonitrile and chloroform. Contrary to expectations no correlation was possible between the k values and the dielectric constant μ of the solvent:-

Measurements were made with the d.d-camphorsulphonate in five solvents at 90°, water, alcohol, acetone, acetonitrile and chloroform. Contrary to expectations no correlation was possible between the k values and the dielectric constant μ of the solvent:-

<u>Solvent</u>	<u>k</u>	<u>μ</u>
Water	0.0009 ₆	80.0
Alcohol	0.0010 ₁	23.5
Acetone	0.0019 ₄	21.4
Acetonitrile	0.0021 ₄	38.8
Chloroform	0.003	5.05

The order of increasing k value does seem, however, to be that of increasing solubility of the camphorsulphonate in the solvents. A theoretical basis for this would be the hypothesis that a good solvent is one in which intermolecular spaces are large, so that many dissolved molecules can be accommodated and if few are present each has freedom for its own motion.

The measurement of the rates of racemisation at three temperatures, 85°, 90°, and 95°, allowed the energy of activation to be calculated. For the d-iodide, the values were 12,900 and 10,400 cal. The difference, 2,500, is the extent of the experimental error (calculated independently), so the value may be given as 11,700 ± 1,250 cal. For the d.d-camphorsulphonate the value was 18,800 ± 1,250 cal. Sidgwick (Annual Reports, 1932) has calculated theoretically that the value for the energy of activation of a diphenyl derivative which has a moderate half-life period (about 60 mins) should be roughly 18,000 cal. Since the "activated" state of a 2:2'-disubstituted derivative may be identified as that in which the energy of thermal agitation overcomes the obstacle effect and 2:2'-substituents pass each other, it is possible to interpret the energy of activation as the energy necessary to rotate one nucleus relative to the other through an angle of 180°. The unstable intermediate compound corresponding to the "enol" form of other asymmetric molecules ("Enol" Theory) has the coplanar configuration. It would seem more probable that the valencies of the ortho carbon atoms only are deflected at the moment of racemisation, rather than that the whole molecule is deformed as, for example, in the configuration of the inactive di-hexamethylene

derivative,  , prepared by Meisenheimer and Höring, (Ber., 1927, 60, 1425). The fact that 2:2':-6'-trisubstituted

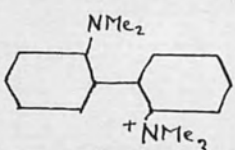
diphenyls are more readily racemised than the corresponding 2:2' -:6:6'-tetrasubstituted ones lends support to this, since the bending of only two, as against four, valencies would be involved.

The fact that Shaw and Turner (loc.cit.) obtained different values for the rates of racemisation of the d.d-camphorsulphonate and the d-iodide suggested that there was some effect due to electrostriction. The d-benzenesulphonate has now been prepared and its rate of racemisation compared with those of the d-iodide and the d.d-camphorsulphonate in dilute aqueous solutions of equimolecular concentrations:-

<u>Salt</u>	<u>k</u>	<u>Half-value period.</u>
benzenesulphonate	0.0014 ₂	210 mins.
iodide	0.0011 ₉	250 "
<u>d</u> -camphorsulphonate	0.0009 ₆	310 "

It is interesting that the loss of activity of the camphor molecule does not obliterate the relative obstacle effect of the camphorsulphonate group. There does not seem to be any correspondance between the values for the benzenesulphonate and the d-camphorsulphonate which would indicate a common effect due to the sulphonate type of linkage. The instability of the benzenesulphonate, as compared with the iodide, strikingly confirms what would have been taken for granted, that dynamic effects (cf. Lesslie and Turner,

J.C.S., 1932, 2021) are not operative in the ionic state; the fact that the values for the iodide and the benzenesulphonate are different, however, suggests that the

ion  does not exist as an entirely independent

entity. There must be some electrostriction which would have to be explained in terms of electronics. This can hardly be regarded as the direct influence of polarity on the obstacle effect of the NMe_3 group, but the two phenomena may be the results of the operation of the same mechanism of electronic displacements.

It is evident that a completely satisfactory interpretation of the polar effects of ortho substituents in the diphenyl molecule is still remote. Any attempt to correlate polar properties with obstacle effect would be premature, and contemporary work must therefore take the form of an interim report.

INDEX TO EXPERIMENTS

I	Hetero-Spiro-Cycle Derivatives of Bicyclopentane	85 - 87
	A. 7-membered Ring Compounds	85 - 86
	1. <i>o,o'</i> -Ditolyl Derivatives: Attempted Synthesis of <i>o,o'</i> -Dibromo- <i>o,o'</i> -ditolyl	85 - 87
	2. <i>o,o'</i> -Tetraethyl- <i>o,o'</i> -ditolyl Derivatives	88 - 89
	3. <i>o,o'</i> -Tetraethyl- <i>o,o'</i> -ditolyl Derivatives	89 - 91
	Experiments on 6-Propylpiperonal	91 - 92
B	E X P E R I M E N T A L .	
	<u>Attempted synthesis of <i>o,o'</i>-dibromo-<i>o,o'</i>-ditolyl</u>	95 - 96
C	1-Ethoxy-2-(<i>o,o'</i> -diethylamino-4'-ethoxy-phenyl)ethane hydrochloride iodide	100 - 102
	1. Synthesis	100 - 102
	2. Measurements of Optical Properties	102 - 103
D	1-Ethoxy-2-(<i>o,o'</i> -diphenylamino-4'-ethoxy-phenyl)ethane hydrochloride iodide	111 - 119
	1. Synthesis	111 - 112
	2. Measurements of Optical Properties	112 - 119
	Solvent Effect	115 - 116
	Temperature Effect	117 - 118
	Ion Effect	118 - 120
	Tables	121 - 122

I N D E X T O E X P E R I M E N T S .

I HETERO-SPIRO-CYCLO DERIVATIVES OF DIPHENYL.

<u>I</u>	Hetero-Spiro-Cyclo Derivatives of Diphenyl	65 - 99
	A. 7-membered Ring Compounds	65 - 96
	1. 2:2'-Ditolyl Derivatives: Attempted Syntheses of 4:4'-Dibromo-2:2'-ditolyl.	65 - 77
	2. w:w'-Tetramethyl-2:2'-ditolyl Derivatives	78 - 88
	3. w:w'-Tetraphenyl-2:2'-ditolyl Derivatives	89 - 91
	Experiments on 6-Bromopiperonal	92 - 96
	B. 9-membered Ring Compounds	
	Attempted syntheses of w:w'-dibromo- 2:2'-diacetyldiphenyl	97 - 99
<u>II</u>	5-Ethoxy-2-(2'-bisdimethylamino-4'-ethoxy-phenyl) phenyltrimethylammonium iodide.	100 - 110
	1. Synthesis	100 - 103
	2. Experiments on Optical Properties	104 - 110
	2-(2'-Bisdimethylaminophenyl) phenyltrimethylammonium iodide	111 - 129
	1. Synthesis	111 - 112
	2. Rates of Racemisation	113 - 129
	Solvent Effect	115 - 116
	Temperature Effect	117 - 119
	Ion Effect	119 - 120
	Tables	121 - 129

(2) Preparation of *o*-nitrobenzyl phenyl ether.

Thiele & Dimroth (Annalen 1885, 305, 113)

I HETERO-SPIRO-CYCLO DERIVATIVES OF DIPHENYL.

A. 7 MEMBERED-SPIRO RING COMPOUNDS.

1. 2:2'-Ditolyl Derivatives:

Attempted Syntheses of w:w'-Dibromo-2:2'-ditolyl

I From *o*-nitrobenzyl phenyl ether.

(1) Preparation of *o*-nitrobenzyl phenyl ether.

The following modification of the method of Thiele & Dimroth (Annalen 1885, 305, 113) was used.

A solution of potassium phenoxide in phenol was prepared by heating 28 g. of caustic potash ($1\frac{1}{2}$ mols) with five drops of water in a Pyrex flask until the liquid was clear, cooling to the point of crystallisation, and adding 94 g. of phenol (3 mols) in small portions, with shaking and occasional warming to keep the melt clear. This was cooled to 100° and treated with 57 g. (1 mol) of *o*-nitrobenzyl chloride. After heating under reflux for 1 hour on the water bath, the product was shaken free from phenol with excess caustic soda and the precipitated ether filtered off. Crystallisation from alcohol gave colourless prisms, m.p. $62-63^{\circ}$. Yield 42 g. (55%).

(2) Preparation of *o*-aminobenzyl phenyl ether.

Thiele & Dimroth (Annalen 1885, 305, 114) used stannous chloride and hydrochloric acid for the reduction of *o*-nitrobenzyl phenyl ether. In the present series of experiments reduction with iron, water and a trace of acid gave good results.

A thin paste of 50 g. of iron filings and water was heated on the water bath for 10 minutes, and a few cc. of glacial acetic acid were added. Whilst the mixture was still frothing, 50 g. of *o*-nitrobenzyl phenyl ether were added and the mixture stirred and kept as hot as possible for half an hour, boiling water being added from time to time to keep the paste thin. The base was extracted with boiling alcohol, the solution filtered from iron, and the solvent removed by evaporation under reduced pressure. The residue was freed from nitro-compound by dissolving in dilute hydro chloric acid filtering and precipitating slowly with ammonia. The base crystallised from alcohol in colourless prisms, m.p. 81-82°. Yield 40 g. (91%).

(3) Action of Potassium Iodide on *o*-Aminobenzyl phenyl ether diazonium salts.

o-Aminobenzyl phenyl ether (20 g.) was heated with 25 cc. of concentrated hydrochloric acid and 40 cc. of water until dissolved. The solution was rapidly cooled,

with stirring, to 0° , and the resulting paste treated with 7 g. of sodium nitrite, ice being added as required. The diazo solution was filtered, freed from nitrous acid with urea, and poured slowly into a solution of 32 g. of potassium iodide and 50 g. of sodium acetate in 70 cc. of water at 40° . A red-brown precipitate appeared, which on heating evolved nitrogen and formed a brownish tar-like mass. On extracting with ether, iodine only dissolved out and the residue had a high melting point (above 200°).

The method was modified:-

- (a) base diazotised in concentrated sulphuric acid
- (b) the diazo solution poured into potassium iodide solution alone.

In each case a similar result was obtained.

On attempting to neutralise the diazo solution with sodium bicarbonate the same precipitate was formed.

Experiments in the p-nitrobenzyl phenyl ether series.

(i) p-Nitrobenzyl chloride was prepared by the method given in the literature. The product was separated from the o-compound by pouring on to ice and filtering, When most of the o-compound filtered through as liquid o-p- mixture.

After melting under successive quantities of boiling water the solid portion was crystallised from alcohol, in which the o-compound is much the more soluble.

Yield 30% (Calculated on total o-p-mixture.)

(ii) p-Nitrobenzyl phenyl ether was prepared from p-nitrobenzyl chloride and potassium phenoxide by the method described for the o-compound ((1) above). m.p. 90-91°.

Yield 25 g. (85%)

(iii) Action of reducing agents on p-nitrobenzyl phenyl ether

(a) Fe and HCl

40 g. of p-nitrobenzyl phenyl ether were dissolved in 70 cc. of alcohol under reflux, 50 cc. of concentrated Hydrochloric acid in 20 cc. of water were added and then 20 g. of iron filings in small quantities, with vigorous shaking. The mixture was heated on the water bath for 2½ hours, and while still warm .880 ammonia was added, drop by drop, till alkaline and the iron filtered off. On evaporating the filtrate, a negligible residue was obtained, which rapidly turned dark in the air and dissolved very readily in dilute hydrochloric acid.

(b) Iron and water.

20 g. of p-nitrobenzyl phenyl ether were added to a hot

paste of 20 g. of iron filings and water with 2 cc. of glacial acetic acid. After stirring for 30 minutes, hot acetone was added, the iron filtered off, and the solution evaporated under reduced pressure until 10 cc. remained. This was treated with dry ether, when a brownish precipitate separated, which had a high melting point and was insoluble in alcohol. After boiling the precipitate with dilute sulphuric acid, and adding excess caustic soda and iodine, a white precipitate appeared and the odour of iodoform was easily detected. The white precipitate was insoluble in organic solvents.

II. From o-Nitrobenzyl benzoate.

(1) Preparation of o-nitrobenzyl benzoate.

50 g. of o-nitrobenzyl chloride were refluxed with 85 g. of sodium benzoate in 100 cc. of water for 8-10 hours at 120° . On cooling, the ester separated, was filtered off and crystallised from aqueous alcohol.

m.p. 93° .

Yield 65 g. (88%)

(2) Preparation of o-aminobenzyl benzoate.

The method described in the literature (reduction with Zinc and Hydrochloric acid - Paal & Bodewig, Ber., 1892,

25, 2963) was first used and did not give satisfactory results. Stannous chloride and hydrochloric acid was found to give a more efficient reducing medium.

10 g. of o-nitrobenzyl benzoate were shaken with 10 cc. of acetic acid in a round flask and 27 g. of stannous chloride added, and then 30 cc. of concentrated hydrochloric acid slowly. The reaction was initiated by heating on the water bath and was complete after 20 minutes. Excess of 40% caustic soda was added with cooling. When the precipitated tin hydroxide had redissolved the precipitated base was filtered off, dissolved in dilute hydrochloric acid, filtered and the hydrochloride precipitated with concentrated hydrochloric acid. Crude yield 5 g. (72%) m.p. of hydrochloride 143° .

(3) Action of Potassium iodide on o-Aminobenzyl Benzoate Diazonium salts.

10 g. of o-aminobenzyl benzoate were dissolved in 10 cc. of concentrated hydrochloric acid and the solution cooled rapidly to 0° , 1.5 g. of sodium nitrite were added, with ice as required. The diazo solution was filtered, treated with urea, and poured into a solution of 8 g. of potassium iodide and 30 g. of sodium acetate in 50 cc. of water at $35-40^{\circ}$. A red-brown precipitate was formed, which

was insoluble in ether and chloroform. The same compound was produced when the diazo solution was neutralised with sodium bicarbonate.

III. From o-Nitrobenzyl alcohol.

(1) Preparation of o-nitrobenzyl alcohol.

The following modification of the method of Paal and Bodewig (Ber., 1892, 25, 2963) gave satisfactory results.

40 g. of o-nitrobenzyl benzoate were shaken with 100 g. of alcoholic potash at 60-70°. The solution was diluted with water and the alcohol extracted with ether. The ethereal solution was dried over potassium carbonate and animal charcoal (to decolourise), filtered, and the ether removed by evaporation.

Yield 17 g. m.p. 70-71°.

(2) Preparation of o-aminobenzyl alcohol.

Various workers - Friedlander & Henriques (Ber. 1882, 15, 2109), Reissert & Cramer (Ber., 1928, 61B, 2555), Gabriel & Posner (Ber., 1894, 27, 3512), Paal & Laudenheim (Ber., 1892, 25, 2968) and Auwers (Ber., 1904, 37, 2260) have experienced difficulty in finding a suitable agent for the reduction of o-nitrobenzyl alcohol. The method of Friedlander & Henriques (loc.cit) was found

satisfactory and gave o-aminobenzyl alcohol in 60% yield.

(3) Preparation of o-iodobenzyl alcohol.

Olivier (Rec. trav. chim. 1923, 516) obtained this compound in small quantities by the hydrolysis of o-iodobenzyl chloride.

9 g. of o-aminobenzyl alcohol were diazotised with 19 cc. of concentrated hydrochloric acid in 10 cc. of water, and 4.5 g. of sodium nitrite at 0°. The solution was filtered, treated with urea and added to 24 g. of potassium iodide in 25 cc. of water. (Presence of sodium acetate caused precipitation of only coloured diazo compound).

A brown granular substance separated, which was extracted with ether, the extract washed with caustic soda till colourless, and dried over potassium carbonate. The ether was evaporated and the residue left in vacuo over concentrated sulphuric acid for 24 hours. Small brownish crystals were obtained, m.p. 86-89°.

Yield (crude) 4 g. (22%)

IV. From o-iodotoluene

(1) Preparation of 2:2'-ditolyl.

(a) Ullmann method.

100 g. of o-iodotoluene were heated to boiling point (204°) in a large boiling tube in a metal bath at 240°.

100 g. of pure copper bronze were stirred in gradually, and the mixture allowed to superheat for 30 minutes. 70 cc. of monochlorbenzene were added and the mixture extracted at the boiling point. The solution was filtered free from copper and cuprous iodide and distilled in a flask fitted with a fractionating column. The chlorbenzene distilled off at 132-140°, unused *o*-iodotoluene (70 g.) at 220°. The residue was distilled under reduced pressure, using Bennett fractionating apparatus, and a small quantity of 2:2'-ditolyl came over as a faintly yellow oil at 140-145° at 20 mm. On cooling in a freezing mixture, the oil deposited small prismatic crystals. Yield 3 g. (7%. 25% allowed for iodotoluene recovered.)

(b) Grignard method.

The Grignard reagent $\text{C}_6\text{H}_5\text{MgI}$ was treated with

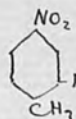
(1) Chromic chloride and (2) Cupric chloride according to the methods described by Bennett & Turner (J.C.S. 1914, 105, 1057), Turner & Krizewsky, (J.C.S. 1919, 559), and Turner (J. Royal Soc., N.S. Wales, 1920).

The dilute Hydrochloric acid - ether mixture tended to emulsify badly (owing to presence of by-products) and only small amounts of ditolyl (8-9%) were obtained from the ethereal layer.

V. From 2-Amino-4-nitrotoluene.

(1) Preparation of 2-iodo-4-nitrotoluene.

Willgerodt & Kok (Ber., 1908, 41, 2077) and Reverdin & Kacor (Ber., 1897, 30, 3000) obtained this iodo compound successfully by adding the diazotised base,



, to potassium iodide solution.

In the present series of experiments, 38 g. (1 mol) of finely powdered 2-amino-4-nitrotoluene were heated with 100 cc. of concentrated hydrochloric acid (4 mols) and 50 cc. of water for 1 hour on the water bath. Diazotisation was carried out between -5° and 0° , and the undissolved hydrochloride recovered by filtering the diazo solution was ground up and treated with dilute hydrochloric acid and more sodium nitrite at -5° . On adding potassium iodide the diazo compound separated as pale brownish yellow granules. It was purified by washing with strong caustic soda, drying and distilling at reduced pressure. Boiling point $170-171^{\circ}$, at 18 mm. m.p. 51° .

Yield 40 g. (60%)

(2) Preparation of 2:2'-dimethyl-5:5'-dinitrodiphenyl.

This compound had previously been obtained by the Ullmann diazo method (Ber., 1905, 38, 728). The following (Ullmann copper bronze) method was found more convenient.

35 g. of 2-iodo-4-nitro-toluene were heated to 205° in a boiling tube in a metal bath at 230-240°. 5 g. of pure copper bronze were stirred in and heating continued gently. At 210° reaction set in, indicated by rapid rise of temperature to 214° and deposit of cuprous iodide on the surface. Further 30 g. of copper bronze were added in small portions at such a rate that the temperature was kept between 210° and 225°. At the end of the addition the mixture was heated for a further 20 minutes at 225-230°, and then extracted with 70 cc. of monochlorobenzene at the boiling point. The solution was filtered off from copper and cuprous iodide and most of the solvent distilled off. The residue was left to cool when crystals of dinitrodiphenyl separated, which were collected, washed first with a little chlorobenzene and then with petroleum ether (b.p. 60-80°.) The chlorobenzene residue left to evaporate spontaneously deposited another crop of crystals. After recrystallisation from glacial acetic acid the 2:2'-dimethyl-5:5'-dinitrodiphenyl had m.p. 178-179°. Yield 10 g. (54%)

(3) Preparation of 2:2'-dimethyl-5:5'-diaminodiphenyl.

(a) Using stannous chloride in hydrochloric acid.

27 g. (1 mol) of 2:2'-dimethyl-5:5'-dinitrodiphenyl were warmed with 20 cc. of glacial acetic acid and 15 cc. of

water in a round flask. 114 g. (6 mols) of stannous chloride and 120 cc. (12 mols) of hydrochloric acid were added and the mixture shaken at 30-40°. When the reaction became vigorous the flask was cooled under the tap. After 20 minutes reaction had ceased, the liquid was filtered free from unused nitro compound (4 g.) and the filtrate basified with 150 g. (36 mols) of caustic soda. The precipitated amino compound was extracted with ether. After removing the ether there was a brown sticky residue which could not be made to crystallise. With benzaldehyde and salicylaldehyde it formed crystalline benzilidine and salicidine derivatives, and the conclusion was drawn that it was a mixture of the monoamino-mononitro- and the diamino-compounds. It was distilled under reduced pressure and the main fraction, boiling 240-241° at 22 mm., was collected separately. After crystallising from benzene / petroleum ether (b.p. 60-80°) this fraction had melting point 95-96°. Yield 9 g. (50%)

(b) Using iron and water.

20 g. of 2:2'-dimethyl-5:5'-dinitrodiphenyl were added to a hot paste of 30 g. of iron and water with 2 cc. of glacial acetic acid and stirred for 40 minutes. When reaction had ceased the base was extracted with boiling alcohol and the solution filtered free from iron. Two

thirds of the alcohol were removed by evaporation at reduced pressure and the residue left to cool. Small yellow crystals separated, which after recrystallisation from benzene / petroleum ether had melting point 96-97°. The alcoholic mother liquor was evaporated and the same sticky residue obtained as in (a). It was vacuum distilled and gave the main fraction boiling at 240-241° at 22 mm. This crystallised from alcohol in colourless rhombohedra. m.p. 96-97°.

Yield 7 g. (52%)

Analysis.

Substance 0.2011 g.

After combustion, volume of nitrogen 23.8 cc.

temp. 24°, pressure 763 mm.

Found 13.2% N.

$C_{14}H_{16}N_2$ requires 13.2% N.

The Grignard reagent was prepared by adding 40 g. (8 mols) methyl iodide to 10 g. (12 atoms) of magnesium in 100 cc. of dry ether. The decanted solution was cooled in ice-water and 9 g. (1 mol) of acid chloride added slowly in 1 g. portions. When the reaction had subsided the mixture was refluxed for 2-3 hours on the water bath. The complex was decomposed with a mixture of 50 cc. of water and 15 cc. of glacial acetic acid, added drop by drop. cautiously at first, the flask being cooled in a freezing

2. w:w'-Tetramethyl-2:2'-ditolyl Derivatives.

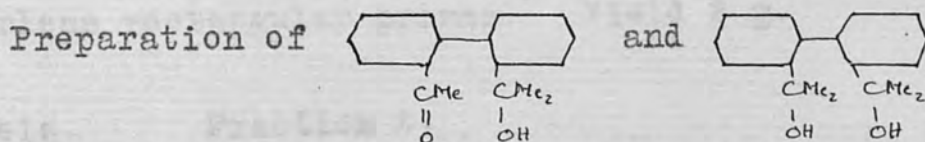
(1) Diphenic acid

was prepared by the Turner modification of the Vorländer method (Annalen 1901, 302, 136).

(2) The acid chloride

was prepared by the action of thionyl chloride on diphenic acid, according to the method described by Bell & Robinson (J.C.S. 1927, 1695).

(3) Action of CH_3MgI on dichloride of diphenic acid.



The Grignard reagent was prepared by adding 40 g. (8 mols) methyl iodide to 10 g. (12 atoms) of magnesium in 100 cc. of dry ether. The decanted solution was cooled in ice-water and 9 g. (1 mol) of acid chloride added slowly in 1 g. portions. When the reaction had subsided the mixture was refluxed for 2-3 hours on the water bath. The complex was decomposed with a mixture of 60 cc. of water and 16 cc. of glacial acetic acid, added drop by drop, cautiously at first, the flask being cooled in a freezing

mixture.

The ethereal layer was washed with water, with dilute caustic soda solution, and again with water, and then dried over anhydrous potassium carbonate. Removal of the solvent gave a yellowish semi-crystalline residue (8 g.) very soluble in alcohol, acetone, benzene, chloroform and glacial acetic acid, fairly soluble in xylene. It was crystallised from light petroleum (b.p. 80-100°) and separated into two fractions, A and B.

Isolation of the Glycol. After fractional crystallisation from light petroleum (b.p. 60-80°) the more soluble fraction, A, had m.p. 138-139°, (successive fractions melted at about 114°, 122°, 129°, 135°, 138°, 138°), and crystallised in colourless rectangular prisms. Yield 2 g.

Analysis. Fraction A.

Found:- (1) C, 80.0 ; H, 8.0%.

(2) C, 79.6 ; H, 7.9%.

C₁₈H₂₂O₂ requires C, 79.95 ; H, 8.20%.

Isolation of the alcohol-ketone. The less soluble residue, B, had m.p. 164-165° (successive values 145°, 158°, 162°, 164°), and crystallised from acetone/P.E. (b.p. 60-80°) in colourless needles. Yield 2 g.

Analysis. Fraction B.

Found:- (1) C, 80.1 ; H, 6.9%
(2) C, 80.0 ; H, 6.8%
 $C_{17}H_{18}O_2$ requires C, 80.27 ; H, 7.13%

Prolonged heating under reflux or addition of benzene to the Grignard complex had the effect of slightly increasing the yield of glycol, but never more than 2.5 g. was obtained. Repeated extraction of the water layer with ether did not materially increase the yield, for although the ethereal layer developed a yellowish colour almost inexhaustibly it was discharged during the caustic-soda washing, and on removal of the solvent 0.2 g of a glue-like residue was obtained.

(2') Esterification of alcohol-ketone.

2.5 g. (1 mol) of the alcohol-ketone were dissolved in 10 cc. of pure, dry pyridine and the solution cooled in ice. 1.2 cc. (1 mol) of benzoyl chloride were added slowly, and the mixture left in a corked flask overnight. A deep red colour developed and a precipitate of pyridine hydrochloride accumulated. Cold, dilute sulphuric acid was added, and then ether. There was immediate hydrolysis, and 2 g. of alcohol ketone were extracted.

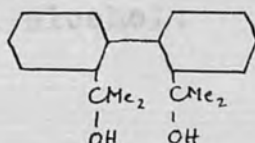
The same quantities of alcohol-ketone and benzoyl chloride were then dissolved in 20 cc. of benzene and 0.7 g.

(1)mol) of pyridine added. After several hours the precipitate of pyridine hydrochloride was filtered off, and the filtrate evaporated in vacuo. The residue was left overnight in a vacuum dessicator, and colourless prisms separated. These had a strong ester-like odour, and were extremely deliquescent, becoming liquid within two minutes of removal from the dessicator.

(3') Phenyl hydrazine in boiling acetic acid solution had no effect on the alcohol-ketone. A solution was formed but on diluting with water the starting material was recovered unchanged.

(4) Action of CH_3MgI on diacetyldiphenyl.

Preparation of



12 g. (1 mol) of diacetyldiphenyl were added slowly in 2 g. portions to the cooled Grignard reagent obtained from 8 g. (8 atoms) of magnesium and 28 g. (4 mols) of methyl iodide in 80 cc. of dry ether. The mixture was heated gently for 3 hours under reflux, and then decomposed with a mixture of 12 cc. of glacial acetic acid and 50 cc. of water, added cautiously at first while cooling the flask in ice-water. The ethereal layer was washed with dilute caustic soda solution and then with water, dried over anhydrous potassium carbonate, and the solvent allowed to

evaporate spontaneously. 10 g. of almost pure glycol separated as large, stout, rhombohedral prisms. These crystallised from light petroleum (b.p. 80-100°) as rectangular prisms m.p. 138-139°.

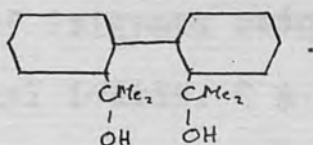
Yield 8 g. 60%.

(5) Dimethyl diphenate was prepared by refluxing 20 g. of diphenic acid with 120 g. of absolute methyl alcohol and 10 g. of conc. sulphuric acid for 3 hours. The product was poured into strong brine (200 g. of salt in 1 litre of water) and extracted with ether. After being washed with dilute sodium carbonate solution, and dried over calcium chloride, the ether was evaporated and the residue crystallised from methyl alcohol.

Yield 21 g. 92%.

(6) Action of CH_3MgI on dimethyl diphenate.

Preparation of



9 g. (1 mol) of dimethyl diphenate were added in three portions to the Grignard reagent obtained from 50 g. (10 mols) of methyl iodide and 10 g. (12 atoms) of magnesium in 100 cc. of dry ether, and the product refluxed for 3 hours. The complex was decomposed with a solution of 16 cc. of glacial acetic acid in 60 cc. of water, added

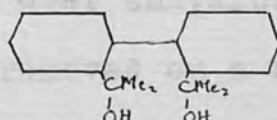
carefully at first with cooling. The ethereal layer was washed three times with dilute caustic soda solution and once with water, dried over anhydrous potassium carbonate, and the ether evaporated. The crystalline residue was crystallised from light petroleum (b.p. 80-100°) and had m.p. 138-139°.

Yield 4 g. 45%.

The alkaline washings were acidified and gave 3 g. of precipitate, probably an acid or lactone, which melted roughly at 150°. Addition of 50 cc. of pure, dry benzene to the refluxing mixture did not affect the yield.

(7) Action of CH_3MgI on the alcohol-ketone.

Preparation of



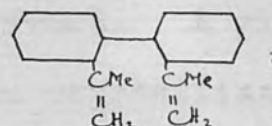
5 g. (1 mol) of alcohol-ketone were added in

3 portions to excess of Grignard reagent prepared from 10 g. (4 mols) of methyl iodide, 2 g. (4 atoms) of magnesium in 50 cc. of dry ether, and the product refluxed for 6 hours. It was decomposed with a solution of 10 cc. of glacial acetic acid in 40 cc. of water. The evolution of large quantities of gas indicated that much of the Grignard reagent had not been used. The ethereal layer was separated, washed with water and dried over anhydrous potassium carbonate and the ether evaporated. Fractional

crystallisation of the residue from petroleum ether (b.p. 60-80°) gave a final crop of pure glycol m.p. 138-139°. Yield 1 g. (10%)

(8) Action of phosphorus tribromide on the glycol.

Preparation of the hydrocarbon



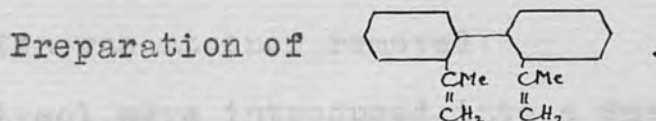
1 g. of the glycol was covered with 5 cc. of phosphorus tribromide in a small, dry flask fitted with a calcium chloride drying tube. A brown-red solution formed, with heat evolution. This was kept warm on the water-bath for 15 mins. and then poured carefully onto ice. When most of the ice had melted the product was extracted with ether, the extract dried over anhydrous potassium carbonate and the solvent rapidly removed on a boiling water-bath (10 mins.) The residue was cooled and readily solidified to a white, opaque mass, which crystallised from light petroleum (b.p. 40-60°) as colourless prisms, m.p. 97-98°. Yield 0.7 g. (87%)

Analysis.

Found:-	C, 92.1(5);	H, 7.8%
C ₁₈ H ₁₈ requires	C, 92.22	; H, 7.74%

Influence of a solvent.

5 cc. of phosphorus tribromide in boiling chloroform solution were treated with 1 g. of the glycol. A homogeneous solution was formed and after 10 mins. on the water-bath this was carefully washed with ice-water, then dried over K_2CO_3 and the chloroform evaporated. A glue-like residue was obtained which, after one crystallisation from petroleum ether (b.p. $60-80^\circ$) had m.p. $138-139^\circ$ and was identified as the glycol.

(9) Action of PBr_3 - PBr_5 mixture on the glycol.

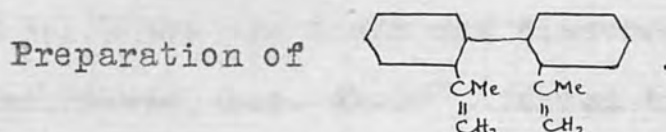
5 g. of phosphorus pentabromide were dissolved in 5 g. of phosphorus tribromide at 100° , and 1 g. of glycol added. After standing on the water-bath for 20 mins. the solution was carefully poured onto ice and the product ether-extracted. Removal of the solvent gave 0.8 g. of residue which crystallised from light petroleum (b.p. $40-60^\circ$) as colourless prisms, m.p. $97-98^\circ$.

(10) Action of phosphorus tribromide on the alcohol-ketone.

1 g. of alcohol ketone was added to 5 cc. of phosphorus tribromide in a small, dry flask fitted with a calcium chloride tube. On warming the flask gently on the water bath a vigorous reaction set in. After 25 mins. the

solution was cooled and poured, very slowly, onto ice. A thick colourless oil settled to the bottom. On adding ether there was immediate hydrolysis, the whole mixture surged and boiled vigorously. After some time, more ether was added and 0.7 g. of alcohol-ketone were recovered.

(11) Action of dry HCl-gas on the glycol.



This reaction was carried out under conditions of special precaution to ensure that all moisture was excluded from the apparatus and that any water formed during the reaction was at once removed.

4 g. of glycol were introduced into a small bolt-head flask, fitted with an inlet tube from an HCl generator and an exit tube leading through two CaCl₂-packed U-tubes to the atmosphere. The flask, tubing, corks and U-tubes had all been dried in an air oven at 120°. The gas was generated by dropping conc. sulphuric acid into conc. hydrochloric acid, and was dried by bubbling through two Drechsel bottles containing conc. sulphuric acid. The exit tube was heavily lagged with cotton wool and asbestos paper, and any water produced by the reaction was collected in two bulbs on the first calcium chloride tube.

The flask was immersed in a bath of paraffin oil and heated to 150° for half an hour. HCl-gas was then passed in

at the rate of one bubble per second (from 0.5 cm tubing). After five minutes water was condensing in the exit tube, and later in the bulb-trap, and soon began to carry with it a volatile product. The temperature was therefore lowered to 120° after 15 minutes, and maintained for a further 50 mins. The HCl was then replaced by a current of nitrogen and the flask allowed to cool.

After several hours the flask was disconnected and 50 cc. of light petroleum, b.p. $60-80^{\circ}$, (dried by refluxing over calcium chloride) were poured onto the product. The solution was transferred to a dry dish and left to evaporate overnight in a desiccator. A semi-crystalline residue was obtained, which was washed with a little alcohol and then crystallised from light petroleum b.p. $40-60^{\circ}$. Colourless prisms m.p. $97-98^{\circ}$.

Analysis.

Found:- C, 92.1(5) ; H, 7.8%.

$C_{18}H_{18}$ requires C, 92.22 ; H, 7.74%.

(12) Action of dry HCl-gas on the alcohol-ketone.

The method was as in the previous experiment. The reaction was started at 170° and completed at 120° . The product was extracted with light petroleum (b.p. $60-80^{\circ}$) but as no crystals could be obtained from this solution the solvent was evaporated, the residue taken up in absolute

alcohol and precipitated with conc. HCl.

Colourless needles separated, which were shown to contain chlorine and melted at 65-66°. Further crystallisation from the same solvent did not change the m.p. although analysis showed that the substance was not a definite compound.

Analysis.

Wt. of substance taken = 0.1266 g.

Wt. of AgCl = 0.0210 g.

Whence Cl = 4.1%.

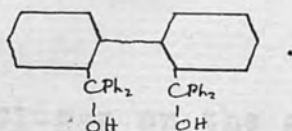
$C_{17}H_{17}OCl$ requires 13.1% Cl.

(3) Action of dimethylsulphide in benzene solution.

A small portion of the crude product in benzene solution was boiled under reflux with a few drops of

3. w:w'-Tetraphenyl-2:2'-ditolyl Derivatives.

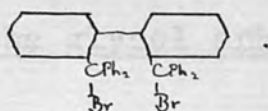
(1) Preparation of

(4) Effect of dry HCl on the glycol.

The method used was that of Tschitschibabin and Ssergejeff. (Ber., 1926, 59, 654).

(2) Action of phosphorus tribromide on the glycol.

(5) Preparation of



5 g. of the glycol was added to 15 g. of phosphorus tribromide under reflux, and the mixture heated gently on the water bath until all had dissolved (10 mins.) The solution was poured carefully onto ice, the white granular precipitate filtered off, washed with ice-water and immediately dried in vacuo.

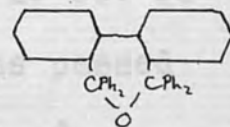
(If the reaction mixture was poured quickly onto ice, vigorous hydrolysis occurred and the glycol was formed.) This crude product was highly hygroscopic. It was shown to contain bromine, and melted at 105° with apparent evolution of HBr. It could not be obtained in a purer condition, all attempts to crystallise it yielded the glycol.

(3) Action of dimethylaniline in benzene solution.

A small portion of the crude product in benzene solution was boiled under reflux with a few drops of dimethylaniline. On cooling, no crystals separated and the bromine compound was unchanged.

(4) Effect of dry HCl-gas on the glycol.

A current of dry HCl gas was passed over 2 g. of the glycol in a flask heated in a paraffin bath. The temperature was raised to 200°, but no change occurred.

(5) Preparation of the glycol anhydride,

The method of Tschitschibabin and Ssergejeff was used (Ber., 1926, 59, 654).

(6) Action of piperidine on the anhydride.

2.5 g. of anhydride and 2 cc. of pure, anhydrous piperidine were heated in a sealed tube on the water bath for 6 hours, and then in a paraffin bath at 120° for a further 2 hours. The product was digested and well washed with alcohol and then left to stand for three days in a vacuum desiccator. It then weighed 2.3 g. and had m.p. 290° and was recognised as unchanged anhydride. The alcohol washings were evaporated and left no residue.

(7) Action of aniline on the anhydride.

5 cc. of pure, redistilled aniline were boiled under reflux with 0.5 g. of anhydride for 5 hours. The solution darkened considerably. Steam was then passed through until all the aniline had been removed (1 hour) and the residue extracted with ether. Removal of the solvent gave 0.2 g. of a dark red-brown residue. This was carefully washed with a little acetone and 0.15 g. of anhydride were recovered.

(8) Action of dry HCl gas on anhydride.

0.5 g. of anhydride were dissolved in 10 cc. of glacial acetic acid at 100° and dry HCl gas was passed in for 2 hours. No change occurred. 0.4 g. of anhydride were recovered.

Yield 27 g. 40%.

Action of copper bronze on 6-bromopiperonal.

50 g. of 6-bromopiperonal were heated with 10 g. of Julex copper bronze in an atmosphere of SO₂ in a boiling tube in a metal bath. The delivery tube from the Kipp's apparatus served conveniently as a stirrer. No reaction occurred below 235°. If the mixture was extracted at

EXPERIMENTS ON 6-BROMOPIPERONAL.

Preparation of 6-bromopiperonal.

50 g. of piperonal were dissolved in 100 cc. of hot carbon tetrachloride. One crystal of iodine was added, and then, slowly, a solution of 20 cc. of bromine in 50 cc. of tetrachloride. Towards the end of the addition the mixture began to boil and was kept boiling for $2\frac{1}{2}$ hours. It was then cooled and left standing overnight, when crystals of bromopiperonal separated. These were filtered off, washed first with carbon tetrachloride, pressed well and then washed with a little alcohol. Crystallisation from alcohol gave colourless needles. m.p. $128-129^{\circ}$.
Yield 27 g. 40%.

Action of copper bronze on 6-bromopiperonal.

50 g. of 6-bromopiperonal were heated with 10 g. of Judex copper bronze in an atmosphere of CO_2 in a boiling tube in a metal bath. The delivery tube from the Kipp's apparatus served conveniently as a stirrer. No reaction occurred below 235° . If the mixture was extracted at

this temperature bromopiperonal was recovered unchanged. At 240° a vigorous reaction set in, the temperature rose rapidly to 280° with boiling and blackening of the whole mass (b.p. of 6-bromopiperonal is 320°).

The mixture was extracted with monochlorobenzene and the solvent removed. A dark-brown glue-like mass remained. On extracting this with sodium bisulphite and basifying a precipitate of piperonal only appeared (m.p. 37°), no trace of a dialdehyde could be detected. It was concluded that some type of auto-reduction had occurred, the blackening probably being due to formation of cupric oxide.

Action of acetic anhydride on 6-bromopiperonal.

(1) 23 g. (1 mol) of 6-bromopiperonal were heated under reflux with 10 g. (1 mole) of acetic anhydride and 2 cc. of glacial acetic acid for three hours. The presence of a few grams of copper sulphate as catalyst was found to improve the yield. The product was poured into water, the precipitate well washed, dried, and crystallised from alcohol or benzene.

m.p. $99-100^{\circ}$.

At 185° apparent boiling occurs with decomposition into acetic acid and 6-bromopiperonal (which sublimes readily). Yield 33 gms. 100%

Analysis.

Wt. of substance 0.2162 g. Wt. of AgBr 0.1382 g.

whence, % Br = 27.2

Diacetate, requires 23.9% Br

Mono-acetic solvate, $C_8H_5O_3Br \cdot C_2H_4O_2$ requires 27.6% Br.

(2) Zinc chloride and (3) conc. sulphuric acid were tried as condensing agents, but both caused considerable charring, the solution turned dark and remained clear when poured into water.

Action of copper bronze on 6-bromopiperonal acetate.

20 g. of bromopiperonal.1 CH_3CO_2H were heated in a boiling tube with 5 g. of copper bronze. At 120° apparent boiling occurred, acetic acid vapour was evolved converting the copper into acetate, and a greenish-white deposit appeared. The product was extracted with chlorobenzene and the solvent removed. Only a small quantity of greyish-coloured powder of high m.p. remained.

Preparation of 6-bromopiperonylideneaniline.

46 g. (1 mole) of bromopiperonal were dissolved in 300 cc. of absolute alcohol under reflux and 18 g. (1 mole) of pure redistilled aniline added, and the mixture boiled for 20 mins. The product separated on cooling, was filtered off, and crystallised from much alcohol in

colourless needles. m.p. 128-129°.

Yield 60 g. 100%.

Analysis.

Wt. of substance 0.3468 g. Wt. of AgBr 0.2147 g.

whence, % Br = 26.2

$C_{14}H_{10}O_2$ Br N requires 26.3% Br.

Preparation of di-(6-bromopiperonylidene) benzidine.

2.3 g. (2 moles) of bromopiperonal were dissolved in 70 cc. of boiling absolute alcohol, 1.8 g. (1 mole) of benzidine added, and the mixture boiled for 5 mins. A yellow product separated, was filtered off and crystallised from nitrobenzene in yellow plates.

Yield 3.5 g. 94%.

Analysis.

Wt. of substance 0.3937 g. Wt. of AgBr 0.2441 g.

whence, % Br = 26.2

$C_{23}H_{18}O_4N_2Br_2$ requires 26.4% Br.

Action of copper bronze on 6-bromopiperonylideneaniline.

30 g. of bromopiperonylideneaniline were heated with 10 g. of copper bronze. No change occurred below 190°. At 200° the temperature rose suddenly to 215° the mass blackened and became very viscous. The temperature was

kept at 215° for a further 20 minutes, and then the product was extracted with chlorobenzene, the solvent distilled off and the residue distilled in vacuum. The first fraction was collected at $90^{\circ}/18\text{m.m}$ and was probably catechol methylene ether. b.p. 170° .

The main fraction was collected at $140^{\circ}/10\text{m.m}$ as a thick yellow oil smelling strongly of carbylamine. On standing on a porous plate yellow needles separated. m.p. 62° , identified as piperonylideneaniline. (m.p. 65°).

Synthesis of 2:6-diacetylphenyl
 2:6-diacetylphenyl was prepared from 2:6-diacetylphenyl (Zincke & Tropp, Annalen 1908, 363, 245), and oxidized to 2:6-diacetylphenyl (Zincke & Tropp, Annalen 1908, 363, 245). The final product, after crystallization from alcohol, had melting point $94-95^{\circ}$. (Zincke & Tropp gave melting point 94° .)
 2:6-diacetylphenyl was prepared from 10 g. of diacetylphenyl (1 mol) dissolved in 50 g. of glacial acetic acid and 15 g. (3 mols) of phenylhydrazine at $50-75^{\circ}$. The hydrazone separated in quantitative yield and after crystallization from benzene / petroleum ether (b.p. $60-65^{\circ}$) had melting point 178° (Zincke & Tropp gave melting point 178°).

Bromination of 2:6-diacetylphenyl

(a) 5.01 g. of bromine were dissolved in 20 cc. of glacial acetic acid and 15.98 cc. of this solution (equivalent to 5.0 g. of bromine) were slowly added to 4.76 g. of

diacetyldiphenyl in 20 cc. of glacial acetic acid at 40°. The mixture was warmed and decolorization began at 50-55°.

B. 9-MEMBERED-SPIRO-RING COMPOUNDS.

The mixture was cooled and crystals separated. These were filtered off and recrystallized from absolute methyl alcohol and then

Synthesis of w:w'-dibromo-2:2'-diacetyldiphenyl.

the product crystallized in colourless hair-like needles.

9: 10-dimethyl-dihydroxy-phenanthrene was prepared from phenanthraquinone (Beil. VII, 797) by the method given by Zincke & Tropp (Annalen 1908, 362, 248), and oxidised to 2:2'-diacetyldiphenyl (Zincke & Tropp, Annalen 1908, 363, 305). The final product, after crystallisation from alcohol, had melting point 94-95°. (Zincke & Tropp gave melting point 84°.)

The bis-phenylhydrazone of diacetyldiphenyl was prepared from 10 g. of diacetyldiphenyl (1 mol) dissolved in 50 g. of glacial acetic acid and 13 g. (3 mols) of phenylhydrazine at 50-70°. The bishydrazone separated in quantitative yield and after crystallisation from benzene / petroleum ether (b.p. 60-80°) had melting point 178° (Zincke & Tropp gave melting point 178°).

Bromination of 2:2'-diacetyldiphenyl.

(a) 8.01 g. of bromine were dissolved in 20 cc. of glacial acetic acid and 15.98 cc. of this solution (equivalent to 6.4 g. of bromine) were slowly added to 4.76 g. of

diacetyldiphenyl in 20 cc. of glacial acetic acid at 40°. The mixture was warmed and decolorisation began at 50-55°. After standing at 60-70° for 15 minutes the solution was cooled and crystals separated. These were filtered off and recrystallised from absolute methyl alcohol and then from petroleum ether (b.p. 80-100°). From both solvents the product crystallised in colourless hair-like needles, m.p. 134-135°. Yield 3 g. 40%. 6 g. of this bromination product were extracted for 6 hours with petroleum ether (b.p. 40-60°) in a Soxhlet apparatus. At the end, no difference in melting point could be detected between the undissolved residue and the crystals which separated from the solution.

(b) 4.76 g. of diacetyldiphenyl were treated with 5.7 g. of bromine (90% theoretical), with 5 g. of anhydrous sodium acetate. Decolorisation occurred after 10 minutes at ordinary temperature, after standing the same product separated as before.

Analysis.

(1) Substance	0.1537 g.	AgBr.	0.1710 g.
whence,	% Br =		47.3%
Dibromination,	$C_{16}H_{12}O_2Br_2$,	requires	40.3% Br.
Tribromination,	$C_{16}H_{11}O_2Br_3$,	requires	50.5% Br.

(2) Found:-	C	42.8%
	H	2.8%
Dibromo derivative, $C_{16}H_{12}O_2Br_2$, requires	C	48.4%
	H	3.0%
Tribromo derivative, $C_{16}H_{11}O_2Br_3$, requires	C	40.3%
	H	2.3%

Chlorination of diacetyldiphenyl.

4.76 g. of diacetyldiphenyl in 20 g. of glacial acetic acid at 30° were treated with 2.84 g. of chlorine. On cooling and diluting with water successive crops of hair-like needles mixed with clusters of prisms were obtained. m.p. 40° . On recrystallising from alcohol the product had m.p. 57° . Recrystallisation from absolute methyl alcohol gave a product of m.p. 78° , while recrystallisation from petroleum ether (b.p. $60-80^{\circ}$) gave product of m.p. 62° . All these substances crystallised in the form of hair-like needles and all contained chlorine.

time to time and the mixture kept well stirred. Heat of
 reaction quickly sent temperature to 180° and the addition
 of copper was regulated to keep the temperature below 205°

II. 5-ETHOXY-2-(2'-BISDIMETHYLAMINO-4'-ETHOXY-PHENYL)

-PHENYLTRIMETHYLAMMONIUM IODIDE.

1. SYNTHESIS.

(1) 3-nitro-4-iodo-phenetole.

was prepared by the method given in the literature (Reverdin, Ber., 1896, 29, 2597, Bull, Soc.chim. 1897, (3), 17, 117), from 3-nitro-4-amino-phenetole which was obtained by the hydrolysis of 3-nitro-4-acetamino-phenetole (nitrophenacetin) with concentrated hydrochloric acid. The crude iodo compound was washed with strong caustic soda solution and hot water, and after drying was distilled in vacuum, boiling point 198-199° at 20 mm.

Crystallisation from petroleum ether (b.p. 60-80°) gave fine yellow needles m.p. 62-63°.

Yield 72%.

(2) Preparation of 4:4'-diethoxy-2:2'-dinitrodiphenyl.

60 g. of 3-nitro-4-iodo-phenetole were heated to 170° in a boiling tube in a metal bath at 180-185°. Small amounts of pure copper bronze (Judex) were sprayed in from

time to time and the mixture kept well stirred. Heat of reaction quickly sent temperature to 190° and the addition of copper was regulated to keep the temperature below 205° (charring occurs at 230°). When 45 g. of copper bronze had been added and the temperature had fallen back to 170° , the dinitrodiphenyl was extracted with 250 cc. of chlorobenzene at the boiling point. The solution was filtered free from copper and cuprous iodide, two thirds of the solvent distilled off and the residue left to cool. Large, pale yellow rhombohedra separated, were collected and washed with a little chlorobenzene.

The chlorobenzene mother liquor was left to evaporate spontaneously and deposited two more crops of equally pure crystals. After recrystallising from alcohol yellow needles were obtained, m.p. $129-130^{\circ}$.

Yield 28 g. (80%).

(3) Preparation of 4:4'-diethoxy-2:2'-diaminodiphenyl.

50 g. of 4:4'-diethoxy-2:2'-dinitrodiphenyl were added to a hot paste of 80 g. of iron filings and water with 5 drops of glacial acetic acid. The mixture was stirred on the water bath and kept as hot as possible until reaction had ceased (80 minutes, the reaction slackened after 30 minutes and then started again). The base was extracted with 500 cc. of boiling alcohol, the solution filtered from iron, and two

thirds of the solvent removed by distillation, and the residue left to crystallise. Small prisms separated, and were recrystallised (1) from petroleum ether (b.p. 80-100°) (2) from acetone/petroleum ether (b.p. 40-60°) (3) from absolute alcohol.

After crystallisation again from absolute alcohol, colourless needles, m.p. 110-111° were obtained.

(4) Preparation of 4:4'-diethoxy-2:2'-bisdimethylamino diphenyl.

30 g. of 4:4'-diethoxy-2:2'-diaminodiphenyl in a Pyrex conical flask were just covered with water. 106 cc. of methyl sulphate were added in three lots, the mixture being shaken and warmed on the water bath for 5 minutes and then treated with caustic soda (20%) solution till alkaline after each addition. The mixture was left on the water bath for 1 hour, then cooled under the tap and the solid tetramethyl base filtered off, washed freely with concentrated ammonia and then with water. Crystallisation from absolute alcohol gave colourless plates m.p. 86-87°. Yield 30 g. (85%)

(5) Preparation of 5-ethoxy-2-(2'-dimethylamino-4'-ethoxy phenyl) phenyltrimethylammonium iodide.

(a) 10 g. of 4:4'-diethoxy-2:2'-bisdimethylamino-diphenyl (1 mol) were heated under reflux in saturated absolute

methyl-alcoholic solution with 8 g. (2 mols) methyl iodide for 2 hours. On cooling, crystals separated, which consisted chiefly of the tetramethyl base (m.p. 66°). Evaporation of the mother liquor gave product of m.p. 160° . It was concluded that methylation had been incomplete.

(b) 20 g. of base were heated on the water bath under reflux for 1 hour with sufficient methyl iodide to cover. The methiodide separated as small prisms which were filtered from the cooled solution and washed with absolute methyl alcohol and dry ether. Recrystallisation from water (3 times) gave colourless needles, m.p. $168-169^{\circ}$. With the bath initially at 170° , the m.p. was $172-173^{\circ}$.

(c) $\frac{1}{2}$ g. of base was left to stand with 1 cc. of methyl iodide in the dark for 24 hours. Colourless crystals of methiodide separated, identical with those obtained in (b).

2. Fractional crystallisation of the camphorsulphonate from carbon tetrachloride (See Table p.109).

46.0 g. of partial racemate were treated with 200 cc. of dry, boiling carbon tetrachloride and the

2. EXPERIMENTS ON THE OPTICAL PROPERTIES.

1. Preparation of 5-Ethoxy-2-(2'-dimethylamino-4'-ethoxyphenyl) phenyltrimethylammoniumcamphorsulphonate

11.7 g. of dl-5-ethoxy-2-(2'-dimethylamino-4'-ethoxy phenyl) phenyltrimethylammonium iodide and the equivalent (8.5 g) freshly-made silver d-camphor 10-sulphonate was boiled under reflux with 150 cc. of absolute alcohol and 20 cc. of water for 30 minutes. The solution was filtered from AgI and evaporated, the residue being freed from water by repeated evaporation with small quantities of absolute alcohol. 23 g. of partial racemate were obtained, deliquescent granules (95%).

These were found to be very soluble in benzene, xylene, and ethyl acetate, and sparingly soluble in light petroleum (b.p. 60-80°). In carbon tetrachloride they showed selective solubility, part dissolving readily and the residue remaining almost insoluble. This was chosen as the solvent for the first set of experiments, and benzene for the second set.

2. Fractional crystallisation of the camphorsulphonate from carbon tetrachloride (See Table p.109).

46.0 g. of partial racemate were treated with 600 cc. of dry, boiling carbon tetrachloride and the

resulting suspension filtered. On cooling in dry air, the filtrate gave 23.3 g. of material (A_1) having $[\alpha]_{579}^{20^\circ} +15.1^\circ$, $[\alpha]_{546}^{20^\circ} +17.8^\circ$, ($\alpha_{579}^{20^\circ} +0.58^\circ$, $\alpha_{546}^{20^\circ} +0.69^\circ$; C, 1.9230; 1, 2) in 99% EtoH. This crop was recrystallised twice, once from a saturated solution, 23.3 g. of A_1 in 250 cc. of solvent gave 13.0 g. of A_2 , and once from a very dilute solution, 13.0 g. of A_2 in 500 cc. of solvent gave 2.0 g. of A_3 . The specific rotation remained unchanged, A_2 having $[\alpha]_{579}^{20^\circ} +14.9^\circ$, $[\alpha]_{546}^{20^\circ} +17.7^\circ$, and A_3 having $[\alpha]_{579}^{20^\circ} +15.1^\circ$, $[\alpha]_{546}^{20^\circ} +17.9^\circ$, ($\alpha_{579}^{20^\circ} +0.61^\circ$, $\alpha_{546}^{20^\circ} +0.72^\circ$; C, 2.0100; 1, 2).

The residue R_1 which remained insoluble at the initial treatment weighed 21.6g. and had $[\alpha]_{579}^{20^\circ} +15.2^\circ$, $[\alpha]_{546}^{20^\circ} +17.9^\circ$, ($\alpha_{579}^{20^\circ} +0.67^\circ$, $\alpha_{546}^{20^\circ} +0.79^\circ$; C, 2.2000; 1, 2).

On recrystallisation, each time necessarily from a large volume of solvent, this gave 18.0 g. of material R_2 having $[\alpha]_{579}^{20^\circ} +15.2^\circ$, $[\alpha]_{546}^{20^\circ} +18.0^\circ$. R_2 was recrystallised and gave a crop R_3 (12.0 g) having $[\alpha]_{579}^{20^\circ} +15.2^\circ$, $[\alpha]_{546}^{20^\circ} +17.9^\circ$ ($\alpha_{579}^{20^\circ} +0.67^\circ$, $\alpha_{546}^{20^\circ} +0.79^\circ$; C, 2.2020; 1, 2).

The mother liquors were fractionally evaporated and the rotations of the various crops were measured. The values of $[\alpha]_{579}^{20^\circ}$ were all between $+15.2^\circ$ and $+14.7^\circ$, with an experimental error of $\pm 0.4^\circ$. The values of $[\alpha]_{546}^{20^\circ}$

lay between $+17.9^{\circ}$ and $+17.5^{\circ}$. This corresponds to differences in the observed angles of $+0.08^{\circ}$ and $+0.11^{\circ}$.

3. Fractional Crystallisation of the Camphorsulphonate
from Benzene. (see Table p.110). Jacoby 1799, 1892.

30.0 g. of partial racemate was dissolved in 75 cc. of hot dry benzene. On cooling in dry air, 25.0 g. of material (A_1) separated; having $[\alpha]_{D^{20}}^{20} +16.6^{\circ}$, $[\alpha]_{D^{20}}^{20} +19.7^{\circ}$ ($d_{D^{20}}^{20} +0.64^{\circ}$, $d_{D^{20}}^{20} +0.76^{\circ}$; C, 1.9280; L, 2) in 99% EtoH. On recrystallisation, this gave successive crops A_2 (19.0g), A_3 (17.0g) and A_4 (6.0 g) having $[\alpha]_{D^{20}}^{20} +17.3^{\circ}$, $+17.7^{\circ}$, and $+17.9^{\circ}$ respectively. The original mother liquor was evaporated and gave first 3.5 g (B_1) having $[\alpha]_{D^{20}}^{20} +17.5^{\circ}$ and then 1.5 g (C_1) having $[\alpha]_{D^{20}}^{20} +16.3^{\circ}$, $[\alpha]_{D^{20}}^{20} +19.1^{\circ}$ ($d_{D^{20}}^{20} +0.70^{\circ}$, $d_{D^{20}}^{20} +0.84$; C, 2.1480; 1, 2). The latter was the smallest (positive) value obtained for the specific rotation of any crop, some fourteen crops having been examined in all. The largest value was $[\alpha]_{D^{20}}^{20} +19.0^{\circ}$, $[\alpha]_{D^{20}}^{20} +22.8$ ($d_{D^{20}}^{20} +0.82^{\circ}$, $d_{D^{20}}^{20} +0.98^{\circ}$; C, 2.1500; 1, 2) for the crop α_1 (3.0 g) obtained from the mother liquor of A_2 . On recrystallising α_1 no material of higher rotatory power could be segregated, either from the crops or from their mother liquors. The difference between the sp. rotations $+16.3^{\circ}$ and $+19.0^{\circ}$ corresponds to a difference of $+0.12^{\circ}$ between the observed angles.

4. Preparation of the α -bromocamphorsulphonate.

The silver salt of \underline{d} - α -bromocamphor- $\overline{\text{II}}$ -sulphonic acid was prepared from the acid by the method of Pope & Read (J. 1910, 97, 2200) the acid itself being obtained from the ammonium salt by the method of Pope & Peachey (Trans. 1898, 73, 893).

12.6 g. of 5-ethoxy-2-(2'-dimethylamino-4'-ethoxy-phenyl) phenyl trimethylammonium iodide were dissolved under reflux in 75 cc. of absolute alcohol, and treated with a solution of 11.2 g. (1 equiv) of silver \underline{d} - α -bromocamphor sulphonate in a mixture of 80 cc. of absolute alcohol and 20 cc. of water. After boiling for 30 minutes the solution was filtered free from silver iodide and then evaporated to dryness. 15 g. of racemate were obtained (100%) as deliquescent granules. These were very soluble in water, alcohol and acetone, moderately soluble in benzene (precipitated) by light petroleum (b.p. 60-80°) and in carbon tetrachloride.

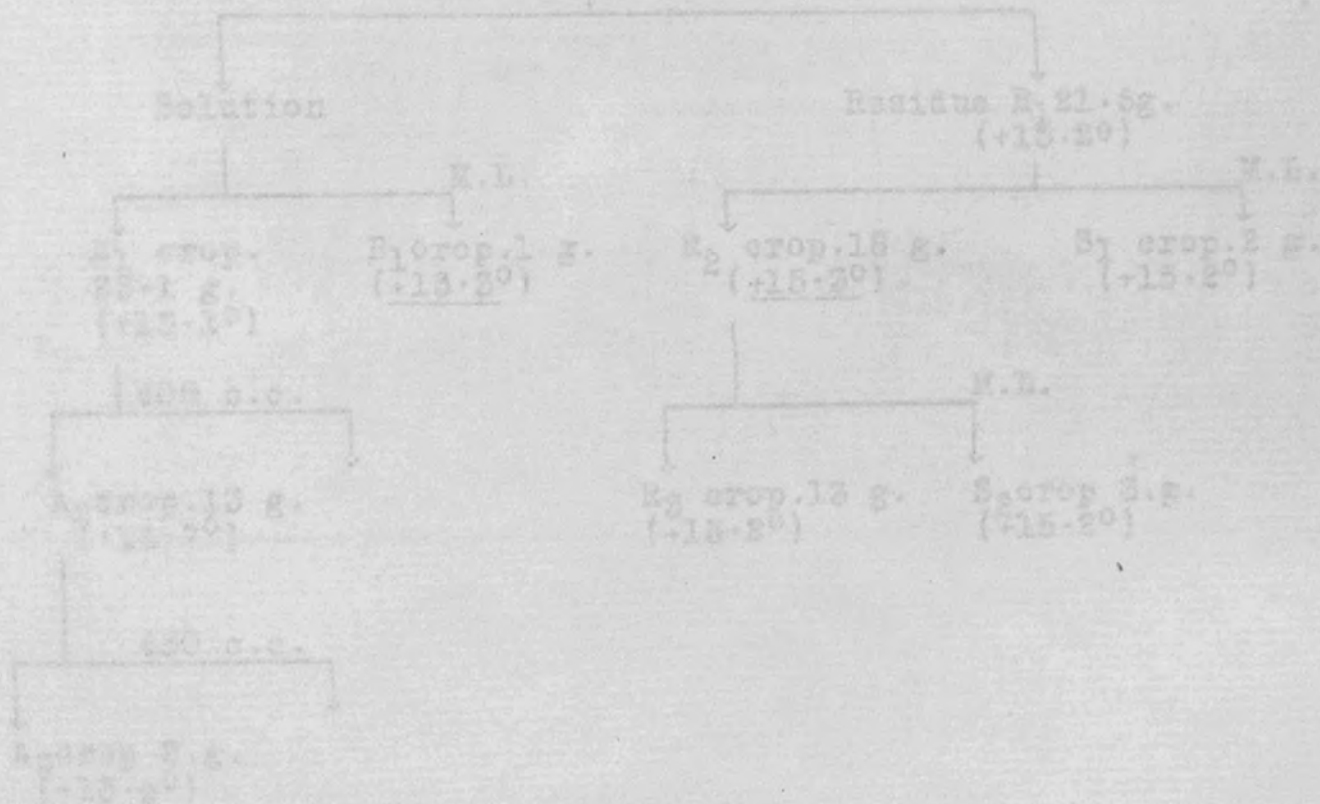
Fractional crystallisation of the α -bromocamphorsulphonate from benzene.

15 g. of partial racemate were dissolved in 70 cc. of dry benzene. First, 8 g. (A_1) separated, having $[\alpha]_{D^{20}}^{20} + 50.5^\circ$ and then 6 g. (B_1) separated, having $[\alpha]_{D^{20}}^{20} + 47.8^\circ$. On recrystallisation, A_1 gave 5 g. (A_2) having $[\alpha]_{D^{20}}^{20} + 47.8^\circ$
 $[\alpha]_{D^{20}}^{20} + 56.9^\circ$ ($\alpha_{D^{20}}^{20} + 2.00^\circ$, $\alpha_{D^{20}}^{20} + 2.38^\circ$;

C, 2.0905; 1, 2). The mother liquor evaporated gave 2 g. (X_1) having $[\alpha]_{579}^{20} + 51.3^\circ$, $[\alpha]_{546}^{20} + 61.3^\circ$ ($\alpha_{579}^{20} + 2.06^\circ$, $\alpha_{546}^{20} + 2.46^\circ$; C, 2.060; 1, 2).

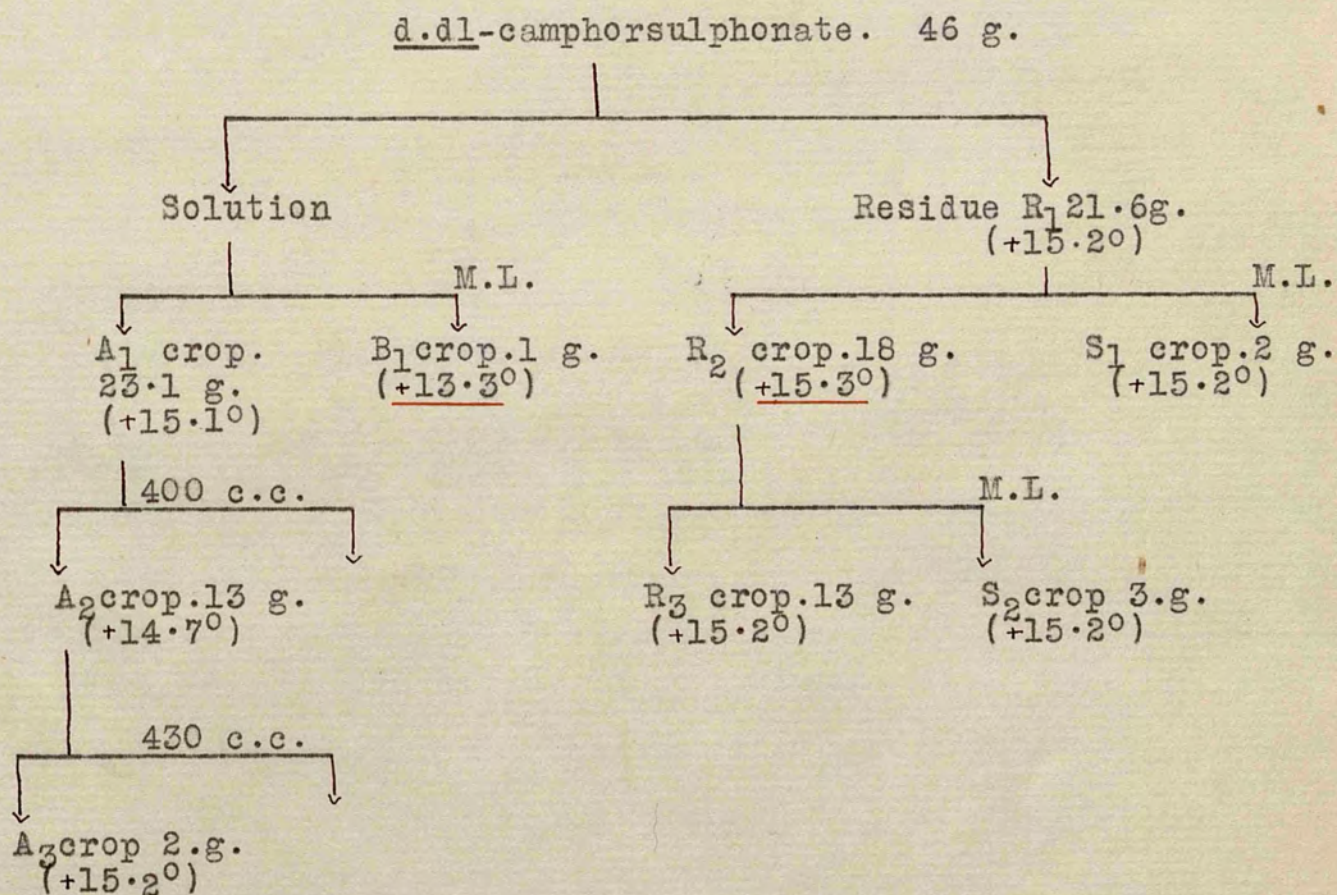
Recrystallisation did not seem to effect further separation, the rotations of the crops remained constant. The greatest difference found between the specific rotations of any two crops was $+52.0^\circ - +47.8^\circ (+4.2^\circ)$ and corresponds to a difference of $+0.06^\circ$ between the observed angles.

d,d-tartronates. 42 g.

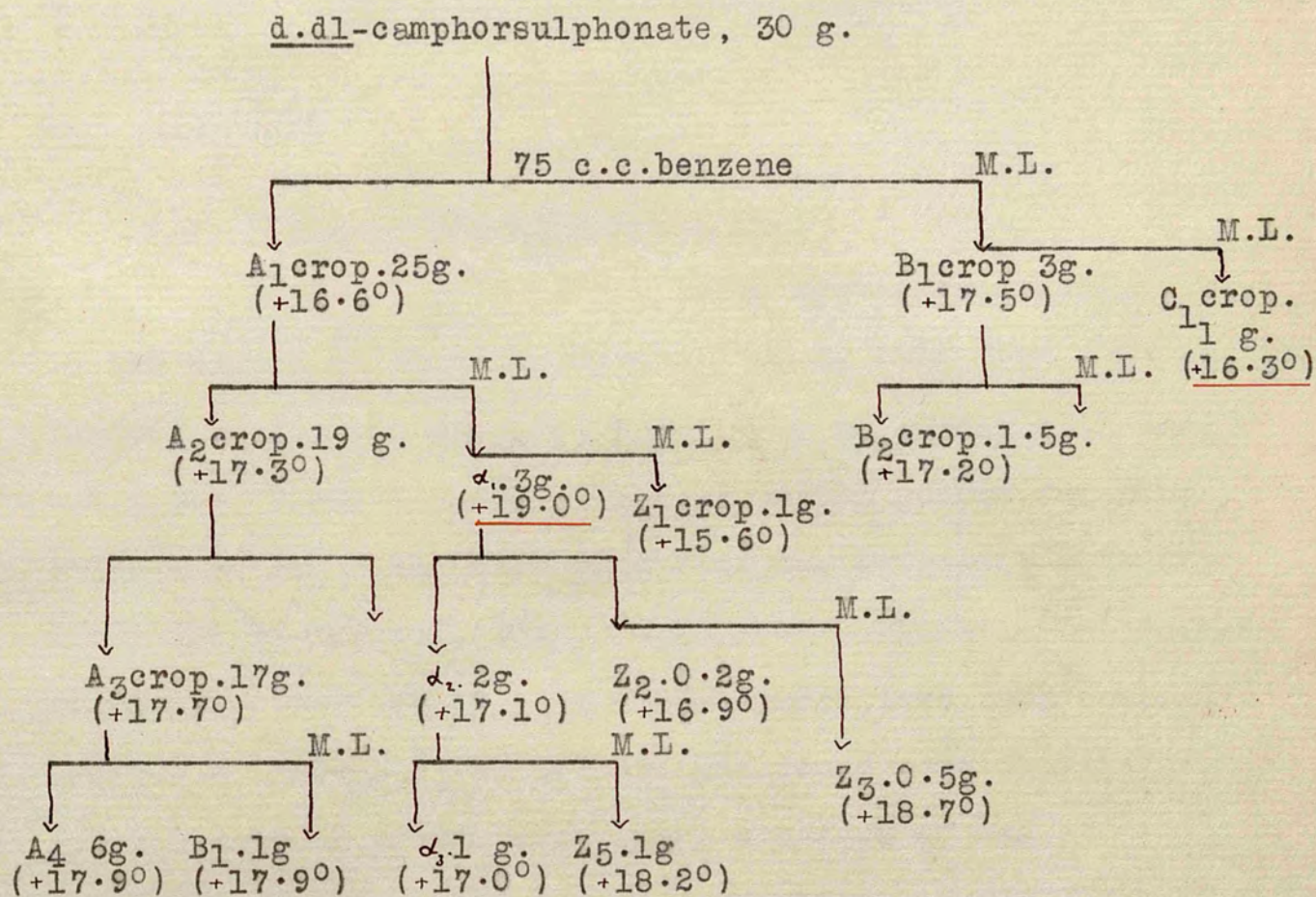


The Effect of Fractional crystallisation on the Specific Rotation of d.dl-Camphorsulphonate.

(1) Carbon tetrachloride solution.



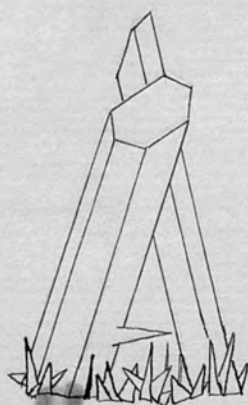
(2) Benzene solution.

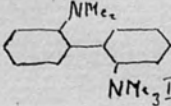


The averaging of consecutive readings in the calculation of k allows a possible error of only 0.0002, and this corresponds to an error in the value of A of 2,500 cal. The difference between the values obtained for the two temperature ranges is therefore just within the experimental error, and the values may be given as:-

A , for the δ -iodide, 11,700 cal. \pm 1,250.

A , for the $\alpha\alpha$ -camphorsulphonate, 18,800 cal. \pm 1,250.



Dimorphism of dl- 

crystallised from neutral aqueous solution.

Fig. VII.

excess hydroxide and then evaporated to dryness. The residue crystallised from water in glistening plates, which were identified as the octahydrate. Yield 13 g. 95%.

Analysis.

Substance 0.5054 g. AgBr 0.2329 g.

whence % Ag = 26.2

$C_6H_5SO_3Ag \cdot 8 H_2O$ requires 26.3%

Preparation of \underline{d} -benzene sulphonate.

4.8 g. of \underline{d} -iodide were dissolved in 10 cc. of cold absolute alcohol, and added to a cold solution of 5.1 g. of silver benzenesulphonate in a mixture of 5 cc. of absolute alcohol and 5 cc. of water. The precipitated silver iodide was filtered off and the solution evaporated at 20° in vacuo. Crystals of the \underline{d} -benzenesulphonate separated out. These were kept in vacuo until their weight was constant.

Analysis.

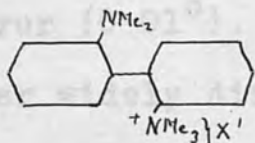
Substance 0.3970 g. Vol. of N_2 22.7 c.c.
(dried at 120°) temp. 20° , pressure 767 m.m.

whence % N = 6.7

$C_{23}H_{28}N_2SO_3$ requires 6.7% N.

line being used for the calculation of k . It was found in some cases that racemisation was slow and the change of

2. MEASUREMENT OF THE RATES OF RACEMISATION OF THE D-SALTS



where X is $d-C_{10}H_{15}\cdot O\cdot SO_3$, $-C_6H_5-SO_3$ and $-I$
IN VARIOUS SOLVENTS AT THREE TEMPERATURES.

The salts were prepared as above and dried in vacuo at 20° , until constant in weight.

Solutions were made in pure solvents, and were necessarily dilute owing to the fact that the l-forms are in each less soluble, and the final readings are complicated by separation of solid material from more concentrated solutions.

A small volume (20 c.c) of solution was used in order to reduce error due to loss by evaporation, technique, and any difference between heating and cooling interval to a minimum. This error was estimated by a control experiment in which 20 c.c of the original solution were heated in a sealed tube at 100° for fifteen hours, and the second reading did not differ from the final experimental reading by more than 0.02° . Heating was carried out in a sealed tube (the temperatures recorded have not been corrected for pressure) in a thermostat regulated to within 0.1° .

The polarimeter readings have a possible error of $\pm 0.01^\circ$, and were taken in a 1 dm. tube at 25° , the mercury yellow

line being used for the calculation of k. It was found in some cases that racemisation was slow and the change of rotation over a given period was within the experimental error (0.01°). Several sets of readings were then taken over widely different periods and the results recorded are average values.

All the readings have been duplicated.

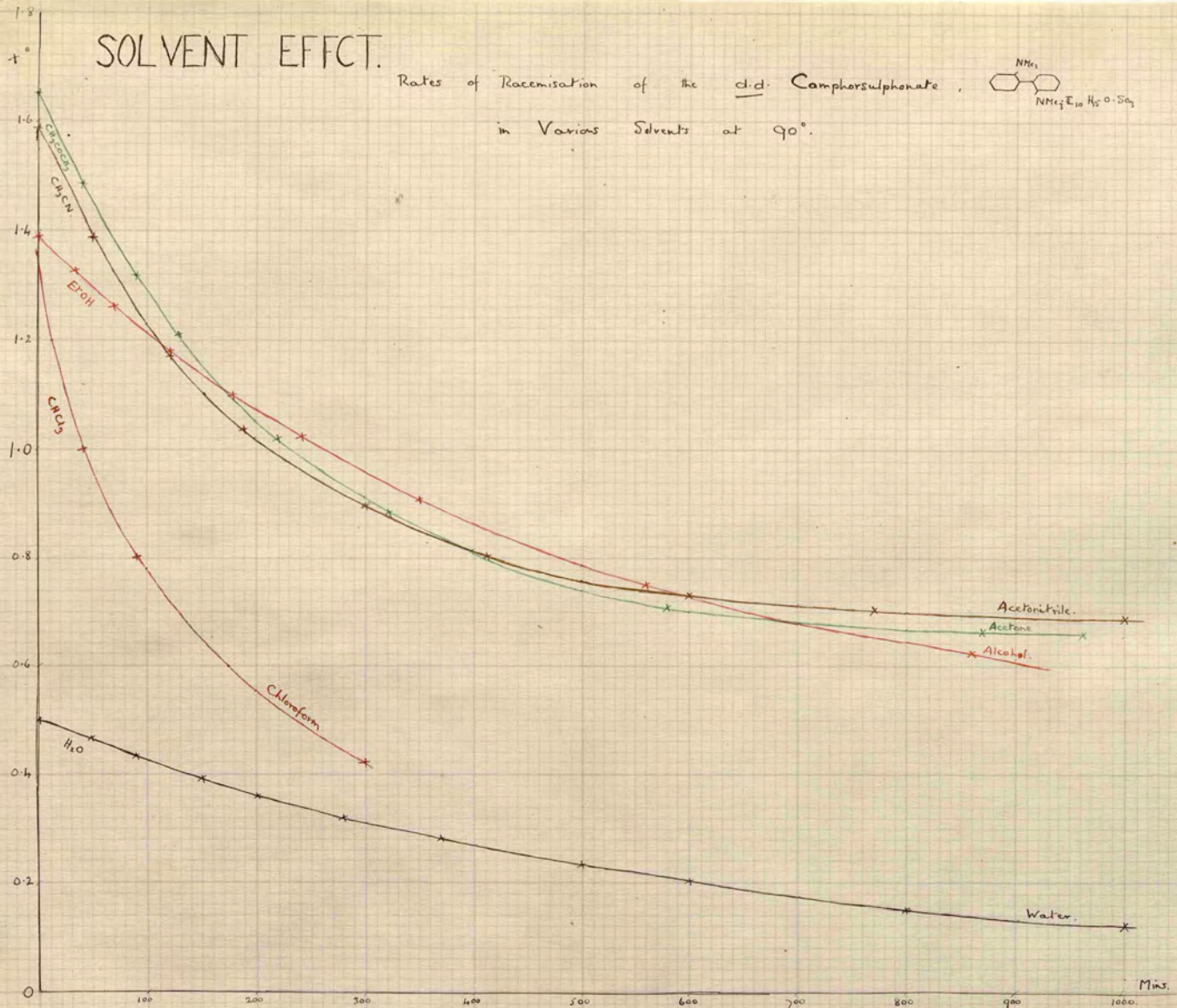
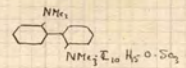
The results are tabulated in Table I. The values are given in degrees. The optical activity was measured at 25°C. The optical activity was measured after 3 hours heating and the results are given in degrees. Contrary to expectation, it was found that the optical activity was not constant but varied with time. The optical activity was measured at 25°C. The optical activity was measured after 3 hours heating and the results are given in degrees.

Substance	Optical activity (degrees)	Time (hours)
Acetone	1.2	3
Water	1.5	3
Alcohol	1.8	3
Diethyl ether	2.1	3
Chloroform	2.4	3

The order of increasing optical activity, acetone, alcohol, water, is the order of increasing solubility of the β -naphthylsulfonate. The optical activity was measured at 25°C. The optical activity was measured after 3 hours heating and the results are given in degrees.

SOLVENT EFFECT.

Rates of Racemisation of the d,l-Camphorsulphonate
in Various Solvents at 90°.



The averaging of consecutive readings in the calculation of k allows a possible error of only 0.0003, and this

The Effect of Temperature on the Rates of Racemisation of the \underline{d} -iodide and the \underline{d} -camphorsulphonate.

Measurements have been taken in aqueous solution (of uniform concentration) at three temperatures, 85°, 90° and 95°, and values have been calculated for the energy of activation A from the Arrhenius Equation:-

$$A = \frac{(\log K_2 - \log K_1) RT_1 \cdot T_2}{0.4343 (T_2 - T_1)}$$

For the \underline{d} -iodide:- (Details on pages 127, 128 & graph on p.119)

<u>Temp:</u>	<u>k</u>	<u>A</u>
85	0.0009 ₃	
90	0.0011 ₉	12,(9)00 cal _s .)
95	0.0014 ₅	10,(4)00 cal _s .)
) mean 11,(7)00 cal _s .

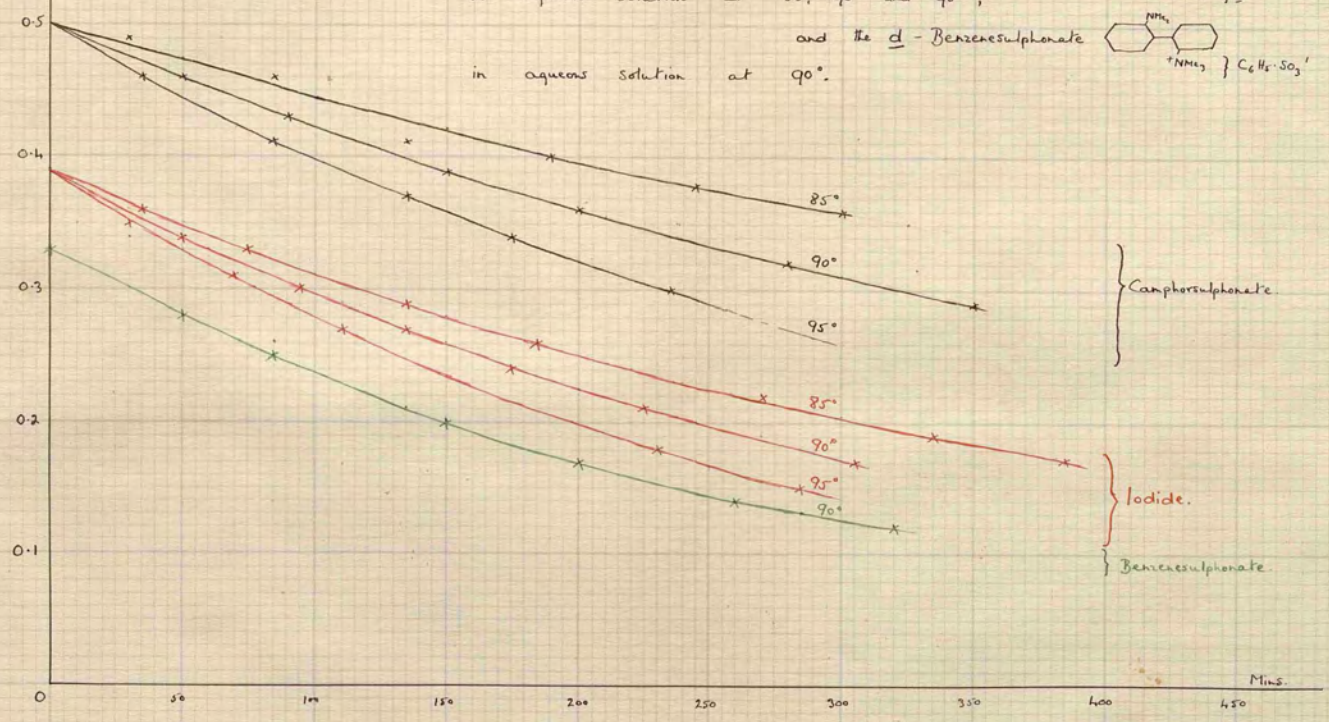
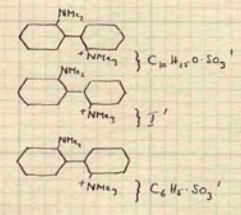
For the \underline{d} -camphorsulphonate:-

(details on pages 121, 125, 126 & graph on p.119)

<u>Temp:</u>	<u>k</u>	<u>A</u>
85	0.0006 ₅	
90	0.0009 ₆	20,(5)00 cal _s .)
95	0.0013 ₃	17,(1)00 cal _s .)
) mean 18,(8)00 cal _s .

TEMPERATURE EFFECT
AND ION EFFECT,

Rates of Racemisation of the d,d- Camphorsulphonate,
and the d- Iodide,
in aqueous solution at 85°, 90° and 95°;
and the d- Benzenesulphonate
in aqueous solution at 90°.



T A B L E S.

Polarimeter zero reading = 359.54°.

k is calculated for the yellow line, k_{5791} .

I. Racemisation of d camphorsulphonate.

(a) In various solvents, at 90°.

1. In water. $c = 0.2634 \times 2$.

Time. in mins.	Polarimeter Readings.		α_{5791}	α_{5461}	$\frac{1}{t_2 - t_1} \cdot \log \frac{\alpha_1}{\alpha_2}$	k.
	k_{5791}	k_{5461}				
0	0.04	0.12	+ 0.50°	+ 0.58		
50	0.00	0.07	0.46°	0.53	0.0009 ₄	
90	359.97	0.04	0.43°	0.50	0.0009 ₈	
150	359.93	359.98	0.39°	0.44	0.0009 ₇	<u>0.0009₆</u>
200	359.90	359.95	0.36°	0.41	0.0009 ₉	
280	359.86	359.91	0.32°	0.37	0.0009 ₅	
370	359.82	359.85	0.28°	0.31	0.0010 ₂	
∞	359.65	359.66	0.11°	0.12		

Half-value period = 310 mins.

2. In Alcohol. $c = 0.2372 \times 5.$

Time.	Polarimeter Readings.		d_{5791}	d_{5261}	$\frac{1}{t_2 - t_1} \cdot \log \frac{d_1}{d_2}$	k.
	λ_{5791}	λ_{5261}				
0	0.93	1.17	+ 1.39	+ 1.63		
35	0.86	1.07	1.32	1.53	0.0010 ₂	
70	0.80	0.97	1.26	1.43	0.0009 ₉	
120	0.73	0.88	1.19	1.34	0.0010 ₅	
180	0.64	0.76	1.10	1.22	0.0010 ₆	
240	0.57	0.69	1.03	1.15	0.0009 ₃	<u>0.0010</u>
350	0.45	0.58	0.91	1.04	0.0012 ₉	
560	0.29	0.41	0.75	0.87		
860	0.16	0.28	0.62	0.74		
(1055	0.07	0.18	0.53	0.64		
(1230	0.07	0.18	0.53	0.64		

Half-value period = 300 mins.

3. In Acetone. $c = 0.2662 \times 5.$

Time.	Polarimeter Readings.		α_{5791}	α_{5461}	$\frac{t}{t_2-t_1} \cdot \log \frac{d_1}{d_2}$	k.
	α_{5791}	α_{5461}				
0	1.19	1.46	+1.65	+1.92		
40	1.03	1.25	1.49	1.71	0.0018 ₉	
90	0.86	1.05	1.32	1.51	0.0019 ₆	
130	0.75	0.90	1.21	1.36	0.0019 ₅	
220	0.56	0.67	1.02	1.13	0.0020 ₀	
320	0.43	0.56	0.89	1.02	0.0018 ₈	0.0019 ₄
580	0.25	0.39	0.71	0.85	0.0023	
870	0.20		0.66			
1050	0.19		0.65			
1130	0.19		0.65			

Half-value period = 155mins

4. In Acetonitrile. $c = 0.2590 \times 5.$

Time.	Polarimeter Readings.		α_{5791}	α_{5461}	$\frac{1}{t_2 - t_1} \cdot \log \frac{a_1}{a_2}$	k.
	α_{5791}	α_{5461}				
0	1.13	1.37	+1.59	+1.83		
50	0.93	1.15	1.39	1.61	0.0021 ₈	
120	0.72	0.90	1.18	1.36	0.0022 ₀)	0.0021 ₅
190	0.58	0.74	1.04	1.20	0.0020 ₉)	
300	0.44	0.68	0.90	1.14	0.0020 ₂)	0.0021 ₁
410	0.35	0.50	0.81	0.96	0.0022 ₀)	
600	0.27	0.40	0.73	0.86	0.0024	<u>0.0021₄</u>
770	0.24	0.36	0.70	0.82		
1050	0.23	0.35	0.69	0.81		
1350	0.23	0.35	0.69	0.81		

Half-value period = 140 mins.

5. In Chloroform.

0	1.11	1.57	+1.36	+1.82		
40	0.80	1.26	1.03	1.49		
90	0.64	1.10	0.82	1.28		0.003
300	0.22	0.68	0.40	0.86		

Half-value period = 100 mins.

(b) At various temperatures, in water.

1. At 85°. $c = 2634 \times 2.$

Time.	Polarimeter λ_{5791}	Readings. λ_{5461}	α_{5791}	α_{5461}	$\frac{1}{t_2 - t_1} \cdot \log. \frac{\alpha_1}{\alpha_2}$	$k.$
0	0.04	0.12	+ 0.50	+ 0.58		
30	0.03	0.10	0.49	0.56	0.0007 ₀	
120	359.98	0.06	0.44	0.52	0.0006 ₁	
130	359.95	9.02	0.41	0.48	0.0006 ₉	
245	359.92	359.98	0.38	0.44	0.0006 ₁	<u>0.0006₅</u>
325	359.89	359.95	0.35	0.41	0.0006 ₄	
445	359.85	359.90	0.31	0.36	0.0006 ₄	
625	359.80	359.85	0.26	0.31	0.0006 ₉	

Half-value period = 460 mins.

2. At 95°. $c = 0.2634 \times 2$.

Time.	Polarimeter Readings.		d_{5791}	d_{5461}	$\frac{1}{t_2 - t_1} \cdot \log \frac{d_1}{d_2}$	k.
	h_{5791}	h_{5461}				
0	0.04	0.12	+0.50	+0.58		
35	0.00	0.07	0.46	0.53	0.0013 ₃	
85	359.95	0.01	0.41	0.47	0.0013 ₄	
135	359.91	359.96	0.37	0.42	0.0012 ₆	
175	359.88	359.92	0.34	0.38	0.0013 ₉	<u>0.0013₃</u>
235	359.84	359.87	0.30	0.33	0.0013 ₈	
∞	359.65	359.66	0.11	0.12		

Half-value period = 230 mins.

3. At 90°. $k = 0.0009_6$.

see p.121.

Half-value period = 310 mins.

II. Racemisation of d-iodide, in water at various temperatures

1: At 85°. $c = 2070 \times 2$.

Time.	Polarimeter Readings.		α_{5791}	α_{5461}	$\frac{1}{t_2 - t_1} \cdot \log \frac{\alpha_1}{\alpha_2}$	k.
	α_{5791}	α_{5461}				
0	359.93	359.98	+ 0.39	+ 0.44		
35	359.90	359.95	0.36	0.41	0.0009 ₅	
75	359.87	359.91	0.33	0.37	0.0009 ₄	
135	359.83	359.87	0.29	0.33	0.0009 ₃	<u>0.0009₃</u>
185	359.80	359.83	0.26	0.29	0.0009 ₅	
265	359.76	359.79	0.22	0.25	0.0009 ₁	
335	359.73	359.75	0.19	0.21	0.0009 ₁	
385	359.71	359.73	0.17	0.19	0.0009 ₇	

Half-value period = 320 mins.

2. At 90°. $c = 0.2070 \times 2.$

Time.	Polarimeter Readings.		α_{5791}	α_{5461}	$\frac{1}{t_2 - t_1} \cdot \log \frac{d_1}{d_2}$	k.
	α_{5791}	α_{5461}				
0	359.93	359.98	+ 0.39	+ 0.44		
50	359.88	359.93	0.34	0.39	0.0011 ₉	
85	359.85	359.89	0.31	0.35	0.0012 ₂	
135	359.81	359.84	0.27	0.30	0.0012 ₅	<u>0.0011₉</u>
175	359.78	359.80	0.24	0.27	0.0011 ₆	
225	359.75	359.76	0.21	0.22	0.0012 ₀	
305	359.71	359.72	0.17	0.18		

Half-value period = 250 mins.

3. At 95°. $c = 0.2070 \times 2.$

0	359.93	359.98	+ 0.39	+ 0.44		
30	359.88	359.94	0.34	0.42)		
50	359.87	359.93	0.33	0.39)	0.0014 ₅	
70	359.85	359.91	0.31	0.37	0.0014 ₃	
110	359.81	359.85	0.27	0.31	0.0014 ₅	<u>0.0014₅</u>
230	359.72	359.76	0.18	0.22	0.0014 ₆	
330	359.67	359.71	0.13	0.17	0.0014 ₁	
380	359.65	359.68	0.11	0.14	0.0014 ₅	
410	359.64	359.67	0.10	0.13	0.0013 ₈	

Half-value period = 210 mins.

III. Racemisation of d-benzenesulphonate in water.At 90°.

$$c = 0.2239 \times 2.$$

Time.	Polarimeter Readings.		α_{5791}	α_{5461}	$\frac{1}{t_2 - t_1} \cdot \log \frac{d_1}{d_2}$	k.
	α_{5791}	α_{5461}				
0	359.87	359.92	+0.33	+0.38		
50	359.82	359.86	0.28	0.32	0.0014 ₂	
85	359.79	359.82	0.25	0.28	0.0014 ₀	
150	359.74	359.76	0.20	0.22	0.0014 ₈	
200	359.71	359.73	0.17	0.19	0.0014 ₁	<u>0.0014₂</u>
260	359.63	359.69	0.14	0.15	0.0014 ₀	
320	359.66	359.67	0.12	0.13	0.0014 ₅	

Half-value period = 210 mins.


III. Racemisation of d-benzenesulphonate in water.At 90° .

$$c = 0.2239 \times 2.$$

Time.	Polarimeter λ_{5791}	Readings. λ_{5461}	α_{5791}	α_{5461}	$\frac{1}{t_2 - t_1} \cdot \log \frac{d_1}{d_2}$	k.
0	359.87	359.92	+0.33	+0.38		
50	359.82	359.86	0.28	0.32	0.0014 ₂	
85	359.79	359.82	0.25	0.28	0.0014 ₀	
150	359.74	359.76	0.20	0.22	0.0014 ₈	
200	359.71	359.73	0.17	0.19	0.0014 ₁	0.0014 ₂
260	359.63	359.69	0.14	0.15	0.0014 ₀	
320	359.66	359.67	0.12	0.13	0.0014 ₅	

Half-value period = 210 mins.

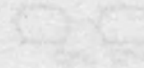

Two lines of investigation have been followed: I on the mechanical aspect and II on the electrical aspect of diphenyl dynamics.

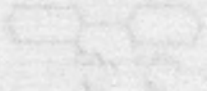
I An attempt has been made to synthesise a 2:2'-hetero-spiro-cyclo-derivative of diphenyl with a view to determining the configuration adopted by the spirocyclic chain. The preparation of halides of the type  has been examined, as it seemed probable that they would undergo ring formation with piperidine:-

S U M M A R Y .

A suitable solvent could not be obtained. It was found in the course of investigation that:-

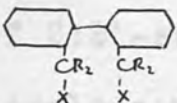
(1) Compounds of the type  do not react with potassium iodide to give an iodo compound, complex intermolecularly associated of high m.p. are formed.

(2) The tetramethyl substituted diphenyl  readily undergoes 100% dehydration in the presence of PBr_3 or dry HI gas to give the corresponding  He replaced the H .

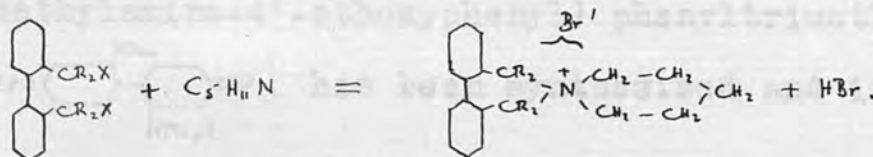
(3) The bromo compound  is extremely labile; with most common solvents it forms deliquescent solutions in which hydrolysis proceeds.

(4) The bromination of 2:2'-dicyclohexyl diphenyl does not proceed smoothly in acetic acid or in chloroform solution.

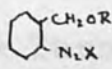
Two lines of investigation have been followed: I on the mechanical aspect and II on the electrical aspect of diphenyl dynamics.

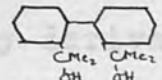
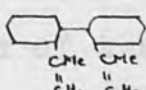
I An attempt has been made to synthesise a 2:2'-hetero-spiro-cyclo derivative of diphenyl with a view to determining the configuration adopted by the spirocyclo chain. The preparation of halides of the type  has been examined, as it

seemed probable that they would undergo ring formation with piperidine:-

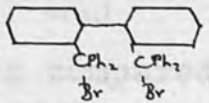


A suitable halide could not be obtained. It was found in the course of investigations that :-

(1) Compounds of the type  do not react with potassium iodide to give an iodo compound, complex intermolecular compounds of high m.p. are formed.

(2) The tetramethyl tolylene glycol  readily undergoes 100% dehydration in the presence of PBr3 or dry HCl gas to give the hydrocarbon .

No replacement occurs.

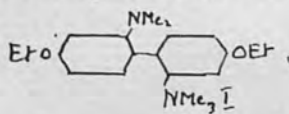
(3) The bromo-derivative, , is extremely labile; with most common solvents it forms deliquescent solutions in which hydrolysis proceeds.

(4) The bromination of 2:2'-diacetyl diphenyl does not proceed smoothly in acetic acid or in chloroform solution.

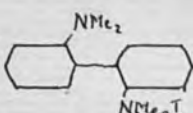
Replacement of the enol group seems to occur, higher bromo-derivatives are formed.

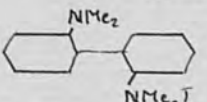
(5) 6-bromopiperonal undergoes autoreduction in the presence of copper bronze in an atmosphere of carbon dioxide, piperonal being formed.

It was concluded that a great deal of preliminary work was needed on the chemistry of 2:2'-substituents themselves, before the synthesis of a spiro-cyclo compound could be completed.

II 5-Ethoxy-2-(2'-dimethylamino-4'-ethoxyphenyl) phenyltrimethylammonium iodide,  has been synthesised and its

optical resolution attempted. It was thought that a comparison of some of its dynamic properties with those of its analogue

 resolved by Shaw & Turner, might lead to some interesting conclusions as to the influence of polarity on optical stability. The d-camphorsulphonate and d-bromocamphorsulphonate of the ethoxy derivative both showed almost constant rotation.

The rates of racemisation of the d.d-camphorsulphonate of the unsubstituted compound, , have been determined in

various solvents, and have been compared with those of the d-iodide in aqueous solution at three temperatures. Values for the energy of activation of both molecules have been calculated. The d-benzenesulphonate has been prepared and its rate of racemisation compared with that of the d-iodide and of the d.d-camphorsulphonate.