S T U D I E S I N

A S Y M M E T R I C T R A N S F O R M A T I O N

A N D

A S Y M M E T R I C S O L V E N T A C T I O N.

A THESIS

Presented by

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SUMMARY

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A number of compounds, which might be expected to be unstably asymmetric, have been prepared with a view to the examination of their behaviour in asymmetric solvents.

5-Substituted derivatives of N-acetyl-N-alkyl-2-amino-4'-methyldiphenylsulphone have been shown to undergo both first and second order asymmetric transformations in ethyl d-tartrate solution, and it has been possible to compare the relative optical stabilities of these compounds, which could not have been resolved in any other way. When the 5-substituent was lacking or was transferred to the 4 position no transformations occurred. Asymmetric derivatives of N-benzoyldiphenylamine have also been shown to undergo asymmetric transformations in ethyl d-tartrate.

Potentially optically active carbonyl compounds, which might have been expected to undergo asymmetric transformations via inactive tautomers, have been examined. Except in one case no evidence of such a compound undergoing an asymmetric transformation in an optically active solvent has been obtained.

The conditions governing the potential asymmetry of derivatives of cyclooctatetraene are discussed and attempts to synthesise such derivatives described. Resolution of a compound owing its asymmetry to the presence of a cyclooctatetraene ring has not been achieved.

4:5-Dimethylbenzcinnoline has been shown to exhibit stereoisomerism

of the 4:5-dimethylphenanthrene type, since its d-camphorsulphonate undergoes a first order transformation in chloroform solution. Dimethylbenzcinnoline itself has not been shown to undergo an asymmetric transformation in an asymmetric solvent.

T A B L E O F C O N T E N T S

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This research had as its primary object the investigation of the possibility of asymmetric transformations taking place in asymmetric solvents.

It is, of course, known that two enantiomorphs cannot be separated by any of the normal processes of separation such as crystallisation, distillation or chromatographic adsorption. The question then arises, what if the medium of separation, that is the solvent in a crystallisation, be itself asymmetric ? In this connection may be noted the resolutions by adsorption on an asymmetric adsopbent which have been reported by Rule (1), and the resolution of Tröger's base by Prelog and Wieland which forms a very successful application of this technique (2).

Several workers have investigated the possibility of separating enantiomorphs by means of an asymmetric solvent, but without success. Tolloczo partitioned r-mandelic acid between ether and an aqueous solution of fructose, and racemic acid between water and l-amyl alcohol. No separation occurred in either case (3). Goldschmidt and Cooper found the solubilities of d and l carvoxime in d-limonene to be the same (4). Cooper also found the solubility curves of sodium ammonium d and l tartrates in dextrose solution to be the same. Schroer dissolved r-mandelic acid in d-carvone and fractionally extracted with water. The acid recovered in this way had a slight laevo rotation which, passing through zero, gradually changed into a dextro rotation. A similar effect in the opposite sense was observed when l-carvone was used.(5) Turner and Harris, discussing the previous work in this field, come to the conclusion that resolution by asymmetric solvent action

is unlikely (6).

Patterson and Buchanan (7) showed, by means of a series of density measurements, that, while the molecular solution volumes of a pair of enantiomorphs were identical, within the limits of experimental error, when measured in a symmetrical solvent, in an asymmetric solvent they differed by an amount outside the limits of possible error. This indicated some difference in the behaviour of an asymmetric solvent towards each of a pair of enantiomorphs and such a difference might extend to the relative stabilities or solubilities of optically unstable enantiomorphs in such a solvent. Though the earlier work referred to had indicated that these solvent effects were so small as to render impracticable resolutions by asymmetric solvent action, the possibility remained that optically active optically unstable compounds, such as are capable of undergoing asymmetric transformations under appropriate conditions, might undergo such transformations in asymmetric solvents.

The phenomenon of asymmetric transformation is observed with readily racemisable compounds, when ready interconversion of the d and l forms may occur. If, say, an optically active optically unstable (racemic) acid is converted to its salt with a dextro rotatory optically stable base, the two diastereoisomers are produced initially in equal amounts: d-base.d-acid and d-base.l-acid. These two compounds may not, however, be equally stable in the given solvent and then the less stable form will undergo conversion to the more stable, the solution will mutarotate and an equilibrium mixture be produced containing an excess of the d-acid salt or the l-acid salt as the case may be. Such a conversion when taking place in one phase is known as a " First Order Asymmetric Transformation ", (cf. Jamison and Turner, 8). Should the

solution of the salt deposit crystals then these may contain an excess of one diastereoisomer, since the solubilities of the two may differ. In this case where two phases are involved the phenomenon is described as a "Second Order Asymmetric Transformation". Second order transformations are distinguished from resolutions by the fact that interconversion of the diastereoisomers takes place: an equilibrium exists in solution,

$$\underline{d}\text{-base}.\underline{d}\text{-acid} \rightleftharpoons \underline{d}\text{-base}.\underline{l}\text{-acid}$$

removal of some of one component (by crystallisation) displaces the equilibrium so that more of the less soluble isomer is produced. Experimentally a second order transformation may be characterised by the isolation of one pure diastereoisomer in more than 50 % yield, or by isolation of successive crops of the salt all possessing the same rotation and yielding optically active acid on decomposition. For conclusive proof that a transformation has taken place removal of the stably asymmetric compound is necessary, though, in the absence of this, other evidence such as mutarotation of the recrystallised salt in another solvent may be considered.

These phemonena have been observed mainly with compounds owing their asymmetry to restricted rotation, such as some ortho substituted diphenyl derivatives, N-benzoyl diphenylamines and other similar compounds. They have also been observed in the cases of compounds where racemisation occurs via an optically inactive tautomer.(cf. Jamison, 9. Harris and Turner, 10).

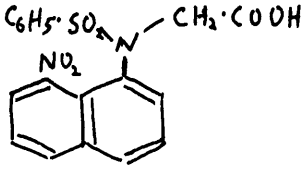
It was thought that such compounds might undergo such transformations in asymmetric solvents.

To test this possibility numbers of optically active, easily racemisable compounds, suitable for asymmetric transformations, were required for examination, and as a secondary object of this research attempts have been made to prepare compounds whose resolution, if achieved, would be of interest in other branches of stereochemistry.

Four classes of compounds have been investigated: compounds owing their asymmetry to restricted rotation, compounds racemising by a mechanism involving tautomeric change, derivatives of cyclooctatetraene, and compounds of the 4:5-dimethylphenanthrene type.

The asymmetric solvent employed most generally was ethyl d-tartrate which, apart from its ready availability, possessed several advantages. It is a most powerful solvent; a large variety of compounds of most diverse type dissolved in it, including the sodium salts of sulphonic acids. Owing to the fact that it is water soluble its removal from solid materials after recrystallisation was a matter of extreme ease, while water soluble compounds could be freed from it by extraction with ether.

Previously B. Douglas (11) had examined the behaviour of N-benzenesulphonyl-8-nitro-1-naphthylglycine (I) in various asymmetric solvents, but did not observe any asymmetric transformations.

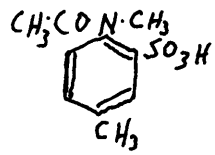


I

COMPOUNDS EXHIBITING RESTRICTED ROTATION

Benzene derivatives.

Mills and Kelham (12) resolved the sulphonic acid II via its brucine salt and found that both the brucine and sodium salts of the optically active acid racemised in solution.



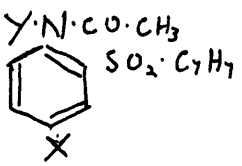
II

The asymmetry of the molecule is due to restricted rotation about the bond joining the nitrogen atom to the benzene ring, owing to the presence of the bulky ortho substituent.

The sodium salt of this acid was found to undergo a first order transformation in ethyl d-tartrate solution. No crystals separated from the solution but the material recovered by precipitation with ether was found to be laevo rotatory: the rotation rose to zero in aqueous solution. The rate of racemisation agreed well with that recorded by Mills, the observed half life period was 150 minutes at 18°c: Mills gives 175 minutes at 16°6°c and 70 minutes at 25°c. This compound underwent a second order transformation in d-sec. butyl alcohol. Almost all the material crystallised from the alcohol and was dextro rotatory. The observed rotations were much smaller than those observed by Mills, the specific rotations were + 0°3° (from d-sec. butyl alcohol) and - 0°4° (from ethyl d-tartrate). Mills measured rotations of about 6°.

The results obtained with sec. octyl alcohol were anomalous. Material recrystallised from l-sec. octyl alcohol was slightly laevo

rotatory, that recrystallised from the d-alcohol was optically inactive. It is possible that the rotation of the sample crystallised from the l- alcohol was due to chance preferential inoculation of the solution, though the experimental conditions rendered this unlikely.

III 

The related sulphone (III where X=Y=CH_3) was examined more extensively. It was prepared by a Witt rearrangement of N-p-toluenesulphonyl-N-methyl-p-toluidine (13), followed by acetylation of the aminosulphone produced. When recrystallised from ethyl d-tartrate the crystallisate was dextro rotatory, while the material remaining in the mother liquors, which could be precipitated by addition of water, was laevo rotatory; the specific rotations were of the order of one degree in each case. Both samples mutarotated in chloroform solution at room temperature, the half-life period being 19 minutes. When a sufficiently dilute solution of the sulphone in ethyl tartrate was allowed to stand at room temperature for a few hours so that no crystallisation occurred, the material in solution was found to be laevo rotatory. As this was the whole amount of the originally optically inactive sulphone a first order transformation must have occurred, while the activity of the material obtained by crystallisation was almost certainly due to a second order transformation. It is of interest to note that this compound obeys the Van't Hoff Dimroth relationship, which states that the less soluble form of the compound should also be the less stable.

In this case the less soluble is the dextro, present in excess in the crystallisate, while the more stable is the laevo, present in excess in solution.

With increase in temperature of the ethyl tartrate the activation effect decreases and is almost negligible at 84°c. This temperature effect was observed to apply to both first and second order transformations.

Effect of temperature change on degree of activation.
(First order transformations)

temperature of tartrate	specific rotation of sample
17°c	= - 1·0°
40°c	= - 0·5°
84°c	= - 0·1°

The value for 17° is the result of a single experiment (as are the values for the other temperatures quoted), but a considerable number of transformations were carried out at or about this temperature (ie. room temperature) with substantially agreeing results.

Experiments carried out at low temperatures gave no conclusive results. Samples of the sulphone in ethyl tartrate solution were maintained at 0° and at - 15° for several hours and the material recovered by precipitation with water. These samples were found to possess specific rotations varying from + 0·3° to - 0·7°. The explanation of these varying results is not known. Perhaps at very low temperatures the possibility of chance preferential crystallisation by inoculation is increased.

The results for second order transformations carried out at room temperature and at 84° confirm those shown above and are given in detail in the experimental section.

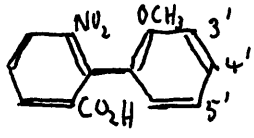
Experiments with this sulphone were also carried out in other asymmetric solvents. It was observed to undergo a second order transformation in l-menthyl acetate. No transformation was observed however when d or l sec. octyl alcohols were used as asymmetric solvents. The solubility of the sulphone in cold octyl alcohol is low and crystallisation took place rapidly, crystallisation of the sulphone from ethyl tartrate took two to three weeks. However crystallisation of the sulphone from menthyl acetate was also rapid so that it is difficult to say whether rate of crystallisation is an important factor.

The related N-ethyl sulphone (III where X = CH_3, Y = C_2H_5) has also been found to undergo both first and second order transformations in ethyl tartrate. As expected it was found to be optically much more stable than the N-methyl compound, having a half life period of about six hours as against nineteen minutes. This is of interest as showing that a compound of such relatively high optical stability is capable of undergoing asymmetric transformations in an asymmetric solvent.

These results showed that optical activation can be achieved by asymmetric solvent action. Moreover this method can be applied to compounds which lack a salt forming group and so cannot be resolved by the normal means. The compounds obtained, although not optically pure, have a sufficiently high rotatory power to allow observations to be made of their rates of racemisation and thus to compare the relative optical stabilities

of related compounds. It was decided to study a series of related sulphones and similar compounds in this way, in the hope that an example exhibiting a more complete activation effect might be obtained.

It has been shown by Adams and his school that, in the case of optically active diphenyl derivatives, substituents other than those actually involved in the steric interference can influence the optical stability of the compound (14, 15, 16). Adams investigated the series of compounds obtained when a substituent X is introduced into positions 3', 4', or 5' of the diphenyl molecule IV.



IV

He found that for each of the three series of compounds, 3', 4' and 5' the optical stability increases in the order

$$H < OCH_3 < CH_3 < Cl < Br < NO_2.$$

The stability of the 4' derivatives is somewhat less than that of the 5' and much less than that of the three 5', the chloro and bromo substituents had somewhat similar effects. The 4' nitro compound is anomalous in being more stable than the corresponding 5' compound.

A similar investigation was carried out on the sulphone type of molecule, the substituents Cl, Br, OCH_3 were successively introduced in place of the para methyl group (III where X = Cl, Br, OCH_3). These compounds were prepared by Witt rearrangement of the appropriate sulphonanilides. The yields varied from 100 % (X = CH_3) to 6 % (X = Br) under the optimum conditions for rearrangement. The N-methyl and N-ethyl

compounds were prepared in each case, though, owing to shortage of material and poor yields in the Witt rearrangement, the N-methyl p-bromo compound was not prepared in sufficient quantity for experiments with ethyl tartrate. The yields were invariably better with the N-ethyl compounds than the N-methyl.

Of these compounds all underwent first order transformations in ethyl tartrate and, with the single exception of the N-ethyl-p-chloro compound, all underwent second order transformations also. The optical stabilities may be arranged in decreasing order of magnitude:

$$OCH_3 > CH_3 > Cl > Br.$$

Relative optical stabilities of sulphones (compound III)

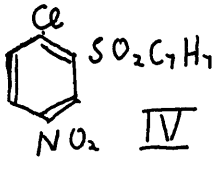
Substituent X	Y = CH_3	Y = C_2H_5
p-Br	——	30 min.
p- Cl	3 min.	120 min.
p- CH_3	19 min.	360 min.
p- OCH_3	41 min.	very slow.

Having regard to the small rotations being measured, these values must be regarded as only approximate, but they allow of the various compounds being arranged in order of increasing optical stability. It will be observed that the substituents fall into the same sequence as observed by Adams but that the order is reversed.

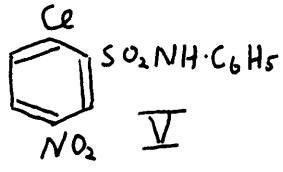
It was desired also to investigate the nitro substituted sulphone (III, X = NO_2), but no route leading successfully to its synthesis could be found.

N-p-Toluenesulphonyl-N-methyl-p-nitraniline did not undergo Witt rearrangement on treatment with sulphuric acid, but was hydrolysed to N-methyl-p-nitraniline. Nor did N-acetyl-N-methyl-p-nitraniline react with sulphuric acid to give N-methyl-p-nitraniline. Nor did N-acetyl-N-methyl-p-nitraniline react with hydrochloric acid to give N-methyl-p-nitraniline hydrochloride.

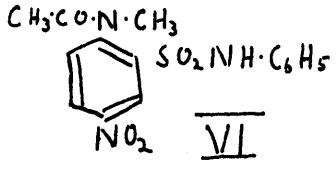
Attempts to prepare 2-chloro-5- nitro-4'-methyldiphenylsulphone (IV), hoping to convert it to the methylamino sulphone by reaction with alcoholic methylamine, were unsuccessful. 2-Chloro-5-nitrobenzenesulphonyl chloride did not react with toluene in the presence of aluminium chloride to produce any purifiable material, in the presence of stannic chloride no reaction whatever took place.



IV



V

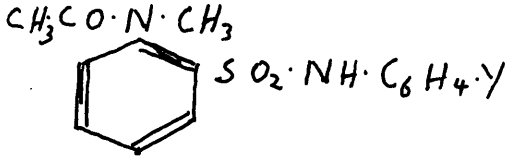


VI

The closely related compound 2-chloro-5-nitrobenzenesulphonanilide (V) was prepared and, on boiling with alcoholic methylamine carbonate followed by acetylation of the product, N-acetyl-N-methyl-2-amino-5-nitrobenzenesulphonanilide (VI) was formed. The steric effect of the sulphonanilide group should be similar to that of the sulphone group. The compound was crystallised from ethyl tartrate, the crystals which separated were optically inactive. The solubility of this compound in ethyl tartrate being low, insufficient material remained in the ethyl tartrate mother liquors for polarimetric examination. This compound was not, however, particularly suitable for such experiments as , owing to its low solubility in all solvents, only dilute solutions could be used for polarimeter readings when the very partial resolution generally by

obtained by crystallisation from ethyl tartrate might be overlooked.

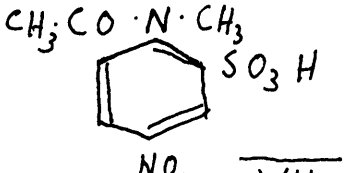
It was accordingly decided to prepare other similar compounds, with a view to obtaining one of higher solubility, and substituents were introduced into the anilide benzene ring (VIa where Y = o or p Cl, CH_3 or OCH_3). Of the six compounds prepared the o-chloro (Y = o-Cl) was selected as the most suitable. This compound was crystallised from ethyl tartrate, but no rotation was detected in the crystals which separated.



VI (a)

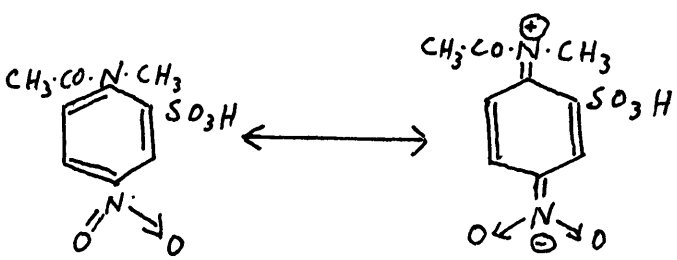
This evidence, however, does not allow of conclusions being drawn regarding the resolvability or optical stability of these nitro substituted sulphonanilides, since it is possible that these compounds, though unstably asymmetric, might fail to undergo asymmetric transformations in ethyl tartrate solution.

N-Acetyl-N-methyl-2-amino-5-nitrobenzenesulphonic acid (VII) was accordingly prepared by sulphonation of N-acetyl-N-methyl-p-nitraniline with chlorosulphonic acid, followed by acetylation of the sulphonation product.

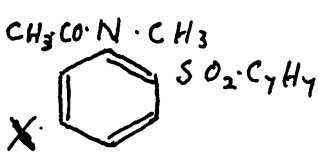


VII

Attempts were made to resolve it via both the brucine and quinidine salts. The brucine salt, which did not crystallise well, had an abnormally low rotation, but it did not mutarotate in solution. Decomposition of the brucine salt yielded an optically inactive sodium salt. The quinidine salt crystallised well, but underwent no change in specific rotation on crystallising from ethyl acetate. It did not mutarotate in solution and on decomposition yielded an optically inactive ammonium salt. Insofar as conclusions may be drawn from such negative evidence it seems that a nitro group para to the methylamino group destroys the asymmetry of the molecule, and it is possible to see how this might come about. Resonance could occur involving both the nitro and amino groups, but resonance can occur only in a planar structure and thus the additional stability produced by the resonance might overcome the steric resistance and favour the planar non - resolvable structure.



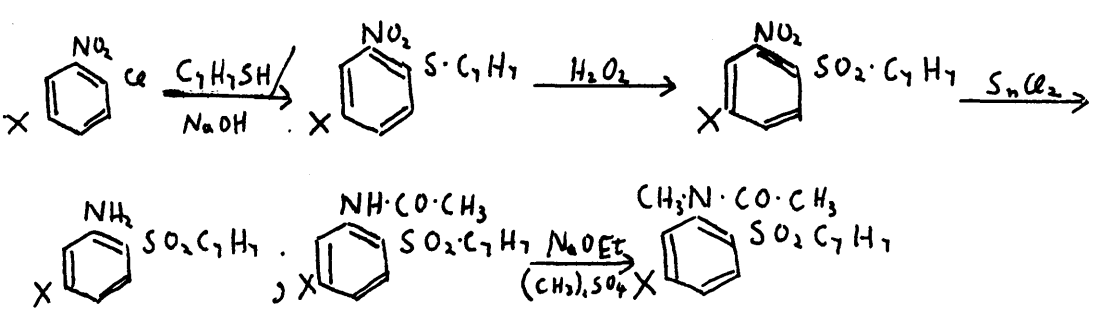
These studies were extended to N-acetyl-N-methyl-2-amino-4'-methyl-diphenylsulphone (VIII where X = H), and to a series of sulphones in which there is a substituent meta to the methylamino group (VIII where X = Br, Cl, CH_3, OCH_3).



VIII

The possibility of preparing these compounds by Witt rearrangement of the appropriately substituted sulphonanilides was considered. In the cases of these compounds which have no substituent para to the amino group there is a possibility that rearrangement might produce a para aminosulphone instead of an ortho. Witt stated that in the case of the p-toluenesulphonyl derivative of N-ethyl-o-toluidine the rearrangement product was the para sulphone, but he produced no proof of this assertion (17). Halberkaan claimed that rearrangement of the p-toluenesulphonyl derivatives of diphenylamine and of phenyl-p-tolylamine gave rise to o-aminosulphones (18). The p-toluenesulphonyl derivatives of N-methyl-m-toluidine and N-ethyl-m-chloraniline were accordingly prepared and treated with concentrated sulphuric acid, no rearrangement products were obtained however, the only action being hydrolysis of the amide linkage. From the p-toluenesulphonyl derivative of N-methylaniline a very small yield of a sulphone was obtained; as this was proved to be different from the o-aminosulphone, prepared by a different route, it was presumably the para rearrangement product.

These compounds were all obtained by the route outlined below.



The starting materials for these syntheses were readily prepared. Where X = Cl or Br they were obtained by nitration of the p-dihalogeno compounds, in the other cases by nitration of the appropriately substituted aniline, followed by a Sandmeyer reaction. The only notable feature of the synthesis is the methylation of the substituted acetanilides by means of alcoholic sodium ethoxide and dimethyl sulphate; normally acetanilides form sodio derivatives by reaction with sodium in an inert solvent. The enhanced acidity of these compounds is due to the presence of the o-sulphonyl group, they are in fact the vinylogues of sulphonamides. This series of reactions was used satisfactorily to prepare the compounds where X = H, Cl, Br, CH_3 and OCH_3 (VIII).

With the exception of the latter compound which was difficult to purify and tended to separate from solution as an oil, these sulphones were all examined in ethyl tartrate solution. The unsubstituted compound (X = H) crystallised from solution, neither the crystals nor the material remaining in the mother liquors were optically active. None of the other compounds crystallised from solution in ethyl tartrate; in no case did the material recovered from the ethyl tartrate by precipitation with water possess any rotation.

These observations were most surprising, having regard to the very consistent results obtained with the closely related para substituted sulphones, and a satisfactory explanation hard to find. It seems unlikely that the shift of the substituent from one position in the benzene ring to the adjacent one could alter the optical stability or resolvability of the compound very profoundly. Moreover it was observed that

compounds of widely differing optical stability will undergo asymmetric transformations in ethyl tartrate, as witness the N-methyl and N-ethyl substituted sulphones. The explanation may lie in the physical properties of these compounds. The unsubstituted and meta substituted sulphones are much more soluble in common solvents than the para substituted compounds and display a great tendency to form supersaturated solutions, the most extreme case being that of the m-chloro compound, solutions of which in acetic acid remained supersaturated for up to two days , crystallising rapidly on inoculation with a crystal of the sulphone. With one exception they did not crystallise from ethyl tartrate and had to be precipitated with water the solute separating first as an oil which solidified on more or less prolonged standing. In these circumstances racemisation of the sulphone might have taken place in the fluid state after removal of the ethyl tartrate, while chance preferential inoculation of the oil could have influenced the composition of the recovered material. Of these two explanations the former is the more probable.

A further member of this series of compounds was prepared, N-acetyl-N-methyl-2-amino-4-nitro-4'-methyldiphenylsulphone (VIII where X = NO_2). As starting material for the preparation of this compound 2-chloro-5-nitroaniline was required. The preparation of this by nitration of o-chloraniline sulphate has been described (19), and also by reduction of 2:4-dinitrochlorobenzene with the theoretical quantity of stannous chloride (Claus and Stiebel, 20). Neither of these methods was found to possess any preparative value. In the first

case, nitration of o-chloraniline with the theoretical quantity of nitric acid in the presence of a large excess of sulphuric acid yielded, apart from unreacted starting material, a compound, sparingly soluble in alcohol, whose melting point (153°) showed it to be most probably a dinitrochloraniline, and also 2-chloro-6-nitraniline (MP 76°). There was left in the mother liquors after the crystallisation of these compounds a mixture of solid products which could not conveniently be separated.

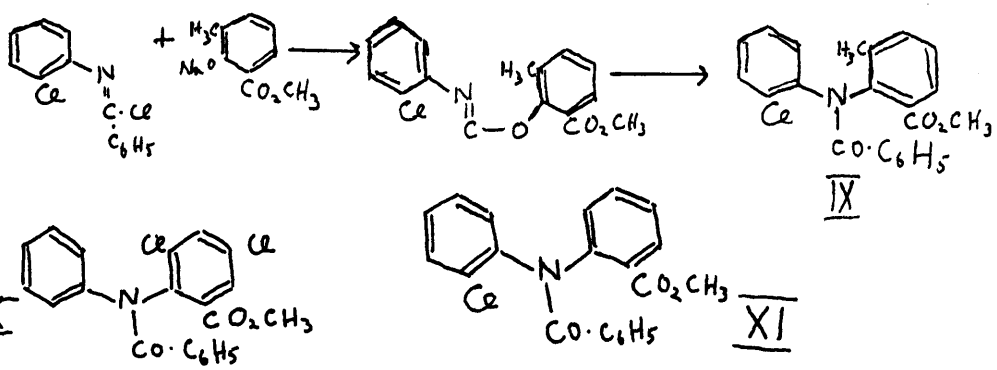
The reaction between stannous chloride and dinitrochlorobenzene was extremely vigorous and, even when moderated by external cooling, the product formed a complex brown mixture which could not be purified.

This compound was finally satisfactorily prepared by nitration of N-(2-chlorophenyl)-phthalimide to give N-(2-chloro-5-nitrophenyl)-phthalimide. This gave, on hydrolysis with aqueous sodium hydroxide, the required 2-chloro-5-nitroaniline free from any isomers. The acetyl derivative of the amine was condensed with sodium p-thiocresate to give a thioether which on oxidation with hydrogen peroxide in acetic acid gave a sulphone. This sulphone could not be methylated, however, owing to its sensitivity to alcoholic sodium ethoxide. The p-toluenesulphonyl derivative of 2-chloro-5-nitroaniline was methylated with dimethyl sulphate and sodium hydroxide, and the methyl derivative hydrolysed to give 2-chloro-5-nitro-N-methylaniline, the melting point found for this compound was substantially higher than that quoted in the literature. The acetyl derivative of this amine was converted to a thioether with sodium p-thiocresate, and this, on oxidation with hydrogen peroxide,

gave the required N-acetyl-N-methyl-2-amino-4-nitro-4'-methyl-diphenylsulphone. This compound, which did not display the same tendency to form supersaturated solutions as the other meta substituted sulphones, was crystallised from ethyl tartrate: both the crystals which separated and the material recovered from the mother liquors were optically inactive.

Derivatives of N-benzoyldiphenylamine.

Also belonging to the class of compounds owing their asymmetry to restricted rotation are the ortho substituted N-benzoyldiphenylamines, compounds of low optical stability investigated by Turner and his school (21). Three compounds of this type were prepared (IX, X and XI) . The method of preparation was that employed by Turner.



The acids corresponding to the first two of these esters have been resolved by Turner who measured their rates of racemisation. Both these esters were observed to undergo both first and second order transformations in ethyl d-tartrate. The rotation of the product of the first order transformation of IX was the largest observed in the course of this research ($[\alpha]_{5461} = -4{\cdot}4^{\circ}$). The

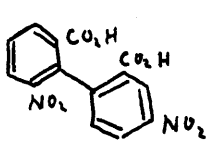
observed rates of racemisation of these esters corresponded fairly satisfactorily with those recorded by Turner for the acids.

	Half life period		Half life period
Acid IX	10·5 min.	Ester IX	8 min.
Acid X	4·6 min.	Ester X	5 min.

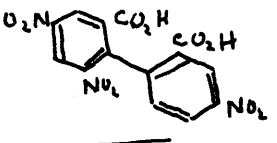
The third ester (XI) was observed to undergo a first order transformation but not a second order transformation. When the compound crystallised from ethyl tartrate the crystals which separated were optically inactive, but the material remaining in the mother liquors was laevo rotatory. When a dilute solution of the compound in ethyl tartrate was allowed to stand so that no crystallisation took place the material recovered from the solution by precipitation with water was laevo rotatory. It is difficult to say why this compound should not have undergone a second order transformation. It had been observed that, in the case of N-acetyl-N-methyl-2-amino-4':5-dimethyldiphenylsulphone, any vigorous agitation of the ethyl tartrate solution while filtering the crystals or any scratching of the walls of the containing vessel caused precipitation of laevo rotatory material along with the dextro rotatory crystals, thus obscuring the rotation of the material actually produced by crystallisation. It is possible that in this case also some form of co-precipitation obscures the effect of a possible second order transformation. The half life period of this compound was large compared with that of X (15 minutes as against 5 minutes). This is not very surprising

having regard to the observations made on the effect of substituents in the optically active sulphones and also that, of the two substituted diphenyls XII and XIII, the former racemises at about three times the rate of the latter (22).

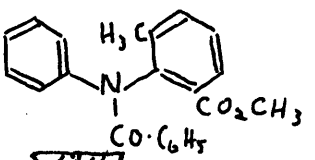
An attempt to prepare another of these compounds (XIV) was also made.



XII



XIII



XIV

The preparation of this compound was described by Turner, who demonstrated the asymmetry of the molecule by means of the addition curve technique; he found that the optical stability of the compound was of an extremely low order. It was thought to be desirable to see if a compound of such low optical ~~optica~~ stability could be obtained in optically active forms by crystallisation from an asymmetric solvent. The attempted preparation of this compound, however, was unsuccessful. The formation of the intermediate imino ether led to the isolation of a pale yellow oil instead of a crystalline solid. The same difficulty was experienced in the preparation of IX, but in that case the oily material, on heating for a while at 260° and trituration of the cooled product with methanol gave the required diphenylamine. Application of the same procedure to the preparation of XIV, however, met with no success, after heating to 260° and cooling the material remained a very viscous oil, extremely soluble in alcohol.

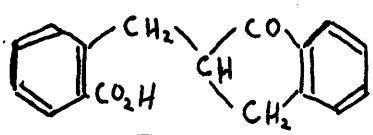
TAUTOMERIC COMPOUNDS

Keto-enol compounds

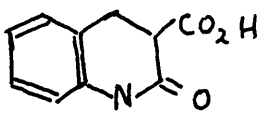
Should a compound exist in solution as an equilibrium mixture of two tautomers, one of which is asymmetric and the other symmetrical, then the optically active forms of the first compound will gradually racemise via the inactive tautomer.

$$\underline{d}\text{-RR'CH·CO·R''} \rightleftharpoons \text{RR'C:C(OH)·R''} \rightarrow \underline{l}\text{-RR'CH·CO·R''}$$

The equation illustrates the racemisation of an optically active ketone via the inactive enol form. Such a compound should be capable of undergoing asymmetric transformations. Only a few instances of this are recorded in the literature and most of the compounds in question were unsuitable for the purposes of the present work. Leuchs and Wutke (23) investigated two compounds of this type XV and XVI: of these the first is difficult to prepare and

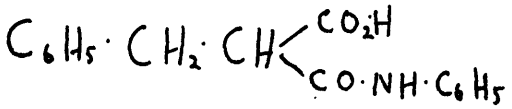


XV



XVI

the second of sparingly soluble. The latter consideration, as has been pointed out is important for the purposes of this work. More recently Turner (24) has shown that compounds of the malonoanilic acid type (XVII) undergo asymmetric transformations with optically active bases, these compounds being readily obtainable and of suitable physical properties.



XVII

One of these compounds, benzylmalono-o-toluidic acid, was prepared and recrystallised from ethyl tartrate. The material which crystallised was laevo rotatory, no mutarotation occurred in alcoholic solution but the rotation disappeared on the addition of alcoholic alkali. These observations are in accord with Turner's findings. No polarimetric measurements could be made on the material recovered from the ethyl tartrate mother liquors owing to the presence of highly coloured impurities.

On the basis of Leuchs' and Wutke's observations on the substituted hydrindone XV it seemed possible that the hydrogen atom attached to a carbon atom adjacent to a single carbonyl group might be sufficiently mobile to permit of asymmetric transformations. An α-alkyldesoxybenzoin was thought to be a suitable compound for experiment and the α-benzyl compound was accordingly prepared.

When α-benzyldesoxybenzoin was crystallised from ethyl tartrate the crystals which separated were laevo rotatory but no mutarotation occurred in chloroform solution at room temperature. No mutarotation occurred on adding piperidine or a mixture of phenol and pyridine to the solution: these catalysts might have been expected to promote tautomeric change. The material recovered from the ethyl tartrate mother liquors, only a very small proportion of the benzyldesoxybenzoin originally used, the solubility of this compound in cold ethyl tartrate being low, was found to be very highly dextro rotatory ($[\alpha]_{5461} = +16°8°$). This material did not racemise in solution either.

Further investigation showed that on recrystallising the laevo rotatory material again from ethyl tartrate the laevo rotation was enhanced, the rotations of the material from successive crystallisations being: $[\alpha]^{17}$ = - 2°1°, - 2°3°, - 3°8°, - 5°2°, - 5°7°, - 5°7°, - 5°7°. While by combining the material recovered from the mother liquors of these crystallisations and again crystallising from ethyl tartrate a dextro rotatory fraction, specific rotation + 17°, was obtained. These results seemed to indicate the possibility of achieving a true resolution by asymmetric solvent action.

It was then found, however, that each of these highly active fractions of benzyldesoxybenzoin could itself be further separated, by crystallisation from alcohol, into two fractions, one of high specific rotation and the other of much lower rotation. Though this separation by crystallisation from alcohol was by no means complete it showed that the optically active material consisted of a highly optically active compound accompanied by a less active, or probably inactive, one. Elementary analysis of the optically active specimens demonstrated the presence of a more highly oxygenated compound than benzyldesoxybenzoin. As, owing to the small quantities involved, it was impossible to achieve other than a partial separation of these compounds by crystallisation, an attempt was made to separate them by chromatography on a column of alumina, following the process polarimetrically. No separation took place. Attempts to separate and identify the optically active components of these mixtures were not prosecuted further.

It seemed obvious that some reaction occurred between the benzyldesoxybenzoin and the ethyl tartrate, or, possibly, with some impurity in the latter since it was observed that the magnitudes of the observed rotations depended on the sample of ethyl tartrate being used. In one case a rotation of - 20° was observed, in another an even more prolonged series of crystallisations failed to lower the rotation beyond - 5·7°. In the absence of any evidence as to the structure of this optically active compound it is impossible to speculate as to whether the separation, by crystallisation from ethyl tartrate, of two fractions of opposing sign of rotation may be regarded as a resolution, but, in view of the findings of other workers in this field, it seems highly improbable.

While these investigations were still in progress, and the possibility of a resolution having been achieved still under consideration, experiments were made to determine to what extent such phenomena were peculiar to the molecular structure of benzyldesoxybenzoin. It was decided to investigate two types of structure largely similar to benzyldesoxybenzoin, but differing in certain features (XVIII and XIX).

$C_6H_5 \cdot CO \cdot CHR' \cdot C_6H_5$ (XVIII) and $C_6H_5 \cdot CO \cdot CH_2 \cdot CHR \cdot C_6H_5$ (XIX)

In the first of these structures the desoxybenzoin structure is retained with the asymmetric carbon atom adjacent to the keto group, but there is no longer a mobile hydrogen atom to form part of a keto - enol system. In the second a keto - enol system still

exists but a methylene group is interposed between the asymmetric carbon atom and the carbonyl group.

The experimental difficulties encountered in the preparation of a compound of type XVIII proved insuperable. Alkylation of a monoalkyldesoxybenzoin is almost impossible (25), and it was found to be impossible to introduce an alkyl group into α-cyanodesoxybenzoin, in which the hydrogen atom to be replaced should be activated by both the carbonyl and nitrile groups.

Attempts to prepare methylethylphenylacetic acid, from which a ketone of the required type should be obtainable by Friedel and Crafts reaction, were unsuccessful. Methylethylphenyl carbinol on treatment with hydrogen chloride gave only an unstable halogen compound which readily lost hydrogen chloride to give α,β-dimethyl-styrene on treatment with aqueous alcoholic potassium cyanide. Attempts to convert this halide to the required acid by Reichstein's method for the preparation of tertiary acids (26) was also unsuccessful, as no simple product could be isolated from the reaction between it and methyl 2-furoate in the presence of aluminium chloride.

Benzylphenyl-p-tolylacetonitrile was readily prepared from phenyl-p-tolylacetic acid but this nitrile could not be hydrolysed to the acid, nor did it undergo alcoholysis to the corresponding ester.

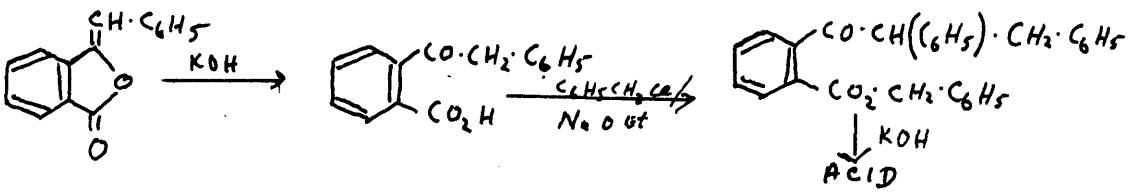
Three compounds of type XIX were prepared and examined. Attempts to prepare compounds of this type by reaction between chalkone and

Grignard reagents failed. Kohler (27) claimed that Grignard complexes add to the 1:4 positions of the conjugated unsaturated system of chalkone (benzylideneacetophenone) producing ketones of type XIX. On attempting to repeat his experiments using the Grignard reagents obtained from methyl iodide, ethyl bromide, p-bromotoluene and benzyl chloride no solid product was obtained in any case. On attempting to distil the yellow oils produced, considerable decomposition took place with darkening and evolution of water. This behaviour seemed more characteristic of the unsaturated carbinols which would have been produced by 1:2 addition of the Grignard reagent to the chalkone and it was thought that these must indeed have been the main products of the reaction.

β-Phenyl-β-9-fluorenylpropiophenone (XIX where R = 9-fluorenyl) was prepared by Michael addition of fluorene to chalkone in the presence of a pyridine catalyst. β-Methyl-β-phenylpropiophenone (XIX where R = CH_3) was prepared by hydrogenation of dypnone over a palladium black catalyst. β-Phenyl-β-p-tolylpropiophenone was prepared by addition of toluene to chalkone in the presence of 96 % sulphuric acid. These compounds were all crystallised from ethyl d-tartrate but in no case was any rotation detected in the crystals which separated or in the materials recovered from the mother liquors.

In view of these results it was considered advisable to synthesise and resolve in the normal fashion an acid more nearly resembling benzyldesoxybenzoin than the substituted hydrindone of Leuchs and

Wutke. α-Benzyldesoxybenzoin-2-carboxylic acid was accordingly synthesised by the route indicated: the 3-benzalphthalide required for the synthesis was readily obtained from phthalic anhydride and phenylacetic acid.



This acid formed a brucine salt from which, after four crystallisations from ethyl acetate, the l-base.d-acid was isolated, $[\alpha]_{5461}^{20} = -12{\cdot}1°$. On treatment with hydrochloric acid the d-acid was produced, $[\alpha]_{5461}^{19} = +27{\cdot}5°$. This acid did not racemise in chloroform solution at room temperature, as did that of Leuchs and Wutke. It racemised slowly, however, on crystallising from hot acetic acid, it also racemised in hot aqueous alcoholic alkali. Esterification of the active acid with diazomethane produced the d-methyl ester, $[\alpha]_{5461}^{21} = +29{\cdot}3°$ This ester was refluxed in alcoholic solution for 48 hours, the recovered ester had rotation $[\alpha]_{5461}^{21} = +31{\cdot}8°$, showing that no racemisation had occurred. The increase in rotation of the ester was presumed to be due to some purification effected in the course of the attempted racemisation.

This result is rather difficult to reconcile with Leuchs' and Wutke's claims, but it indicates that benzyldesoxybenzoin itself would be unlikely to undergo an asymmetric transformation.

Optically inactive methyl α-benzyldesoxybenzoin-2-carboxylate was

crystallised from ethyl d-tartrate solution. Almost all the ester separated from the solution: the crystals showed no rotation.

Hoping that the replacement of the α-benzyl group by some activating group might increase the mobility of the hydrogen atom attached to the asymmetric carbon atom, and thus produce a compound capable of undergoing asymmetric transformations, phenylbenzoyl - acetic ester (XX) was prepared and crystallised from ethyl tartrate solution. On some occasions the crystals which separated were laevo rotatory, no mutarotation occurred, however, in chloroform or acetonitrile solution at room temperature. Sometimes under apparently identical conditions no optical activity was detected in the recrystallised material.

$C_6H_5 \cdot CO \cdot CH(CO_2C_2H_5) \cdot C_6H_5$
XX

$R \cdot CO \cdot CH(CO \cdot R') \cdot CO \cdot R''$
XXI

In search of tautomeric compounds capable of undergoing asymmetric transformations it was decided to investigate triacyl - methanes of the type XXI.

The first compound of this type which was examined was benzoyl-p-toluylacetone (XXI where R = C_6H_5, R' = CH_3 and R" = $C_6H_4 \cdot CH_3$). This was prepared from benzoylacetone and p-toluyl chloride. Dibenzoylacetone occurs in three forms, the triketo, the diketo - enol and another very unstable form which was stated by Michael to be also a triketone (28). The triketo form is the

most stable, on treatment with alkali it is converted to the diketo - enol but on crystallisation this tends to revert to the triketo form. The benzoyl-p-toluylacetone was crystallised from ethyl d-tartrate. Decomposition of the compound or reaction with the ethyl tartrate seemed to occur, for the crystals which separated were badly discoloured while addition of water to the mother liquors produced a viscous oil which crystallised only slowly. No rotation was detected in the crystals or in the material recovered from the mother liquors.

It was therefore decided to prepare a triacylmethane in which all the acyl groups should be aroyl groups, in the hope that it would be more stable, and crystallise better than the benzoyl-p-toluylacetone. Tribenzoylmethane has been investigated by Abell (29). It exists as both triketo and diketo - enolic forms, the latter is unstable and passes into the former on recrystallisation. The compound exists in solution to a small extent as the diketo - enolic form. Benzoyl-p-toluylmethane was prepared from ethyl benzoate and p-methylacetophenone, also from ethyl p-toluate and acetophenone , the melting point agreed with that reported by Weygand who prepared it by a different route via its isomeric O - methyl ethers, (30).

The reaction between benzoyl-p-toluylmethane and α-naphthoyl chloride is, however, exceedingly complex and the products have not been identified. The diketone forms a sodio derivative with a suspension of sodium in ether. On treating this with α-naphthoyl

chloride two neutral, highly crystalline products result. As they are neutral they are obviously neither of them the desired triacyl - methane. Their analyses correspond best with the following empirical formulae:

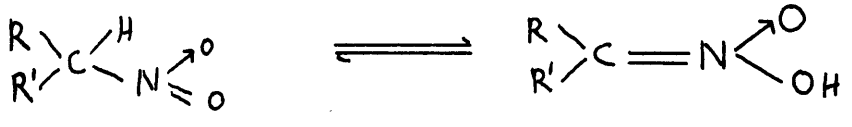
compound A: white prisms from dioxan, MP 148°; $C_{22}H_{14}O_3$;

compound B: white needles from benzene, MP 160°; $C_{22}H_{16}O_4$.

On reaction with alcoholic sodium ethoxide and α-naphthoyl chloride the benzoyl-p-toluylmethane was recovered almost entirely unchanged, only traces of another acidic compound, MP 143°, being obtained. The quantity of this latter was insufficient for analysis and it was not, therefore, further investigated.

Nitro aci-nitro compounds.

Another tautomeric system, which, in suitable optically active compounds, might cause them to undergo asymmetric transformations, is the nitro aci-nitro system.



No compounds of this type have previously been shown to undergo asymmetric transformations. One of the difficulties likely to be encountered was the fact that many otherwise suitable compounds are somewhat unstable, while aliphatic nitro compounds are in general rather low melting solids or oils, so that the hydrocarbon residues R, R' would have to be of fairly high molecular weight.

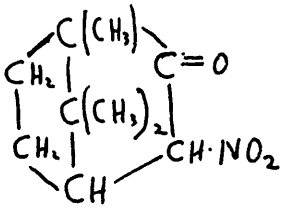
Only one nitro compound was examined, α,β-dinitrodibenzyl, which has been shown to exist in two isomeric forms, one MP 235° and the other MP 152°, (31). This compound contains two asymmetric carbon atoms and one of these isomers will be the racemic form of the compound and the other the meso. No means of distinguishing them exists, since, lacking any salt forming group, no method of resolution, other than asymmetric solvent action, is applicable. It was hoped that the racemic form might undergo an asymmetric transformation in ethyl d-tartrate, while there was a possibility that the meso form might undergo partial conversion to its isomer under the influence of the ethyl tartrate.

The higher melting isomer crystallised rapidly from ethyl tartrate. In the first experiment the crystals were found to be laevo rotatory, mutarotation occurred at room temperature. A certain amount of decomposition of the dinitrodibenzyl had occurred, however, as shown by the evolution of nitrous fumes: it had been necessary to heat the dinitrodibenzyl and ethyl tartrate for rather a long time near the boiling point of the tartrate in order to bring the sparingly soluble nitro compound into solution. The experiment was repeated, care being taken to avoid any decomposition of the nitro compound, the crystals which separated were optically inactive . No rotation was detected in the crystals when the first crystals were allowed to separate at 86° (to permit of slow crystallisation). The rotation observed in the first instance was possibly due to chance preferential inoculation of the solution,

or to an asymmetric decomposition. All these samples melted at 235° there was no indication of conversion to the lower melting isomer.

When the other isomer was crystallised from ethyl tartrate there was no indication of any asymmetric transformation of of any conversion to the high melting isomer.

Attention was then turned to α-nitro-ketones. Compounds of this type should be suitable for asymmetric transformations when the carbon atom carrying the nitro group is asymmetric and has one hydrogen atom attached. Most of these compounds, unfortunately, are unstable, as for instance α-nitrodesoxybenzoin (32). α-Nitro-d-camphor, however, is known and is a fairly stable compound. It was therefore decided to prepare α-nitro-dl-camphor (XXII) and examine its behaviour in ethyl d-tartrate solution. This compound possesses three asymmetric carbon atoms, only that to which the nitro group is attached would be expected to be involved in an asymmetric transformation.



XXII

The method of synthesis was to form iso-nitroso-dl-camphor by treating dl-camphor with amyl nitrite in the presence of sodium, and then oxidise this with alkaline ferricyanide to the nitrocamphor. Iso-nitroso-d-camphor occurs in two forms, MP's 114° and 150°, the former passes into the latter on heating above its melting point.

On treating synthetic (dl) camphor with amyl nitrite and sodium a crystalline iso-nitroso compound, MP 111 - 114°, was obtained, this did not isomerise on heating above its melting point. On oxidation with potassium ferricyanide in aqueous potassium hydroxide a bulky white precipitate, presumably a peroxide, was initially obtained, and this decomposed gradually with evolution of a gas. These phenomena are entirely in accord with those recorded for the preparation of α-nitro-d-camphor. Subsequently there was obtained, however, only an acidic yellow oil which did not crystallise alone or in contact with various solvents.

DERIVATIVES OF CYCLOOCTATETRAENE

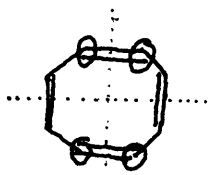
Cyclooctatetraene was first prepared by Willstatter from N-methylgranatenine (33). Its stability and general properties differed to such an extent from those of benzene that many workers rejected the eight membered ring formula and believed the compound to be a form of styrene. The compound has since been prepared from acetylene by controlled catalytic polymerisation and the identity of this preparation with Willstatter's compound proved (34).

The modern view of the structure of aromatic compounds is that the stability of the aromatic ring is due to resonance between all possible bond isomers. Now the benzene molecule is planar and strainless but a planar cyclooctatetraene molecule would be highly strained and it is believed that this molecule is in fact non - planar. As resonance is impossible in a non - planar structure the differences between cyclooctatetraene and aromatic compounds can thus be explained.

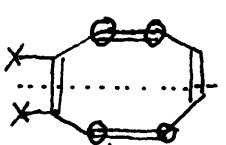
Experimental proof of the non - planarity of the cyclooctatetraene molecule has been supplied by Brockway, who carried out X -ray diffraction measurements on tetrabenzcyclooctatetraene, and showed the eight membered ring in this compound to be non - planar (35).

A suitably substituted cyclooctatetraene should therefore be asymmetric and potentially resolvable. There are several factors to be considered regarding the stereochemistry of cyclooctatetraenes.

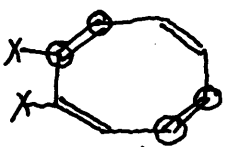
In the cyclooctatetraene molecule as shown the four carbon atoms enclosed by a circle may be regarded as lying in the plane of the paper, the other four lie in a plane parallel to that but slightly above or below it.



Any derivative of cyclooctatetraene with an uneven number of substituents, or an uneven number of any one substituting radical, will be asymmetric. When those compounds with an even number of substituents are considered the question of the position of the substituents with regard to the double bonds becomes important. If there is no resonance in a cyclooctatetraene ring there should exist two isometic adjacent disubstituted compounds.

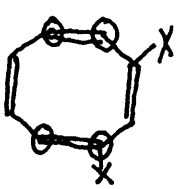


(a)

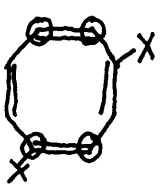


(b)

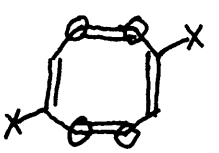
Of these (a) has a plane of symmetry as shown, (b) has none and should therefore be resolvable. Of the other four possible disubstituted cyclooctatetraenes (f) alone possesses a plane of symmetry.



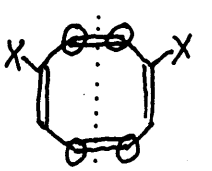
(c)



(d)

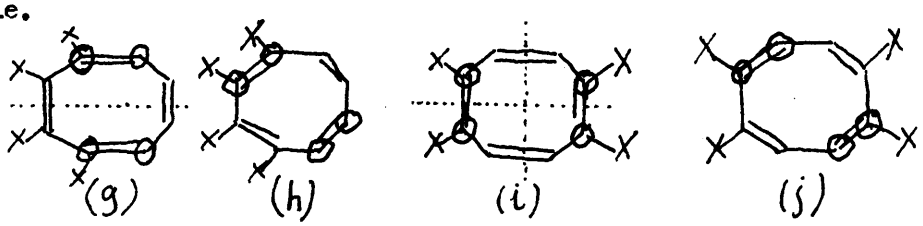


(e)



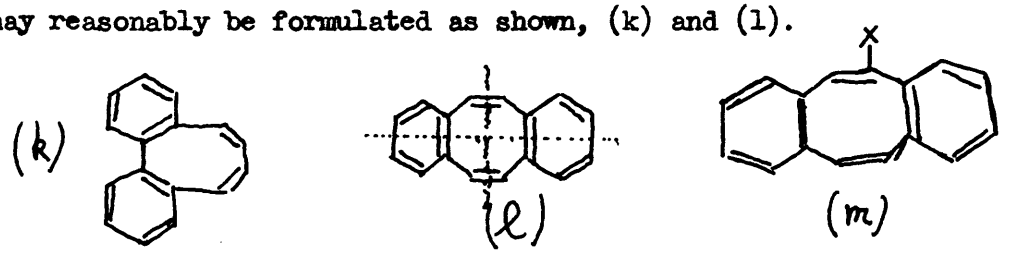
(d)

Of more immediate concern for the purposes of this work are the 1:2:3:4 and 1:2:5:6 tetrasubstituted cyclooctatetraenes, since the dibenzcyclooctatetraenes, which were used experimentally, fall into this class. A 1:2:3:4 tetrasubstituted cyclooctatetraene may exist in forms (g) or (h). Of these (g) has a plane of symmetry while (h) is resolvable.



Similarly there are two forms of a 1:2:5:6 tetrasubstituted compound of which the first (i) has two planes of symmetry while the second (j) is resolvable.

Coming now to the dibenzcyclooctatetraenes it seems probable that the fusion bonds of the molecule which are held in common by the benzene and octatetraene rings may be regarded from the point of view of the latter as double bonds, and that the two compounds may reasonably be formulated as shown, (k) and (l).

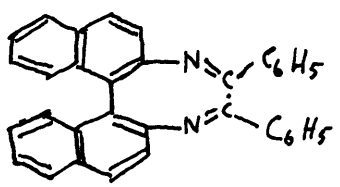


On the basis of these formulae 1:2:3:4-dibenzcyclooctatetraene and any of its derivatives should be asymmetric, but a derivative of 1:2:5:6-dibenzcyclooctatetraene would not be asymmetric unless asymmetrically substituted, as in (m).

Apart from the degree of fixation of the octatetraene double bonds

the most important factor is the rigidity of the eight membered ring. The carbon atoms need not necessarily be held firmly in one configuration, but might undergo an inversion of configuration, the ring passing temporarily through a planar arrangement. On the ease with which this inversion took place would depend whether such a compound would be capable of undergoing asymmetric transformations, or whether it would be resolvable at all. If the inversion were extremely rapid the net effect would be that of a planar ring.

The only analogous case of a compound containing an eight membered ring is that of the condensation product of benzil and 2:2'-diamino-1:1'-dinaphthyl. Kuhn and Goldfinger (36) condensed the optically active (dextro rotatory) base with benzil and obtained an optically active product (XXIII) which was optically stable.



XXIII

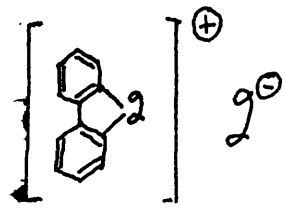
The demonstration of the asymmetry of this compound tells us little, however, regarding the configuration of a normal cyclooctatetraene ring since a non - planar configuration would be imposed on the molecule because of the steric interference of the hydrogen atoms in the peri positions of the naphthyl nuclei. It may be noted that this compound is of type (h) above and its existence in an optically active form confirms the conclusions already arrived at.

It was decided to attempt to prepare a derivative of cyclooctatetraene

and see if it would undergo asymmetric transformation. The benzcyclooctatetraenes, of which some are known, are more stable than the parent compound and more suitable as regards physical and chemical properties in general.

The first attempt was to prepare tetrabenzcyclooctatetraene (tetraphanylene), the formation of which from magnesium 2:2'-diphenylene dibromide has been described by Rapson and Shuttleworth (37). Attempts to repeat their work were, however, unsuccessful. 2:2'-Dibromodiphenyl was recovered unchanged even after refluxing with magnesium in dry ether for 72 hours, nor did attempts to prepare the Grignard complex in dry diamyl ether meet with any more success. It seems that some impurity in one of the reagents must have acted as an inhibitor.

As the Grignard reaction on 2:2'-dibromodiphenyl had failed, it was decided to explore the possibilities of the Ullmann reaction. Lothrop (38) had found that dibromodiphenyl is not dehalogenated by reaction with copper, but that it would react with cuprous oxide. By heating dibromodiphenyl,or better diphenylene-iodonium iodide (XXIV), with a large excess of cuprous oxide he obtained a

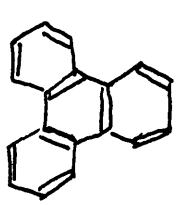
XXIV 

mixture from which he isolated diphenylene (dibenzcyclobutadiene). This compound was also obtained by Rapson and Shuttleworth as a by - product in the preparation of tetraphenylene.

Lothrop's experiments with diphenylene-iodonium iodide were repeated and it was found that under appropriate conditions a small amount of a compound corresponding to tetraphenylene could be isolated, accompanied by a large amount of 2:2'-diiododiphenyl, separation being effected by crystallisation from alcohol. This compound yielded a scarlet picrate MP 182°, probably identical with one (MP 175°) isolated but not further investigated by Lothrop. Rapson and Shuttleworth stated that tetraphenylene did not form a picrate.

Only a small yield of tetraphenylene could be obtained by this method, however, under a wide range of experimental conditions. Diphenylene was obtained in about the same yield as that claimed by Lothrop. It was attempted to prepare the Grignard complex from 2:2'-diiododiphenyl, hoping that this would prove more reactive than the corresponding dibromo compound. This was not the case, however, the diiododiphenyl was recovered unchanged after 48 hours refluxing with magnesium in dry ether.

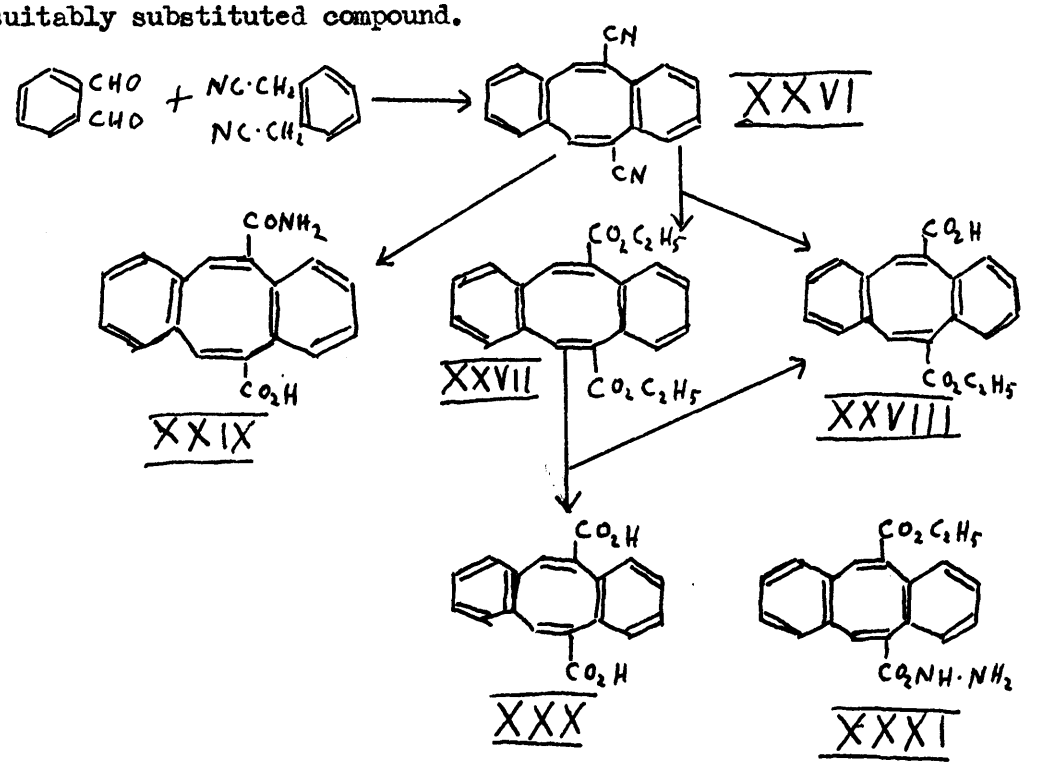
As a model experiment the Grignard reagent from o-dibromobenzene was prepared and treated with cupric chloride. A minute yield (about 1 %) of a substance corresponding in melting point and general properties with 9:10-benzphenanthrene (XXV) was obtained, accompanied by traces of diphenyl. The product of the reaction consisted almost entirely of resinous matter.



XXV

As the available amount of tetrabenzcyclooctatetraene was insufficient for further work, attention was turned to the dibenzcyclooctatetraenes.

Fieser and Pechet (39) prepared 1:2:5:6-dibenz-3:8-dicyano-cyclooctatetraene by condensing o-phthalaldehyde with o-phenylenediacetonitrile, and they described the preparation of several derivatives of this compound. Their work was repeated and the dinitrile (XXVI) obtained in good yield. As was pointed out above, however, a 1:2:5:6-dibenzcyclooctatetraene requires itself to be asymmetrically substituted before it becomes potentially resolvable, and great difficulty was experienced in obtaining a suitably substituted compound.



The half ester (XXVIII) was obtained in only a small yield, as a by - product in the preparation of the diester (XXVII). Attempts to increase the yield of the half ester during the alcoholysis of the dinitrile by employing aqueous alcohol, or to obtain it by partial hydrolysis of the diester were unsuccessful. In the latter case a little of XXVIII was produced along with some of the diacid (XXX). Attempts to prepare the half hydrazide (XXXI) by the method of Davidis (40) as used for dimethyl terephthalate were unsuccessful, XXVII failing to react with hydrazine hydrate.

The half amide (XXIX) was obtained in poor yield. Under the conditions described by Fieser and Pechet for its preparation the dinitrile was unaffected. Conditions were found, however, which produced a small amount of the desired compound. This compound formed a brucine salt, but no evidence of the asymmetry of the acid was obtained. The recrystallised salt did not mutarotate in solution and the recovered acid was optically inactive.

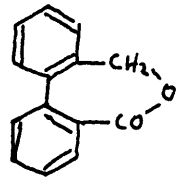
Attention was then turned to derivatives of 1:2:3:4-dibenzcyclooctatetraene. As reasoned above both this compound and all its derivatives should be asymmetric so that the difficulty of introducing the proper substituents does not arise.

Rapson and Shuttleworth (41) had tried unsuccessfully to prepare compounds of this type by condensing diphenyl-2:2'-dialdehyde with succinic acid and succindialdehyde: no reaction took place. It was thought that diphenyldialdehyde might possibly condense with an acitve methylene compound of greater reactivity than

those tried by Rapson and Shuttleworth, such as succinonitrile. Succinonitrile will condense with benzaldehyde in the presence of sodium ethoxide (42).

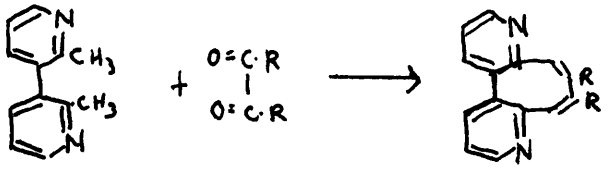
When a mixture of succinonitrile and diphenyldialdehyde was treated with sodium ethoxide, however, the only product isolated was the lactone XXXII, formed by an intramolecular Cannizzarro reaction of the aldehyde.

XXXII

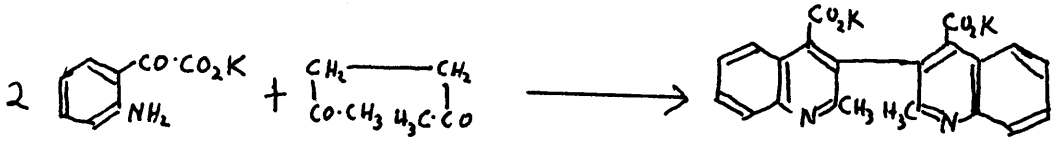


The use of other more weakly basic condensing agents, such as diethylamine or pyridine, was ineffectual: no reaction occurred. The use of acid catalysts was contemplated, but as a result of model experiments with benzaldehyde and succinonitrile using zinc chloride and acetic anhydride as condensing agents, when only hard resins were produced, the project was abandoned.

Another reaction which was considered to hold out the possibility of a practicable cyclooctatetraene synthesis was the reaction between an α or γ methyl pyridine or quinoline and an aldehyde, producing a styryl pyridine or quinoline. This reaction has been investigated Knoevenagel and others (45). A 2:2'-dimethyl-3:3'-dipyridyl might, by condensing with an α-diketone, produce a cyclooctatetraene.



Derivatives of 3:3'-dipyridyl are rather inaccessible, but 2:2'-dimethyl-3:3'-diquinolyl may be obtained from o-aminobenzaldehyde and acetonylacetone (44) and this compound was accordingly synthesised. Owing to the limited availability of o-nitro and o-aminobenzaldehyde an attempt was made to prepare the dimethyldiquinolyl via the corresponding γγ-dicarboxylic acid, obtained from acetonylacetone and isatin.



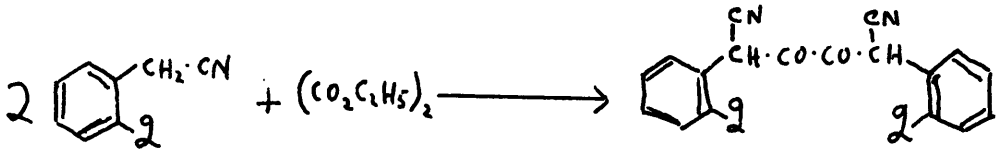
XXXIII

No pure product could be isolated from the action between isatin and acetonylacetone, no doubt owing to the sensitivity of the latter to the alkali in which the reaction was carried out, (45): but on refluxing an alkaline solution of acetonylacetone dioxime with isatin 2:2'-dimethyl-3:3'-diquinolyl-4:4'-dicarboxylic acid (XXXIII) was obtained. It proved to be a high melting solid, completely insoluble in all common solvents, which could be purified only via its potassium salt, which crystallised readily from water. The salt, however, decomposed somewhat on drying so that concordant analyses could not be obtained. The S-benzyl-thiuronium salt was readily prepared and purified and served to characterise the acid. This acid, however, unlike most α or γ quinolinic acids, was difficult to decarboxylate, possibly owing to the fact that the carboxyl groups are sterically hindered.

Using a copper chromite catalyst a very small yield of dimethyldiquinolyl was obtained. The acid could not be esterified by either the Fischer - Speier or the silver salt methods.

Attempts to condense dimethyldiquinolyl with benzil, and with 2-carbomethoxybenzil, using acetic anhydride as condensing agent were unsuccessful. Dark brown solids were obtained which could not be purified by crystallisation or chromatographic adsorption. The reaction was also attempted using zinc chloride as condensing agent whena similar result was produced. When no condensing agent, or when hydrochloric acid, was used no reaction took place.

Another route investigated was based on the condensation of diethyl oxalate and phenylacetonitrile (46). Diethyl oxalate will condense with benzyl cyanide to produce the dinitrile of diphenylketipinic acid, phenylacetic ester does not undergo this reaction as it more readily forms a self condensation product. It was intended to prepare diiododiphenylketipinicdinitrile (XXXIV) and cyclise this by an internal Ullmann reaction.

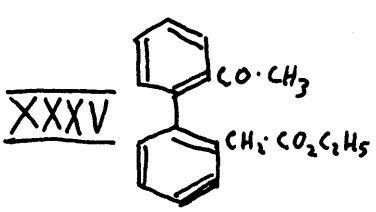


XXXIV

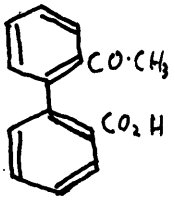
The dinitrile was obtained, but in such poor yield that the investigation was not pressed further.

A final attempt to prepare a 1:2:3:4-dibenzcyclooctatetraene was aimed at the synthesis of the intermediate XXXV, 2-acetyldiphenyl-

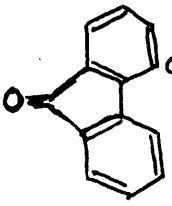
2'-acetic ester, which should on ring closure give a cyclooctadiene ring. Rapson and Shuttleworth (41) tried unsuccessfully to prepare this compound by the action of copper on a mixture of o-iodoacetophenone and o-iodophenylacetic ester.



XXXV



XXXVI



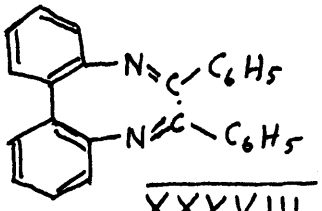
XXXVII

Diphenic anhydride was treated with dimethyl cadmium (cf. de Benneville, 47)to produce 2-acetyldiphenyl-2'-carboxylic acid,(XXXVI), which was obtained as a yellow oil which crystallised after about 7 days, it was characterised as its methyl ester and its structure confirmed by its cyclisation to 4-acetylfluorenone (XXXVII).

The acid chloride of XXXVI was very unstable , cyclising readily to the acetyl fluorenone, this behaviour being characteristic of this type of compound. The next stage of the projected synthesis was an Arndt Eistert reaction to produce the acetic acid XXXV. Though diazomethane reacts with keto groupings, successful Arndt Eistert syntheses have been carried out on keto acids (48). On treatment of the acid chloride of XXXV with excess diazomethane no solid diazoketone could be isolated. Attempts to convert the gums which were obtained to the ester or amide of XXXV were unsuccessful: only oils were produced which could not be hydrolysed to give any acid.

As, with one exception, all attempts to produce a potentially

resolvable cyclooctatetraene derivative had failed, it was decided to investigate one of the more easily obtained heterocyclic analogues, by attempting the resolution of the condensation product of benzil and 2:2'-diaminodiphenyl (XXXVIII). The work of Kuhn and Goldfinger on the related compound from 2:2'-diamino-1:1'-dinaphthyl has already been referred to. In the case of the diphenyl derivative there is no steric interference as there is with the dinaphthyl compound so that any asymmetry found in this molecule could be ascribed to the non - planar nature of the cyclooctatetraene ring.



XXXVIII

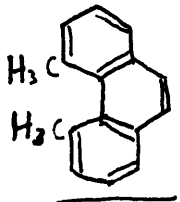
This compound, like all 1:2:3:4-dibenzcyclooctatetraenes, should be asymmetric without the need for any further substitution.

Benzil and diaminodiphenyl were readily condensed by refluxing in acetic acid containing a trace of hydrogen chloride. This method proved much superior to that described by Tauber (49), which consisted in fusing the constituents together at 160°.

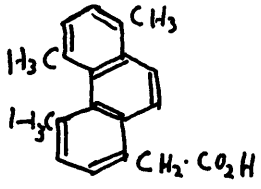
This compound was recrystallised from ethyl tartrate: the crystals which separated were optically inactive, insufficient material remained in the mother liquors for polarimetric examination.

DERIVATIVES OF 4:5-DIMETHYLPHENANTHRENE

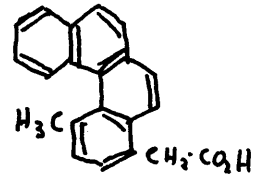
Finally some investigations were carried out on stereoisomerism of the 4:5-dimethylphenanthrene type. It has for a considerable number of years been realised that in a molecule such as 4:5-dimethylphenanthrene (XXXIX)there would be steric interference between the two methyl groups, and, indeed, some workers had considered that such a compound would be incapable of existence (50, 51). Such a compound, a dimethylchrysene, was,however, prepared by Newman (52), who later claimed the resolution of two derivatives of 4:5-dimethylphenanthrene, XL and XLI (53, 54). The experimental evidence in the case of the second of these compounds seemed to be not altogether satisfactory, but the asymmetry of the first molecule seems to be established.



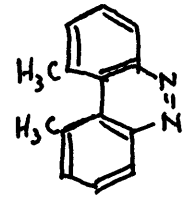
XXXIX



XL



XLI



XLII

The asymmetry of these compounds may be ascribed to distortion of the central six membered ring, or to distortion of the bonds joining the methyl groups to the phenanthrene nucleus. The latter explanation is to be preferred as the absorption spectra of these compounds definitely conform to the phenanthrene type (53).

Though Newman was apparently unaware of the fact, a similar investigation had previously been carried out on this subject by

Wittig and Stichnoth (55). They attempted to resolve 4:5-dimethylbenzcinnoline (XLII) via its salt with d-bromocamphorsulphonic acid, but failed to achieve a resolution. It is not apparent from their published results, however, whether these workers were expecting their compound to be optically stable, in which case they might have failed to detect any asymmetric transformations which might have occurred. Newman reported that XL racemised readily at room temperature.

Ritchie proposed to attempt the resolution of a derivative of 4:5-dimethylphenanthridine, but was unable to obtain suitable experimental material for this purpose (56).

In view of the doubt regarding the results of Wittig and Stichnoth it was considered to be profitable to reinvestigate dimethylbenzcinnoline. This compound, also, is somewhat more accessible than the phenanthrene. derivatives of Newman.

The dimethylbenzcinnoline was prepared by the method of Kenner (57), that is by reduction of 6:6'-dinitro-2:2'-ditolyl with sodium amalgam and alcohol. This was preferred to the electrolytic reduction of Wittig and Stichnoth as electrolytic reductions proceed only under carefully defined conditions which are sometimes difficult to reproduce.

An attempt to prepare the compound by reduction of dinitroditolyl with sodium sulphide to the corresponding azoxy compound, and reduction of the latter to the cyclic azo compound with the theoretical amount of stannous chloride was unsuccessful. The azoxy

compound was obtained, though purification was difficult as the compound was contaminated with unreacted starting material which was difficult to remove. Stannous chloride however reduced this substance to the corresponding diamine (cf. Ullmann, 58).

The possibility of preparing the compound by treating 6:6'-tetrazo-2:2'-ditolyl with sodium arsenite (cf. Sandin and Cairns, 59) was also investigated, intending to carry out the reaction with optically active diaminoditolyl. Bell (60) has shown that in reactions involving the replacement of the amino groups in optically active diaminoditolyl via the tetrazo compound the asymmetry is largely retained. The reaction, however, was unsuccessful, no dimethylbenzcinnoline could be isolated from the complex product obtained: this reaction would only have been of use, of course, had the dimethylbenzcinnoline been formed in a fair state of purity since any extensive process of purification might have resulted in the loss of any optical activity the material might have possessed.

Dimethylbenzcinnoline did not crystallise from ethyl tartrate, its solubility in all organic solvents was high, and on precipitating the compound from solution in ethyl tartrate it was found to be optically inactive.

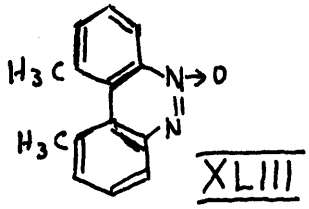
It was therefore decided to investigate the behaviour of this base with an optically active acid, d-camphorsulphonic acid being selected for this purpose.

4:5-Dimethylbenzcinnoline d-camphorsulphonate (acid:base ratio

of 1:1) underwent a first order transformation in chloroform solution, the rotation falling to an equilibrium value. The observed change in rotation was quite unambiguous (0·46° over a period of 6 hours).

The free base was recovered from the equilibrium mixture. In the process of recovery, however, some oxidation always occurred, though several methods of recovery were attempted. Consequently the recovered base was contaminated with the brown azoxy compound (XLIII), and, though it was possible to observe that the base indeed possessed a rotation in the laevo sense which mutarotated to zero in a few hours, it was impossible to make any measurement of the rate of racemisation as accurate polarimetric readings were impossible.

A convenient solvent for the crystallisation of the camphorsulphonate could not be found, consequently it was impossible to investigate any second order transformations with this salt.



XLIII

EXPERIMENTAL

All polarimeter readings were made in a 2 dm tube, using mercury green light, λ = 5461 A° . MP's are uncorrected.

Sodium N-acetyl-N-methyl-p-toluidine-3-sulphonate.

N-Methyl-p-toluidine was prepared by the method of Halberkaan (61).

The acetyl derivative of the methyl-p-toluidine was sulphonated by the method of Mills and Kelham (12) and the product acetylated. The hydrated salt melted at 83 - 85°, the anhydrous decomposed at 275 - 280°.

Sodium N-acetyl-N-methyl-p-toluidine-3-sulphonate in ethyl d-tartrate.

The salt (2 gms) was dissolved in ethyl tartrate (5 cc) by heating. After being allowed to stand for 5 hours at room temperature the salt was precipitated by the addition of moist ether (if dry ether were used difficulty was experienced in obtaining a solid precipitate). The precipitate, which was very retentive of ethyl tartrate was extracted with ether in a Soxhlet apparatus, filtered, dried in vacuo and examined polarimetrically.

Solution of 1·627 gm in 15 cc water, 18°c.

Rotation	- 0·08°	- 0·07°	- 0·06°	- 0·05°	- 0·04°	- 0·02°	- 0·00°
Time	10 min.	26	44	132	160	308	∞

Sodium N-acetyl-N-methyl-p-toluidine-3-sulphonate in d-sec. butyl alcohol.

The salt (2 gms) was recrystallised from moist d-sec. butyl alcohol (7·5 cc), the salt was insoluble in the dry alcohol. The crystals which separated were dried at the pump and washed with ether (120 cc) in six portions, the salt formed white needles of the dihydrate, MP 84°.

Solution of 1·563 gm in 15 cc water, 18°c, the rotation rose from - 0·08° to zero in about 5 hours.

Sodium N-acetyl-N-methyl-p-toluidine-3-sulphonate in d and l-sec. octyl alcohol.

The salt (2gms) was recrystallised from l-sec. octyl alcohol (60 cc) care being taken not to heat the solution above 100° since at higher temperatures the salt was dehydrated and rendered insoluble. Some of the salt which did not dissolve in the alcohol was filtered off and the filtrate allowed to crystallise. The crystals were filtered, washed thoroughly with ether and dried in vacuo, MP 84°.

Solution of 0·527 gm in 15 cc water, 14°c, the rotation rose from - 0·04° to zero in 4 hours.

The experiment was repeated using the d alcohol. In this case no rotation was detected in the crystals: solution of 0·583 gm in 15 cc water.

N-Acetyl-N-methyl-2-amino-4':5dimethyldiphenylsulphone.

This compound was prepared by the method of Halberkaan (61). The melting point found (268°) was substantially higher than that

quoted by Halberkaan (138°) and the constitution of the preparation obtained was confirmed by analysis. (Found: C, 64·45; H, 5·82. Calculated for $C_{17}H_{19}O_3NS$ C, 64·35; H, 6·00 %).

N-Acetyl-N-methyl-2-amino-4':5-dimethyldiphenylsulphone in ethyl d-tartrate.

a). The sulphone (3 gms) was dissolved in ethyl tartrate (10 cc). After standing at room temperature for 5 hours the sulphone was precipitated by addition of water, filtered, washed with water and dried in vacuo.

Solution of 1·336 gm in 15 cc chloroform, 17·7°c.

Rotation	-0·2°	-0·18°	-0·15°	-0·13°	-0·12°	-0·10°	-0·08°
Time (min.)	9	14	23	29	32	37	45
Rotation	-0·07°	-0·05°	-0·03°	-0·02°	-0·00°		
Time (min.)	48	56	70	80	120		

b). The sulphone (5 gms) was recrystallised from ethyl tartrate (7 cc). After standing at room temperature for 14 days the crystals were carefully drained free of ethyl tartrate as far as possible, washed with a little alcohol, then washed thoroughly with water and dried in vacuo. It was essential not to scratch or in any way agitate the crystals while still in contact with ethyl tartrate as this caused precipitation of laevo rotatory material from the ethyl tartrate mother liquors. The material still remaining in the mother liquors was precipitated and treated as in a) above.

Crystals: solution of 2·034 gm in 15 cc chloroform, 17°c.

Rotation	+ 0·17°	+ 0·16°	+ 0·14°	+ 0·12°	+ 0·10°
Time (min)	14	19	26	31	37
Rotation	+ 0·09°	+ 0·07°	+ 0·06°	+ 0·00°	
Time (min)	43	48	52	∞	

Precipitate: solution of 1·271 gm in 15 cc chloroform, 16°c.

Rotation	- 0·15°	- 0·14°	- 0·13°	- 0·11°	- 0·10°
Time (min)	7	11	14	20	24
Rotation	- 0·08°	- 0·07°	- 0·04°	0·00°	
Time (min)	29	34	45	∞	

Effect of temperature changes: high temperatures.

A solution of the sulphone (5 gms) in ethyl tartrate (7 cc) was allowed to crystallise at 84° for 5 days, the crystals were filtered and washed with the same precautions as before.

Solution of 1·84 gm in 15 cc chloroform, 18°c, had rotation + 0·1°(5 minutes after wetting).

Solutions of the sulphone (2 gms) in ethyl tartrate (5 cc) were maintained at 42° and at 84° for several hours, water was then added to precipitate the solute which was filtered, washed and dried.

42° sample: $[\alpha]^{17^\cdot}$ = - 0·5° (7 minutes after wetting, c = 11)

84° sample: $[\alpha]^{17^\cdot}$ = - 0·01°(4 minutes after wetting, c = 12).

Low temperatures.

Solutions of the sulphone (1·5 gms) in ethyl tartrate (15 cc)

were allowed to stand at room temperature for 24 hours and were then cooled to - 10° to - 15° in a freezing mixture (ice and 66 % sulphuric acid), and maintained there for 4 hours. The solute was then recovered by precipitation with water in the usual way.

1) $[\alpha]^{18}$ = + 0°3° (10 minutes after wetting, c = 10)
2) $[\alpha]^{19}$ = 0°0° (4 minutes after wetting, c = 5)
3) $[\alpha]^{17}$ = - 0°7° (5 minutes after wetting, c = 9)

These experiments were repeated cooling the samples to 0° in an ice bath for 5 hours the rest of the procedure being as above.

1) $[\alpha]^{19}$ = - 0°4° (9 minutes after wetting, c = 7),
2) $[\alpha]^{18}$ = - 0°1° (15 minutes after wetting, c = 9).

N-Acetyl-N-methyl-2-amino-4':5-dimethyldiphenylsulphone in l-menthyl acetate.

The sulphone (3 gms) was crystallised from l-menthyl acetate (20 cc). The crystals were filtered, and washed free as far as possible from menthyl acetate with cold methanol and dried.

The rotation of a solution of 1°03 gms in 15 cc chloroform fell from + 0°08° to - 0°10° in 80 minutes. The final laevo rotation was presumably due to menthyl acetate which had not been completely removed from the crystals.

N-Acetyl-N-methyl-2-amino-4':5-dimethyldiphenylsulphone in d and l sec. octyl alcohols.

The sulphone (3 gms) was recrystallised from both d and l sec. octyl alcohols (10 cc), in each case the crystals which separated, representing almost the whole of the solute, were optically inactive: solution of approx. 2 gm in 15 cc chloroform.

N-Acetyl-N-ethyl-2-amino-4':5-dimethyldiphenylsulphone.

Was prepared in the same way as the N-methyl compound. It crystallised from alcohol in white needles, MP 144 - 145°.

N-Acetyl-N-ethyl-2-amino-4':5-dimethyldiphenylsulphone in ethyl d-tartrate.

The sulphone (5 gm) was recrystallised from ethyl tartrate (10 cc). The crystals which separated were dextro rotatory, the material remaining in the mother liquors laevo rotatory.

Crystals: solution of 1°8164 gm in 15 cc chloroform, 22°c.

Rotation	+ 0°11°	+ 0°10°	+ 0°09°	+ 0°06°	+ 0°05°	+ 0°00°
Time (min)	13	60	120	360	480	∞

Precipitate: solution of 1°254 gm in 15 cc chloroform, 20°c.

Rotation	- 0°08°	- 0°06°	- 0°05°	- 0°04°	- 0°00°
Time (min)	7	120	240	380	∞

A solution of the sulphone (3 gm) in ethyl tartrate (15 cc) was allowed to stand at room temperature for 5 days, the solute was then recovered by precipitation with water.

Solution of 1°5177 gm in 15 cc chloroform, 20°c.

Rotation	- 0°08°	- 0°07°	- 0°05°	- 0°04°	- 0°00°
Time (min)	4	60	220	350	∞

Substituted N-acetyl-N-alkyl-2-amino-4'-methyldiphenylsulphones.

The p-toluenesulphonyl derivatives of p-methoxy, p-chloro and p-bromo N-methyl and N-ethyl anilines were all prepared by the normal methods. Rearrangement to the o-aminosulphones was carried out by heating at 100° with an equal weight of 96 % sulphuric acid for 2 hours, on cooling and pouring into water the sulphones were precipitated.

Methoxy compounds.

N-p-toluenesulphonyl-N-methyl-p-anisidine, prisms from alcohol, MP 70 - 72°, gave N-methyl-2-amino-5-methoxy-4'-methyldiphenylsulphone, MP 150°, in 40 % yield. The acetyl derivative crystallised from alcohol in prisms, MP 137 - 138°.

N-p-toluenesulphonyl-N-ethyl-p-anisidine, prisms from alcohol, MP 94°, gave in 50 % yield N-ethyl-2-amino-5-methoxy-4'-methyldiphenylsulphone, prisms from alcohol, MP 94°. (Found: C, 63°13; H, 6°28; N, 4°84. $C_{16}H_{19}O_3NS$ requires C, 62°95; H, 6°23; N, 4°59 %).

N-acetyl-N-ethyl-2-amino-5-methoxy-4'-methyldiphenylsulphone, prisms from alcohol, MP 145°. (Found: C, 63°04; H, 6°11; N, 4°26. $C_{18}H_{21}O_4NS$ requires C, 63°11; H, 6°04; N, 4°02 %).

Chloro compounds.

N-p-toluenesulphonyl-N-methyl-p-chloraniline, thick needles from alcohol, MP 94 -95° gave in 10 % yield N-methyl-2-amino-4-chloro-4'-methyldiphenylsulphone. small needles MP 155°

(Found: C, 57°11; H, 4°82; N, 5°13. $C_{14}H_{14}O_2NClS$ requires C, 56°87; H, 4°74; N, 4°74 %).

N-acetyl-N-methyl-2-amino-5-chloro-4'-methyldiphenylsulphone, needles from alcohol, MP 159°. (Found: C, 57°03; H,4°69; N,4°44. $C_{16}H_{16}O_3NClS$ requires C, 56°89; H, 4°74; N, 4°15 %).

N-p-toluenesulphonyl-N-ethyl-p-chloraniline, needles from alcohol MP 104°, gave in 15 % yield N-ethyl-2-amino-5-chloro-4'-methyldiphenylsulphone, needles from alcohol, MP 136°. (Found: C, 58°1; H, 5°13; N, 4°79. $C_{15}H_{16}O_2NClS$ requires C, 58°18; H, 5°17; N, 4°73 %).

N-Acetyl-N-ethyl-2-amino-5-chloro-4'-methyldiphenylsulphone, small plates from alcohol, MP 153°. (Found: C, 58°05; H, 5°42; N, 3°67. $C_{17}H_{18}O_3NClS$ requires C, 58°02; H, 5°12; N, 3°96 %).

Bromo compounds.

N-p-toluenesulphonyl-N-methyl-p-bromaniline, prisms from methanol, MP 80°, gave in 6 % yield N-methyl-2-amino-5-bromo-4'-methyldiphenylsulphone, needles from alcohol, MP 160 - 161°. (Found C, 49°98; H, 4°27. $C_{14}H_{14}O_2NBrS$ requires C, 49°7; H, 4°15 %). N-Acetyl-N-methyl-2-amino-5-bromo-4'-methyldiphenylsulphone, white needles from alcohol, MP 173°. (Found: C, 50°11; H, 4°28. $C_{16}H_{16}O_3NBrS$ requires C, 50°3; H, 4°22 %).

N-p-toluenesulphonyl-N-ethyl-p-bromaniline, elongated prisms from alcohol, MP 90°, gave in 25 % yield N-ethyl-2-amino-5-bromo-4'-methyldiphenylsulphone, needles from alcohol, MP 141 °.

(Found: C, 50°92; H, 4°79. $C_{15}H_{16}O_3NBrS$ requires C, 50°9; H, 4°55 %).

N-Acetyl-N-ethyl-2-amino-5-bromo-4'-methyldiphenylsulphone, needles from alcohol, MP 143 -144°. (Found: C, 51°5; H, 4°64. $C_{17}H_{18}O_3NBrS$ requires C, 51°58; H, 4°58 %).

N-Acetyl-N-ethyl-2-amino-5-methoxy-4'-methyldiphenylsulphone in ethyl d-tartrate.

The sulphone (3 gms) was crystallised from ethyl tartrate (7 cc). Crystals: solution of 0°432 gm in 15 cc chloroform, 21°c.

Rotation	- 0°10°	- 0°09°	- 0°08°	- 0°06°	- 0°05°
Time (min)	4	15	20	35	45
Rotation	- 0°03°	- 0°02°	0°00°		
Time (min)	80	120	∞		

Precipitate: solution of 0°9616 gms in 15 cc chloroform, 20°c.

Rotation	- 0°11°	- 0°10°	- 0°08°	- 0°06°	- 0°06°
Time (min)	4	8	25	30	40
Rotation	- 0°05°	- 0°04°	- 0°02°	0°00°	
Time (min)	50	70	120	∞	

The sulphone (1 gm) was dissolved in ethyl tartrate (10 cc). After several days it was precipitated by addition of water. Solution of 0°7458 gms in 15 cc chloroform, 20°c, had rotation - 0°08° fising to zero.

N-Acetyl-N-ethyl-2-amino-5-methoxy-4'-methyldiphenylsulphone in ethyl d-tartrate.

The sulphone (3 gms)was crystallised from ethyl tartrate (6 cc).

Crystals: solution of 0·4944 gms in 15 cc chloroform, 19°c, had rotation + 0·03° falling to zero over a period of a few hours.

Precipitate: solution of 1·065 gms in 15 cc chloroform ; 18°c.

Rotation	+ 0·10°	+ 0·09°	+ 0·06°	0·00°
Time (min)	8	50	200	∞

N-Acetyl-N-methyl-2-amino-5-chloro-4'-methyldiphenylsulphone in ethyl d-tartrate.

The sulphone (3 gms) was recrystallised from ethyl tartrate (9 cc).

Crystals: solution of 1·0776 gms in 15 cc chloroform, 22°c.

Rotation	- 0·20°	- 0·15°	- 0·09°	- 0·06°	- 0·04°
Time (min)	4	5	6	10	12
Rotation	- 0·03°	- 0·02°	0·00°		
Time (min)	14	15	19		

Precipitate: solution of 0·9746 gms in 15 cc chloroform, 22°c.

Rotation	- 0·10°	- 0·08°	- 0·06°	- 0·03°	- 0·02°	0·00°
Time (min)	4	6	9	13	15	18

The sulphone (1 gm) was dissolved in ethyl tartrate (10 cc), after 24 hours the solute was recovered in the usual way. Solution of 0·9547 gm in 15 cc chloroform, 21°c, had an initial rotation of - 0·04°.

N-Acetyl-N-ethyl-2-amino-5-chloro-4'-methyldiphenylsulphone in ethyl d-tartrate.

The sulphone (3 gm) was crystallised from ethyl tartrate (9 cc).

Crystals: solution of 0·9584 gms in 15 cc chloroform, 20°c, had no rotation.

Precipitate: solution of 0·7558 gms in 15 cc chloroform, 20°c.

Rotation	+ 0·14°	+ 0·12°	+ 0·11°	+ 0·09°	+ 0·08°	+ 0·06°	0·00°
Time (min)	18	60	90	150	180	300	∞

The sulphone (1gm) was dissolved in ethyl tartrate (10 cc), and recovered after several days.

Solution of 0·9368 gms in 15 cc chloroform, 20°c.

Rotation	+ 0·16°	+ 0·12°	+ 0·10°	+ 0·07°	0·00°
Time (min)	18	80	150	300	∞

N-Acetyl-N-ethyl-2-amino-5-bromo-4'-methyldiphenylsulphone in ethyl d-tartrate.

The sulphone (2 gms) was crystallised from ethyl tartrate (5 cc).

Crystals: solution of 0·720 gms in 15 cc chloroform, 15°c.

Rotation	- 0·13°	- 0·11°	- 0·09°	- 0·07°	- 0·06°
Time (min)	5	10	20	30	35
Rotation	- 0·05°	- 0·02°	- 0·00°		
Time (min)	45	74	135		

Precipitate: solution of 0·750 gms in 15 cc chloroform, 15°c. The rotation fell from + 0·12° ± 0·04° to zero in 2 - 3 hours, owing to the presence of coloured impurities in the solution no rate measurements could be made.

N-p-toluenesulphonyl-N-methyl-p-nitraniline, formed pale yellow prisms from dioxan, MP 178°. On warming with 96 % sulphuric acid at 100° for 1 hour it was quantitatively converted to N-methyl-p-nitraniline.

Attempted preparation of N-methyl-2-amino-5-nitro-4'-methyldiphenylsulphone.

N-Acetyl-N-methyl-p-nitraniline (3·64 gm) in carbon disulphide (30 cc) was mixed with powdered aluminium chloride (3 gms) and p-toluenesulphonyl chloride (4 gms) added at 0° with stirring. The mixture was heated at 50° on the water bath for 2 - 3 hours without reaction occurring. It was possible to separate both reactants from the cooled reaction mixture, no other material was found in it.

2-Chloro-5-nitrobenzenesulphonic acid, (cf. Ullmann and Juntzel, 77). p-Chloronitrobenzene (160 gms) was stirred mechanically with 20 % oleum (200 cc) and heated in an oil bath at 140 - 145° (thermometer in flask) for 5 hours. The cooled reaction mass was poured on crushed ice (500 gms) and the crude sulphonic acid filtered off. It was crystallised from hydrochloric acid solution, yield 200 gms.

The sulphonyl chloride was prepared via the potassium salt, it crystallised from light petroleum in colourless needles, MP 90°.

Attempted preparation of 2-chloro-5-nitro-4'-methyldiphenylsulphone.

2-Chloro-5-nitrobenzenesulphonyl chloride (2·56 gms) was dissolved in pure dry toluene (7 cc) and finely powdered anhydrous aluminium chloride (1·4 gms) added in one portion, a deep red colour developed. The solution was warmed gently on the steam bath

for 4 hours while hydrogen chloride was evolved. The cooled reaction product was decomposed with ice and hydrochloric acid and the toluene layer separated. No pure material could be separated from it however.

If the reaction was carried out in nitrobenzene at room temperature, or the aluminium chloride replaced by stannic chloride (1·5cc), the chloronitrobenzenesulphonyl chloride could be recovered unchanged.

2-Chloro-5-nitrobenzenesulphonanilide, was prepared from the sulphonyl chloride (20·3 gms), aniline (9·3 gms) and pyridine (50 cc). It crystallised from acetic acid in small colourless needles, MP 169°. (Found: C, 46·16; H, 2·79; N, 8083. $C_{12}H_9O_4N_2ClS$ requires C, 46·2; H, 2·89; N, 8·88 %).

2-(N-methylamino)-5-nitrobenzenesulphonanilide. 2-Chloro-5-nitrobenzenesulphonanilide (20 gms), methylamine hydrochloride (11·5 gms) and potassium carbonate (10 gms) were dissolved in alcohol (200 cc) and water (20 cc). The whole was boiled for 48 hours, carbon dioxide was evolved steadily. On cooling lemon yellow prisms were deposited mixed with methylamine hydrochloride. They were filtered off, washed with water to remove methylamine hydrochloride and recrystallised from alcohol (150 cc), MP 167°.
(Found:C, 50·95; H, 4·45; N, 13·81. $C_{13}H_{13}O_4N_3S$ requires C, 50·7; H, 4·24; N, 13·7 %).

N-acetyl-N-methyl-2-amino-5-nitrobenzenesulphonanilide, colourless prisms from dioxan, MP 220 - 222°. (Found: C, 51·83; H, 4·36;

N, 12°16. $C_{15}H_{15}O_5N_3S$ requires C, 51°6; H, 4°29; N, 12°03 %).

N-Acetyl-N-methyl-2-amino-5-nitrobenzenesulphonanilide in ethyl d-tartrate.

The anilide (2 gms) was crystallised from ethyl tartrate (10 cc). Solution of 0°1945 gms of the crystals in 15 cc dioxan, 18°c, rotation = 0°00°.

2-Chloro-5-nitrobenzenesulphon-2'-chloranilide, prepared from the sulphonyl chloride (12°8 gms), o-chloraniline (6°4 gms) and pyridine (30 cc). Colourless plates from alcohol, MP 171°. (Found: C, 41°67; H, 2°43; N, 8°4. $C_{12}H_8O_4N_2Cl_2S$ requires C, 41°5; H, 2°3; N, 8°1 %).

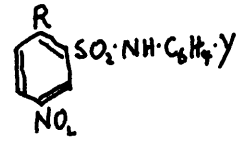
2-(N-methylamino)-5-nitrobenzenesulphon-2'-chloranilide. The above anilide (11 gm), methylamine hydrochloride (5 gms) and potassium carbonate (4°6 gms) were refluxed in 80 % alcohol (200 cc) for 48 hours. The product formed pale yellow prisms from alcohol, MP 197°. (Found: C, 46°85; H, 3°36; N, 12°44. $C_{13}H_{12}O_4N_3ClS$ requires C, 46°65; H, 3°51; N, 12°3 %).

N-Acetyl-N-methyl-2-amino-5-nitrobenzenesulphon-2'-chloranilide. Colourless prisms fron acetic acid, MP ~~280°~~ 145°. (Analysis results are not available for this compound but there is little doubt of its constitution as the acetyl derivative of the above amine).

N-Acetyl-N-methyl-2-amino-5-nitrobenzenesulphon-2'-chloranilide in ethyl d-tartrate.

The anilide (4 gms) was crystallised from ethyl tartrate (10 cc).

Crystals: solution of 0·921 gms in 15 cc dioxan, 18°c, rotation = 0·00°.

Compounds of type 

Several compounds of this type were prepared where R = Cl, [illegible] $NHCH_3$ or $N(CH_3)COCH_3$. They were not analysed, with the exception of those compounds selected for further experiment but by analogy with these compounds, which have been described above, the structures of the other compounds in the group may be assumed to be correct. The melting points of all these compounds are tabulated here.

Y	R = Cl	R = $NHCH_3$	R = $N(CH_3)COCH_3$
o-Cl	171°	197°	175°
p-Cl	185°	204°	214°
o-CH_3	174°	157°	174°
p-CH_3	173°	152°	152°
o-OCH_3	164°	203°	237°
p-OCH_3	148°	193°	207°
H	168°	167°	222°

N-Acetyl-N-methyl-p-nitraniline was prepared by the method of Morgan and Grist (62).

Sodium N-acetyl-N-methyl-p-nitraniline-2-sulphonate. Dry N-acetyl-N-methyl-p-nitraniline (21·6 gms) was thoroughly mixed with chlorosulphonic acid (13 gms). The mixture was heated to 120° in an oil bath and the temperature allowed to rise to 138° over a period of 30 minutes, stirring continuously with the thermometer. The temperature was maintained at 138° for 4 hours stirring being

continued till the reaction mass became so viscous as to render it impossible. The mass was allowed to cool and dissolved in cold water (50 cc). After filtering from N-methyl-p-nitraniline the aqueous solution was boiled with charcoal and evaporated to dryness. The residue was extracted with 95 % alcohol (120 cc), sodium sulphate filtered off and the filtrate, on cooling, deposited yellow needles of sodium N-methyl-p-nitraniline-2-sulphonate sesquihydrate. (Found: C, 29·99; H, 3·78, $C_7H_7O_5N_2SNa$ $1{\cdot}5H_2O$ requires C, 29·90; H, 3·56%).

Sodium N-acetyl-N-methyl-p-nitraniline-2-sulphonate. The above salt (7 gms) was heated with acetic anhydride (5·5 cc) at 120° for 1·5 hours. The cold product was triturated with ether, ground up and extracted with ether in a Soxhlet apparatus till free from acetic anhydride. It was then recrystallised from alcohol (35 cc) as white needles of the hydrated salt and dehydrated at 100°. (Found: C, 36·33; H, 3·17; N, 9·49· $C_9H_9O_6N_2SNa$ requires C, 36·5; H, 3·04; N, 9·46 %).

l-Brucine N-acetyl-N-methyl-p-nitraniline-2-sulphonate. The sodium salt (1·5 gms) in water (4 cc) was treated with a solution of brucine (2·3 gms) in water (10 cc) containing acetic acid (0·41 gms). The solution immediately became a deep red colour and on standing the brucine salt separated. (Found: C, 57·37; H, 5·50; N, 8·56. $C_{32}H_{34}O_{10}N_4S$ requires C, 57·4; H, 5·42; N, 8·42 %).

Attempted resolution via brucine salt. The salt was recrystallised from water, alcohol, in which it was sparingly soluble, and from

nitrobenzene (readily soluble). The rotation in each case was zero.

No change in rotation occurred on further crystallisation from water, no mutarotation occurred. The salt was allowed to crystallise from water at 48°, the salt was optically inactive.

A saturated solution of the brucine salt in chloroform was treated with the theoretical quantity of alcoholic sodium ethoxide at 0°, after a few minutes stirring the sodium salt separated. It was optically inactive.

Quinidine N-acetyl-N-methyl-p-nitraniline-2-sulphonate. A solution of the sodium salt (8·88 gms) in water (35 cc) was mixed with a solution of quinidine (9·72 gms) in water (25 cc) containing acetic acid (1·8 gms). A yellow viscous oil was precipitated immediately. The oil was left in contact with the aqueous mother liquors, evaporation being prevented. After a fortnight the oil had crystallised completely giving very pale yellow prisms of the quinidine salt, yield 10 gms. This salt was extremely soluble in most organic solvents except light petroleum, and separated from solutions as a viscous oil which crystallised in contact with water. It crystallised in prisms from ethyl acetate.

Attempted resolution via the quinidine salt. The salt (5 gms) of specific rotation + 210·5°, was recrystallised from ethyl acetate giving 3·05 gms of pale yellow prisms, $[\alpha]^{19}$ = + 210·5° (c = 2·4 in chloroform)

No mutarotation was observed with these solutions. A solution of

the quinidine salt (2·3841 gms) in chloroform (50 cc) was extracted with dilute ammonium hydroxide (15 cc). The aqueous layer was separated, extracted with chloroform (75 cc) in three portions and filtered. The resulting solution of the ammonium salt was optically inactive and displayed no mutarotation.

N-p-toluenesulphonyl-N-methyl-m-toluidine was prepared from N-p-toluensulphonyl-m-toluidine (60 gms) aqueous sodium hydroxide (9·2 gms in 300 cc of water) and dimethyl sulphate (30 gms). It crystallised from alcohol in white prisms, MP 62°. On treatment with 96 % sulphuric acid at 100° for 1 hour the sole product was N-methyl-m-toluidine, identified as its acetyl derivative MP 66°.

N-p-toluenesulphonyl-N-ethyl-m-chloraniline. Prepared from p-toluenesulphonyl-m-chloraniline (67 gms) sodium hydroxide (10 gms in 250 cc water) and dimethyl sulphate (38 gms), It crystallised from alcohol in white needles, MP 69°. Treatment with 96 % sulphuric acid at 100° for 1 hour converted it completely to N-ethyl-m-chloraniline.

N-p-toluenesulphonyl-N-methylaniline, white prisms from alcohol, MP 95°.

Witt rearrangement with N-p-toluenesulphonyl-N-methylaniline. On warming the compound with an equal weight of 96 % sulphuric acid at 100° for 1 hour a small yield (1 %) of a sulphone was obtained, it crystallised in needles from alcohol, MP 139°. The acetyl derivatiwe formed small white prisms from methanol, MP 114 -116°, depressed on

admixture with N-acetyl-N-methyl-2-amino-4'-methyldiphenylsulphone.

N-Acetyl-N-methyl-2-amino-4'-methyldiphenylsulphone and its 4-substituted derivatives.

The general procedure was as follows: the appropriate o-nitrohalogeno compound(1 mol) was dissolved in hot alcohol and treated with an aqueous alcoholic solution of p-thiocresol (1 mol) and sodium hydroxide (1 mol). After a few minutes refluxing the solution was allowed to cool when it deposited crystals of the thioether.

Oxidation of thioether. The thioethers were oxidised with excess hydrogen peroxide (5 cc per gram of thioether) in acetic acid at 100° the hydrogen peroxide being added over a period of 1 hour.

Reduction of nitro group. The nitrosulphone (1 mol) was added in portions to a hot solution of pure stannous chloride in hydrochloric acid (3 mols stannous chloride in 6 mols acid) with good shaking. The mixture was then warmed on the steam bath for a further 30 minutes, cooled and diluted with water. The precipitated base was filtered off and recrystallised. The reduction of halogen substituted compounds was carried out below 50° and the reaction mixture allowed to stand at room temperature for 30 minutes instead of being heated on the water bath.

Methylation. The acetylamine (1 mol) was added to a 5 % alcoholic sodium ethoxide solution (1 mol) and warmed for a few minutes on the steam bath. In some cases a crystalline sodio derivative

separated. Freshly distilled acid free dimethyl sulphate (1 mol) was then added to the cooled sodium salt and the whole cautiously warmed till a clear solution was obtained. After a few minutes a gelatinous precipitate of sodium sulphate separated with vigorous boiling. The reaction was completed with an hours warming on the steam bath. On pouring the reaction mixture into water the acetylmethylamine was precipitated and could be filtered off. The halogen substituted compounds were contaminated with highly coloured impurities, these formed separate crystals on recrystallisation and could be separated mechanically.

2-nitro-4'-methyldiphenylsulphide: fine orange needles from acetic acid, MP 118°.

2-nitro-4'-methyldiphenylsulphone, white needles from acetic acid MP 158°.

2-amino-4'-methyldiphenylsulphone, white needles from methanol MP 117°.

N-p-toluenesulphonyl-2-amino-4'-methyldiphenylsulphone needles from acetic acid, MP145°. (Not analysed.)

N-acetyl2-amino-4'-methyldiphenylsulphone prisms from alcohol MP 128°.

N-p-toluenesulphonyl-N-methyl-2-amino-4'-methyldiphenylsulphone, needles from methanol, MP 132°. (Not analysed).

N-acetyl-N-methyl-2-amino-4'-methyldiphenylsulphone, prisms from alcohol MP 121°. (Found: C, 63·54; H, 5·01. $C_{16}H_{17}O_3NS$ requires C, 63·4; H, 5·3 %).

N-acetyl-N-methyl-2-amino-4'-methyldiphenylsulphone in ethyl d-tartrate.

The sulphone (2 gms) was crystallised from ethyl tartrate (5 cc)

Crystals: solutionof 0·2 gms in 15 cc chloroform, 20°,

rotation = 0·00°

Precipitate: solution of 0·398 gms in 15 cc chloroform, 20°c ,

rotation = 0·00°.

3-nitro-p-toluidine was prepared by the method of Noyes (63). It crystallised from alcohol in dark red plates, MP 117°.

3-nitro-4-bromotoluene. Crystallised in needles from alcohol, MP 34°.

2-nitro4:4'-dimethyldiphenylsulphide, flat yellow needles or plates from alcohol, MP 118°.

2-nitro-4:4'-dimethyldiphenylsulphone, needles from alcohol, MP 114°.

2-amino-4:4'-dimethyldiphenylsulphone, thick needles from methanol MP 143°.

N-acetyl-2-amino-4:4'-dimethyldiphenylsulphone, needles from alcohol MP 121°.

N-acetyl-N-methyl-2-amino-4:4'-dimethyldiphenylsulphone, needles from alcohol, MP 161°. (Found: C, 64·47; H, 5·71; N, 4·97. $C_{17}H_{19}O_3NS$ requires C, 64·37; H, 6·03; N, 4·47 %).

N-acetyl-N-methyl-2-amino-4:4'-dimethyldiphenylsulphone in ethyl d-tartrate.

A solution of the sulphone (2gms) in ethyl tartrate (15 cc) was allowed to stand at room temperature for a few days and the solute recovered by precipitation with water.

Precipitate: solution of0·63 gms in 15 cc chloroform, 18°c,

rotation = 0·00°.

3-Nitro-p-anisidine. Dry finely powdered N-acetyl-p-anisidine (30 gms) was added in portions to 12 % nitric acid which had been warmed to 40° on the water bath. The acetylanisidine dissolved after a short time at 40°, heating was discontinued and the mixture well shaken. In a few minutes the nitration product commenced to separate and some heat was evolved, the temperature was maintained below 50° by cooling under the tap. When the temperature showed no further tendency to rise the mixture was left at room temperature for a further hour and then diluted with an equal volume of water. The crystalline orange precipitate was filtered off and freed from acid by thorough washing with water. The crude nitration product was dissolved in hot methanol (250 cc) and aqueous potassium hydroxide (16 gms in 25cc water) added slowly to the hot solution, the colour became dark red and the base began to crystallise almost immediately. After cooling the 3-nitro-p-anisidine was filtered off, it formed bright red prisms, MP 122°. Yield 28 gms.

3-Nitro-4-chloroanisole. The above amine (25·5 gms) in 10N hydrochloric acid (150 cc) and water (200 cc) was diazotised by the addition at 0° of a solution of sodium nitrite (11 gms) in water (20 cc). The diazo solution was added to a solution of cuprous chloride (35 gms) in 10 N hydrochloric acid (200 cc) at 50° and warmed for an hour on the steam bath. The nitrochloroanisole crystallised on cooling, was filtered off and recrystallised from methanol as yellow needles MP 45°.

2-Nitro-4-methoxy-4'-methyldiphenylsulphide, orange prisms from methanol, MP 96°. (Found: C, 61°33; H, 4°6. $C_{14}H_{13}O_3NS$ requires C, 61°1; H, 4°76 %).

2-Nitro-4-methoxy-4'-methyldiphenylsulphone, fine white needles from alcohol, MP 126 - 127°. (Found: C, 54°8; H, 4°22. $C_{14}H_{13}O_5NS$ requires C, 54°78; H, 4°27 %).

2-Amino-4-methoxy-4'-methyldiphenylsulphone, small white needles from benzene, MP 153°. (Found: C, 60°73; H, 5°48. $C_{14}H_{15}O_3NS$ requires C, 60°7; H, 5°46 %).

N-Acetyl-2-amino-4-methoxy-4'-methyldiphenylsulphone, needles from alcohol, MP 115°. (Found: Analysis results are not available for this compound).

N-Acetyl-N-methyl-2-amino-4-methoxy-4'-methyldiphenylsulphone, prisms from methanol, MP 147°. (Found: C, 61°27; H, 5°82; N, 4°4. $C_{17}H_{19}O_4NS$ requires C, 61°3; H, 5°75; N, 4°21 %).

2:5-Dichloronitrobenzene. p-Dichlorobenzene (50 gms) was suspended in 96 % sulphuric acid (75 cc) and fuming nitric acid (25 cc) added with shaking. The mixture was heated on the steam bath to 40° when the dichlorobenzene became molten and an exothermic reaction took place: the temperature was maintained at 45 - 50° by cooling under the tap. After the reaction had subsided the mixture was heated to 50° on the steam bath for a few minutes and left for an hour at room temperature, the organic layer had resolidified in the course of the reaction. The acid was diluted with water, the nitro

compound filtered, washed thoroughly and crystallised from acetic acid, prisms MP 54°. Yield 64 gms.

2-nitro-4-chloro-4'-methyldiphenylsulphide, orange prisms from acetic acid, MP 121°.

2-nitro-4-chloro-4'-methyldiphenylsulphone, fine white needles from alcohol, MP 124°

2-amino-4-chloro-4'-methyldiphenylsulphone, white platelets from alcohol, MP 137°. (Found: C, 55°6; H, 4°29. $C_{13}H_{12}O_2NClS$ requires C, 55°4; H, 4°29 %).

N-acetyl-2-amino-4-chloro-4'-methyldiphenylsulphone, needles from methanol, MP 129°. (Found: C, 55°76; H, 4°25. $C_{15}H_{14}O_3NClS$ requires C, 55°69; H, 4°36 %).

N-acetyl-N-methyl-2-amino-4-chloro-4'-methyldiphenylsulphone, white prisms from acetic acid, MP 175°. (Found: C, 57°12; H, 4°55; N, 4°26. $C_{16}H_{16}O_3NClS$ requires C, 56°9; H, 4°78; N, 4°15 %).

N-Acetyl-N-methyl-2-amino-4-chloro-4'-methyldiphenylsulphone in ethyl d-tartrate.

A solution of the sulphone (2 gms) in ethyl tartrate (15 cc) was allowed to stand for a few days at room temperature and the sulphone recovered by precipitation with water.
Solution of 1°479 gms in 15 cc chloroform, 19°c, rotation = 0°00°.

2:5-Dibromonitrobenzene; was prepared in the same way as the dichloro compound, a higher reaction temperature was required. The mixture was heated to 55° when reaction set in, and maintained thereafter,

by cooling, at 60 - 62°. The product crystallised from acetic acid in white needles, MP 84°. Yield 53 gms.

2-nitro-4-bromo-4'-methyldiphenylsulphide, elongated orange prisms from dioxan, MP 124°. (Found: C, 48°62; H, 3°29. $C_{13}H_{10}O_2NBrS$ requires C, 48°35; H, 3°11 %).

2-nitro-4-bromo-4'-methyldiphenylsulphone, white needles from alcohol, MP 132°. (Found: C, 43°85; H, 2°82. $C_{13}H_{10}O_4NBrS$ requires C, 43°83; H, 2°83 %).

2-amino-4-bromo-4'-methyldiphenylsulphone prisms from alcohol, MP 154°. (Found: C, 47°7; H, 3°77. $C_{13}H_{12}O_2NBrS$ requires C, 47°9; H, 3°71 %).

N-acetyl-2-amino-4-bromo-4'-methyldiphenylsulphone, white prisms from methanol, MP 132°. (Found: C, 48°97; H, 4°1. $C_{15}H_{14}O_3NBrS$ requires C, 48°95; H, 3°9 %).

N-acetyl-N-methyl-2-amino-4-bromo-4'-methyldiphenylsulphone, white prisms from alcohol, MP 160°. (Found C, 50°17; H, 4°19; N, 4°00. $C_{16}H_{16}O_3NBrS$ requires C, 50°3; H, 4°22; N, 3°7 %).

N-Acetyl-N-methyl-2-amino-4-bromo-4'-methyldiphenylsulphone in ethyl d-tartrate.

A solution of the sulphone (2 gms) in ethyl tartrate (15 cc) was allowed to stand at room temperature for a few days and the sulphone recovered by precipitation with water.

Solution of 0°87 gms in 15 cc chloroform, 20°c, rotation = 0°00°.

Nitration of o-chloraniline sulphate. o-Chloraniline (25·4 gms) was added with stirring to 96 % sulphuric acid (200 cc) cooled in a bath of ice and salt, the temperature rose to 10°. When the temperature had dropped to - 3° a solution of 68 % nitric acid (12·5 cc) in 96 % sulphuric acid (40 cc) was added with stirring at such a rate that the temperature did not rise above 0°. The mixture was left in the ice bath for 4 hours, poured into ice water (500 cc) and neutralised by the addition of solid sodium carbonate. The precipitated amines were filtered at the pump and drained free from accompanying oil. On crystallisation from alcohol (75 cc) light brown prisms, MP 150 -151°, were obtained (7·1 gms), further crystallisation raised the melting point to 153°.

On pouring the alcoholic mother liquors into water a brown solid was precipitated which was crystallised from alcohol (15 cc), after three crystallisations it formed scarlet needles, MP 76°.

N-(2-Chlorophenyl)-phthalimide. o-Chloraniline (27·5 gms) and phthalic anhydride (29·6 gms) were mixed in a flask without reflux condenser and heated in an oil bath at 240° when a vigorous reaction set in with evolution of water. After 30 minutes the temperature was gradually raised to 260° and later to 270° and there maintained for 2 hours. The mass was allowed to cool partially and then poured into cold spirits with good stirring when a white solid crystallised. It was recrystallised from acetic acid in matted needles, MP 140 -141°. Yield 45 gms. (Found: C, 65·5; H, 3·02. $C_{14}H_8O_2NCl$ requires C, 65·5; H, 3·13 %).

N-(2-Chloro-5-nitrophenyl)-phthalimide. N-(2-Chlorophenyl)-phthalimide (30 gms) was suspended in 96 % sulphuric acid (110 cc) and 68 % nitric acid (25 cc) added gradually with shaking. The temperature tended to rise and was maintained at 30 - 40° by cooling under the tap. The suspended material went into solution and then, when nearly all the nitric acid had been added, the nitration product began to separate. After addition of the acid was complete the mixture was allowed to stand for 30 minutes and was then poured into water (500 cc) and the nitro compound filtered off. The solid was washed free of acid and crystallised from acetic acid as pale yellow prisms, MP 197°. Yield 33 gms.
(Found: C, 55°58; H, 2°49. $C_{14}H_7O_4N_2Cl$ requires C, 55°62; H, 2°33 %).

2-Chloro-5-nitro-aniline. The nitrated phthalimide (30 gms) was dissolved in 2 N aqueous sodium hydroxide (250 cc) and the solution boiled for 2 hours, when the amine separated. The solution cooled the amine filtered off and crystallised from alcohol in bright yellow needles, MP 120°. Yield 14 gms.

2-Chloro-5-nitroacetanilide, large white needles from alcohol, MP 160°.

N-Acetyl-2-amino-4-nitro-4'-methyldiphenylsulphide, very pale yellow matted silky needles from acetic acid, MP 125°.
(Found: C, 59°76; H, 4°79. $C_{15}H_{14}O_3NS$ requires C, 59°65; H, 4°67 %).

N-Acetyl-2-amino-4-nitro-4'-methyldiphenylsulphone, white matted silky needles from alcohol, MP 149 - 150°. (Found: C, 53°87; H, 4°07. $C_{15}H_{14}O_5N_2S$ requires C, 53°9; H, 4°22 %).

N-p-Toluenesulphonyl-2-chloro-5-nitroaniline was prepared from the amine (15 gms) p-toluenesulphonyl chloride (17 gms) and pyridine (50 cc) by 45 minutes heating on the steam bath. Some of the N:N-bis-toluenesulphonyl derivative was produced, alcoholic sodium ethoxide readily converted this to the mono-toluenesulphonyl derivative which crystallised from acetic acid in diamond shaped prisms, MP 159°.

N-p-Toluenesulphonyl-N-methyl-2-chloro-5-nitroaniline, soft white prisms from alcohol, MP 89°. (Analysis results are not available for this compound).

2-Chloro-5-nitro-N-methylaniline was obtained hydrolysis of its toluenesulphonyl derivative with 80 % sulphuric acid at 140°. It formed orange prisms from methanol, MP 110°. (Found: C, 45°08; H, 3°60. Calculated for $C_7H_7O_2N_2Cl$ C, 45°05; H, 3°78 %).

N-Acetyl-N-methyl-2-chloro-5-nitroaniline, white prisms from alcohol, MP 90°. (Analysis results are not available for this compound).

N-Acetyl-N-methyl-2-amino-4-nitro-4'-methyldiphenylsulphide, dull yellow prisms from alcohol, MP 157°. (Found: C, 60°83; H, 5°05. $C_{16}H_{16}O_3N_2S$ requires C, 60°75; H, 5°1 %).

N-Acetyl-N-methyl-2-amino-4-nitro-4'-methyldiphenylsulphone, white platelets from alcohol, MP 170 - 171°. (Found: C, 55°24; H, 4°60. $C_{16}H_{16}O_5N_2S$ requires C, 55°2; H, 4°63 %).

N-Acetyl-N-methyl-2-amino-4-nitro-4'-methyldiphenylsulphone in ethyl d-tartrate.

The sulphone (1·5 gms) was recrystallised from ethyl tartrate (5 cc).

Crystals: solution of 0·60 gms in 15 cc chloroform , 18°c ,

rotation = 0·00°.

Precipitate: solution of 0·471 gms in 15 cc chloroform, 18°c,

rotation = 0·00°.

o-Chlorophenylbenzimino-2'-carbomethoxy-6'-methylphenyl ether could not be obtained as a crystalline solid, the yellow oil which was obtained was heated at 260° over a free flame for 15 - 20 minutes, cooled and triturated with cold methanol to give Methyl 2-chloro-N-benzoyl-6'-methyldiphenylamine-2'-carboxylate, prisms from methanol, MP 169°.

Methyl 2-chloro-N-benzoyl-6'-methyldiphenylamine-2'-carboxylate in ethyl d-tartrate.

The compound (3 gms) was crystallised from ethyl tartrate (20 cc).

Crystals: solution of 1·1022 gms in 15 cc chloroform, 20°c.

Rotation	- 0·11°	- 0·09°	- 0·07°	- 0·05°	- 0·03°	- 0·01°	- 0·00°
Time (min)	4	7	10	18	21	26	35

Precipitate: solution of 0·4623 gms in 15 cc chloroform, 20°c.

Rotation	- 0·27°	- 0·25°	- 0·23°	- 0·18°	- 0·14°
Time (min)	4	6	9	12	16
Rotation	- 0·11°	- 0·08°	- 0·05°	- 0·03°	- 0·00°
Time (min)	20	24	28	32	40

A solution of the compound (2 gms) in ethyl tartrate (30 cc) was allowed to stand overnight at room temperature and the solute recovered by precipitation with water.

Solution of 1·0899 gms in 15 cc chloroform, 22°c.

Rotation	- 0·32°	- 0·30°	- 0·26°	- 0·19°	- 0·16°	- 0·12°
Time (min)	7	9	11	14	16	20
Rotation	-0·07°	- 0·06°	- 0·05°	- 0·03°	- 0·01°	0·00°
Time (min)	24	26	28	30	35	40

Phenylbenzimino-4:6-dichloro-2-carbomethoxyphenyl ether, prisms from alcohol, MP 113°.

Methyl 4:6-dichloro-N-benzoyldiphenylamine-2-carboxylate, prisms from alcohol, MP 119°.

Methyl 4:6-dichloro-N-benzoyldiphenylamine-2-carboxylate in ethyl d-tartrate.

The compound (3 gms) was crystallised from ethyl tartrate (9 cc).

Crystals: solution of 2·025 gms in 15 cc chloroform, 19°c.

Rotation	- 0·09°	- 0·06°	- 0·04°	- 0·03°	- 0·01°	0·00°
Time (min)	6	9	12	14	19	25

Precipitate: solution of 0·57 gms in 15 cc chloroform, 19°c.

rotation = - 0·03° rising to zero.

The compound (2 gms) was dissolved in ethyl tartrate (20 cc) and after standing at room temperature for 24 hours was recovered as usual.

A solution of 1·55 gms in 15 cc chloroform, 18°c.

Rotation	- 0·11°	- 0·08°	- 0·06°	- 0·05°	- 0·02°	0·00°
Time (min)	6	9	11	13	21	30

2-Chlorophenylbenzimino-2'-carbomethoxyphenyl ether, white elongated prisms from methanol, MP 89°. (Found: C, 68·63; H, 4·4. $C_{21}H_{16}O_3NCl$ requires C, 68·8; H, 4·4 %).

Methyl 2-chloro-N-benzoyldiphenylamine-2'-carboxylate, prepared by rearrangement of the above ether at 270 - 290°. White prisms from methanol, MP 123°. (Found: C, 68·95; H, 4·53. $C_{21}H_{16}O_3NCl$ requires C, 68·8; H, 4·4 %).

Methyl 2-chloro-N-benzoyldiphenylamine-2'-carboxylate in ethyl d-tartrate.

The compound (3 gms) was crystallised from ethyl tartrate (10 cc).

Crystals: solution of 1·072 gms in 15 cc chloroform, 18°, rotation = 0·00°

Precipitate: solution of 1·653 gms in 15 cc chloroform, 17°c.

Rotation	- 0·13°	- 0·11°	- 0·10°	- 0·08°	- 0·07°
Time (min)	6	8	10	15	20
Rotation	- 0·04°	- 0·02°	0·00°		
Time (min)	30	40	60		

The compound (1 gm) was dissolved in ethyl tartrate (5 cc) and recovered as usual after 24 hours at room temperature.

A solution of 0·955 gms in 15 cc chloroform, 19°

Rotation	- 0·10°	- 0·09°	- 0·07°	- 0·06°	- 0·04°	- 0·02°	0·00°
Time (min)	5	9	15	20	30	45	60

2-Methylphenylbenzimino-2'-carbomethoxyphenyl ether. Only a pale yellow oil was produced by the action of the imino chloride from benz-o-toluidide on methyl salicylate in the presence of sodium ethoxide. This oil was heated for a while at 260 - 270°, but on cooling and trituration with cold methanol no solid product could be obtained.

Benzylmalono-o-toluidic acid. (cf. Turner, 24; Chattaway, 64). Diethyl benzylmalonate (40 gms) and o-toluidine (11 gms) were heated at 190° in an oil bath in a flask equipped with a fractionating column and condenser. The alcohol produced distilled off at the top of the column, the reaction being almost complete after 3 hours. On cooling, alcohol (150 cc) was added and the crystalline ditoluidide filtered off (12 gms). The alcohol mother liquors were evaporated and the residue distilled in steam with excess sodium carbonate solution. The crystalline sodium salt which separated on cooling was filtered off, suspended in a small quantity of water and decomposed with dilute hydrochloric acid. The precipitated acid was recrystallised from aqueous alcohol as clusters of white needles, MP 154 - 155°(dec).

Benzylmalono-o-toluidic acid in ethyl d-tartrate. The acid (3·1 gms) was dissolved in ethyl tartrate (30 cc) at 100° and allowed to crystallise. A solution of 1·3305 gms in 15 cc chloroform, 17°c, had rotation = - 0·13°. No mutarotation occurred.

The acid did not seem to be sufficiently soluble in formic acid to allow of measurements being made in this solvent, Turner observed

that the active acid racemised in formic acid but he was working with acid of much higher optical purity than that referred to in the present work and so could work with more dilute solutions.

To a solution of 0·8gms of the acid in 15 cc alcohol was added 3 cc of a solution of potassium hydroxide (0·281 gms) in alcohol (25 cc), the rotation of the acid rose from - 0·08° to zero on addition of the alkali.

α-Benzyldesoxybenzoin (cf. Meyer, 25) crystallised from alcohol in white needles, MP 124°.

α-Benzyldesoxybenzoin in ethyl d-tartrate. The compound (8 gms) was recrystallised from ethyl tartrate (40 cc).
Crystals: total weight of crop = 6·5 gms. Solution of 1·047 gms in 15 cc chloroform, 15°c, had rotation - 0·16°. No mutarotation occurred. To this solution were added 1 cc of an equimolecular mixture of pyridine and phenol. The observed rotation was - 0·12°, no mutarotation occurred.

The material remaining in the ethyl tartrate mother liquors was recovered in the usual way and extracted with water in a Soxhlet apparatus to remove ethyl tartrate and then dried in vacuo.
A solution of 0·1380 gms in 15 cc chloroform, 17°c, had rotation = - 16·8°. No change was observed in this rotation over a period of several hours.

Fractional crystallisation of benzyldesoxybenzoin from ethyltartrate.

Benzyldesoxybenzoin (30 gms) was recrystallised from ethyl tartrate

(170 cc) to give crystals (25·3 gms), $[\alpha]^{17} = -2{\cdot}11°$.

The crystals were again recrystallised from ethyl tartrate (200 cc), and then crystallised successively from 4 portions of ethyl tartrate (50 cc each). The rotations at each stage of the process were:

$[\alpha] = -2{\cdot}3°; -3{\cdot}8°; -5{\cdot}2°; -5{\cdot}7°; -5{\cdot}7°; -5{\cdot}7°.$

The benzyldesoxybenzoin recovered from the mother liquors of the first three crystallisations was combined and crystallised from ethyl tartrate (30 cc). This gave 5·8 gms crystals $[\alpha]^{18} = +5{\cdot}7°$, and the precipitate from the mother liquors (approx 0·3 gms) which had $[\alpha]^{18} = +17°$.

In a parallel experiment with another sample of ethyl tartrate a less soluble fraction was obtained with $[\alpha]^{19} = -20°$, the soluble fraction had $[\alpha]^{20} = +20°$.

Attempted separation of optically active mixtures containing benzyldesoxybenzoin.

~~benzyldesoxybenzoin.~~

Benzyldesoxybenzoin (0·5 gms) of $[\alpha]^{18} = +17°$ was recrystallised from ethyl alcohol (20 cc), the crystals (0·3 gms) had $[\alpha]^{18} = +5{\cdot}8°$, $[\alpha]^{18} = +30{\cdot}9°$.

Similarly the laevo rotatory material of $[\alpha]^{19} = -20°$, on crystallisation from alcohol (20 cc/ gm) gave crystals of $[\alpha]^{19} = -14°$, and residue from the mother liquors which had $[\alpha]^{19} = -34°$.

Owing to the small amount of material available it was not possible to carry this separation further.

Attempted chromatographic separation. A solution of the optically active compound, $[\alpha]^{19} = -24°$, (0·32 gms) in benzene (50 cc) was run through a column of activated alumina. Polarimetric readings were taken of each 10 cc of elute. All the dissolved material ran through the column immediately giving 0·31 gms of material, $[\alpha]^{18} = -13·9°$.

Effect of prolonged heat on α-benzyldesoxybenzoin and ethyl tartrate. α-Benzyldesoxybenzoin (1 gm), $[\alpha]^{20} = -5·65°$, which, when crystallised from ethyl tartrate in the normal way, gave material of $[\alpha]^{20} = -5·75°$, was heated at 100° for 7 hours with 5 cc ethyl tartrate. The crystals which separated on cooling had $[\alpha]^{26} = -8·32°$.

Methylethylphenylcarbinol. To the Grignard reagent prepared from ethyl bromide (33 gms) and magnesium (7·2 gms) was added freshly distilled acetophenone (35 gms). After reaction was complete the complex was decomposed with dilute acid, the carbinol extracted with ether, dried and distilled, BP 102° / 16 mm. Yield 28 gms.

Attempted preparation of methylethylphenylacetonitrile. A solution of the carbinol in dry ether (10 gms in 100 cc) was saturated with dry hydrogen chloride at 0° in the presence of calcium chloride. After standing 24 hours at room temperature the ether was evaporated leaving a reddish brown oil. This was refluxed for 3 hours with a solution of potassium cyanide (5 gms) in 60 % aqueous alcohol (20 cc) and then poured into water. The oil which separated was extracted with ether. The ether extract, after drying, was evaporated and the residue distilled, BP 79° / 12mm. The distillate was an oil which

decolourised bromine water and corresponded with αβ-dimethylstyrene.

Attempted reaction with methylethylphenyl-methyl chloride and methyl 2-furoate.

Methylethylphenylcarbinol (21·3 gms) was dissolved in carbon disulphide (100 cc) and a few lumps of calcium chloride added. The solution was cooled in ice and saturated with dry hydrogen chloride. The solution was filtered and mixed with methyl 2-furoate (17·9 gms). This mixture was added to aluminium chloride (38 gms) suspended in carbon disulphide (100 cc) at 0° with mechanical stirring over a period of 30 minutes, stirring was continued for a further 2·5 hours. After a further 20 hours the mixture was decomposed with icw cold hydrochloric acid. The organic layer was separated, filtered from much black solid, washed, dried and evaporated. The residue consisted of a black gum which could not be purified further.

Phenyl-p-tolylacetic acid was prepared by the method of Gyr (65). The crude acid was immediately converted into the amide and then into the nitrile, MP 62°.

Benzylphenyl-p-tolylacetonitrile. Phenyl-p-tolylacetonitrile (3·3 gms) was added to a solution of sodium (0·365 gms) in alcohol (10 cc) and warmed on the water bath for 15 minutes. Benzyl chloride (2·1 gms) was then added and the mixture heated for a few more minutes before being cooled and poured into water. The precipitated nitrile crystallised from alcohol in needles, MP 125°. Yield 3·3 gms.

Attempted alcoholysis of above. The nitrile (0·5 gms) was heated at 120 - 130° for 6 hours with absolute alcohol (5 cc) and 96 % sulphuric acid (0·58 cc). On cooling colourless needles separated MP 125° not depressed on admixture with the starting material.

α-Cyanodesoxybenzoin was prepared by the method of Ghosh (66), plates from acetic acid, MP 95°.

Attempted alkylation of α-cyanodesoxybenzoin. α-Cyanodesoxybenzoin (5 gms) was added to a solution of sodium (0·51 gms) in alcohol (15 cc) and the whole heated on the water bath for 2 hours. Benzyl chloride (3 gms) was then added and heating continued for a further 2 hours. The mixture was cooled, poured into water, filtered and crystallised from alcohol, prisms, MP 95° not depressed by starting material.

Reactions between chalkone and Grignard reagents. The Grignard reagent was prepared from methyl iodide (7 gms) in ether (20 cc) and magnesium (1·2 gms). A solution of chalkone (10 gms) in ether (30 cc) was then added at 0° and the whole stirred mechanically for 30 minutes at 0°, allowed to come to room temperature and finally heated to gentle reflux for about a further hour. The complex was decomposed by the cautious addition to the ice cold mixture of ice cold hydrochloric acid. The ethereal layer was separated, the aqueous layer extracted twice with ether (30 cc), the combined ether extracts washed, dried over sodium sulphate and the ether evaporated. The

residue was a pale yellow gum which did not crystallise on standing. Trituration with various solvents did not produce any solid material, the gum was soluble in all organic solvents except light petroleum. After it had been standing 3 weeks an attempt was made to distill the material at 10 mm pressure, no distillate could be obtained, at indefinite tempetatures above 100° the mixture darkened in colour and water was evolved.

Similarly chalkone (10 gms) was added to the Grignard reagents from ethyl bromide (5·3 gms), benzyl chloride (6·2 gms) and p-bromotoluene (8·3 gms) and magnesium (1·2 gms). Except for a small quantity of dibenzyl (MP 52°) isolated in the experiment involving benzylchloride, the product was in each case a pale yellow oil or gum which could not be distilled. Tests for the presence of carbonyl groupings with 2:4-dinitrophenylhydrazine did not give any positive results.

β-Phenyl-β-9-fluorenylpropiophenone was prepared by the method of Pink and Hilbert (67). It was crystallised first from acetic acid and then from benzene forming colourless prisms, MP 129°.

β-Methyl-β-phenylpropiophenone. Dypnone, prepared by the method of Kohler (68), (20 gms) was dissolved in absolute alcohol (150 cc) and the solution hydrogenated over palladium black (1 gm) at 1 atmosphere and room temperature. The theoretical quantity of hydrogen (1900 cc) was absorbed in 7 hours and on concentrating the alcoholic solution the product was obtained as white glistening platelets,

MP 74° after one crystallisation from alcohol.

β-Phenyl-β-p-tolylpropiophenone. Chalkone (10 gms) was shaken for six days at room temperature with toluene (100 cc) and 96 % sulphuric acid (10 cc). The dark red acid layer was then diluted with water and the toluene layer separated. The aqueous layer was extracted with ether, the combined organic extracts washed, dried and evaporated. The residue consisted of a dark brown oil which crystallised on addition of 4 volumes of alcohol and chilling. It formed soft white needles , MP 97°, after two crystallisations from alcohol. (Found: C, 87·38; H, 6·5. $C_{21}H_{20}O$ requires C, 87·51; H, 6·8 %).

β-Phenyl-β-9-fluorenylpropiophenone in ethyl d-tartrate. The ketone (4 gms) was crystallised from ethyl tartrate (15 cc).

Crystals: solution of 1·221 gms in 15 cc chloroform, 19°c.

rotation = 0·00°.

Residue in mother liquors was insufficient for examination.

β-Methyl-β-phenylpropiophenone in ethyl d-tartrate. The ketone (5 gms) was crystallised from ethyl tartrate (7 cc).

Crystals: solution of 1·857 gms in 15 cc chloroform, 19°c.

rotation = 0·00°

Residues in mother liquors: solution of 1·796 gms in 15 cc chloroform,

19°c, foration = 0·00°

β-Phenyl-β-p-tolylpropiophenone in ethyl d-tartrate. The ketone (3 gms) was crystallised from ethyl tartrate (8 cc).

Crystals: solution of 0·995 gms in 15 cc chloroform, 19°c, rotation = 0·00°

Residues in mother liquors: solution of 1·667 gms in 15 cc chloroform 19°c, rotation = 0·00°.

3-Benzalphthalide was prepared by the method of Gabriel (69).

Desoxybenzoin-2-carboxylic acid. Benzalphthalide (40 gms) was heated for half an hour on the steam bath with potassium hydroxide (30 gms) and water (40 cc). The mixture was then diluted with water to give a homogeneous red solution. On acidification with dilute hydrochloric acid a red oil was precipitated and rapidly crystallised to a white solid, MP 72 - 75° after drying over concentrated sulphuric acid in vacuo. Yield 46 gms.

Methyl desoxybenzoin-2-carboxylate. A solution of the acid (20 gms) in methanol (50 cc) was saturated with a slow stream of dry hydrogen chloride over a period of 3 hours, so that no warming occurred. On standing overnight the ester crystallised. It was filtered off, washed with dilute sodium carbonate and water and recrystallised from methanol as white prisms, MP 109 - 110°. Yield 19 gms.

Benzyl α-benzyldesoxybenzoin-2-carboxylate. To a hot solution of sodium (5·1 gms) in methanol (60 cc) was added methyl desoxybenzoin-2-carboxylate (32 gms). The dark red solution was heated on the steam bath for a few minutes and then benzyl chloride (22 gms) added gradually over a period of 10 minutes with vigorous shaking. The solution boiled vigorously as sodium chloride separated, and the

whole was then heated on the steam bath for 30 minutes to complete the reaction. Methanol (200 cc) was added and the solution filtered hot. The product separated rapidly as long thick white needles which were filtered and washed with methanol till colourless, MP 75°. Yield 28 gms. (Found: C,.83·12; H, 5·62. $C_{29}H_{24}O_3$ requires C, 82·9; H, 5·7 %).

α-Benzyldesoxybenzoin-2-carboxylic acid. The ester (28 gms) and potassium hydroxide (20 gms) were dissolved in 75 % alcohol (75 cc) and refluxed for 2 hours, on cooling, dilution and acidification an oil separated which almost immediately crystallised. The solid was filtered off and recrystallised from acetic acid (60 cc) as white prisms, MP 170 - 171°. (Found: C, 79·67; H, 5·4. $C_{22}H_{18}O_3$ requires C, 79·9; H, 5·45 %).

Brucine α-benzyldesoxybenzoin-2-carboxylate. Brucine (16·8 gms) and α-benzyldesoxybenzoin-2-carboxylic acid (11·8 gms) were dissolved together in hot ethyl acetate (80 cc). The crystals which separated on cooling were washed with a little ethyl acetate.

Solution of 0·784 gms in 15 cc chloroform , α = - 1·60°.

$[\alpha]^{20}$ = - 15·3°.

Brucine d- - benzyldesoxybenzoin-2-carboxylate. The salt was recrystallised from ethyl acetate (300 cc) giving 15 gms of salt, $[\alpha]^{19}$ = - 14·4°. Two more crystallisations from ethyl acetate (200 cc) gave 7 gms of salt, $[\alpha]^{20}$ = - 12·1° not changed on further crystallisation.

d-α-Benzyldesoxybenzoin-2-carboxylic acid. The brucine salt, $[\alpha]_D^{20} = -12{\cdot}1°$, (7 gms) was decomposed with dilute hydrochloric acid to give 4 gms of acid.

Solution of 0·8106 gms in 15 cc chloroform, $\alpha = +2{\cdot}97°$

$$[\alpha]_D^{19} = +27{\cdot}5°.$$

No mutarotation occurred in chloroform solution.

Methyl d-α-benzyldesoxybenzoin-2-carboxylate. d-α-Benzyldesoxybenzoin-2-carboxylic acid (2 gms) was added to excess ethereal diazomethane. The ether and excess diazomethane were then evaporated and the residual gum triturated with light petroleum. The resulting solid was recrystallised from methanol (4 cc), white prisms, MP 110°. (Found: C, 79·96; H, 5·66. $C_{23}H_{10}O_3$ requires C, 80·25; H, 5·81 %).

Solution of 0·3502 gms in 15 cc methanol, $\alpha = +2{\cdot}54°$

$$[\alpha]_D^{20} = +29{\cdot}3°.$$

The ester was refluxed in methanol for 48 hours and the methanol evaporated to small bulk when the ester crystallised.

Solution of 0·4364 gms in 15 cc methanol, $\alpha = +1{\cdot}85°$

$$[\alpha]_D^{15} = +31{\cdot}8°.$$

Racemisation of benzyldesoxybenzoin-2-carboxylic acid. A sample of the acid, $[\alpha]_D^{22} = +4{\cdot}85°$, was heated at 100° for 33 hours with excess aqueous alcoholic sodium ethoxide, a solution of 0·3308 gms in 15 cc chloroform was then found to be optically inactive. On crystallising some of the same sample of acid from acetic acid the crystals were also found to be optically inactive (c = 2 in chloroform).

Methyl -α-benzyldesoxybenzoin-2-carboxylate in ethyl d-tartrate.

The ester (4·7 gms) was crystallised from ethyl tartrate (9 cc).

Crystals: solution of 1·1180 gms in 15 cc methanol had $\alpha = 0·00°$.

Residues: solution of 1·2370 gms in 15 cc methanol had $\alpha = 0·00°$.

Phenylbenzoylacetic ester was prepared by alcoholysis of α-cyanodesoxybenzoin, it crystallised from aqueous alcohol in white needles, MP 94°.

Phenylbenzoylacetic ester in ethyl d-tartrate. The ester (4 gms) was crystallised from ethyl tartrate (8 cc).

Crystals: solution of 1·5733 gms in 15 cc chloroform, 17°c,

rotation = - 0·13° No mutarotation took place.

Residues: solution of 0·5350 gms in 15 cc chloroform, 18°c,

rotation = 0·00°.

This experiment was several times repeated and in some cases, under apparently identical experimental conditions, the crystals were optically inactive. The optically inactive samples were examined in chloroform and acetonitrile solution, no mutarotation took place in either solvent.

Benzoylacetone was prepared from ethyl acetate and acetophenone by the method of Claisen using sodium as condensing agent (70).

Benzoyl-p-toluylacetone. Benzoylacetone (16·2 gms) was dissolved in absolute alcohol (75 cc) and cooled to 0° in a bath of ice water. A solution of sodium (0·46 gms) in alcohol (100 cc) was prepared. To the solution of the diketone were added 10 cc of ethoxide solution

followed by p-toluyl chloride (1·5 gms) with good shaking. The mixture was removed from the ice bath and shaken for 5 minutes, then cooled once more in ice and the process repeated. After all the ethoxide solution and 15 gms p-toluyl chloride had been added the mixture was left in the ice for a further hour, and then overnight at room temperature. The mixture was diluted with water and acidified with dilute acetic acid. The precipitated oil crystallised on chilling in ice and was filtered off. The crude material was dissolved in dilute sodium hydroxide solution, almost neutralised with acetic acid and the oily impurities extracted with ether. The aqueous layer was freed from ether by a rapid stream of air and acidification with acetic acid gave a precipitate of benzoyl-p-toluylacetone. The compound crystallised from methanol in white needles, MP 139°. (Found: C, 77·08; H, 5·9. $C_{18}H_{16}O_3$ requires C, 77·2; H, 5·75 %).

Benzoyl-p-toluylacetone in ethyl d-tartrate. The ketone (2 gms) was crystallised from ethyl tartrate (10 cc). When the material remaining in the mother liquors was precipitated it came down at first as an oil which only gradually solidified.

Crystals: solution of 0·32 gms in 15 cc chloroform, α = 0·00°

Residues: solution of 0·78 gms in 15 cc chloroform, α = 0·00°

Benzoyl-p-toluylmethane. Sodium (9·3 gms) was atomised under xylene and, after cooling and washing with ether, was suspended in dry freshly distilled ethyl benzoate (150 cc). The success of the reaction

depended very considerably on the state of division of the sodium, since any but the very smallest particles failed to react completely. To the suspension was added p-methylacetophenone (52 gms) in portions with shaking. Some heat was generated during the course of the reaction which was modified by cooling occasionally in a bath of cold water, the temperature being kept at about 50° as judged by touch: the addition required about an hour. After standing for a further hour the flask was closed with a ground glass stopper and left at room temperature for 2 days. During this time the sodium reacted to produce a brown gelatinous precipitate of sodio benzoyl-p-toluylmethane. After the reaction was complete the mixture was added cautiously to ice water (500 cc) and light petroleum (300 cc) and well stirred, each portion being completely acted on by the water before the addition of another; a white solid separated at the interface of the two layers but this gradually dissolved. When solution was complete the layers were separated. Acidification of the aqueous layer with acetic acid produced scarcely any precipitate. The petroleum layer was extracted with aqueous potassium hydroxide in 100 cc portions till the alkaline extracts were colourless. The combined alkaline extracts were then acidified with acetic acid and a red oil, rapidly crystallising to a pale yellow solid, was precipitated. It was crystallised from methylated spirits (2 cc / gm) giving pointed white prisms, MP 87°. Yield 38 gms.

It was observed that if very concentrated alkali were used to extract the diketone three layers were formed, a very heavy red oil,

a colourless aqueous layer and the petroleum layer which contained unreacted starting materials. On separating the oil and the aqueous layer from the petroleum and acidifying, the oil crystallised to a pale yellow mass of benzoyl-p-toluylmethane.

Reaction between benzoyl-p-toluylmethane and α-naphthoyl chloride.

a) Sodium as condensing agent. Atomised sodium (1 gm) was suspended in dry ether (100 cc) and benzoyl-p-toluylmethane (10 gms) added. After about 30 minutes the mixture was refluxed gently on the water bath for 5 hours. The sodium dissolved with evolution of gas and the sodio derivative separated as a bulky white solid. After standing overnight the salt was treated with α-naphthoyl chloride (8·7 gms) and the whole refluxed on the water bath for 5 hours. The product was then cooled and poured into water. The ethereal layer was separated and extracted with dilute sodium hydroxide solution. The combined alkaline extracts were acidified but scarcely any precipitate was produced. The ethereal solution was dried over sodium sulphate and evaporated. The oily residue was treated with methanol when crystals were produced. They were recrystallised from dioxan as hard white prisms, MP 148°. (Found: C, 81·16, 80·95; H, 4·53, 4·24. $C_{23}H_{14}O_3$ requires C, 81·00; H, 4·3 %).

The methanolic mother liquors were allowed to evaporate at room temperature, the oily residue crystallised partially after standing for 3 - 4 weeks. The crystals were filtered and cautiously washed with a little cold methanol , the solid was then crystallised twice from benzene giving long white needles, MP 160°.

(Found: C, 76·91, 76·89; H, 4·68, 4·49. $C_{22}H_{16}O_4$ requires C, 76·83; H, 4·65 %).

b) alcoholic sodium ethoxide as condensing agent. Benzoyl-p-toluylmethane (10 gms) was dissolved in absolute alcohol (100 cc). To the mixture cooled in ice water was added 10 cc of a solution of sodium (1 gm) in alcohol (100 cc) followed by α-naphthoyl chloride (0·75 cc). After 5 minutes a further portion of ethoxide solution and naphthoyl chloride were added and the process continued till all the ethoxide and 7·5 cc naphthoyl chloride had been added, the mixture was then allowed to stand overnight at room temperature and poured into water. The ethereal layer was separated and extracted with dilute sodium hydroxide solution till no more acidic material was obtained. Nothing then remained in the ethereal layer. Acidification of the combined alkaline extracts gave the enol form of benzoyl-p-toluylmethane, an insoluble white powder, MP 166°. This slowly dissolved in boiling methanol and on cooling crystals of the diketo form were deposited, MP 87°.

On pouring the methanolic mother liquors into water a solid was precipitated which crystallised from concentrated solution in methanol in needles, MP 158°.

α,β-Dinitrodibenzyl, was prepared from stilbene by the method of Schmidt (71). From 30 gms stilbene were obtained 12 gms of the high melting isomer, MP 233 -235° and 7 gms of the low melting isomer, MP 142 - 146° (after two crystallisations from acetic acid).

αβ-Dinitrodibenzyl in ethyl d-tartrate.

a) High melting isomer. The compound (3 gms) was dissolved in boiling ethyl tartrate (45 cc), some nitrogen dioxide was evolved. The solution crystallised rapidly and completely.

Crystals: solution of 0·9467 gms in 15 cc nitrobenzene, 20°c,

rotation = - 0·28° rising to zero in about an hour.

This experiment was repeated using 3 gms dinitrodibenzyl in 60 cc ethyl tartrate, care being taken to avoid any decomposition, as evidenced by the evolution of nitrous fumes, occurring. In these cases both the crystals and the material remaining in the mother liquors were optically inactive. The experiment was repeated using these quantities but allowing the first crystals to separate while the solution was maintained at 86° for 50 hours in a thermostat. The solution was then cooled very slowly to ensure slow crystallisation. The materials produced in this way were optically inactive.

b) Low melting isomer. The compound (2 gms) was recrystallised from ethyl tartrate (10 cc) care being taken not to heat the solution above 140° (this isomer undergoes conversion to the higher melting isomer above 152°). Both the crystals and the material recovered from the mother liquors were optically inactive, both samples melted at 147°.

iso-Nitroso-dl-camphor. Dry synthetic camphor (10·2 gms) was dissolved in dry ether (50 cc) and clean sodium wire (1·52 gms) added. The mixture was cooled in ice and freshly distilled amyl nitrite (7·8 gms)

added slowly with shaking, the mixture was left for an hour at room temperature when there was little sign of reaction. The ether was then refluxed gently for four hours on the steam bath, when most of the sodium reacted and a gelatinous precipitate was produced. After cooling the mixture was cautiously poured into ice water, the ether layer separated and the aqueous layer extracted several times with ether. On acidification of the aqueous layer with dilute acetic acid an oil separated which was extracted with ether, After drying and evaporation of the ether the residual oil crystallised partially on standing for 24 hours. Addition of light petroleum caused the rest of the material to crystallise also. The solid was recrystallised from light petroleum and was obtained as white prisms, MP 111 - 114° (1·8 gms). On heating for a few hours above its melting point this compound decomposed to a dark resinous mass, instead of yielding a higher melting isomer.

Oxidation of the product. The crystals obtained from the above reaction (1·5 gms) were dissolved in 15 % aqueous potassium hydroxide (15 cc). On addition of a freshly prepared solution of potassium ferricyanide (3·75 gms) in water (15 cc) a bulky colourless precipitate separated, but redissolved in about 5 minutes with evolution of gas to give a brown solution. After an hour this solution was acidified with dilute hydrochloric acid, the precipitated oil extracted with ether and recovered by evaporation of the ether, after washing and drying. This oil did not crystallise even after being kept for several weeks at 0°.

2:2'-Dibromodiphenyl was prepared by the method of Schwechten (72). This consists in treating diphenyl-2:2'-bisdiazonium sulphate with excess potassium mercuri-bromide solution, it was found to be necessary to employ 100 % excess of the mercury salt solution. The resulting tetrazonium-mercury double salt was readily decomposed to give dibromodiphenyl. The product, which was contaminated with a brown impurity, was purified by distillation in vacuo followed by crystallisation from methanol, when it formed white needles, MP 81°.

Attempted Grignard reaction with 2:2'-dibromodiphenyl. Dibromodiphenyl was recovered largely unchanged even after 72 hours refluxing with magnesium in dry ether. It was also recovered after 5 - 6 hours refluxing with magnesium in dry diamyl ether. Rapson and Shuttleworth (37) obtained a Grignard complex after 48 hours refluxing with magnesium in ether, and this on treatment with anhydrous cupric chloride gave tetraphenylene.

Diphenylene-iodonium iodide was prepared by the method of Lothrop (38).

Tetraphenylene. Dry diphenylene-iodonium iodide (12 gms) was mixed thoroughly with cuprous oxide (150 gms) and the mixture heated at 215 - 220° for 3 hours in an oil bath. The cold reaction mixture was extracted with ether (300 cc) in three portions. The ether was evaporated and the residue distilled in vacuo, a fraction boiling at 140° / 1 mm being collected. The distillate was dissolved in alcohol (15 cc) when diiododiphenyl crystallised, MP 109° after one more crystallisation from alcohol (2·3 gms): the mother liquors from

the first crystallisation were poured into water and the precipitate extracted with ether (75 cc) in three portions, the ether extract was dried and evaporated. The residue was crystallised from benzene (1 cc) giving white plates, MP 236° (literature MP of tetraphenylene 230 - 233°.

On treating a cold saturated alcoholic solution of this substance with an equal volume of a cold saturated alcoholic solution of picric acid, scarlet needles, MP 180 - 182°, separated after 3 hours at 0°.

If the mixture of ouprous oxide and diphenylene-iodonium iodide was heated strongly on the sand bath water was free, even though both reactants had previously been thoroughly dried. If the reaction was carried out under reflux , diphenyl BP 105° / 1 mm, and a high boiling oil, BP 240° / 1 mm, which solidified to a glassy solid were obtained, This latter was thought to be a mixture of 2:2'-diphenyldiphenyl and tetraphenylene. If the water was distilled off as the reaction proceeded a 10 % yield of diphenylene, MP 111°, was obtained as well as small amounts of tetraphenylene accompanied by 2:2'-diiododiphenyl.

Attempted Grignard reaction with 2:2'-diiododiphenyl. 2:2'-Diiodo-diphenyl (obtained by heating diphenylene-iodonium iodide for a short time at 215°) was refluxed with one molecular proportion of magnesium in dry ether for 48 hours. No reaction took place.

o-Dibromobenzene was prepared by the method of Hollemann (73).

Action of cupric chloride on the Grignard reagent from o-dibromobenzene.

A solution of o-dibromobenzene (5 gms) in dry ether (30 cc) was refluxed with magnesium (0·52 gms) for 48 hours. The solution was then cooled to 0° and anhydrous cupric chloride (2·8 gms) added with efficient stirring. The mixture was then refluxed for a further 2 hours with stirring: it was then cooled to 0° and ice water (300 cc) added. Hydrochloric acid (10 N) was added to dissolve the copper salts, the ethereal layer was separated and the aqueous layer was extracted twice with ether (30 cc). The combined ethereal extracts were washed, dried over sodium sulphate, the ether distilled and the residue distilled in vacuo. A small amount of diphenyl was obtained followed by a fraction BP 190° / 1 mm. This was an oil which, on treatment with light petroleum, gave a light brown solid. This was recrystallised from methanol (1·5 cc) (charcoal). The crystals which separated were again crystallised from alcohol giving thin white needles, MP 196 - 197°. Yield 20 mgms.

1:2:5:6-Dibenzcyclooctatetraene was prepared by the method of Fieser and Pechet (1939).

1:2:5:6-Dibenz-3carboxy-8-carbamidocyclooctatetraene. The dinitrile (1 gm) was heated with sulphuric acid of density 1·64 gm/ cc (150 cc) at 120 - 125° for four hours the mixture being stirred mechanically. The resulting brown solution was cooled and poured on ice, the grey solid which separated was filtered and, after freeing from acid, was leached with several portions of hot alcohol, being

finally crystallised from a large volume of alcohol, it formed a white microcrystalline powder, MP 283 - 284°(dec). Yield 0·5 gms.

Hydrolysis of the dinitrile. When the dinitrile was heated with 50 % sulphuric acid (D = 1·4 gm/ cc) at 135° for 5 hours as described by Fieser and Pechet it did not go into solution and could be filtered off unchanged. At 150° reaction took place to give a product fairly soluble in alcohol and difficult to purify, probably mainly the diacid. With 62 % acid (D = 1·52 gm/ cc) at 135° for 5 hours a small yield of the half amide was obtained accompanied by a larger amount of the diacid.

1:2:5:6-Dibenz-3-carboxy-8-carboethoxycyclooctatetraene was prepared along with the diester according to the method of Fieser . An an attempt to obtain it from the diester the latter was refluxed with one molecular proportion of alcoholic potash till neutral to litmus (5 hours). The alcohol was evaporated and the residue, after extraction with ether was acidified to give a white solid, MP 240 - 255°, probably a mixture of the diacid and the acid [illegible].ester. Evaporation of the ethereal layer gave back some of the diester.

Attempted preparation of the half hydrazide. The diester (0·348 gms) was heated with hydrazine hydrate (0·08 gms) in alcohol (1 cc) at 120° for 1 hour. Crystals of the diester separated on cooling and were pure after one crystallisation from alcohol.

Brucine 1:2:5:6-dibenz-8-carbamidocyclooctatetraene-3-carboxylate. The half amide (0·455 gms) and brucine (0·728 gms) were dissolved hot methanol (7 cc), filtered hot and the methanol evaporated. The residue was crystallised from benzene (3 cc). This salt had $[\alpha]^{20} = -3·64°$. (c = 2 in methanol), no mutarotation occurred. Evaporation of the mother liquors yielded a further crop, probably contaminated with brucine however: $[\alpha]^{20} = -15·5°$ (c = 3 in methanol).

The solutions of both samples were evaporated to dryness and the residue partitioned between [illegible] chloroform and 15 cc of 2 % aqueous potassium hydroxide. The aqueous layer was extracted with chloroform till free from brucine, in neither case was the resulting solution of the potassium salt optically active.

o-Iodobenzoic acid was prepared from anthranilic acid by diazotisation and decomposition of the diazonium iodide. It formed light brown needles from acetic acid, MP 160 - 162°, yield 153 gms from 133 gms of anthranilic acid.

o-Iodobenzaldehyde was prepared by the method of Rapson and Shuttleworth (41).

Diphenyl-2:2'-dialdehyde. o-Iodobenzaldehyde (10 gms) was mixed with clean dry sand (15 gms) and copper bronze (15 gms) in a flask fitted with inlet and outlet tubes through which a slow stream of nitrogen was passed. After the nitrogen had been passing for 15 minutes the flask was heated to 140° in an oil bath and the temperature then raised to 200° over a period of 30 minutes, and maintained there

for 20 minutes before being allowed to cool, still in an atmosphere of nitrogen. The cooled mass was extracted with ether (200 cc) in eight portions. Evaporation of the ether left a yellow oily residue which soon crystallised. The crystals were pressed between filter paper to remove adhering oil and recrystallised from a mixture of ether and light petroleum, giving yellow platelets, MP 63°. Yield 2·8 gms.

Attempted condensation of diphenyl-2:2'-dialdehyde and succinonitrile.

a) Sodium ethoxide as condensing agent. The dialdehyde (2·1 gms) and succinonitrile (0·80 gms) were dissolved in absolute alcohol (20 cc) and 10 % alcoholic sodium ethoxide (2·8 cc) was added with shaking. After the ethoxide had been added the mixture was left for 1·5 hours at room temperature and then refluxed on the steam bath for 3 hours. The alcohol was then evaporated in vacuo and the residue dissolved in ether and dilute hydrochloric acid. The ethereal extract was filtered, washed with water and dried over sodium sulphate. Evaporation of the ether left an oil which soon crystallised and was recrystallised from methanol as light brown prisms, MP 132 - 133·5°. Literature MP of XXXII = 132° (Kenner, 74). (Found: C, 80·07; H, 4·89. Calculated for $C_{14}H_{10}O_2$ C, 80·0; H, 4·76 %).

b) Diethylamine as condensing agent. The dialdehyde (1·05 gms) and succinonitrile (0·4 gms) were melted together by gentle heat and 6 drops diethylamine added, crystals of the dialdehyde separated in a few days , MP 60 - 61 °, not depressed by mixture with starting material.

c) Pyridine as condensing agent. The dialdehyde (1·05 gms) and succinonitrile (0·4 gms) were heated together in pyridine (3 cc) on the water bath for 5 hours. After cooling the mixture was dissolved in ether and washed with dilute hydrochloric acid and water. Evaporation of the dried ether solution left a residue which did not crystallise.

2:2'-Dimethyl-3:3'-diquinolyl-4:4:-dicarboxylic acid. Acetonylacetone dioxime (3 gms) isatin (12 gms) and 40 % aqueous potassium hydroxide (45 cc) were refluxed for 40 hours. Crystals separated on cooling and, after standing 4 hours, were filtered off, washed with 40 % potassium hydroxide solution and recrystallised from water (5 cc). Yield, after drying at 100°, 2·8 gms. This material was readily soluble in hot water, less soluble in cold and sparingly soluble in potassium hydroxide solution. It decomposed somewhat on drying and concordant analyses dould not be obtained.

Decomposition of the potassium salt with dilute hydrochloric acid gave 2:2'-dimethyl-3:3'-diquinolyl-4:4'-dicarboxylic acid as an insoluble white powder, MP 326 - 330° (dec).

Treatment of the aqueous solution of the potassium salt with S-benzylthiuronium chloride gave the S-benzylthiuronium salt , crystallising as the dihydrate in white needles from aqueous alcohol, on heating the crystals decomposed at 180°. (Found: C, 62·21; H, 5·4; N, 11·53. $C_{38}H_{34}O_4N_6S_2 2H_2O$ requires C, 62·5; H, 5·25; N, 11·7 %).

Decarboxylation of above acid. The acid (1 gm) was mixed with copper chromite catalyst (5 gms), placed in a vacuum sublimation apparatus and covered with a thin layer of copper chromite. The mixture was sublimed at 200° / 10 mm for 3 hours. The rather gummy sublimate was triturated with light petroleum and crystallised from benzene, clusters of needles MP 144° not depressed by mixture with 2:2'-dimethyl-3:3'-diquinolyl.

2:2'-Dimethyl-3:3'-diquinolyl was prepared by the method of Friedlander (44). After dehydration over concentrated sulphuric acid in vacuo and crystallisation from benzene it formed needles MP 144°.

Attempted condensation of benzil and 2:2'-dimethyl-3:3'-diquinolyl. 2:2'-Dimethyl-3:3'-diquinolyl (0·71 gms) and benzil (0·525 gms) were dissolved in acetic anhydride (1 cc) and heated at 150 - 160° for 12 hours. After cooling water was added and the resulting black gum triturated with 50 cc boiling alcohol, when a dark brown solid was produced (0·55 gms). This decomposed at 200 - 210°, it was very insoluble in alcohol, soluble in ether and benzene, but it could not be made to crystallise from either of these solvents, nor could it be sublimed in vacuo. The benzene solution was dark brown in colour with a red fluorescence, chromatography on a column of alumina did not give satisfactory material.

When the acetic anhydride was replaced by hydrochloric acid or when no condensing agent was used no reaction took place.

Benzil-2-carboxylic acid. Oxidation of a solution of desoxybenzoin-2-carboxylic acid (5 gms) and sodium carbonate (1·1 gms) in water (50 cc) with an aqueous solution of potassium permanganate (0·65 gms) at room temperature gave benzil-2-carboxylic acid (3·7 gms), MP 71 - 73° after drying over concentrated sulphuric acid in vacuo. The methyl ester was prepared by the action of ethereal diazomethane.

Attempted condensation of 2-carbomethoxybenzil and 2:2'-dimethyl-3:3'-diquinolyl.

Dimethyldiquinolyl (0·72 gms), 2-carbomethoxybenzil (0·6 gms) and acetic anhydride (1 cc) were heated at 150 - 160° for 6 hours. To the resulting dark brown viscous liquid water was added drop by drop with shaking. A dark brown solid was obtained and filtered off. It could not be recrystallised from any solvent or purified in any way. It much resembled the material obtained from benzil and dimethyldiquinolyl.

o-Iodobenzyl cyanide was prepared by the method of Rapson and Shuttleworth (41). It was obtained as a colourless oil BP 167° / 10 mm.

2:2'-Diiododiphenylketipiniodinitrile. To a solution of sodium (0·6 gms) in alcohol (10 cc) was added diethyl oxalate (1·8 gms). After shaking for a few minutes a homogeneous solution was obtained. o-Iodobenzyl cyanide (6·1 gms) was added with shaking when a yellow colour developed and the mixture was warmed for a few minutes on the water bath when it became brown in colour and a colourless flocculent solid separated. The mixture was then cooled and water

added, some of the material dissolved but a considerable amount of tar remained. The aqueous solution was decanted from the tar and acidified, after 5 - 6 hours a pale yellow solid separated which melted with decomposition at 140 - 155°. The tar was dissolved in glacial acetic acid and the solution added slowly to water with stirring. The resulting brown solid was triturated with 2 N sodium hydroxide solution and the alkaline solution decanted from the tar, on acidification a small amount of yellow flocculent precipitate was obtained. The solid was washed with hot methanol and crystallised from acetic acid as bright yellow prisms, melting with decomposition at 240 - 242° (0·4 gms). (Found: C, 41·01; H, 2·12. $C_{18}H_{10}O_2N_2I_2$ requires C, 41·01; H, 1·9 %).

2-Acetyl-2'-carboxydiphenyl. An 8·66 % solution of methyl bromide in pure dry ether was prepared. The Grignard reagent was prepared by gradual addition of this solution (40 cc) to dry magnesium (0·9 gm) under reflux, after addition was complete the mixture was heated to boiling for 45 minutes. The cooled ethereal solution was then decanted from the magnesium into a three necked flask equipped with mechanical stirrer and reflux condenser and cooled in ice. Anhydrous cadmium chloride was added with vigorous stirring and stirring was continued in the ice bath for a further 1·5 hours. Finely powdered diphenic anhydride (1·6 gms) was added in portions over a period of 15 minutes, the flask was then removed from the ice bath and the mixture refluxed for 3 hours, stirring being maintained. A viscous oil separated during the heating process.

The mixture was cooled in ice and the complex decomposed with ice cold 6 N sulphuric acid (50 cc). Ether (100 cc) was added, some solid (unreacted anhydride) filtered off, and the two layers separated. The aqueous layer was extracted with ether (75 cc), the combined ethereal solutions washed with 4 N sodium carbonate (150 cc) in three portions. The alkaline solution was washed several times with ether and acidified. The oil which separated was extracted with ether and, after drying over sodium sulphate, the ether evaporated. The residue consisted of a viscous yellow oil, which crystallised to a sticky solid after 10 days. Trituration of this with light petroleum gave a white solid, MP 110 - 114°, yield 0·65 gms of 2-acetyl-2'-carboxydiphenyl. Analytical results are not available for this compound which did not crystallise well, it was characterised in the form of its derivatives.

Evaporation of the neutral solution gave a solid crystallising from alcohol in needles, MP 73 - 75°. This compound which was available only in small amounts was not analysed, from analogous reactions however it is probably 3:3-dimethyldiphenide (cf. Wang Isensee, Griffith and Christensen, 75)

Methyl 2-acetyldiphenyl-2'-carboxylate. Esterification of the acid by the Fischer - Speier method gave the methyl ester, BP 140° /2 mm. It crystallised from alcohol in white needles, MP 73 - 75°. (Found: C, 75·34; H, 5·34. $C_{16}H_{14}O_3$ requires C, 75·6; H, 5·3 %).

4-Acetylfluorenone. 2-Acetyl-2'-carboxydiphenyl was refluxed with

excess thionyl chloride in benzene solution for 1 hour. Evaporation of the excess thionyl chloride and benzene left a black gum from which, on sublimation at 170 - 180° / 2 mm, was obtained a pale yellow crystalline solid. This was recrystallised from benzene to give almost colourless prisms of 4 -acetylfluorenone, MP 139 - 141°. (Found: C, 80·9; H, 4·5. $C_{15}H_{10}O_2$ requires C, 81·1; H 4·7 %).

Attempted Arndt - Eistert synthesis with 2-acetyl-2'-carboxydiphenyl.

The acid (2 gms) was dissolved in benzene (20 cc) and pure thionyl chloride (20 cc) added, the whole was warmed to 50° for 1 hour. The benzene and thionyl chloride were then evaporated in vacuo below 50°. Benzene (10 cc) was then added and the evaporation repeated, two more portions of benzene were evaporated in this way. The residue was then dissolved in dry ether (10 cc) and added to the ethereal solution of diazomethane obtained from 10 gms N-nitrosomethylurea. After standing 2 days the ether and excess diazomethane were evaporated . The gummy residue was dissolved in methanol (40 cc) silver oxide (1 gm) added and the whole refluxed for 8 hours. After filtering from silver oxide the solution was boiled with charcoal, filtered and distilled in vacuo. A small amount of distillate, BP 140° / 2 mm, was obtained as a viscous oil. It did not crystallise nor could it be hydfolysed to a solid acid.

In another experiment the residue, after evaporation of ether and diazomethane, was refluxed with silver oxide in a mixture of dioxan and aqueous ammonium hydroxide solution: the only product which

could be isolated was an uncrystallisable oil.

Condensation of benzil and 2:2'-diaminodiphenyl. Benzil (5·5 gms) and 2:2'-diaminodiphenyl (4·5 gms) were refluxed together in acetic acid (70 cc) containing a trace of hydrochloric acid for 3 hours. The condensation product began to separate from the boiling solution after 1 hour , crystallisation was complete on cooling. The product consisted of pale yellow prisms; MP 238°. Yield 7 gms.

This condensation product in ethyl d-tartrate. The compound (3 gms) was crystallised from ethyl tartrate (30 cc).
Crystals: solution of 0·5680 gms in 15 cc chloroform, α = 0·00°.

3-Nitro-o-toluidine. The methods of preparation of this compound described in the literature being found unsatisfactory (76, 78), the following procedure was adopted.

A solution of fuming nitric acid (110 cc) in acetic anhydride (250 cc) was cooled to below 10° in an ice bath and stirred mechanically. To this was added powdered acet-o-toluidide (100 gms) in portions at such a rate that the temperature rose above 15° but not above20°, with efficient cooling in the ice bath fairly rapid addition was possible. The toluidide dissolved to give a yellow brown solution, in some experiments when nearly all the toluidide had been added the nitration product commenced to separate, this occasioned a slight rise in temperature and it was necessary to suspend further addition

of acetyltoluidine till the temperature fell: in other experiments it was possible to add all the reactant before the product started to separate. After addition was complete stirring was continued in the ice bath for a further 1·5 hours and then water (1 l) added. The mixture of nitration products was filtered and washed thoroughly to remove acid. The solid was then suspended in 10 N hydrochloric acid (400 cc) and distilled in steam. After a short time an orange solid began to distill and distillation was continued till no further solid was obtained in the distillate, about 16 litres of distillate. The 3-nitro-o-toluidine was filtered, dried at the pump and crystallised from methylated spirits as large orange needles or elongated prisms, MP 97°. Yield 48 gms.

3-Nitro-2-iodotoluene was prepared by diazotisation of the amine and decomposition of the diazonium iodide in the usual manner, it formed pale yellow prisms from alcohol, MP 55°.

6:6'-Dinitro-2:2'-ditolyl. 3-Nitro-2-iodotoluene (30 gms) was heated to 200 - 210° and copper bronze added in portions, stirring with a thermometer. Considerable heat was evolved at first and external heating was discontinued, the rate of addition of the copper being adjusted to maintain the temperature at about 215°. When the heat of reaction was insufficient to maintain this temperature the mixture was once more heated to 210 - 215° in an oil bath while the rest of the copper (25 gms in all) was added. Heating was continued for 30 minutes after all the copper had been added and then

the mixture allowed to cool to about 90° when methylated spirits (330 cc) was added with good stirring, the alcoholic solution was heated to boiling for a few minutes and filtered hot, the residue being extracted with two more portions of spirits (200 cc). The combined extracts were then boiled with charcoal, filtered hot and concentrated to about 250 cc . Dinitroditolyl crystallised as cream coloured needles, MP 110°. Yield 11 gms.

4:5-Dimethylbenzcinnoline oxide. A solution of dinitroditolyl (0·67 gms) in alcohol (65 cc) was warmed and a hot solution of sodium sulphide (4·7 gms) in water (3 cc) added in one portion. The whole was refluxed on the water bath for 1 hour, most of the alcohol evaporated and the residue poured into water. The product was crystallised from alcohol giving a mixture of needles and brown prisms. The needles were identical with the starting material, the prisms, which melted at 132° consisted of the azoxy compound. Treatment of this azoxy compound with the theoretical quantity of stannous chloride in hydrochloric acid gave a black tar accompanied by some diaminoditolyl, MP 135°.

4:5-Dimethylbenzcinnoline. A solution of dinitroditolyl (10 gms) in absolute alcohol (350 cc) was stirred mechanically while being cooled in a stream of running water. 3 % Sodium amalgam (500 gms) was added in portions during 50 minutes at 15 - 25°, stirring was maintained for a further 15 minutes and the temperature just raised to 40°. The alcohol layer was separated and poured into water

(1·5 l). The solid which separated was filtered , dissolved in 6 N hydrochloric acid , the solution of the hydrochlorides filtered and made alkaline with ammonium hydroxide. The mixed bases were filtered (6·3 gms) and crystallised from alcohol (25 cc) giving a mixture of white prisms and yellow needles. Further alcohol was added to dissolve the needles, the prisms were filtered off, they melted at 135° and consisted of 6:6'-diamino-2:2'-ditolyl (3 gms). The alcoholic mother liquors were evaporated and the residue crystallised from methanol (10 cc) giving fine yellow needles, MP 95 - 100° (2·5 gms). Two more crystallisations from methanol gave bright yellow needles of 4:5-dimethylbenzcinnoline, MP 113°. Yield 1·5 gms.

Action of sodium arsenite on 2:2'-ditolyl-6:6'-tetrazonium chloride

Diaminoditolyl (1·4 gms) was dissolved in 2 N hydrochloric acid (17 cc) and cooled to 0°. 2N Sodium nitrite (7 cc) was then added drop by drop. After 30 minutes the tetrazo solution was made neutral to congo red paper with 2 N sodium carbonate solution and siphoned into an ice cold solution of arsenious oxide (2 gms) in 2 N sodium carbonate (20 cc) containing some cupric sulphate. A brown solid was precipitated and was filtered off. It was non - basic and was not investigated further.

4:5-Dimethylbenzcinnoline in ethyl d-tartrate. A solution of the base in ethyl tartrate (2 gms / 5 cc) was allowed to stand at room temperature for several days and then the solute recovered as usual.

A solution of 0·25gms in 15 cc chloroform, α = 0·00°

First order asymmetric transformation of 4:5-dimethylbenzcinnoline d-camphorsulphonate.

Dimethylbenzcinnoline (0·104 gms) was dissolved in 10 cc chloroform and d-camphorsulphonic acid added (0·111 gms). As soon as all the acid had dissolved the volume was made up to 15 cc, 19°c.

Rotation	+ 1·23°	+ 1·18°	+ 1·15°	+ 1·11°	+ 0·95°
Time (min)	8	20	26	43	115
Rotation	+ 0·85°	+ 0·80°	+ 0·77°	+ 0·77°	
Time (min)	180	263	310	360	

Total change in specific rotation was from + 16·8 ° to + 10·5 °

Preparation of a sample of 4:5-dimethylbenzcinnoline containing an excess of the l form.

Dimethylbenzcinnoline (0·4815 gms) and d-camphorsulphonic acid (0·7610 gms)were dissolved in chloroform and the solution diluted to 50 cc. Two portions of 20 cc each were removed from the solution.

a) The chloroform solution of the camphorsulphonate was extracted with dilute ammonium hydroxide solution, the chloroform layer separated and extracted with dilute hydrochloric acid. The colour of the dimethylbenzcinnoline hydrochloride being too intense to allow of polarimeter readings being taken, the solution was therefore made alkaline and the base extracted with chloroform, the chloroform solution was dried roughly by passing through a paper filter . The solution was optically inactive,

b) The other portion of the solution was quickly evaporated at 23° in vacuo. The residue was treated with ammonium hydroxide and the precipitated base filtered, washed and dried.

Solution of 0·1488 gms in 15 cc chloroform, 20°.

Initial rotation (16 minutes after wetting) = - 0·12° ± 0·04°

rising to zero in a few hours.

Owing to the intense colour of the solution no rate measurements could be made.

B I B L I O G R A P H Y

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