

THE CONFIGURATION OF 2:2'-BRIDGED DIPHENYLS

By

Gwendoline Ruth Bird,
Bedford College.

Thesis presented for the Degree of Doctor of Philosophy
in the University of London.

October, 1952.

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ABSTRACT

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Summary.

The thesis is divided into five sections.

1. A review is given of some of the aspects of the stereochemistry of diphenyl and its derivatives.
2. The attempt has been made to resolve a diphenyl derivative in which the 2 and 2' positions in diphenyl are linked by a 7-membered ring and the 6 and 6' positions are free from substituents. Such a compound should be capable of existing in enantiomorphous forms as it possesses no element of symmetry. No optically active compound has been isolated, but in one case two diastereoisomeric quinine salts of widely different rotation were obtained which yielded an inactive acid on decomposition. The idea is put forward that non-resolution of such compounds is due to the difference in specific rotation of the enantiomers and/or diastereoisomers being extremely small. It is shown that the compounds are not optically labile.
3. An attempt has been made to ascertain whether the "crowding" effect of the two nitro substituents on the two carboxyl groups in 3:3'-dinitrodiphenic acid is such as to render the acid sufficiently optically unstable to show first and/or second order asymmetric transformation at room temperature. No sign of optical instability was apparent in the dimethyl ester: the acid could not be obtained pure.

4. The reactivity of certain diphenyl derivatives with a variety of reagents has been investigated.
5. The ultraviolet absorption spectra of certain diphenyls containing the 7-membered ring bridging the 2:2' positions have been determined, in order to find out how much reliance can be placed on the previous assumption that such spectra are a valuable guide to configuration in the diphenyl series. It is shown that the ultra-violet absorption spectrum of a substituted diphenyl must be used with considerable reserve as a criterion of coplanarity or otherwise.

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My grateful thanks are due to the following:-

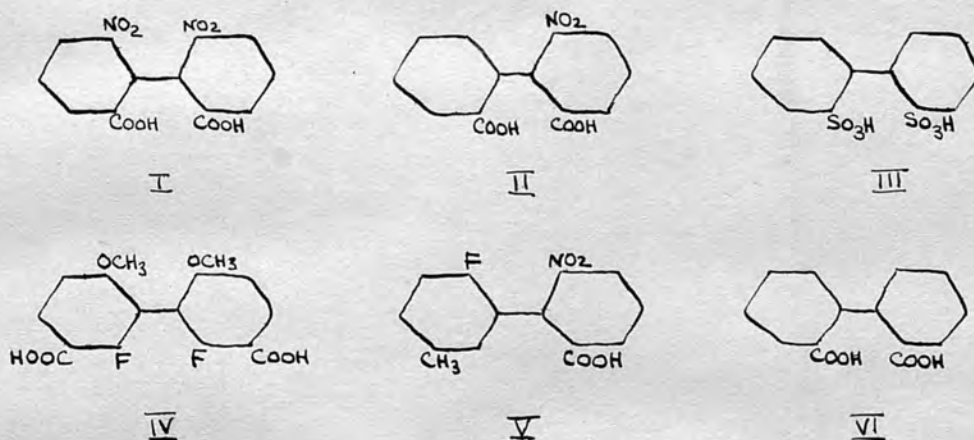
Professor E.E.Turner, Dr.M.S.Lesslie and Dr.D.M.Hall for help and advice during the period of research.

The Council of Bedford College for awarding me a Post-graduate Research Fellowship for two years which enabled me to carry out the work.

Dr.G.H.Beaven for determining the ultraviolet absorption spectra of certain compounds.

A. Introduction: A review of some of the aspects of the stereochemistry of diphenyl and its derivatives.

The resolution of 6:6'-dinitrodiphenic acid into optically active forms by Christie and Kenner in 1922 [J., 1922, 614], opened up an entirely new field of stereochemistry, and stimulated the preparation and attempted resolution of many diphenyl derivatives. Certain of these derivatives containing two, three or four ortho-substituents were found to be resolvable (I, II, III), while others (IV, V, VI) resisted all attempts at resolution.

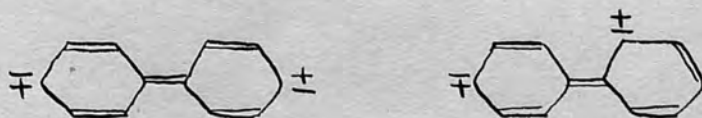


From a detailed study (see Adams and Yuan, [Chem. Rev., 1933, 12, 262], for a summary of earlier work) of the compounds which could be resolved and those which could not, it became clear that the optical activity was due to an obstacle effect. Because of the size of the ortho substituents, the benzene rings are unable to assume the coplanar position although they remain coaxial. The molecules as a whole therefore possess none of the elements of symmetry, and exist in two enantiomorphous forms provided neither benzene nucleus is

symmetrical about the co-axes. These extensive investigations were concerned with demonstrating that the diphenyl skeleton could be forced to take up a non-coplanar configuration, but the question of the coplanarity or otherwise of those diphenyls which could assume a coplanar position also attracted attention.

The configuration of the parent hydrocarbon diphenyl may be considered first. Dhar [Indian J. Physics, 1932, 2, 43] and Pickett [Nature, 1933, 131, 513] showed by X-ray crystallographic analysis that in the diphenyl crystal the two benzene rings are coaxial and coplanar, the 1:1'-bond distance being 1.48\AA compared with $C-C_{\text{aliphatic}} 1.54\text{\AA}$ and $C=C_{\text{olefinic}} 1.38\text{\AA}$. This work does not however necessarily throw much light upon the question of the preferred configuration of an isolated molecule.

The resonance energy of diphenyl as calculated by Pauling and Sherman [J. Chem. Phys., 1933, 1, 606] is greater by about 8 kcal/mol than twice that of benzene, suggesting that the contribution of structures such as VII to the ground state of the molecule cannot be left unconsidered.

VII

Various workers have stressed the fact that any tendency for the pivot bond to assume double bond character implies coplanarity of the two benzene nuclei. It has been

reported Wheland, [The Theory of Resonance, 1944, p.69] that the unconjugated structure diphenylmethane has a comparable resonance energy, and obviously no conclusions as to the configuration of diphenyl can be drawn from such calculations.

Electron diffraction studies in the vapour phase do give information concerning the single molecule. Karle and Brockway [J. Amer. Chem. Soc., 1944, 66, 1974] concluded that electron diffraction data alone could not decide whether diphenyl was coplanar or not, but favoured the non-coplanar structure as it avoids steric hindrance between the ortho hydrogen atoms. They pointed out that in the coplanar model, the separation of the hydrogen atoms is 1.84\AA , whereas the nearest approach between two molecules of e.g. methane is 2.0\AA . Bastiansen [Acta Chem. Scand., 1949, 3, 408] agreed with the non-coplanar model and calculated an angle of $45^{\pm 10^\circ}$ between the two benzene nuclei.

The characteristic absorption in the quartz region of the ultraviolet ($4000-2000\text{\AA}$) is attributed to electrons which are in π -type bond orbitals, or electron pairs not in a bond. Hence a study of the ultraviolet absorption spectra of diphenyl and its derivatives should give information concerning the conjugation between the two benzene rings. A comparison of the spectra of diphenyl and benzene fig. I shows that they differ greatly from

one another, the intensity of the main absorption band being increased by about 90 times [benzene λ_{\max} 2550Å, ϵ 213; diphenyl λ_{\max} 2500Å, ϵ 18,000]. This implies considerable interaction between the electronic systems of the two aromatic rings across the pivot bond, involving structures such as VII. One of the accepted generalizations of absorption spectroscopy is that an increase in the number of conjugated double bonds in a system results in a displacement of the absorption maxima to longer wavelengths, together with an increase in the intensity of absorption. The near coincidence of the absorption maxima of benzene and diphenyl, with that of benzene being somewhat higher than that of diphenyl, is merely fortuitous. The first absorption band of benzene, which is of low intensity, is almost certainly due to a transition to an excited state that results largely from resonance between the Kekulé structures. The first absorption band of diphenyl, which is of high intensity, is probably due to an excited state which results from resonance principally among ionic structures such as VII. It has been pointed out several times that this implies coplanarity of the benzene rings: for example, O'Shaughnessy and Rodebush [J. Amer. Chem. Soc., 1940, 62, 2906] state: "for resonance or conjugation to involve two rings as in biphenyl, it is necessary that the π -orbitals of the adjacent 1:1'-carbons be parallel, and this requires the coplanarity of the two rings." On the other hand, Merkel and Wiegand [Z. Natur-

Ultraviolet Absorption Spectra of diphenyl
and benzene.

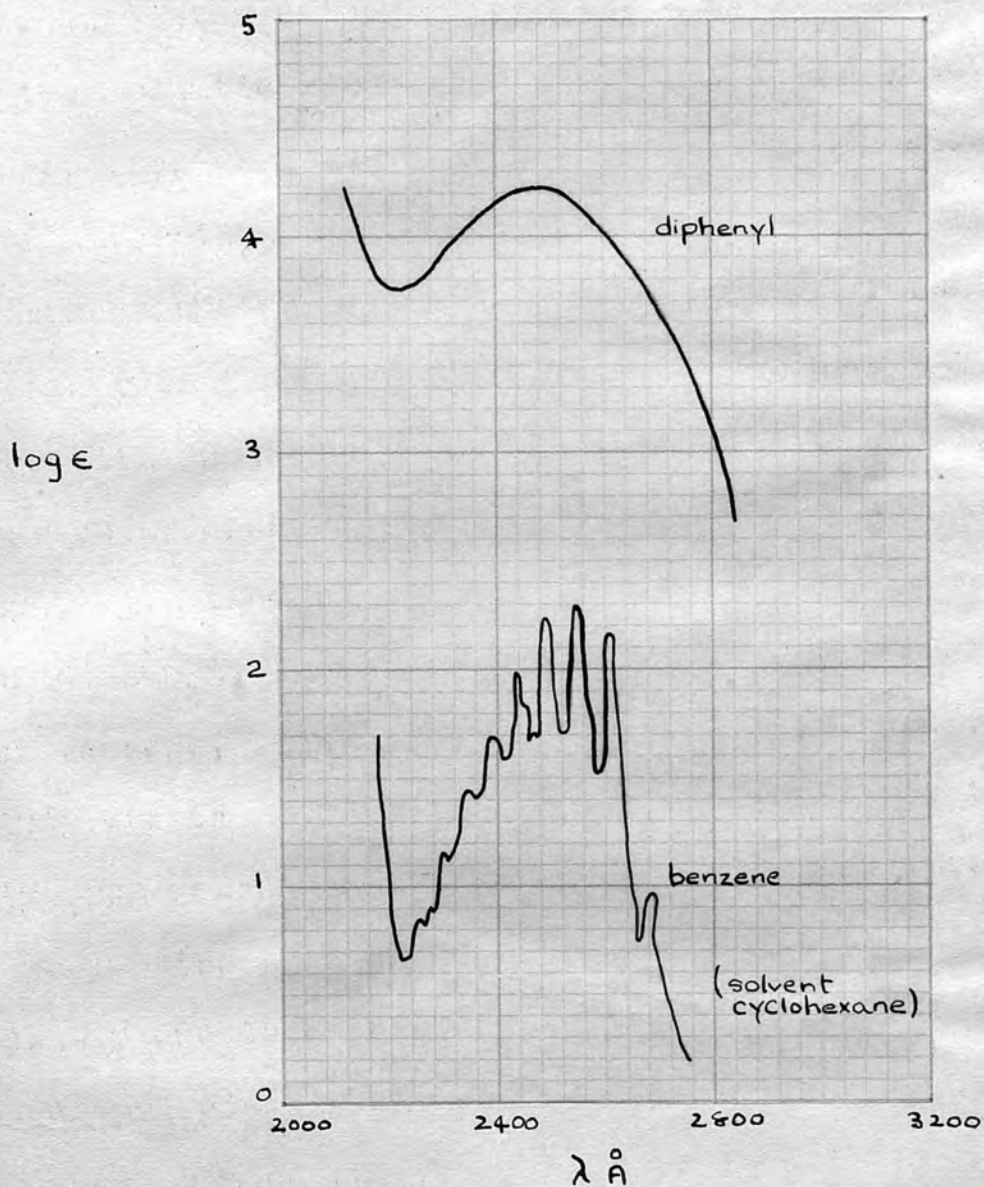


Fig I

forsch., 1948, 36, 93 and Naturwissenschaften, 1947, 34, 122] claim to have found that diphenyl is planar in the crystal but non-planar in the vapour state and in hexane solution. This conclusion was based on the idea that aromatic molecules of flat structure tend to show a fine-

structure in their long-wave absorption bands, and if the structure is not flat, this fine structure is not apparent. The effect is claimed to be most pronounced in the vapour form, diminishing in solution, although hexane has little effect on the fine structure.

The various pieces of evidence relating to diphenyl derivatives may now be considered. Since a coplanar model implies a possibility of conjugation across the pivot bond, it would appear at first sight that where the molecule could become flat, it would do so in order to increase the resonance energy. On the other hand, interatomic repulsions would make a completely flat molecule seem improbable, particularly as there is evidence of hindered rotation in ethane and its simple derivatives. Which tendency would be the greater? If some departure from coplanarity is permissible without loss of conjugating power, some compromise might be effected. There is little in the chemical literature concerning the degree of non-coplanarity which would make the contribution of the conjugated molecule negligible.

Dipole moments of 2:2'-disubstituted diphenyls should show whether the molecule is entirely trans ($\mu=0.00D$), or cis (when the moment is readily calculable). Measurements made imply a non-coplanar configuration; for example Hampson and Weissberger [J.Amer.Chem. Soc., 1936, 58, 2111] found that for 2:2'-dichlorodiphenyl $\mu = 1.45 D$, whereas the calculated value is 1.31D for the cis molecule. Le Fèvre

and Vine [J., 1938, 967] compared the moments of 2:2'-disubstituted compounds with those of their analogues substituted also in the 4:4'-positions. The changes in moment were greater than could be attributed to the polarity of the substituents, and this was also thought to favour a non-coplanar model. As Hampson and Weissberger [loc.cit.] point out: "the forces regulating the probabilities of the various configurations are (a) electrostatic repulsions and attractions, (b) quantum mechanical attractions (London forces), (c) quantum mechanical repulsions (impenetrability of colliding atoms)". Since there are insufficient data as to the precise effect of these factors, these results again give little information as to the preferred configuration of the diphenyl molecule itself. Le Fèvre and Le Fèvre [J., 1936, 1130] attempted to find information concerning the resonance interaction between the two benzene rings by studying the moments of 4:4'-disubstituted diphenyls, the 4- and 4'- groups being dissimilar, and comparing them with the moments of the corresponding para-disubstituted benzenes. These workers inferred that there was some resonance interaction between the groups and hence between the two rings, which implied coplanarity.

With regard to X-ray data, Toussaint [Acta Cryst., 1948, 1, 43] considered 3:3'-dichlorobenzidine to be planar or nearly so, with the chlorine atoms in the trans position. Smare however [ibid., 150] found that the molecules of 2:2'-

dichlorobenzidine show a tendency to adopt the cis-configuration, steric hindrance demanding an angle of 72° between the rings. The 1:1'-bond is $1.53\overset{\circ}{\text{Å}}$, which is almost the exact C-C_{aliphatic} bond distance. Again, Fowweather and Hargreaves [ibid., 1950, 3, 81] found that the two phenyl rings in 2:2'-dimethylbenzidine dihydrochloride are mutually inclined at an angle of 70.6° , which brings the two methyl groups in contact. The pivot bond is $1.52\overset{\circ}{\text{Å}}$ and the separation of the two methyl groups $3.54\overset{\circ}{\text{Å}}$, which is considerably less than the usual methyl-methyl separation between two discrete molecules of about $4\overset{\circ}{\text{Å}}$. This would seem to imply that crystallographic data are probably of little use in determining preferred configurations in a free molecule of the diphenyl type as the intramolecular repulsive forces have obviously been overcome by some other factor in the formation of the crystal unit.

Bastiansen [loc.cit.] studied 3:3'-dichlorobenzidine and 3:3'-dibromodiphenyl by the electron diffraction rotating sector method, and concluded that in the first compound the rings are inclined at an angle of about $52\pm 10^\circ$, while in the bromo-compound the angle is about $54\pm 10^\circ$. He also found [Acta Chem. Scand., 1950, 4, 926] the cis configuration for 2:2'-dichloro-, 2:2'-dibromo- and 2:2'-di-iodo-diphenyl, with interannular angles of 74° , 75° and 79° , the length of the pivot bond being $1.50\pm 0.03\overset{\circ}{\text{Å}}$.

The ultraviolet absorption spectra of many diphenyl derivatives have been studied, and the various workers have

postulated that the two main spectra types (vide infra) can be correlated with planarity or non-planarity of the molecules, thus affording a diagnosis of the presence of steric hindrance in such molecules. Pickett, Walter and France [J. Amer. Chem. Soc., 1936, 58, 2296] showed that the spectra for 2:4:6:2':4':6'-hexachlorodiphenyl and dimesityl were similar to those for the corresponding benzene derivatives [fig. II], whereas 3:3'- and 4:4'- dimethyldiphenyl and 4:4'- dichlorodiphenyl gave markedly different spectra from toluene and monochlorobenzene [fig. III]. They suggested that the increased absorption of the meta- and para-substituted compounds might depend on the planar form of the molecule and that a study of ultraviolet absorption spectra

Ultraviolet Absorption Spectra of hexachlorodiphenyl, trichlorobenzene, dimesityl and mesitylene.

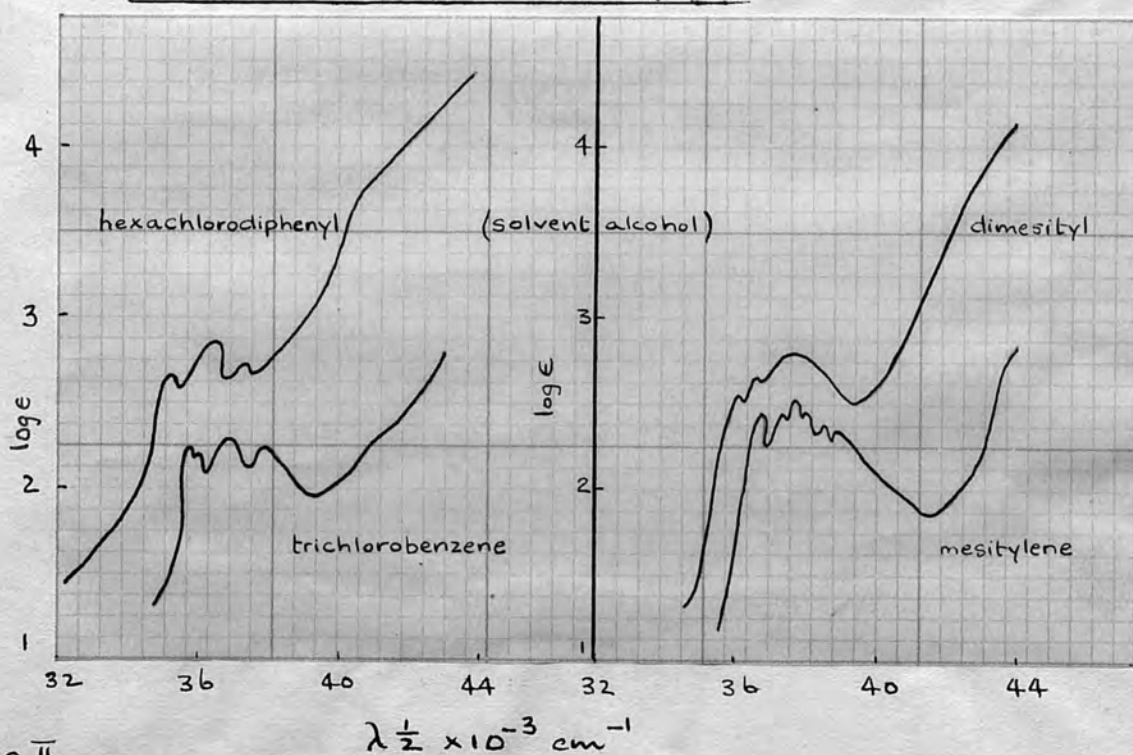


Fig. II.

might be a means of distinguishing compounds of restricted rotation. Calvin [J.Org.Chem., 1939, 4, 256] also suggested that certain non-resolvable tetraorthosubstituted diphenyls should show the conjugation type spectrum whereas other tetraorthosubstituted diphenyls in which the coplanar arrangement is out of the question would have an absorption spectrum very similar to that of the uncoupled parts.

O'Shaughnessy and Rodebush [loc.cit.] studied the absorption spectra of substituted diphenyls in which the various effects of conjugation, coplanarity and restricted rotation might be investigated. They considered that any considerable interference must turn the rings out of coplanarity and prevent conjugation between the rings. 2:2'-Dimethyldiphenyl shows greatly decreased absorption, whereas the 3:3'- and 4:4'-compounds show only effects which might be expected from interaction of the methyl groups with the benzene rings [fig.IV] 2:2':4:4'-Tetramethyldiphenyl has increased absorption over the 2:2'- compound, and the authors suggest that this might be attributed to the effect of the para substituents in "promoting the ionic state and the planar configuration." The spectra of 3:3'- dimethoxydiphenyl and 2:2'-dimethyl-5:5'-dimethoxydiphenyl [fig.V.] illustrate the effect of meta- and ortho- substituents on the diphenyl absorption. Meta-substituents reduce the general diphenyl absorption, but a maximum appears corresponding to the absorption of the two

Ultraviolet Absorption Spectra of toluene and 3:3'-dimethyldiphenyl.

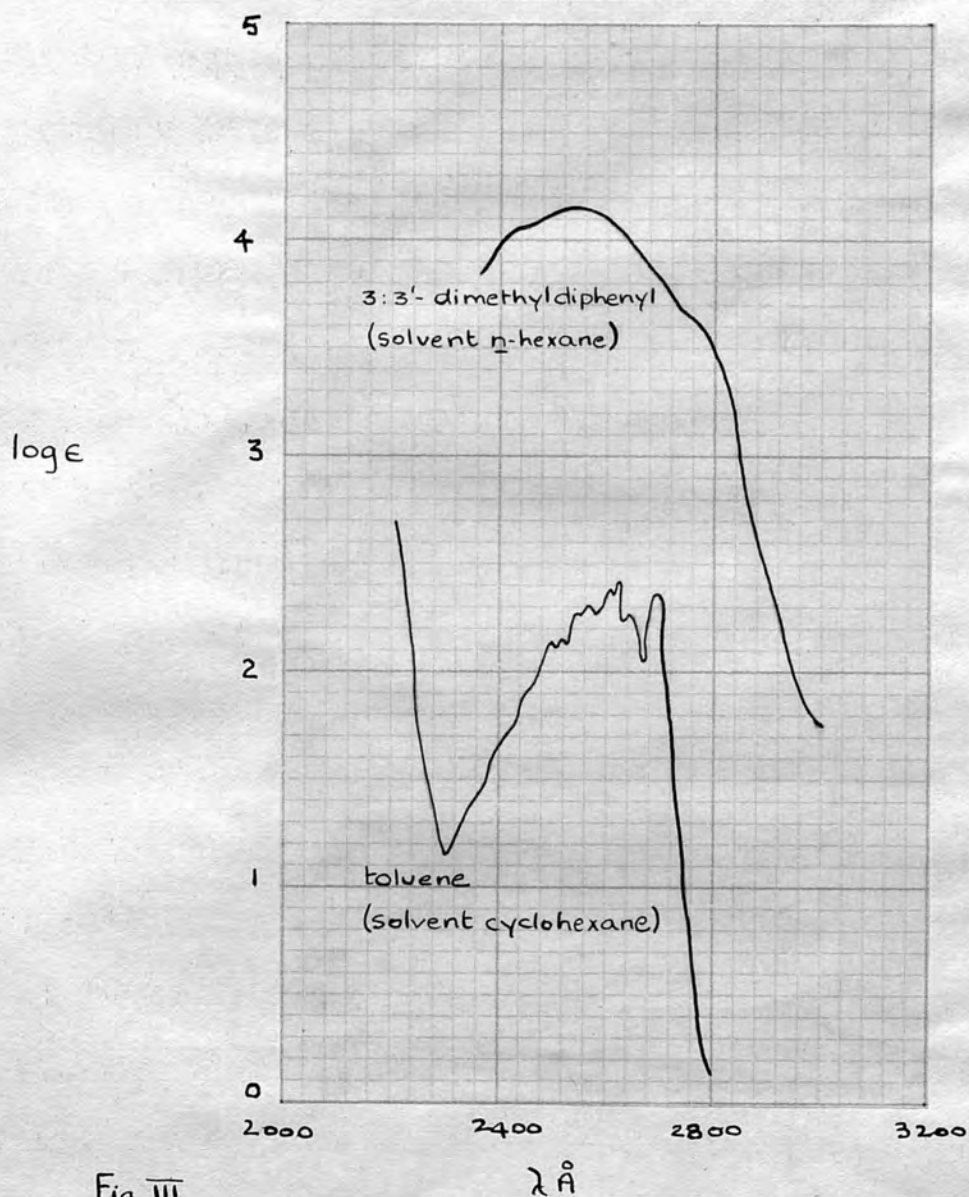
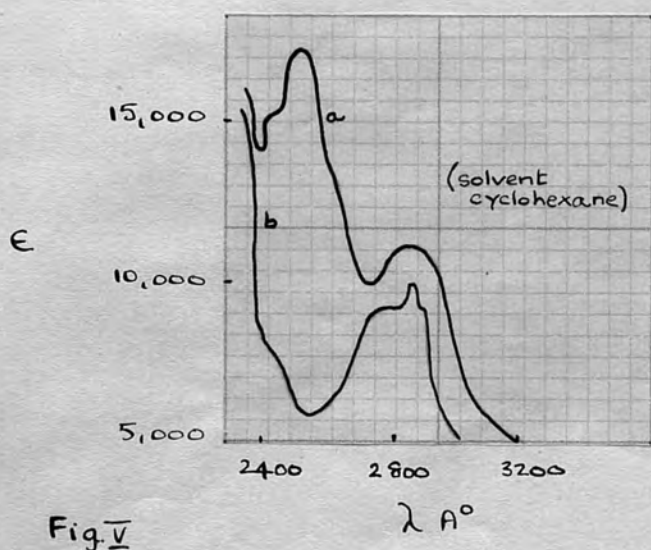
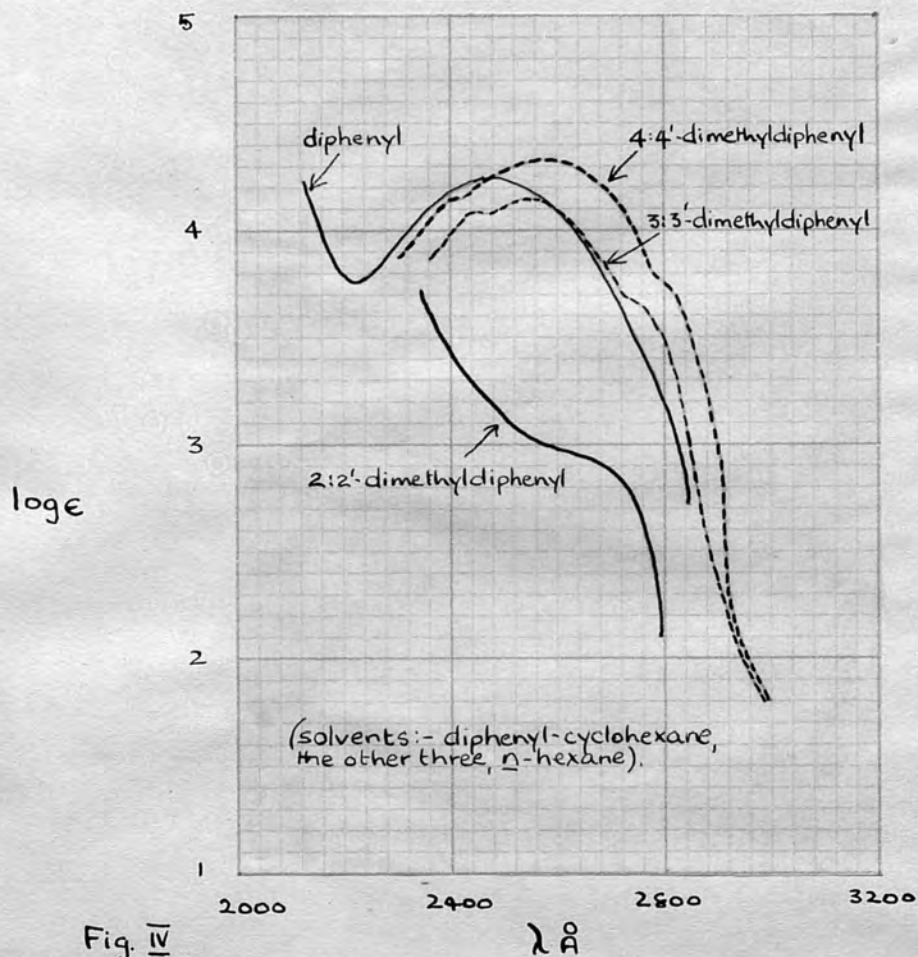


Fig. III

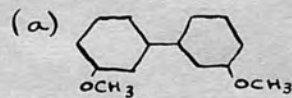
halves of the molecule.

Similar effects were seen in the spectra of the compounds VIII and IX, where the linking of the meta carbon atoms by a many-membered ring bridge had little or no effect

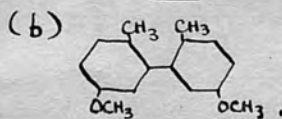
Ultraviolet Absorption Spectra of diphenyl and its 2:2', 3:3' and 4:4'-dimethyl derivatives.



Ultraviolet Absorption Spectra of



and



on the spectra, the macro-ring behaving as two ordinary meta substituents.



Williamson and Rodebush [J. Amer. Chem. Soc., 1941, 63, 3018] compared the ultraviolet absorption spectra of various 2:2'-disubstituted diphenyls. If the assumption is made that the interference between ortho-substituents is purely mechanical, departure from coplanarity should be proportional to the size of the blocking group, i.e. $\text{SO}_3\text{Na} > \text{NO}_2 > \text{Cl} > \text{CH}_3 > \text{COOH} > \text{NH}_2 > \text{OH} > \text{OCH}_3$. Comparison of the ϵ/λ curves for the diphenyl derivatives with the $2\epsilon/\lambda$ curves for the corresponding benzene derivatives, indicated that there is great departure from coplanarity with COOH , NO_2 and NH_2 in the 2:2'-positions, but, with OCH_3 , resonance involves both rings as the absorption is much greater. The results for the 2:2'-, 3:3'- and 4:4'- diphenic acids are interesting [fig. VI]. The spectrum for the 2:2'- compound is similar to that for benzoic acid, whereas the 4:4'-compound shows great absorption, the absorption maximum being near 2800\AA , and the intensity of absorption being much greater than for diphenyl itself. This is attributed to the resonance between the carboxyl groups and the diphenyl nucleus. The absorption for the 3:3'- compound is greater than that for the 2:2'- compound, but

Ultraviolet Absorption Spectra of diphenyl and
2:2'-, 3:3'- and 4:4'- diphenic acids.

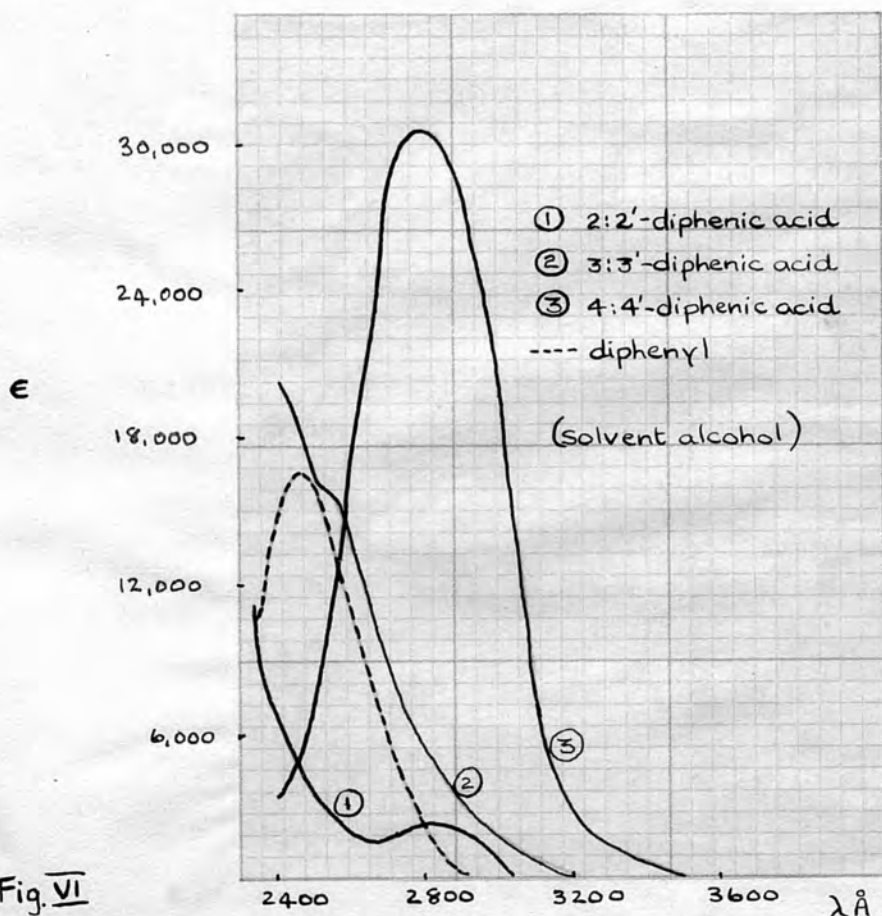


Fig. VI

considerably less than that for the 4:4'- compound, and the absorption maximum is shifted to a shorter wavelength beyond the range of the medium quartz spectrograph. It is not possible for a structure to exist which involves double bonds between the rings and between the ring and the carbon atom of the carboxyl group at the same time. Thus competition between the various permissible structures results in a decreased amount of conjugation. In order to account for the increased absorption over diphenyl itself with the meta-directing meta substituents, the authors state that "the piling up of the electron charge in the bond between the

rings favours the existence of some sort of ionic structure." These authors also concluded that if a small group such as hydroxyl is in the 2:2'- positions, the molecule is part of the time in a coplanar configuration. 2:2'- Dihydroxydiphenyl exhibits a spectrum in which the diphenyl absorption is reduced in intensity, and in which an absorption maximum characteristic of phenol appears. This was the only 2:2'- derivative studied in which the two absorption maxima were found.

Jones [ibid., 1658] studied the ultraviolet absorption spectra of 9:10- dihydrophenanthrene and 4:5- methylene-9:10- dihydrophenanthrene, which may be considered as diphenyls with the ortho positions linked by 6-membered and 5-membered rings, and compared them with the spectrum of diphenyl itself. [fig.VII]. The free rotation of the benzene rings about the pivot bond is restricted, so that the phenyl groups must be approximately coplanar. The secondary absorption maximum in the spectrum of 9:10- dihydrophenanthrene was attributed to the normal bathochromic effect of alkyl substituents, and the general similarity of this spectrum to that of diphenyl led Jones to conclude that "either the bond angles are deformed sufficiently to bring the rings into the same plane, or a small rotation of this order (this was referring to the angle of $15^{\circ}2'$ between the two rings) does not affect the polarizability of the bond." Braude however [J., 1949, 1902] believed the secondary maximum to be due to interaction

Ultraviolet Absorption Spectra of diphenyl, 9:10-dihydrophenanthrene and 4:5-methylene-9:10-dihydrophenanthrene.

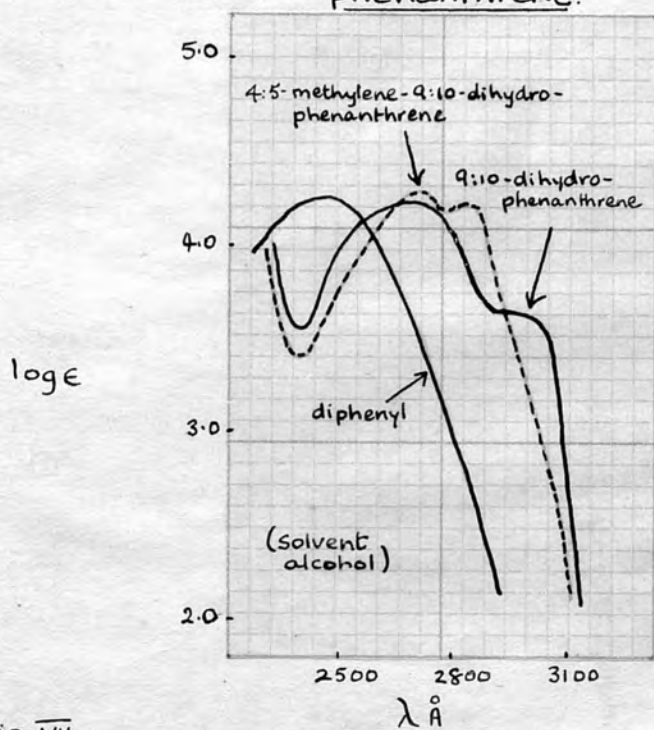


Fig. VII.

Ultraviolet Absorption Spectrum of fluorene

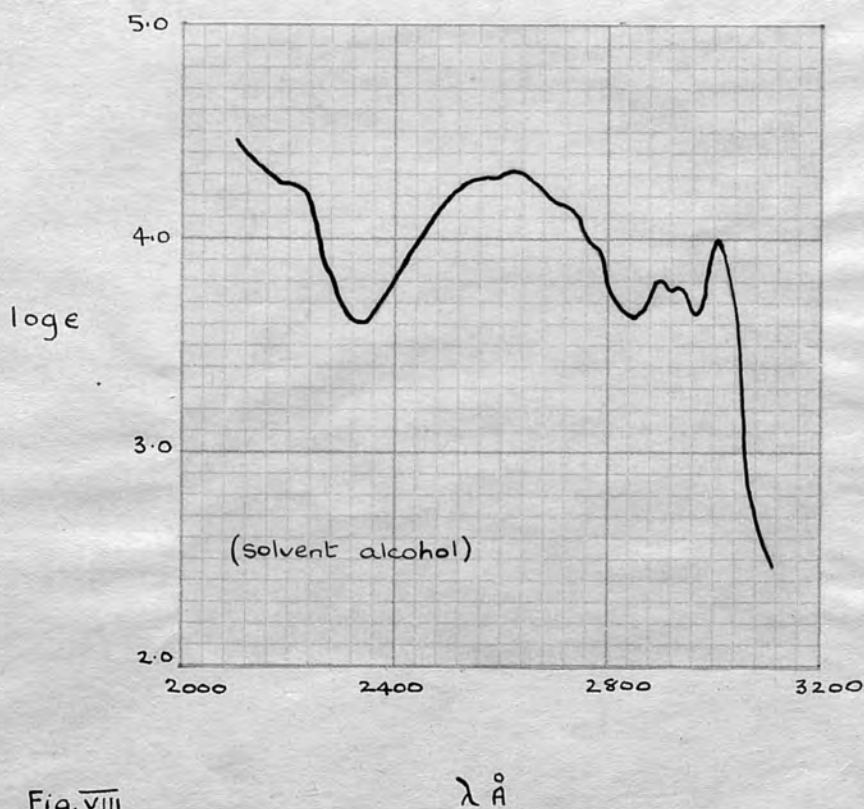


Fig. VIII.

through the $-\text{CH}_2-\text{CH}_2-$ bridge. In this respect the origin of the long wave band is the same as that in fluorene where it is believed to be due to interaction between the two phenyl groups and the methylene bridge. Beaven, Hall, Lesslie and Turner [ibid., 1952, 854] regard it as more satisfactory to consider 9:10-dihydrophenanthrene as a diphenyl which is sufficiently non-coplanar for the contribution of separate phenyl chromophores to appear. In the case of 4:5-methylene - 9:10-dihydrophenanthrene, Jones maintained that the spectrum resembles that of diphenyl with the secondary maximum increased in intensity. In the ultraviolet absorption spectrum of fluorene [Mayneard and Roe, Proc.Roy.Soc., 1937, A, 158, 634], this secondary maximum develops into a system possessing considerable fine structure [fig.VIII]. The spectrum of 4:5-methylene - 9:10-dihydrophenanthrene was thus regarded by Jones as showing a compromise between the fluorene and 9:10-dihydrophenanthrene spectral types, the configuration being approximately planar.

Friedel, Orchin, and Reggel [J.Amer.Chem.Soc., 1948, 70, 199] considered that the spectra of 2-methyl-, 2-methoxy- and 2-hydroxydiphenyl all showed some signs of steric hindrance [fig. IX], and believed the bands at about 2840\AA in the last two compounds to be "phenoxy" bands originating in the unconjugated benzene rings containing the OH and OCH_3 substituents.

As a general conclusion it may be stated that various

Ultraviolet Absorption Spectra of diphenyl, 2-methyl, 2-hydroxy- and 2-methoxy-diphenyl.

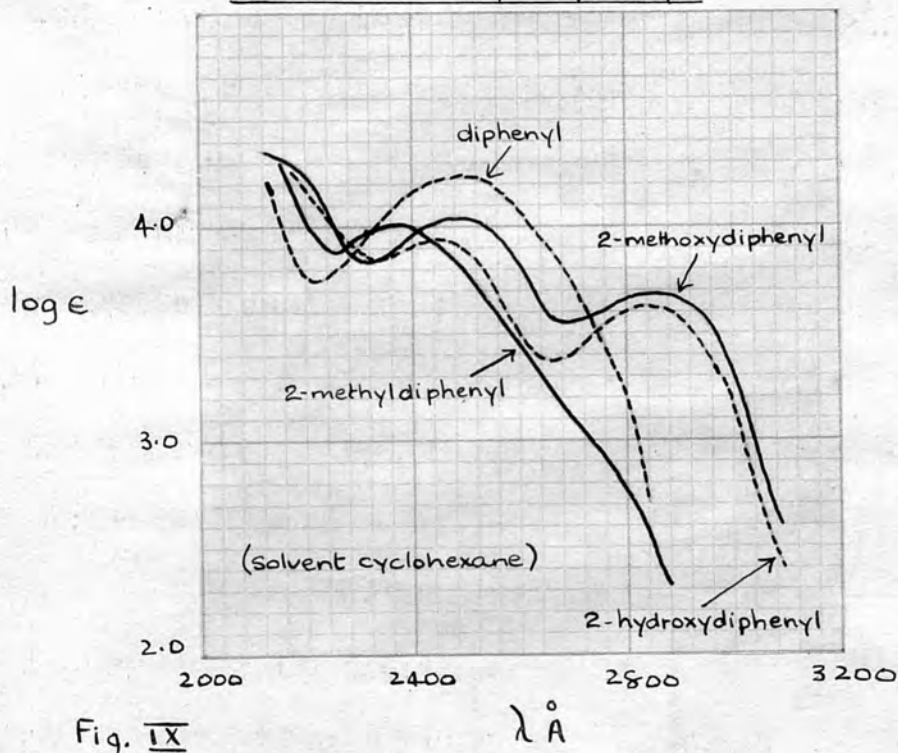


Fig. IX

λ Å

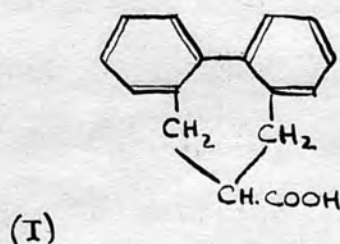
workers have found evidence to suggest that the ultraviolet absorption spectra of diphenyl derivatives give an indication as to whether or not the molecular configuration is coplanar. Nevertheless some anomalies have appeared which spoil this clear-cut picture of the relationship between configuration and absorption. For example, Sherwood and Calvin [ibid., 1942, 64, 1350] found that although in the spectrum of 2:2'-dimethyldiphenyl the conjugation band is practically eliminated O'Shaughnessy and Rodebush, [loc.cit. and fig.IV], in the spectrum of 2:2'-dimethyl-4:4'-dinitrodiphenyl, the conjugation band is restored in full. Although many of the workers quoted assume that the appearance of the conjugation band implies coplanarity or near coplanarity, there is little indication of how near to coplanarity the molecule must be to

ensure resonance interaction across the pivot bond. Jones [loc.cit.] implies that the calculated angle of about 15° between the rings in 9:10-dihydrophenanthrene allows conjugation to occur. Guy [J.Chim.Phys., 1949, 46, 469] attempted to calculate how the degree of delocalization of the π electrons would alter in a diphenyl with increase in the angle between the two aromatic nuclei. He concluded that the angle could increase from 0° to about 22.5° without the resonance interaction being affected to any extent. For values of the interannular angle of from 22.5° (θ_1) to somewhere between 45° and 67.5° (θ_2) the resonance interaction decreases rapidly to practically zero, and if steric hindrance should hold the rings in an average configuration such that the angle between the phenyl nuclei (α) is between θ_1 and θ_2 , there would be a greater or less displacement of the first ultraviolet absorption band (depending on the value of α) showing itself generally as a hypsochromic effect. For values of the angle between the aromatic nuclei of from θ_2 to 90° , Guy calculated that the resonance between the two halves of the molecule is completely inhibited, the π -electrons separating into two independent groups. The two halves of the molecule would then behave independently as regards absorption in the near ultraviolet.

B. Section I.

The attempt has now been made to resolve a diphenyl in which the 2:2'-positions are joined by a 7-membered-ring bridge, and the 6:6'-positions are free from substituents. The 7-membered ring would assume a multiplanar configuration in order to be strainless, and the two benzene rings would be forced to take up a noncoplanar configuration. A model shows that the angle between the rings is of the order of 50°, and as the molecule has none of the elements of symmetry, the compound should be capable of resolution into optically active forms.

The formation of the 7-membered ring is particularly easy, and the acid (I) [Kenner, J., 1913, 103, 621] was selected as a suitable compound for attempted resolution.



This acid did not form crystalline salts readily from a wide range of alkaloids and solvents, but a crystalline brucine salt was obtained from carbon tetrachloride, which contained one molecule of solvent of crystallization. Repeated crystallizations gave rise to crops with considerably different values of $[\alpha]_{5461}^{20}$, but no consistent change in rotation with crystallization was observed, and no active acid was obtained from the decomposition of any crop of crystals. The acid

also gave a crystalline salt with ephedrine from ether, but it proved impossible to recrystallize this salt from any solvent or mixture of solvents in a satisfactory manner.

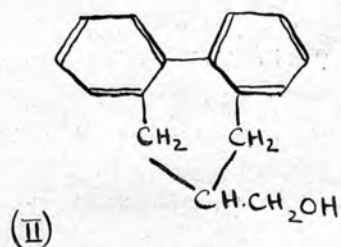
With quinine, the acid gave a gum from aqueous ethanol, which readily solidified on "scratching." The amorphous white powder produced was crystallized from ethanol and the crystals thus obtained corresponded to the formula 1 mol.acid. 1 mol.base, and had m.p.128°. Repeated crystallization from ethanol led to no significant change in specific rotation, the extreme values in chloroform of $[\alpha]_{5461}^{20}$ being -86.9° and -85.4°. Decomposition yielded an inactive acid. The acid and quinine also gave a crystalline salt from ether with m.p.103-5°(decomp.). This was recrystallized from an ether-acetone mixture and gave a crystalline solid with formula corresponding to 1 mol.acid.1 mol.base and m.p.150°. Repeated crystallization gave no significant change in rotation, the extreme values in chloroform of $[\alpha]_{5461}^{20}$ over a series of crystallizations being -119° and -122°. Decomposition of any crop always yielded an inactive acid. It would appear that two distinct diastereoisomers were produced, and the failure to obtain an active acid might be due to the fact that (a) the acid is extremely optically labile or (b) the specific rotation of the enantiomers is too small to be detected with ease. It may be noted here that Bell [J.,1952, 1527] failed to obtain a crystalline brucine salt of the acid, and obtained an inactive acid from the quinine and cinchoni-

dine salts which were crystallized from ethanol.

The methyl ester of 1:2-3:4-dibenzocyclohepta-1:3-dione-6-carboxylic acid (I) was prepared, dissolved in (+)-diethyl tartrate and allowed time to undergo any probable equilibration following the method of Buchanan and Graham [J., 1950, 500] and Glazer, Harris and Turner [ibid., 1753] who showed that optical activation could be achieved by asymmetric solvent action. Rapid precipitation with water in the cold yielded an inactive ester. An optical activation of the acid by brucine was also attempted by rapidly mixing equivalent amounts of the pure acid and pure anhydrous brucine in chloroform in a jacketted polarimeter tube. No evidence was obtained of an asymmetric transformation occurring in solution.

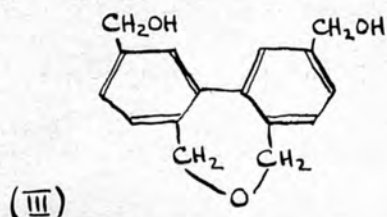
As it seemed unlikely that the acid was optically unstable, the working hypothesis was adopted that compounds of the type of (I) should be optically stable if capable of resolution, and other derivatives were prepared in the hope that either their salt-forming properties would be superior or their optical rotation greater than in the case of the Kenner acid.

As the (-)-menthyl ester of the acid (I) proved unsuitable for attempted resolution, the methyl ester was prepared and reduced with lithium aluminium hydride to give the alcohol (II).



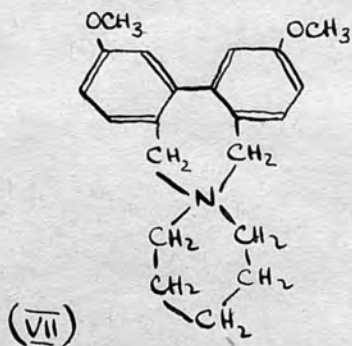
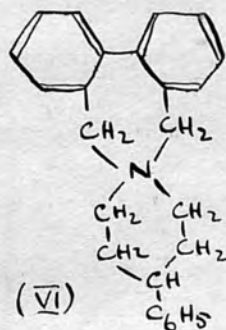
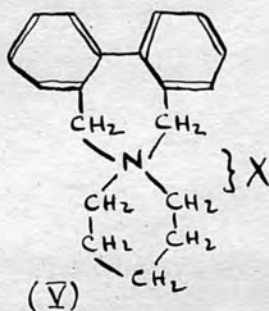
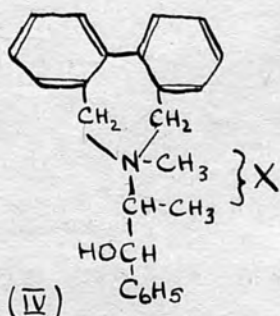
This was converted into its hydrogen phthalate, which was combined with brucine in acetone to form a salt. Repeated crystallization from acetonitrile failed to produce any change in rotation, and on decomposition, an inactive hydrogen phthalate was obtained. The (-)-menthoxyacetate of the alcohol (II) was then prepared which was crystallized repeatedly from 40-60° petroleum ether. A considerable range of specific rotation was observed in various crops ($[\alpha]_{5461}^{20}$ from -57.4° to -63.9° in chloroform), but again no consistent change in the degree of rotation with crystallization could be obtained. It is perhaps noteworthy that the melting points of various crops differ slightly, and in each case there was some softening prior to melting. It is possible that two diastereoisomeric compounds were present with closely similar solubility and/or optical rotation. Unfortunately no other solvent suitable for crystallization could be found.

2:7-Dihydro-3':2"-hydroxymethyl-3:4-5:6-dibenzoxepin (III) was prepared in the hope that the presence of two substituents in the meta positions might increase the optical rotatory power of the molecule.



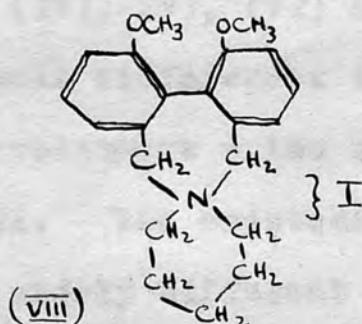
As the di-(-)-menthoxyacetate proved unsuitable for resolution, the dihydrogen phthalate was prepared. Unfortunately no suitable salt could be obtained using a wide range of alkaloids and solvents, and the attempt to resolve (III) had to be abandoned.

Similar types of compound containing a nitrogen atom in the 7-membered ring have been prepared Beaven, Hall, Lesslie and Turner, [J., 1952, 854 (IV,V,VI), and unpublished work (VII)]. These workers failed to resolve the following four compounds (IV-VII).



There is no case therefore where compounds containing the

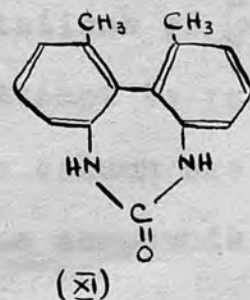
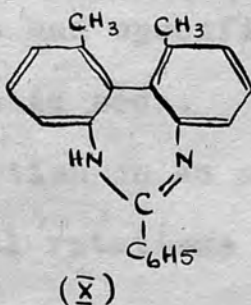
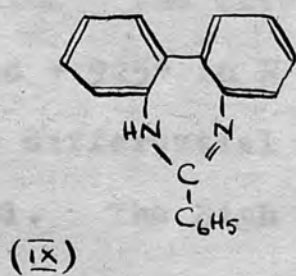
diphenyl nucleus with the 2:2'-positions linked by a 7-membered ring and no 6:6'-substituents have been resolved, and yet such compounds do not appear to be optically labile. Beaven, Hall, Lesslie and Turner [loc.cit.] managed to achieve the resolution of (VIII) by laborious fractional crystallization of the (+)- and (-)-camphorsulphonates. The specific rotations of the two enantiomorphs were $[\alpha]_{5461}^{22}$ $-3.8 \pm 0.2^\circ$ and $[\alpha]_{5461}^{22} + 4.0 \pm 0.4^\circ$, and the active forms were



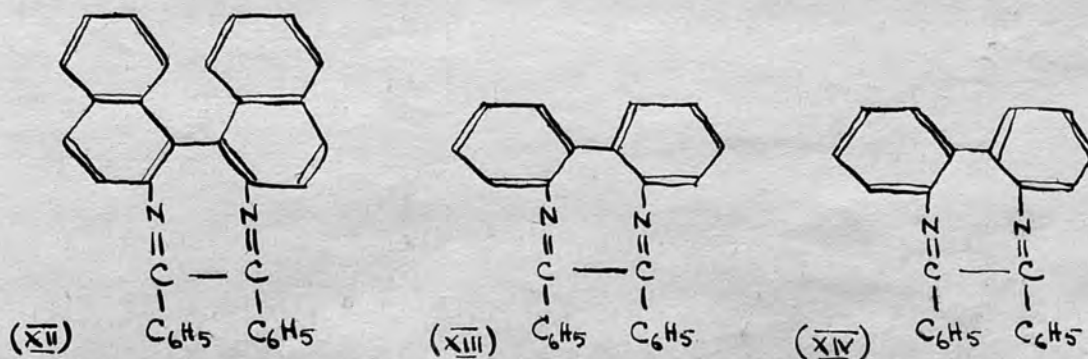
found to be highly optically stable. Since it had been shown previously [Van Arendonk, Cupery and Adams, J. Amer. Chem. Soc., 1933, 55, 4225] that the dicamphorsulphonate of 3:3'-diamino-2:2':6:6'-tetramethoxydiphenyl mutarotated rapidly in solution at -17° , while the alkaloidal salts of 3:3'-dicarboxy-2:2':6:6'-tetramethoxydiphenyl showed no mutarotation even at -17° , and gave inactive acid on decomposition, it is evident that the methoxy group is of little consequence as a "blocking" agent in the ortho positions. Hence the activity of 2:7-dihydro-4':1"-dimethoxy-3:4-5:6-dibenzazepinium-1-spiro-1"-piperidinium bromide (VIII) must be due to the asymmetry of the molecule caused by the

enforced non-coplanarity of the benzene rings. It is to be noted that the specific rotations of the active iodides are very small, and it is at least possible that the resolution of (VIII) as compared with the non-resolution of (V) is to be attributed to the methoxy groups increasing the optical rotatory power of the molecule, although it is difficult to understand why they should not display a similar effect in (VII). It may be considered therefore that the non-resolution of compounds (II), (IV), (V), (VI) and (VII) may be ascribed to the extremely small differences in rotation between the two expected diastereoisomers - too small in fact to make resolution practical. The existence of two quinine salts of the acid (I) of widely different specific rotation is difficult to account for, particularly as the acid shows no sign of being optically unstable, and is indeed unlikely to be so, considering the optical stability of (VIII).

It is of some interest to note here that Sako [Mem. Coll. Eng. Kyushu, 1932, 6, 263 (C.A., 1932, 26, 3246)] was unable to resolve 2-phenyldiphenimidine (IX) via the tartrate or (+)-camphorsulphonate into optically active forms. The compound (X) could not be resolved either, but when it was



prepared from pure (-)-2:2'-diamino-6:6'-dimethyl diphenyl, an optically active compound resulted. This possessed the extremely high value of $[\alpha]_D$ of -986.3° in benzene. Sako also prepared the laevorotatory form of (XI) starting from (-)-2:2'-diamino-6:6'-dimethyldiphenyl and urea ($[\alpha]_D$ not quoted). Kuhn and Goldfinger [Annalen, 1929, 470, 183] obtained the compound (XII) in an active form by condensing (+)-2:2'-diamino-1:1'-dinaphthyl with benzil and showed that it had an extraordinarily high specific rotation ($[\alpha]_D^{21}$ - -1910°) in pyridine. In this compound as in Sako's compounds (X) and (XI) there are large substituents in the ortho positions, and these were considered necessary for the preservation of the non-coplanar position in both the 7- and 8- membered ring compounds. Very recently, Bell [loc. cit.] succeeded in resolving (XIII), prepared from 2:2'-diamino - 4:4'-dicarboxydiphenyl and benzil, via the brucine



salts. The free acids had specific rotations of $[\alpha]_D$ -955° and $+925^\circ$ in N/2 caustic soda. An attempt to resolve (XIV) by differential adsorption on an active column was unsuccessful. The high optical rotations of the compounds prepared

from 2:2'-diaminodiphenyl derivatives are remarkable compared with the low values exhibited by the enantiomers of (VIII), and this must be due to some factor inherent in the bridge-ring system.

EXPERIMENTAL

1. Preparation and attempted resolution of 3:4-5:6dibenzo-cyclohepta-3:5-diene-1-carboxylic acid.

(a) Diphenic acid was prepared by a modification of the methods due to Vorländer and Meyer [Annalen, 1902, 320, 122], Atkinson, Lawler, Heath, Kimball and Read [J. Amer. Chem. Soc., 1941, 63, 730] and Professor E. E. Turner [private communication].

100 g. of anthranilic acid in 300 c.c. of water and 300 c.c. of concentrated hydrochloric acid were diazotized between 0° and 5° using 48 g. of solid sodium nitrite. The diazo solution was filtered prior to use, and added to the catalytic solution by means of a long-stemmed dropping-funnel, the end of which was turned up and constricted to a fine opening. The opening was placed well down in the catalytic solution which was made by adding 800 g. of sodium metabisulphite and 800 c.c. of 0.880 ammonia to a solution of cuprammonium sulphate at 10°. This latter was prepared by dissolving 352 g. of hydrated copper sulphate in 2000 c.c. of water and adding 400 c.c. of 0.880 ammonia. The diazo-solution was run in at a rate not exceeding 5 c.c. per minute, and the temperature of the catalytic solution, which was mechanically stirred throughout, was maintained at about 15°. When the evolution of nitrogen had ceased, a solution

of 520 g. of anhydrous ferric chloride in 800 c.c. of water and 2,600 c.c. of concentrated hydrochloric acid was added carefully. After standing overnight, the precipitated diphenic acid was filtered off, washed well with water and dried. It was obtained in 88% yield as an almost white powder, m.p. 228° , which could be used without further purification.

(b) Dimethyl diphenate was prepared by refluxing diphenic acid with its own weight of concentrated sulphuric acid and ten times its weight of methanol for six hours. After pouring into water, the ester was filtered and stirred with sodium bicarbonate solution. After filtering again and washing, it was crystallized from methanol. The ester was obtained in about 80% yield as colourless prisms m.p. $74-5^\circ$.

(c) 2:2'-di(hydroxymethyl)diphenyl was prepared by reducing dimethyl diphenate with lithium aluminium hydride according to Hall, Lesslie and Turner [J., 1950, 711]. 38 g. of finely ground dimethyl diphenate were dissolved in 400 c.c. of anhydrous ether. The solution was slowly run into a solution of 8.5 g. of lithium aluminium hydride in 350 c.c. of anhydrous ether, at such a rate as to maintain a gentle reflux. When the reaction was over, water was added very cautiously, followed by dilute sulphuric acid. When two clear layers were obtained, the ether was distilled off on a water-bath, and the diol set to a white solid on top of

the aqueous layer. It was filtered off, dried and crystallized from benzene, whence it was obtained in 90% yield as beautiful white needles m.p. 111-112°.

(d) 2:2'-di(bromomethyl)diphenyl [idem. *ibid.*]. 15 g. of 2:2'-di(hydroxymethyl)diphenyl were added gradually to 800 c.c. of 48% W/W hydrobromic acid at 90°. When all the diol had been added the mixture was boiled under reflux for about 20 minutes. It was then poured into a beaker and allowed to cool, when the 2:2'-di(bromomethyl)diphenyl solidified. This was filtered off through a sintered glass funnel and the excess hydrobromic acid was removed over potash in a vacuum desiccator. When it was dry, the dibromide was crystallized from 60-80° petroleum ether, whence it was obtained in 90% yield as faintly brown prisms m.p. 90-2°.

(e) 3:4-5:6-dibenzocyclohepta-3:5-diene-1-carboxylic acid. [Kenner, *loc. cit.*]. 2.3 g. of sodium were dissolved in about 50 c.c. of absolute ("super dry") ethanol. 8.8 g. of freshly distilled diethyl malonate in 120 c.c. of anhydrous ether were run in gradually, followed by a solution of 17 g. of 2:2'-di(bromomethyl)diphenyl in 140 c.c. of anhydrous ether. The mixture was heated in a water-bath on a hot-plate (about 60°) for three hours, during which time it was mechanically stirred. The ether was distilled off from the now neutral-reacting mixture, and 250 c.c. of ethanol were added,

together with a solution of 10 g. of caustic potash in 10 c.c. of water. The mixture was refluxed for half an hour, then about 100 c.c. of water were added prior to distilling off the ethanol. The aqueous solution left in the reaction flask was extracted with ether, and the alkaline layer was acidified with dilute sulphuric acid. The precipitated dicarboxylic acid was filtered and dried, and decarboxylated by heating at about 172° in an oil-bath until evolution of carbon dioxide ceased. The product was cooled, dissolved in hot 10% sodium carbonate solution, and the cooled alkaline solution was extracted with ether. The alkaline layer on acidification yielded a white solid which was filtered and crystallized from aqueous ethanol. The 3:4-5:6-dibenzo-cyclohepta-3:5-diene-1-carboxylic acid was obtained in 80% yield as white needles m.p. 160-1°.

(f) No satisfactory salt could be made from the acid using morphine, quinidine, strychnine, cinchonine, α -phenyl-ethylamine or arginine with a wide variety of solvents.

(g) A crystalline salt m.p. 113-4° was obtained from ephedrine using ether as solvent, but this could not be recrystallized from any solvent or mixture of solvents in a satisfactory manner. On decomposition an inactive acid was obtained showing that no second-order asymmetric transformation had occurred.

(h) A crystalline salt was obtained using brucine and carbon tetrachloride as solvent.

(i) 2.38 g. of acid and 4.30 g. of brucine dihydrate were dissolved separately in carbon tetrachloride. The hot solutions were mixed, boiled for a short time and filtered. 5.8 g. of crystals were obtained which had m.p. 86-7° (decomp). The melting-point was unchanged after drying in vacuo for several hours. The salt was recrystallized from carbon tetrachloride, and the specific rotations of successive crops was determined. For this purpose, about 0.2 g. of salt was dissolved in 20 c.c. of absolute ethanol. A 2 d.m. tube was used, and readings were taken using the mercury green line $\lambda 5461 \overset{\circ}{\text{A}}$.

The following results were obtained:

	Wt. in g.	m.p.	$[\alpha]_{5461}^{20}$
Crop 1.	1.55	90°(decomp.)	-32.1
2.	2.45	85° "	-29.5
3.	0.75	90° "	-32.1
4.	0.80	85° "	-24.4
	<u>5.55</u>		

The salt separated as small round crystalline aggregates, or as a microcrystalline powder. Between crops 3 and 4, a small quantity (about 0.1 g.) of a fawn powder was obtained, m.p. 158° (decomp.), $[\alpha]_{5461}^{20} -16.0^{\circ}$.

1.75 g. of crops 1 and 3 combined were recrystallized from carbon tetrachloride. The first solid to separate was about 0.25 g. of fawn powder with a high indefinite melting point which crystallized from warm ethanol: $[\alpha]_{5461}^{20} -17.3^\circ$.

The second crop was a white microcrystalline powder: 0.5 g., m.p. 90° (decomp.), $[\alpha]_{5461}^{20} -30.8^\circ$. Further evaporation of the mother liquor yielded only successive small quantities of the fawn powder and the experiment was repeated to see if these results were reproducible.

(ii) 2.38 g. of acid and 4.30 g. of brucine dihydrate were combined to form a salt as in (i). On recrystallization, a small residue would not dissolve in carbon tetrachloride, and on warming with ethanol gave small clusters of prisms, about 0.1 g., with no definite melting point and $[\alpha]_{5461}^{20} -10.51^\circ$. Successive crops were obtained from the carbon tetrachloride solution as follows:

	Appearance	Wt. in g.	m.p.	$[\alpha]_{5461}^{20}$
Crop 1.	Fawn, amorphous	0.5	80° (decomp.)	-14.0°
2.	White, microcryst.	1.5	90° "	-31.8°
3	" "	1.7	90° "	-32.0°
4	Fawn, amorphous	0.3	90° "	-18.8°
5	" "	0.2	80° "	-18.7°
6	" "	0.3	80° "	-19.8°

The amorphous crops would only dissolve in ethanol on slight warming.

Crop 1.

Found: C 60.88; H 5.3; Cl 18.5. 1 mol. acid 1 mol. base. CCl_4
requires C 61.1; H 5.1; Cl 18.1.

Crop 3.

Found: C 61.1; H 5.1; N 4.2; Cl 18.2. 1 mol. acid. 1 mol.
base. CCl_4
requires C 61.1; H 5.1; N 3.6; Cl 18.1.

There seemed to be a possibility, disregarding the high melting crops, of there being two different types of salt, one more laevorotatory than the other. Decomposition of a specimen of each type gave an inactive acid m.p. 160-161°.

Crops 2 and 4 from (i) and 2 from (ii) (3.5 g.) were recrystallized from carbon tetrachloride. At first 0.2 g. of high melting fawn powder was obtained which crystallized from ethanol to give slightly fawn prisms $[\alpha]_{54.61}^{20} -7.6^\circ$.

Found: C 58.34; H 6.72; N 6.05 which does not correspond to any reasonable formula.

Finally about 2.5 g. of white crystals m.p. 80° (decomp.), $[\alpha]_{54.61}^{20} -30.6^\circ$ were obtained.

(iii) A further quantity of salt was made from 2.38 g. of acid and 3.94 g. of anhydrous brucine. The acid was dissolved in carbon tetrachloride, and the brucine was added gradually to the hot solution which was boiled for a short time and

then filtered. The first four crops were small amounts of fawn powder which were combined and warmed with ethanol. No crystals were obtained, and on pumping off the solvent, a gel was obtained which solidified on "scratching". The solid had $[\alpha]_{5461}^{20} -31.3^{\circ}$.

Crop 5. white crystalline clusters m.p. 80° (decomp.)
 3.0 g. $[\alpha]_{5461}^{20} -30.9^{\circ}$

Crop 6. white microcrystalline powder m.p. 90° (decomp.)
 2.9 g. $[\alpha]_{5461}^{20} -33.7^{\circ}$

It was decided to attempt recrystallization from another solvent, most common solvents having been previously found unsuitable. Ethyl acetate dissolved the salts readily, and it was found that they would crystallize very slowly from this solvent.

Crop 5.

recryst. ethyl acetate - m.p. 92° (decomp.) $[\alpha]_{5461}^{20} -36.2^{\circ}$
 crop from mother liquor - m.p. 92° (decomp.) $[\alpha]_{5461}^{20} -38.7^{\circ}(\alpha)$

Crop 6.

recryst. ethyl acetate - m.p. 100° (decomp.) $[\alpha]_{5461}^{20} -38.5^{\circ}(\beta)$

Crops (α) and (β) were combined and recrystallized from ethyl acetate. Three successive crops had m.p. between 92° and 100° (decomp.) and values of $[\alpha]_{5461}^{20}$ as follows:

1. -40.1°
2. -40.3°
3. -39.0°

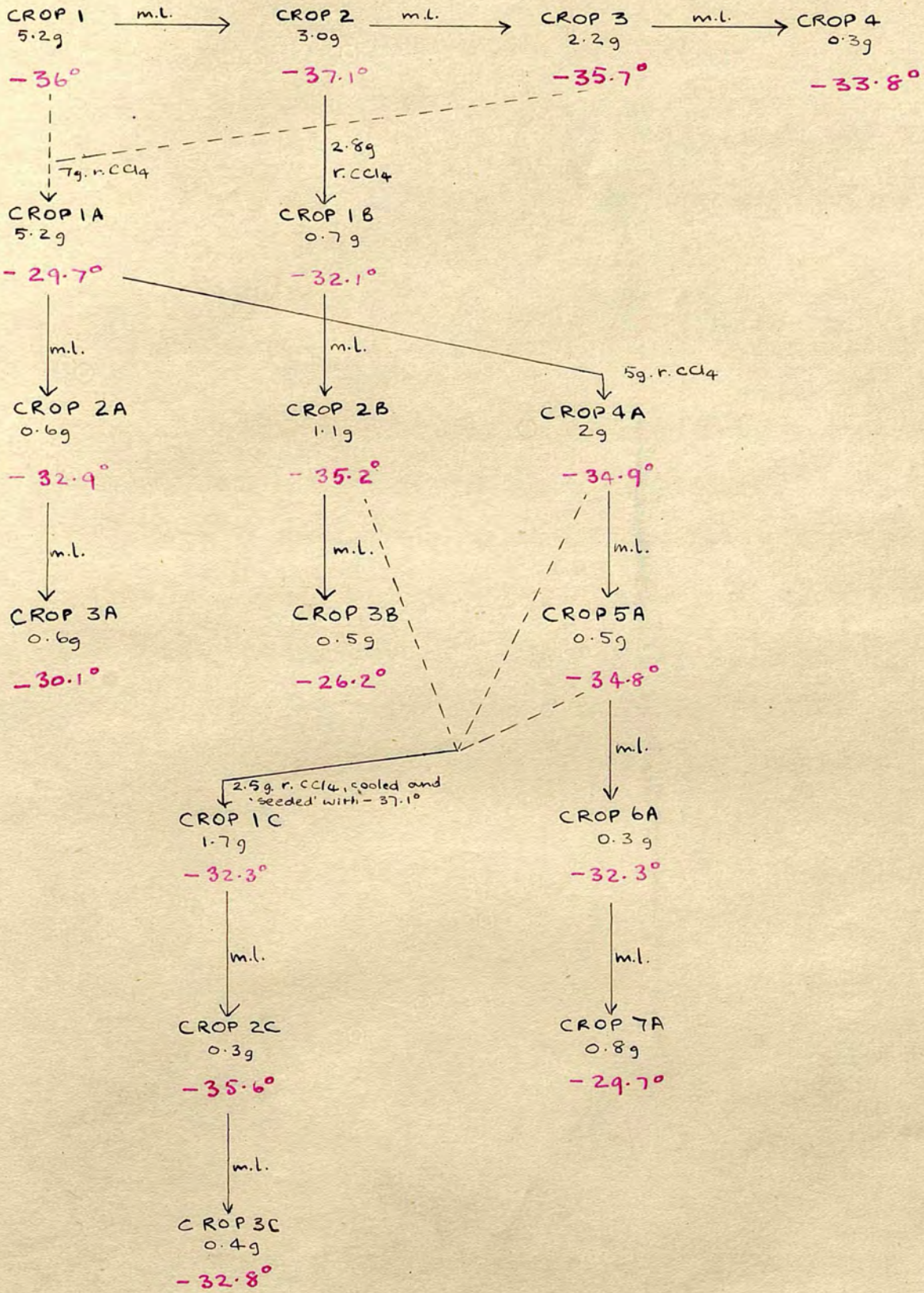
These differences in rotation were shown by analysis to be due probably to differences in solvation, so that ethyl acetate was discarded as a solvent.

Found: Crop 5.	$[\alpha]_{5461}^{20}$	-36.2°	C 72.0; H 5.9.
Crop (a).	$[\alpha]_{5461}^{20}$	-38.7°	C 70.2; H 6.6.
Crop 2.	$[\alpha]_{5461}$	-40.3°	C 70.5; H 6.4.
1 mol. acid. 1 mol. base.	$\text{CH}_3\text{COOC}_2\text{H}_5$	requires	C 71.7; H 6.7.
1 mol. acid. 1 mol. base.	2 $\text{CH}_3\text{COOC}_2\text{H}_5$	"	C 69.8; H 6.9.

(iv) A final attempt at resolution was made with carbon tetrachloride as solvent using 4.76 g. of acid and 7.88 g. of anhydrous brucine. A summary of results is shown in the chart below: m.l. = mother liquor; r. = recrystallized.

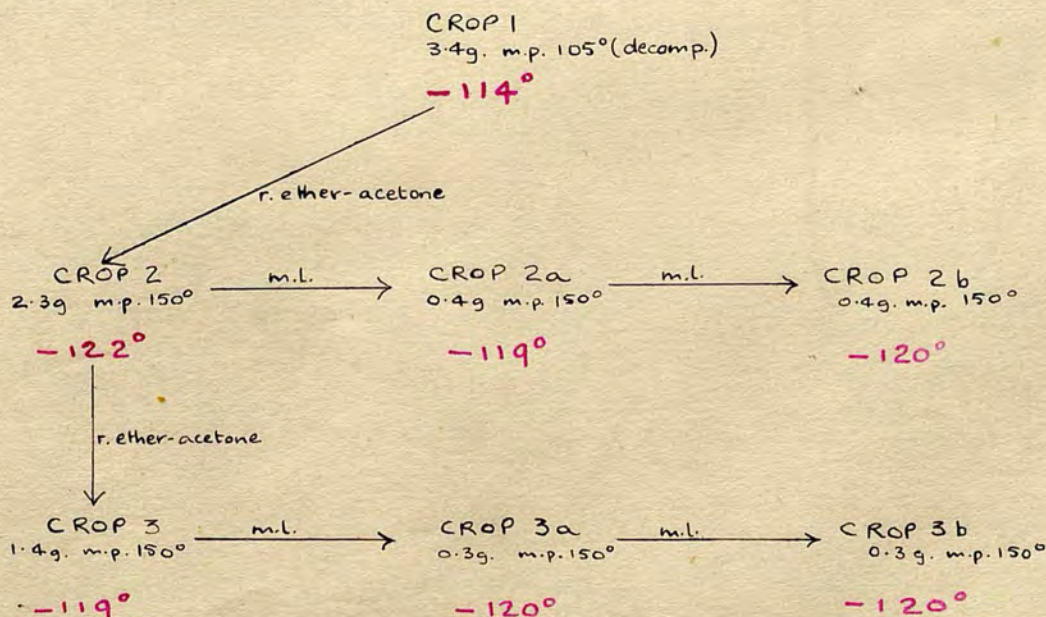
XIXa

1 mol acid + 1 mol base



Some of the differences in specific rotation may be due to differences in solvation. In this last experiment, no amorphous crops with low specific rotations were obtained.

(i) 4.76 g. of acid and 3.60 g. of quinine dihydrate were dissolved separately in ether, and the solutions after mixing were boiled and filtered. The salt obtained had m.p. 105°(decomp.) which was unchanged after drying in vacuo for several hours. It had a specific rotation $[\alpha]_{5461}^{20} -114^\circ$ in ethanol. The salt would not redissolve in ether, but could be obtained as long silky needles by recrystallizing from an ether-acetone mixture. These needles had m.p. 150° and a specific rotation $[\alpha]_{5461}^{20} -122^\circ$ in ethanol, so that the salt first obtained was no doubt solvated. No significant change in specific rotation with recrystallization was obtained as shown in the chart below. A duplicate experiment gave practically identical results.



After a considerable time no further deposition of crystals took place from the mother liquor of CROP 1 which should contain a considerable amount of salt. This solution was chilled and decomposed in the cold. The acid recovered was inactive.

A crop with $[\alpha]_{5461}^{20} -122^{\circ}$ from a duplicate experiment was decomposed, and found to yield an inactive acid. In each case, about 1.5 g. of acid was dissolved in 20 c.c. of solvent in case the activity should be slight.

Found for CROP 2 $[\alpha]_{5461}^{20} -122^{\circ}$: C 76.8; H 6.7.
 1 mol. acid. 1 mol. base requires : C 76.9; H 6.8.

The rotations of the salt in chloroform were found to be identical with those in ethanol.

(j) 2.38 g. of acid were dissolved in a little hot ethanol, and 1.80 g. of quinine dihydrate were added. Boiling water was added until the solution was slightly turbid. It was warmed to clear and allowed to cool. The oil which separated could be solidified by "scratching".

The amorphous powder was crystallized from ethanol whence beautiful clusters of long rectangular prisms were obtained, 2.8 g., m.p. 128° , $[\alpha]_{5461}^{20} -86.9^{\circ}$ in chloroform.

Repeated crystallizations from ethanol led to no significant change in rotation, the lowest value of $[\alpha]_{5461}^{20}$

being -85.4° . The rotations in ethanol were found to be identical with those in chloroform.

Found crop of highest	$[\alpha]_{5461}^{20}$	-86.9°	C 76.6; H 6.8.
Found crop of lowest	$[\alpha]_{5461}^{20}$	-85.4°	C 76.5; H 6.7.
1 mol. acid. 1 mol. base requires:			C 76.9; H 6.8.

On decomposition, an inactive acid was obtained.

(k) 1 equivalent (0.238 g.) acid and 1 equivalent (0.394 g.) pure anhydrous brucine were dissolved separately in pure dry chloroform containing a known amount of ethanol. The acid solution was placed in a jacketted polarimeter tube, and the base solution was added rapidly, the stop-clock being started simultaneously. A reading was taken as soon as possible (0.5 minute) which was completely unchanged after several hours. This suggested that no first order asymmetric transformation occurred in solution.

(e) The acid was converted into its methyl ester by heating with its own weight of concentrated sulphuric acid and ten times its weight of methanol on a water-bath for four hours. A viscous gum was formed on pouring into water. Solid sodium bicarbonate was added until the aqueous solution was neutral, and the ester was extracted with ether. The extract was dried and on removal of the ether, the ester was obtained as colourless rather waxy plates m.p. $47-48^{\circ}$, yield 89%

theoretical. It could not be readily crystallized, but came out with some difficulty from 60-80° petroleum ether (melting point unchanged). (Kenner [loc. cit.] gives the m.p. of the ester, prepared by the Fischer-Speier method as 44-45°).

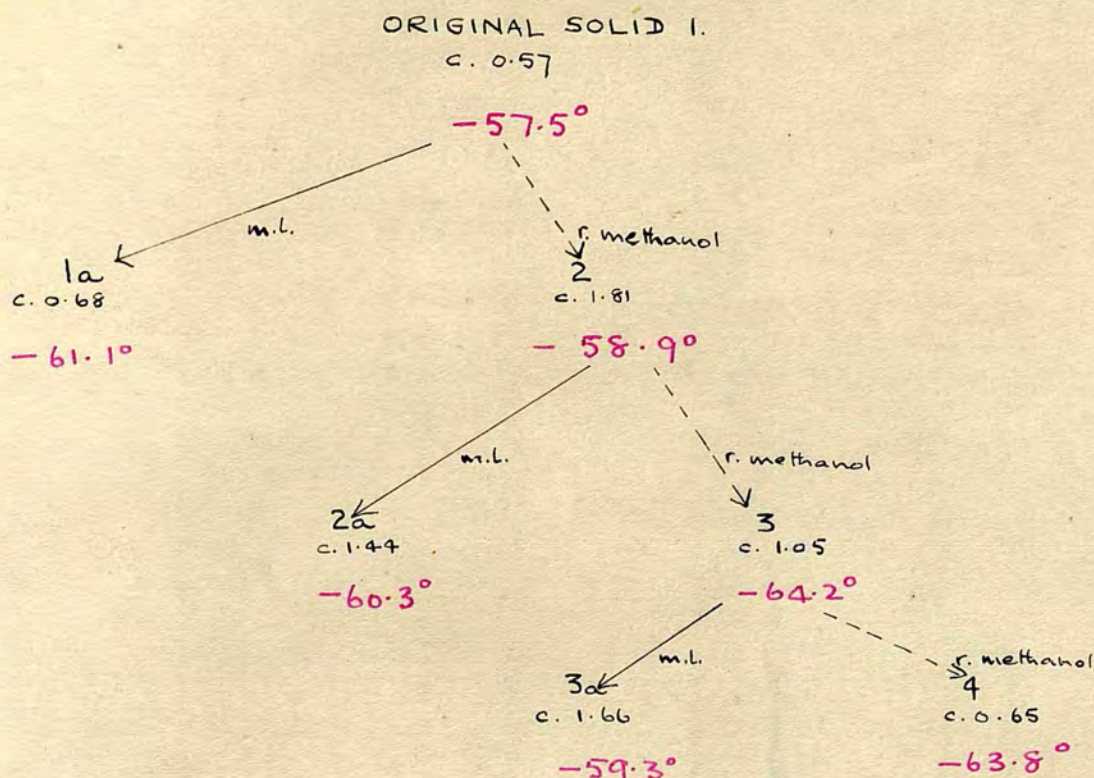
Approximately 1 g. of ester was dissolved in 20 c.c. of (+)-diethyl tartrate by warming and the solution was left to equilibriate for 1½ hours. After this time, a little of the solution was added to water at 0°, and the gum first formed was solidified by "scratching". The remainder of the solution was poured into cold water, and "seeded" with the previously formed solid. When the ester had been entirely precipitated, it was filtered, washed well with water, and dried, m.p. 47-48°. It was dissolved quickly in chloroform and transferred to a jacketted polarimeter tube as rapidly as possible. No trace of activity was detected. The experiment was repeated, the solution being allowed to equilibriate over a weekend. Again an inactive ester m.p. 47-48° was obtained.

(m) The (-)-menthyl ester was made from 12 g. of acid and 34 g. of (-)-menthol using the Fischer-Speier method. (The method using the acid chloride, made from purified thionyl chloride, and pyridine had been found unsuitable for a small scale preparation).

The acid and (-) menthol were heated in an oil-bath at

110° for eight hours, hydrogen chloride being passed in for ten minutes every two hours. After eight hours, the mixture was left overnight and the thick syrup was dissolved in ether and washed with 10% sodium carbonate. The ether layer was separated and the solvent removed. The excess (-) menthol was steam-distilled from the ester which remained as a semi-solid gum in the water. The ester was dissolved in ether, and the extract was dried before distilling off the solvent. A light brown residue which set to a stiff gum was obtained. This would not solidify and would not crystallize from any solvent at room temperature. If it was dissolved in methanol and cooled in a CO₂ -alcohol bath, white crystals separated which could be filtered rapidly through a chilled Buchner and washed with chilled solvent. The stiff gum which formed at room temperature from these crystals was thoroughly dried in vacuo and the rotation taken in chloroform solution. The concentrations were not comparable as it was difficult to gauge the quantities of gum required. As this procedure was unsatisfactory and the ester could not be vacuum distilled without much decomposition, the attempted resolution was abandoned. On distilling at atmospheric pressure, the ester decomposed smoothly into (+) menthene and the acid which was thus readily recovered.

XXVa



2. Preparation and attempted resolution of 3:4-5:6-dibenzo-1-hydroxymethylcyclohepta-3:5-diene.

(a) 8.9 g. of methyl 3:4-5:6-dibenzocyclohepta-3:5-diene-1-carboxylate were dissolved in 100 c.c. of anhydrous ether. This solution was run into one of 2 g. of lithium aluminium hydride in 100 c.c. of anhydrous ether. The reaction mixture was decomposed with water and dilute sulphuric acid as described previously, and on distilling off the ether, a white solid was obtained on the aqueous layer. This was crystallized from a benzene-60-80° petroleum ether mixture, being obtained in 90% yield as needles m.p. 131.5°.

Found: C 85.5; H 7.18. $C_{16}H_{16}O$ requires C 85.7; H 7.14.

(b) 4.4 g. of 3:4-5:6-dibenzo-1-hydroxymethylcyclohepta-3:5-diene and 2.9 g. of pure sublimed phthalic anhydride were mixed with 3 g. of pure dry pyridine and the mixture was heated on a water-bath for three hours. The product was poured into excess ice and hydrochloric acid, and left overnight. The almost solid ester was filtered off, and ground with dilute hydrochloric acid to remove pyridine. It was then washed, dried, and crystallized from dilute acetic acid. The hydrogen phthalate was obtained as a fine white microcrystalline powder (4.5 g.) m.p. 145°.

Found: C 77.10; H 5.37. $C_{24}H_{20}O_4$ requires C 77.43; H 5.38.

(c) After attempting to prepare a salt from various alkaloids and solvents without success, a salt was made using brucine. 3.3 g. of hydrogen phthalate were dissolved in ether, and 3.5 g. of anhydrous brucine were dissolvedⁱⁿ acetone. The solutions were mixed, boiled and filtered, and on cooling, beautiful clusters of prisms were obtained, 6.5 g. m.p. 129° (decomp.), $[\alpha]_{546}^{20} -20.6^\circ$ in chloroform. The salt could not be recrystallized from most common solvents; it would come out of ethyl acetate in small rhombic plates m.p. 139° $[\alpha]_{546}^{20} -21.0^\circ$, but a very large quantity of solvent was needed for complete solution. It was best crystallized from acetonitrile from which it separated as rhombic crystals m.p. 139°, $[\alpha]_{546}^{20} -21.9^\circ$. Repeated crystallization from

acetonitrile caused no change in rotation, the extreme values of $[\alpha]_{546}^{20}$ being -21.9° and -21.3° . On decomposition, an inactive ester m.p. 145° was obtained.

(d) 9.3 g. of 3:4-5:6-dibenzo-1-hydroxymethylcyclohepta-3:5-diene were dissolved in 50 c.c. of pure dry pyridine, and the solution was cooled in ice. 11.8 g. of freshly prepared and distilled (-)menthoxyacetyl chloride were slowly added to the mixture which became warm. A white crystalline precipitate of pyridine hydrochloride separated out. The reaction mixture was left overnight and was then poured into dilute hydrochloric acid when a thick oil separated. This was extracted with ether and the ethereal layer was washed with hydrochloric acid, dilute caustic soda and water. After drying, the ether was distilled off and a yellowish oil remained which gradually solidified. It was heated with a mixture of benzene and 60-80° petroleum ether from which needles separated which proved to be mostly alcohol. By partial evaporation of solvent the alcohol was removed, and on removing the solvent completely, a yellow, very viscous oil with a pungent odour was obtained. On heating with methyl alcohol and cooling, 7.5 g. of a white solid m.p. 62° were obtained, corresponding to a 42% yield. The recovered alcohol was treated with twice the calculated amount of (-) menthoxyacetyl chloride, whereupon a complete conversion to the ester took place, no alcohol being recovered.

The ester was best crystallized from 40-60° petroleum ether, from which it separated in long needles. Found: C 82.9; H 8.6. $C_{28}H_{36}O_2$ requires C 83.1; H 8.9.

The results of repeated crystallizations are shown on the chart. The rotations were taken in chloroform, c =about 1.0. Although the range of specific rotation is considerable, $[\alpha]_{5461}^{20}$ from -57.4° to -63.9°, there was no clear separation into two types of crops, and the investigation was abandoned. (There was softening a few degrees below the actual recorded melting point in each case).

The oil recovered from the solutions used for the determination of specific rotation by evaporation of the chloroform was crystallized from 40-60° petroleum ether and 'seeded' with the crop with $[\alpha]_{5461}^{20}$ -63.9°.

FIRST CROP 0.5g m.p. 63° -61.8°	$\xrightarrow{\text{m.l.}}$	SECOND CROP 0.8g m.p. 62° -57.4°
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3. Preparation and attempted resolution of 2:7-dihydro-3':2"-hydroxymethyl-3:4-5:6-dibenzoxepin.

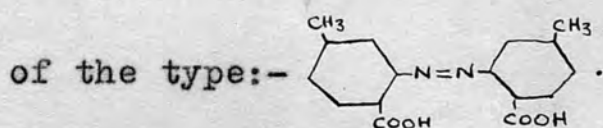
(a) m-amino-p-toluic acid was prepared according to a modification of the general directions given by Kloeppel [Ber., 1893, 26, 1733].

Pure p-toluic acid (100 g.) was slowly added to 500 g. of fuming nitric acid. The solution became warm, and after standing for about an hour, it was poured into a large volume of cold water. Crude m-nitro-p-toluic acid was precipitated as a very pale yellow solid m.p. 188-9°. It was found to be unnecessary to crystallize the solid before the next stage. The theoretical yield of crude material was obtained.

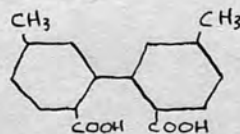
148 g. of m-nitro-p-toluic acid were dissolved in the least possible amount of hot glacial acetic acid. This solution was added gradually to a hot solution of 610 g. of stannous chloride in 770 c.c. of concentrated hydrochloric acid. There was a vigorous reaction after each addition of the acetic acid solution, the contents of the flask refluxing briskly. After the reaction was over, the mixture was poured into a beaker and allowed to cool, about 250 c.c. of concentrated hydrochloric acid being added. On cooling, the amine hydrochloride was obtained as colourless needles, which were filtered, washed with concentrated hydrochloric acid and

dried. Yield almost theoretical.

(b) 11.1 g. of base hydrochloride were dissolved in 3.3 g. of concentrated hydrochloric acid and water, and diazotized at 0-2° by addition of 4.6 g. of sodium nitrite. The diazo solution was slowly added to a well-stirred solution containing 33.2 g. of hydrated copper sulphate in 190 c.c. of water and 38 c.c. of 0.880 ammonia, to which 26 g. of sodium metabisulphite and 26 c.c. of 0.880 ammonia had been added at 10°. A brisk evolution of nitrogen occurred, and after standing for some time, the solution was acidified with a solution of 16.9 g. of anhydrous ferric chloride in 26 c.c. of water and 85 c.c. of concentrated hydrochloric acid. An orange precipitate was obtained, which was filtered and suspended in water. On addition of sodium bicarbonate, carbon dioxide was evolved and the substance went into solution. On boiling with charcoal, filtering and acidifying, 3 g. of an orange powder m.p. 145° were obtained. This compound contained nitrogen and was presumably an azo compound



No trace of the desired compound:-
could be detected.



(c) m-iodo-p-toluic acid was made according to Kloeppel's directions [loc. cit.]. 110 g. of m-amino-p-toluic acid

hydrochloride were dissolved by heating in water with 85 g. of concentrated sulphuric acid. The solution was diazotized at 0-2° with a solution in water of 41 g. of sodium nitrite. The diazo solution was filtered and added slowly to a cooled, saturated solution of 195 g. of potassium iodide in water. The flask was then warmed on the water-bath until no further evolution of nitrogen took place. After adding a few grams of sodium metabisulphite to remove iodine, the iodo-acid was obtained as a light pink powder, which was filtered and washed with water. 125 g. of crude product m.p. 206-6.5° were obtained, and it was not necessary to purify the compound before the next stage.

(d) The iodo-acid was oxidized to iodoterephthalic acid according to the method of Abbes [Ber., 1893, 26, 2952]. It was found that the yield did not decrease on a 20 g. scale, but that it dropped considerably for 30 g. and larger quantities.

20 g. of iodo-acid were dissolved in about 3.5 g. of caustic soda in a little water, and the solution was heated on the water-bath. A solution of 26 g. of potassium permanganate in 2600 c.c. of water was added, and after 4-5 hours' heating on the water-bath, decolourization had occurred. SO₂ was passed into the cold solution until all the manganese dioxide disappeared. The solution was made

rather more acid with dilute sulphuric acid, and the precipitated iodoterephthalic acid was obtained as a light yellow powder. Yield about 18 g., m.p. $>275^{\circ}$. Again, no purification was necessary.

(e) (i) dimethyliodoterephthalate was prepared according to Kenner and Witham [J., 1913, 237] by suspending 32 g. of iodoterephthalic acid in 320 c.c. of cold methanol and saturating the suspension with hydrogen chloride. The mixture was warmed on the water-bath for about 4 hours, and on cooling the dimethyl ester separated out. It was filtered and recrystallized from methanol. Yield 24 g. of yellow microcrystalline powder, m.p. 80° .

(ii) 30 g. of iodo-acid were refluxed on a water-bath for about 4 hours with 30 g. of concentrated sulphuric acid and 300 g. of methanol. The solution was poured into water and the crude ester was filtered off. After removal of any unchanged acid with sodium bicarbonate solution, the ester was crystallized from methanol and obtained as colourless rectangular plates m.p. $81-2^{\circ}$, yield 22 g. This latter method was preferred as it gave a cleaner product.

(f) Tetramethyldiphenyl-2:2'-5:5'-tetracarboxylate was prepared from the dimethyl ester according to Kenner and Witham [loc. cit.] with slight modifications.

(i) 10 g. of ester were heated in a metal bath to 260°, then 10 g. of copper bronze were added gradually. After the addition was complete, the mixture was heated for 45 minutes, and after cooling somewhat, was extracted with boiling chlorobenzene. A very dark solution resulted, and on boiling off the solvent, a dark residue was left. Crystallization from a benzene - 60-80° petroleum ether mixture gave a yellowish crystalline powder (small rhombs) m.p. 144-6°. On cooling and remelting, the melting point was 160-2° Kenner and Witham gave m.p. 156°. Yield about 50%.

(ii) 10 g. of ester were treated with copper bronze as above, but the extraction was carried out with boiling o-dichlorobenzene, and on cooling, the greenish-brown solution deposited almost colourless rhombs m.p. 145-6°, with second m.p. after solidification 160-1°. Yield about 50%.

(iii) A further Ullmann reaction was carried out, the extraction being done with benzene after cooling, as did Kenner and Witham. The first crop of crystals was small colourless plates m.p. 158-61°. A further crop obtained by partial evaporation of the solvent, consisted of almost colourless rhombs m.p. 144 -5°, with second m.p. 159-61°. Hence the tetramethyldiphenyltetracarboxylate appears to be dimorphic. Method (ii) was preferred. The best yield obtained was 62% compared with 70% recorded by Kenner and

Witham.

(g) The tetra-ester was reduced to the corresponding tetra-hydric alcohol with lithium aluminium hydride. As it was only sparingly soluble in ether, the Soxhlet technique was used. 1.5 mols. of reducing agent per mol. of ester were used.

During the reduction, a thick white precipitate formed, and after decomposition with water and acidification, some white solid was still apparent. The ether layer was removed on the water-bath, and a white solid remained in suspension. This was filtered off, and crystallized from a large volume of ethanol from which it separated as a white microcrystalline powder (needles) m.p. 202-3°.

Yield 76%.

Found: C 69.8; H 6.9. $C_{16}H_{18}O_4$ requires: C 70.1; H 6.6.

(h) The above alcohol was converted to the oxepin by heating in a water-bath for about an hour with excess 2N sulphuric acid. (Dark coloured, high melting products were obtained if 50% or rather more dilute sulphuric acid was used.) A white crystalline substance was obtained which was readily recrystallized from ethanol. Colourless plates m.p. 192° (decomp.) were obtained. Yield almost theoretical.

Found: C 74.89; H 6.24. $C_{16}H_{16}O_3$ requires: C 75.0; H 6.25.

(i) 8 g. of oxepin were dissolved in about 30 c.c. of pure dry pyridine. 25 g. of (-) menthoxyacetyl chloride were added to the cooled solution. A dark red colour developed, and pyridine hydrochloride was precipitated. The solution was allowed to stand overnight, and was then poured into excess dilute hydrochloric acid. A red oil separated which gradually became very viscous. The whole mass was extracted with ether and the extract was washed in turn with dilute hydrochloric acid, sodium carbonate and water. On drying the extract and removing the ether, a reddish glass-like substance was obtained which would not solidify with any of the usual solvents. On vacuum distillation, a reddish fairly mobile liquid b.p. $182^{\circ}/22$ mm. was obtained, which had a very pungent odour.

(j) 6.5 g. of oxepin were heated in a water-bath with 7.5 g. of pure sublimed phthalic anhydride and about 10 g. of pure dry pyridine for three hours. On pouring into ice and dilute hydrochloric acid, a solid was obtained which was washed well, and ground with hydrochloric acid to remove pyridine. After washing with water, the solid was crystallized from dilute acetic acid. Colourless needles m.p. $179-9.5^{\circ}$ were obtained. Yield 10.5 g.

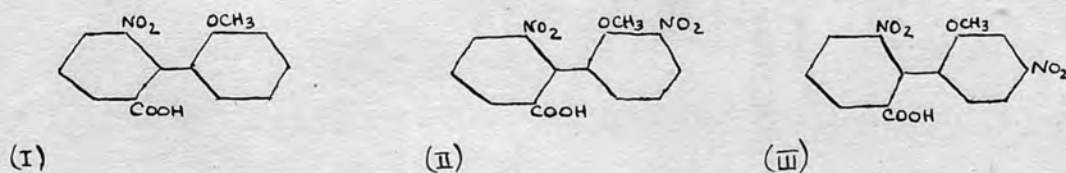
Found: C 69.10; H 4.45. $C_{32}H_{24}O_9$ requires C 69.56; H 4.35.

(k) No satisfactory salt could be made from the dihydrogenphthalate and brucine, strychnine, quinine, cinchonine, cinchonidine or quinidine, using a wide variety of solvents. Either gums were obtained which could not be crystallized, or solids which did not crystallize satisfactorily.

C. Section II.

An attempt was made to prepare 3:3'-dinitro-diphenic acid, in order to ascertain whether it would undergo first and/or second order asymmetric transformation in suitable solvents. Diphenic acid itself cannot be resolved, but the ultraviolet absorption spectrum indicates a non-coplanar structure (see introduction), and Lesslie, Turner and Winton (J., 1941, 257) found that it underwent a rapid optical activation with nor-(+)- ψ -ephedrine at -30° in chloroform or acetone-chloroform.

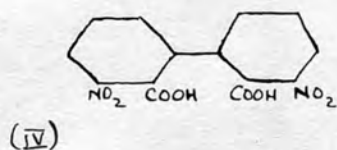
In the following series of three optically unstable substituted diphenyls, (I) has a half-life period of 9.4 minutes in alcohol at 25° [Stoughton and Adams, J. Amer. Chem. Soc., 1932, 54, 4426]. Compound (II) has a half-life



period in alcohol at 25° of 1905 minutes [Chien and Adams, *ibid.*, 1934, 56, 1737], while (III) has a half-life period in acetone at 25° of 115 minutes [Hanford and Adams, *ibid.*, 1935, 57, 1592].

Since the 3'-nitro group in (II) cannot interfere with the 6-nitro or 2-carboxyl groups, it must somehow increase the interference of the methoxyl group with these substituents.

Some repulsive force may account for this apparent "crowding" effect of the 3'-nitro group. That this effect may be transmitted to some extent by a group not adjacent to the ortho methoxyl is shown by the increased optical stability of (III). Some effect similar to this may be expected to show in 3:3'-dinitro-diphenic acid (IV).



The "crowding" effect of the nitro groups might be expected to increase the interference of the carboxyl groups to such an extent that an optical activation might be observable at room temperature. As is shown in the experimental attached to this section, it proved impossible to obtain the pure acid. The dimethyl ester however was readily obtained, and was dissolved in (+) diethyl tartrate and allowed to equilibriate. On reprecipitation with water, an inactive ester was recovered, so that it appears that the "buttressing" effect of the nitro substituents is insufficient to show any trace of optical instability by this technique.

EXPERIMENTAL

(a) 100 g. of 3-nitrophthalic anhydride were heated in a metal-bath at 300° with 66 g. of ammonium carbonate, using an air condenser, until no more water-vapour came off. On cooling, the contents of the flask were boiled with acetone

when complete solution occurred. On filtering, removing some of the solvent and cooling, yellow plates were obtained m.p. 218-9°, yield 78g.

(b) 3-nitrophthalamic acid was prepared according to the method of Moser and Gompf [J. Org. Chem. 1950, 15, 583]. 20 g. of 3-nitrophthalimide were added to a well-stirred solution of 11.7 g. of caustic potash in 417 c.c. of water. The stirring was continued for about two hours until solution was complete. The solution was cooled and carefully acidified while stirring was continued. 3-nitrophthalamic acid was obtained in about 80% yield as a cream or fawn crystalline powder m.p. 150° with resolidification and decomposition at 206°. (In one experiment m.p. 160-2°, then 206° (decomp)).

On repeating this experiment with a further 58 g. of 3-nitrophthalimide, the latter dissolved almost immediately in caustic potash, and on acidification, no 3-nitrophthalamic acid was obtained. Ether extraction yielded only 4 g. of the required product. By slow evaporation on the water-bath, 57 g. of solid were obtained which effervesced with cold sodium bicarbonate solution and which gave off ammonia on warming with caustic soda, m.p. 265-70° (decomp.). As this was certainly ammonium hydrogen 3-nitrophthalate it

was stirred with hydrochloric acid and the remaining solid was boiled with charcoal and water. On filtering and cooling, yellow crystals m.p. 210° were obtained which effervesced with cold sodium bicarbonate solution but did not evolve ammonia on warming with alkali. This impure 3-nitrophthalic acid was converted to the β -monomethyl ester by heating with ten times its weight of methanol and four times its weight of concentrated sulphuric acid on the water-bath for one hour. The reaction mixture was poured into water and when cold the solution was extracted with ether. On removing the ether from the dried extract, 27 g. of yellowish crystalline powder were obtained. On washing with chloroform, in which the ester was found to be practically insoluble, the 3-nitrophthalic acid- β -monomethyl ester was obtained as a white crystalline powder m.p. $166-8^{\circ}$. This ester was converted to 3-nitrophthalamic acid according to the method of Kahn [Ber., 1902, 35, 3857]. The ester was dissolved in 200 c.c. of 0.880 ammonia and left in a stoppered flask for two days, after which time it was poured into an evaporating dish and left until no smell of ammonia could be detected. On acidifying with hydrochloric acid, 24 g. of white crystalline powder m.p. 155° with resolidification and final m.p. 206° (decomp.) were obtained. The old method therefore gives a cleaner product.

(c) 40 g. of 3-nitrophthalamic acid were added slowly to a stirred solution of sodium hypobromite at 0° , made by adding 11.4 c.c. of bromine to a stirred solution of 45.6 g. of caustic soda in 380 c.c. of water at 0° . When solution was complete, the flask was warmed to $70-80^\circ$ for half an hour to effect rearrangement. On cooling and acidifying with hydrochloric acid, 6-nitroanthranilic acid was precipitated, which was filtered and crystallized from water. It was obtained in 70% yield as light brown prisms m.p. 184° .

(d) (i) It has been reported by Atkinson, Morgan, Warren and Manning [J. Amer. Chem. Soc., 1945, 67, 1513] that 3:3'-dinitrodiphenic acid can be obtained in 40% yield using the same method as for diphenic acid (see section I). All diazotizations were carried out in hydrochloric acid solution and the hydroxylamine catalyst favoured by the American workers was used. No details of appearance, melting point etc. are given in the paper, but it is stated that some 6-chloro-2-nitrobenzoic acid was also isolated (amount not given).

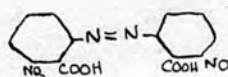
As the cuprammonium-sulphite catalyst had been found suitable for the diphenic acid preparation this was used here.

21 g. of 6-nitroanthranilic acid were dissolved in water and 50 c.c. of concentrated hydrochloric acid by

heating. The mixture was cooled, and 8.5 g. of sodium nitrite were added at 0-2°. The diazo-solution was filtered before use, as a considerable amount of a brownish solid was left. The catalytic solution was made as follows: 61 g. of hydrated copper sulphate were dissolved in 346 c.c. of water and 35.2 c.c. of 0.880 ammonia. When the diazo solution was ready, 138.5 g. of sodium metabisulphite and 138.5 c.c. of 0.880 ammonia were added at 10°. The diazo solution was added slowly with stirring when evolution of gas occurred and a dark, sticky substance separated. When the addition was over, the whole mixture was filtered through a sintered glass funnel before adding a solution of 90 g. of anhydrous ferric chloride in 138.5 c.c. of water and 450 c.c. of concentrated hydrochloric acid. The solution was only slightly cloudy, but on cooling a small amount of oil separated. The solution was extracted with ether, but again, only a small amount of oil was obtained. After standing for two days, the aqueous solution deposited a considerable amount of a brick-red powder. This (4 g.) was insoluble in sodium bicarbonate solution but contained nitrogen, m.p. indefinite, darkening at 225° with decomposition at 243°. The substance gave an intense violet colour with caustic soda, and could be crystallized with difficulty from glacial acetic acid when an orange powder was obtained.

On warming with sodium carbonate solution there was a considerable evolution of carbon dioxide, and the purple colouration appeared.

Found: C 43.3; H 2.7; N 15.9.


 requires: C 46.6; H 2.2; N 15.5.

(ii) 10 g. of 6-nitroanthranilic acid were dissolved in water and 14 c.c. of concentrated hydrochloric acid were added. The solution was cooled to 0° and diazotized with 4 g. of sodium nitrite. The diazo solution was filtered and added to the catalytic solution slowly with stirring. The catalytic solution which was cooled in ice was prepared as follows: 19 g. of hydrated copper sulphate were dissolved in 75 c.c. of water and 32 c.c. of 0.880 ammonia. The solution was cooled to 10°. 5.4 g. of hydroxylamine hydrochloride were dissolved in 18 c.c. of water and cooled to 10°. 12.8 c.c. of 6N caustic soda solution were added, and this solution was immediately added to the cuprammonium sulphate solution. When the diazo solution was added, copious evolution of nitrogen occurred and some tarry matter separated. The solution was therefore filtered before it was heated to boiling and acidified with about 38 c.c. of concentrated hydrochloric acid. On standing only a little tar separated, so after filtering, the green solution was

extracted with ether. The yellow ether extract was dried and the ether removed. A somewhat tarry residue remained which was treated with cold bicarbonate solution. The solution which resulted was boiled with charcoal, filtered and acidified. On cooling, a bright yellow powder melting above 270° was obtained. This was taken up in sodium bicarbonate solution, boiled with charcoal and acidified, whence, on cooling, 1 g. of yellow plates was obtained. This corresponds to an 11% yield if the product is 3:3'-dinitrodiphenic acid.

Found: C 49.9; H 2.15; N 8.12.

$C_{14}H_8O_8N_2$ requires: C 50.6; H 2.41; N 8.43.

By evaporation of the mother liquor, colourless needles m.p. 161° were obtained. These were 6-chloro-2-nitrobenzoic acid, and about 1 g. was isolated corresponding to a 9% yield.

On repeating the experiment on about $2\frac{1}{2}$ times the scale, much more tarry matter was produced. The working up was carried out as before, and an orange powder m.p. $> 270^{\circ}$ was isolated. On boiling with alcohol, however, a deep orange solution was obtained from which

an almost white solid separated. This was taken up in sodium bicarbonate, boiled with charcoal, filtered and acidified. About 2 g. ^{of} colourless plates m.p. $> 270^{\circ}$ were obtained.

Found: C 50.5; H 2.33; N 7.32.

$C_{14}H_8O_8N_2$ requires: C 50.6; H 2.41; N 8.43.

2.5 g. of the chloro compound were obtained.

(e) As the diazotization in hydrochloric acid was not altogether satisfactory, another method was sought, from which 2-nitro-6-iodobenzoic acid might be prepared.

(i) Hodgson and Walker's method [J., 1933, 1620] was used on 5 g. of 6-nitroanthranilic acid, and the diazo-solution was added to a cold saturated solution of potassium iodide. 2 g. of light brown needles were obtained, and a further 2 g. by ether extraction; m.p. 188° , yield 50%. On a larger scale, however, not such good results were obtained.

(ii) Witt's method was tried on 5 g. and 10 g. of 6-nitroanthranilic acid as this was reported by Rule and Smith to give a 77% yield [J., 1937, 1096]. However, only poor yields were obtained.

(iii) Schoutissen's method of diazotization was found to give consistently good results on a small and large scale.

9 g. of 6-nitroanthranilic acid were dissolved in about 125 c.c. of concentrated sulphuric acid, and the solution was cooled to 0°. A solution of 5 g. of sodium nitrite in 75 c.c. of concentrated sulphuric acid was added, then 300 c.c. of syrupy phosphoric acid were run in at 0-5°. After half an hour, 20 g. of urea were added and the mixture was poured on to ice. The diazo solution was slowly added to a cold solution of 82.5 g. of potassium iodide in water. 9 g. of 2-nitro-6-iodobenzoic acid were obtained after crystallization from water as light brown needles m.p. 189°. Yield 62%.

(f) (i) 2 g. of the iodoacid were refluxed for several hours with 2 g. of concentrated sulphuric acid and 20 g. of methanol, but the acid was recovered entirely unchanged.

(ii) 10 g. of iodoacid were dissolved in 20 c.c. of 2N ammonium hydroxide and the solution was boiled to expel ammonia. On cooling, freshly prepared silver nitrate

solution was added to the dark brown solution, and a peach-coloured precipitate was obtained. This was filtered away from light, washed well with water and dried in vacuo in the dark. The silver salt was suspended in anhydrous ether, and refluxed with 4.1 g. of methyl iodide for several hours. The reaction mixture was filtered through a sintered glass funnel, and the silver iodide was washed well with ether. The orange ethereal solution on distilling off the ether left an orange residue which on crystallization from methanol gave light yellow rectangular plates m.p. $94-5^{\circ}$. 6 g. only of methyl 2-nitro-6-iodo-benzoate were obtained.

(g) 4 g. of the above ester were heated in a metal bath to 200° . 4 g. of copper bronze were added gradually, and after addition heating was continued at 210° for one hour to complete the reaction. On cooling to room temperature the mixture was extracted with boiling ethanol, and when it was cold the yellow alcoholic solution deposited buff-coloured needles of dimethyl 3:3'-dinitrodiphenate m.p. $144-5^{\circ}$.

Yield 50%

Found: C 53.1; H 3.39; N 7.97.

$C_{16}H_{12}O_8N_2$ requires: C 53.3; H 3.33; N 7.78.

(h) 1 g. of dimethyl 3:3'-dinitrodiphenate was dissolved in 40 c.c. of (+) diethyl tartrate by warming. The solution was left overnight to equilibrate. On addition of cold

water, the ester was precipitated immediately as a buff powder which was filtered and dried in vacuo. It was dissolved in purified chloroform containing a known amount of absolute ethanol and transferred to a jacketted polarimeter tube. A reading was taken within 30 seconds of wetting the solid, but no trace of optical activity was detected.

(i) (i) The ester was dissolved in glacial acetic acid, and dilute sulphuric acid (1 pt. acid: 12 parts water by volume) was added till the solution was turbid. The mixture was boiled for some hours under reflux. (Method of Mills and Elliott, [J., 1928, 1299]). On cooling and diluting with water, a yellowish powder was obtained m.p. $143-4^{\circ}$, which proved to be unchanged ester.

(ii) The ester was boiled under reflux with 10% aqueous caustic soda for about two hours. On acidifying and cooling, gradually brilliant yellow crystals formed m.p. $> 270^{\circ}$. These dissolved with effervescence in cold bicarbonate solution.

Found	(a)	C 47.6; H 2.2; N 7.5.
Found	(b)	C 46.24; H 2.8; N (not det.)
$C_{14}H_8O_8N_2$ requires:		C 50.6; H 2.41; N 8.43.
$C_{15}H_{10}O_8N_2$ ($\frac{1}{2}$ ester) requires:		C 51.9; H 2.88; N 8.59.

This does not appear to be the same as the bright yellow compound obtained previously ((d) (ii)).

(iii) The ester was boiled with methyl alcoholic potash for one hour. After distilling off most of the methanol and acidifying, a buff crystalline precipitate m.p. $> 270^{\circ}$ and soluble with effervescence in cold bicarbonate solution was obtained. It was refluxed with ethanol and charcoal and filtered. On cooling a white crystalline powder was obtained m.p. $> 270^{\circ}$.

Found: C 50.13; H 2.88.

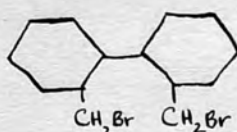
$C_{14}H_8O_8N_2$ requires: C 50.6; H 2.41.

This again gives a different analysis from the previously obtained colourless product ((d) (ii)).

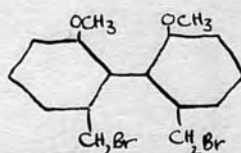
D. Section III.

The preparation of various diphenyl derivatives has been attempted. In some cases the reactivity of certain diphenyl derivatives was being investigated from the point of view of general chemical interest; in other cases, an attempt was made to prepare a compound for attempted resolution and/or study of its ultraviolet absorption spectrum. The attempts in this second category which failed are recorded in this section together with the compounds which make up the first category.

1. Beaven, Hall, Lesslie and Turner [J., 1952, 854] showed that 2:2'-bisbromomethyldiphenyl (I) reacts vigorously with strong secondary bases to give dibenzazepinium compounds.



(I)



(II)

Thus compounds are readily formed with (+) ephedrine, piperidine and phenylpiperidine, while 2:2'-bisbromomethyl-6:6'-dimethoxydiphenyl (II) reacts readily with diethylamine and piperidine.

It was decided to determine whether the dibromide reacted easily with tertiary bases. Diquaternary salts

are formed relatively easily with pyridine, dimethylaniline, triethylamine and $\alpha:\alpha'$ -dipyridyl; the reaction with quinoline seems to yield a mixture of mono- and di-quaternary salts.

EXPERIMENTAL

(a) 0.5 g. of pure dry quinoline and 0.34 g. of 2:2'-bis-bromomethyldiphenyl were dissolved separately in chloroform and the solutions were mixed. There was no reaction in the cold, so the solution was warmed to 70° for a short time. After standing for about a minute a white precipitate formed which was filtered off and washed with acetone; m.p. 216° with previous softening. It was completely soluble in water and gave an immediate precipitate with silver nitrate solution.

Found: N 3.4; Br 31.4.

$C_{23}H_{21}NBr_2$ requires: N 2.98; Br 34.1.

$C_{32}H_{30}N_2Br_2$ requires: N 4.7; Br 26.7.

(b) 0.2 g. of dry pyridine and 0.3 g. of dibromide were dissolved separately in chloroform and the solutions were mixed. On placing in warm water, a white precipitate formed immediately, which was filtered off and washed with acetone; m.p. 270° . It was soluble in cold water and gave an immediate precipitate with silver nitrate solution.

Found: N 5.5; Br 31.9.

$C_{24}H_{22}N_2Br_2$ requires: N 5.6; Br 32.1.

(c) Solutions of 0.2 g. of dimethylaniline and 0.3 g. of dibromide in chloroform were mixed. After warming no precipitation occurred, neither did a precipitate form on standing overnight. On adding acetone a white precipitate formed which was filtered and washed with acetone m.p. 138-9°. It was water-soluble and gave a precipitate with silver nitrate solution.

Found: N 4.6; Br 27.1;

$C_{30}H_{34}N_2Br_2$ requires: N 4.8; Br 27.5.

(d) 0.1 g. of triethylamine and 0.3 g. of dibromide were dissolved separately in chloroform and the solutions were mixed. On mixing some heat was evolved but there was no precipitation. After warming in a water-bath a white turbidity appeared. On cooling and adding acetone, a white precipitate was obtained which was filtered and washed with acetone m.p. 165°(decomp.). It was soluble in water giving a precipitate with silver nitrate.

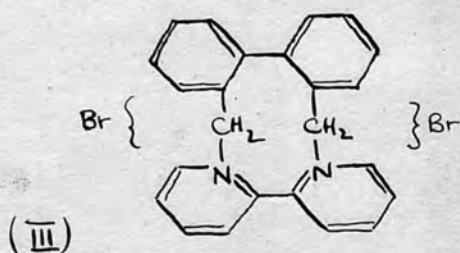
Found: N 5.3; Br 29.0.

$C_{26}H_{42}N_2Br_2$ requires: N 5.2; Br 29.5.

(e) (i) 0.16 g. of $\alpha:\alpha'$ -dipyridyl and 0.34 g. of dibromide were dissolved separately in chloroform and the solutions were mixed. There was no reaction even on warming. On cooling, acetone was added but there was no precipitation.

(ii) 0.16 g. of $\alpha:\alpha'$ -dipyridyl and 0.34 g. of dibromide were warmed together in 60-80° petroleum ether. On cooling, a crystalline precipitate formed which proved to be a mixture of the two components.

(iii) 0.16 g. of $\alpha:\alpha'$ -dipyridyl and 0.34 g. of dibromide were heated together on a water-bath. The mixture melted but after some time became solid again. On cooling, the substance proved to be very deliquescent, but on boiling with alcohol and cooling, fine white needles were obtained which were stable in air, m.p. 137°(decomp.). These were soluble in cold water giving an immediate precipitate with silver nitrate. If the diquaternary salt were formed from the monomethyl groups in the 'cis' position, the 10-membered ring compound (III) would be obtained.



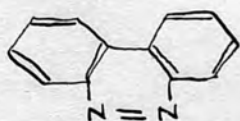
Found	(a)	N 5.42; Br 30.80.
	(b)	N 5.41; Br 30.91.

$C_{24}H_{20}N_2Br_2 \cdot H_2O$ requires: N 5.45; Br 31.09.

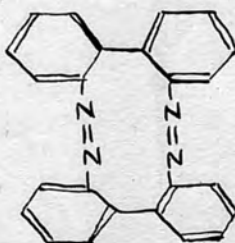
The molecular weight of this compound, assuming it to be a monohydrate, is 514. 514 g. of the salt should therefore contain 159.8 g. of bromide ion. Titration of a solution

of the dibromide with standardized silver nitrate solution gave a value of 159.5 g. of bromide ion per 514 g. of salt.

2. The reduction of 2:2'-dinitrodiphenyl with lithium aluminium hydride was carried out in order to determine what type of azo compound is produced. With the nitro groups in the trans position a complex polymer might form. With the nitro groups in the cis position, either (IV) or (V) might result. Alternatively a mixture of products might be obtained.



(IV)



(V)

The product (IV) was obtained in high yield.

EXPERIMENTAL

2 g. of 2:2'-dinitrodiphenyl which is sparingly soluble in ether were reduced in a Soxhlet apparatus with an ethereal solution of 0.7 g. of lithium aluminium hydride. During the reduction, the solution went from yellow to brown and finally almost black. On adding water, the black colour was displaced and a yellow precipitate was observed. On acidification, the ether layer was orange, the aqueous

blackish-green. The ether layer was separated and partly evaporated, when yellow rectangular prisms separated out m.p. 157° , yield over 90%. The solid dissolved very readily in dilute acids.

Found: C 79.8; H 4.45; N 15.3.

Calculated for $\text{C}_{12}\text{H}_8\text{N}_2$: C 80.0; H 4.44; N 15.6.

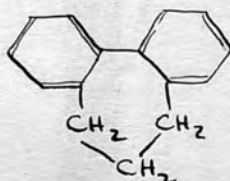
M.W.: 178. Required for (IV): 180.

The reduction product was therefore 0:0'-azodiphenyl.

3. An attempt was made to decarboxylate 3:4-5:6-dibenzocyclohepta-3:5-diene-1-carboxylic acid (VI) in order to



(VI)



(VII)

prepare the parent hydrocarbon (VII). The decarboxylation was unsuccessful, some (VI) being recovered unchanged, and a product of doubtful composition being isolated.

EXPERIMENTAL

2 g. of 3:4-5:6-dibenzocyclohepta-3:5-diene-1-carboxylic acid were heated with 0.1 g. of copper bronze and 20 c.c. of pure dry quinoline in a metal bath at 260° for three

hours. At the end of this time, the liquid in the flask had become dark brown. Dilute hydrochloric acid was added to take up the quinoline, whereupon a viscous brown oil separated. On shaking with ether, some black solid separated which was filtered off. The ethereal extract was washed in turn with dilute hydrochloric acid, water, sodium carbonate and water. The sodium carbonate extract on acidification yielded about 1 g. of the original acid (VI). The ether was removed from the dried ether extract, and a brown oil with a pungent 'phenolic' odour was left. On adding to this a cold saturated solution of picric acid in alcohol, a brownish precipitate formed immediately. This was filtered and crystallized by dissolving in alcohol and adding a cold saturated solution of picric acid in alcohol. Brown needles were obtained m.p. 113-4°, yield 0.5g.

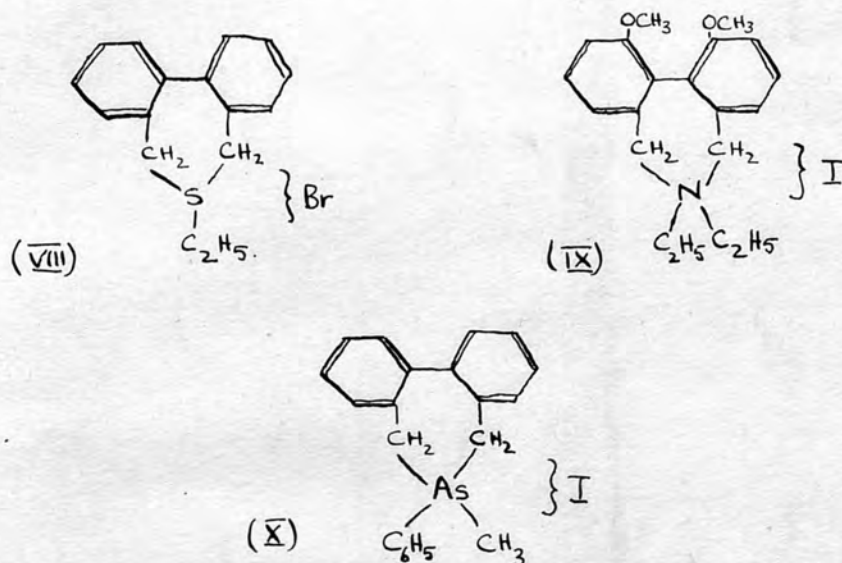
Found: C 54.5; H 3.5; N 11.3.

$C_{21}H_{17}O_7N_3$ requires: C 59.6; H 4.0; N 9.9.

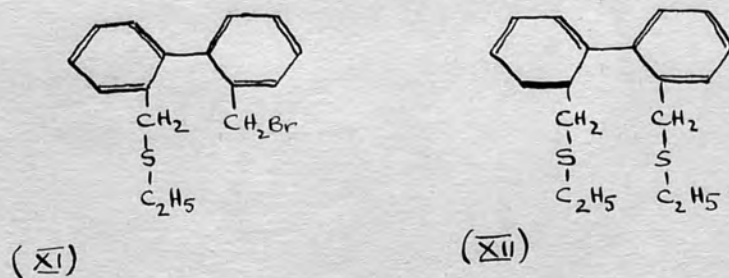
After recrystallization the melting point was unchanged, but analysis gave C 54.8; H 3.4; N 10.6.

Rapoport and Williams [J. Amer. Chem. Soc., 1949, 71, 1774] report that they could not make a picrate from 3:4-5:6-dibenzocyclohepta-3:5-diene, so that the structure of the above compound is doubtful.

4. An attempt was made to prepare the cyclic sulphonium salt (VIII) from 2:2'-bisbromomethyldiphenyl.



Apart from its interest as the sulphur analogue of compounds such as (IX) (Beaven, Hall, Lesslie and Turner, [loc. cit.]) and (X) (Beeby, Mann and Turner, [J., 1950, 1923]), this sulphonium salt should be capable of resolution owing to the dissymmetry of the molecule. On treatment with ethyl mercaptan, however, no sulphonium salt was formed, but two liquid products, which were probably (XI) and (XII).

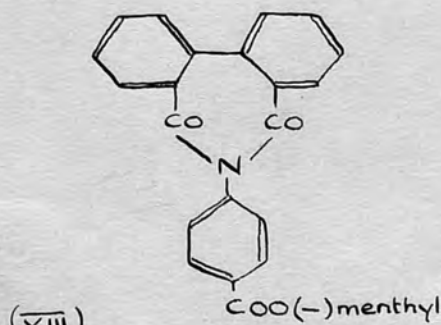


EXPERIMENTAL

0.68 g. of clean, dry sodium were dissolved in 30 c.c.

of absolute ethanol, and 1.5 c.c. of ethyl mercaptan were added. This solution was run into a boiling, well-stirred solution of 10 g. of 2:2'-bisbromomethyldiphenyl in ethanol. A white precipitate started to form immediately, and the refluxing was continued for about an hour. The sodium bromide was filtered off, and the bulk of the ethanol removed by distillation. On pouring the residue into water, a thick yellow oil was obtained, which was extracted with ether. The dried extract after removal of ether yielded just over 6 g. of yellow oil. This oil was distilled under reduced pressure when an evil-smelling liquid came off over the range 170-200°/10 m.m. On redistillation, a liquid b.p. 174-8/10m.m. with an onion-like odour was obtained which contained sulphur but no bromine, and an unpleasant smelling viscous liquid which partly solidified b.p. 16-189-92°/10m.m., containing both sulphur and bromine. No trace of sulphonium salt could be detected in the aqueous solution.

5. An attempt was made to condense diphenic anhydride with (-) menthyl p aminobenzoate to give the substituted imide (XIII).



This should exist in diastereoisomeric forms, unfortunately the desired product could not be obtained.

EXPERIMENTAL

(a) 6.5 g. of diphenic acid was converted to its anhydride by heating in an oil-bath at 120° for an hour with 10 g. of acetic anhydride. On cooling, beautiful colourless crystals were obtained which were washed with glacial acetic acid and dried, m.p. 225°. The recorded melting-point is 217°, but successive preparations gave the same product, the mixed melting-point with diphenic acid being 202°.

(b) (i) 25 g. of *p*-aminobenzoic acid were refluxed with about 100 g. of thionyl chloride until no further evolution of hydrogen chloride occurred. The thionyl chloride was distilled off, and the residue was distilled under reduced pressure, when a yellow liquid b.p. 144°/14 m.m. was obtained which readily solidified to give a yellow solid m.p. 35°. About 36 g. were obtained. 8.1 g. of (-) menthol were dissolved in 81 g. of dry pyridine. 10g. of yellow solid were added slowly while the flask was cooled. After leaving overnight the mixture was poured into dilute hydrochloric acid and ice, when an oil was obtained which was extracted in ether. When the ether extract had been dried and the ether removed, the residue was vacuum distilled. A considerable

amount of decomposition seemed to occur, and a viscous yellow liquid b.p. $192^{\circ}/10$ mm. was obtained which smelled of menthol and slowly solidified to a waxy solid. Both this product and the yellow solid from the acid chloride preparation diazotized and coupled with β -naphthol, but both were found to contain a considerable amount of sulphur.

(ii) It was decided therefore to prepare (-) menthyl p-aminobenzoate by reduction of the nitro compound according to McCluskey and Sher [J. Amer. Chem. Soc., 1947, 49,452].

16.7 g. of p-nitrobenzoic acid was refluxed with 59.5g. of thionyl chloride for about an hour. The thionyl chloride was distilled off, and 39 g. of menthol were added. The mixture was heated in an oil-bath at 130° until no more hydrogen chloride was evolved. The excess menthol was distilled off ($91^{\circ}/9$ mm.) and the dark residue was refluxed with alcohol and charcoal, and filtered. 17 g. of slightly grey rectangular prisms m.p. $62-3^{\circ}$ were obtained.

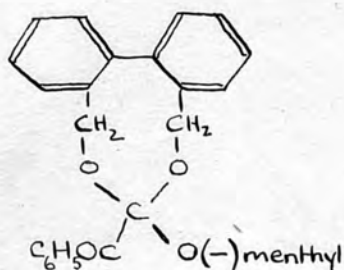
The ester was intimately mixed with 119 g. of iron powder, and sufficient water was added to form a paste. The mixture was heated and stirred for 20 hours at $50-60^{\circ}$, a little water being added at intervals to offset evaporation. At the end of this time, the mixture was evaporated to dryness and transferred to a Soxhlet thimble from which it was extracted with ether. An orange solution was obtained

which left a dark orange oil on removal of ether. This was heated with 60-80° petroleum ether and a little charcoal, and filtered. On cooling, 6g. of buff prisms m.p. 88° were obtained.

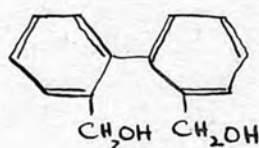
(c) (i) Following the general method given by Warren and Briggs [Ber., 1931, 64 B, 26], 1.1 g. of diphenic anhydride and 1.4 g. of (-) menthyl *p*-aminobenzoate were dissolved separately in benzene, and the solutions were mixed. A small crystalline precipitate came down on standing, but this proved to be diphenic anhydride and not the required anilic acid. No anilic acid was produced using acetone as solvent. The sparing solubility of diphenic anhydride restricted any further choice of solvent.

(ii) Following the method of Vanags [Acta Univ. Latviensis, 1939, 4, 405] for *N*-substituted phthalimides, 1.1 g. of diphenic anhydride and 1.4 g. of (-)menthyl *p*-aminobenzoate were heated together under reflux in glacial acetic acid for about an hour. On cooling, no solid separated, and treatment with water precipitated a mixture of the original components.

6. The attempt was made to prepare the cyclic ketal(XIV) from 2:2'-di(hydroxymethyl)diphenyl (XV) and (-)menthyl benzoyl formate. Apart from finding out whether the diol



(XIV)



(XV)

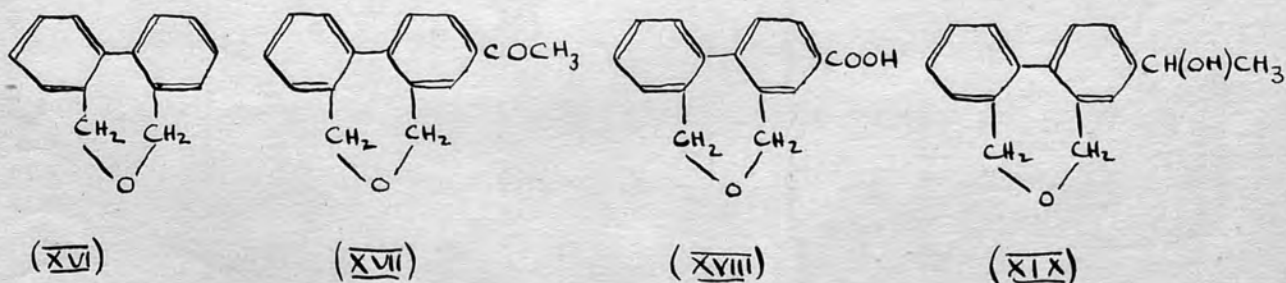
would form the ketal or shut too readily to form the oxepin under the influence of the acid catalyst, the compound if formed should exist in diastereoisomeric forms. The oxepin was formed, and the (-)-menthyl benzoyl formate was recovered unchanged.

EXPERIMENTAL

The general method of Salmi [Ber., 1938, 71 B, 1803] was used. 2.3 g. of 2:2'-di(hydroxymethyl)diphenyl and 2.9 g. (-)-menthyl benzoyl formate were heated in an oil-bath with 50 c.c. pure dry benzene and a few crystals of *p*-toluene sulphonic acid, until no more water came off. The benzene was then mostly distilled off, when some solid separated on cooling. This when crystallized from methylated spirit gave about 1 g. of white needles m.p. 71-2, mixed m.p. with (-)-menthyl benzoyl formate 70-2°. On completely removing the benzene, about 2.5 g. of yellowish gel was obtained which went solid on scratching. This solid gave

white needles from aqueous methanol m.p. 69-70° with softening from about 45°, and was impure (-)-menthylbenzoylformate. On evaporation of the mother liquor a solid was obtained which was low melting but could not be satisfactorily crystallized. A little of this solid was added to hydrobromic acid at 90°, and the mixture was boiled for twenty minutes. On cooling a solid formed which on crystallization from 60-80° petroleum ether melted at 90-2°, the mixed melting point with 2:2'-bisbromomethyldiphenyl being 90-2° also.

7. A Friedel-Crafts reaction was carried out with 2:7-dihydro-3:4-5:6-dibenzoxepin (XVI) and acetic anhydride or acetyl chloride, in the hope of preparing the ketone (XVII). This could then be oxidized to the acid (XVIII) or reduced to the alcohol (XIX), and either of these should be capable of resolution.



Only a liquid of uncertain composition could be isolated from the reaction mixture, and the yield of this was low.

EXPERIMENTAL

(a) In the course of preparing 2:2'-di(hydroxymethyl)-diphenyl by reducing dimethyl diphenate with lithium aluminium hydride, in a few cases, the reaction apparently failed, only a few grams of the diol being obtained on crystallization. On evaporating the benzene used for crystallization off completely, a solid was left which could be crystallized from methanol. White needles m.p. $71-2^{\circ}$ were obtained which proved to be 2:7-dihydro-3:4-5:6-dibenzoxepin.

Found: C 85.8; H 6.25.

$\text{C}_8\text{H}_{12}\text{O}$ requires: C 85.7; H 6.12.

It was found that the diol is readily converted to the oxepin by heating with 50% sulphuric acid on a water bath for a short time. The ether is unaffected by boiling for a prolonged period with 50% sulphuric acid or 50% potassium hydroxide solution. It is, however, readily converted to 2:2'-bisbromomethyldiphenyl by treatment with hydrobromic acid.

(b) (i) The reaction was carried out according to the general directions of Noller and Adams [J. Amer. Chem. Soc., 1924, 46, 1889]. To about 20 c.c. of carbon disulphide in

a 100 c.c. flask were added 10 g. of 2:7-dihydro-3:4-5:6 dibenzoxepin and 14.8 g. of aluminium chloride. 5.2 g. of acetic anhydride were run in slowly with stirring. The flask became warm, and the contents were a resinous mass. On heating on a water bath a rapid evolution of hydrogen chloride occurred and heating was continued for about an hour. The viscous mass was poured on to ice and the carbon disulphide was allowed to evaporate. A semi-solid substance and a dark oil separated, and the mixture was extracted with ether. The extract was washed with water, 10% caustic soda and water, and finally dried. After removing the ether, an orange, somewhat viscous liquid remained which was vacuum distilled. A considerable amount of decomposition occurred, and a viscous almost colourless oil b.p. about $181^{\circ}/^{\circ}\text{m.m.}$ was collected. On redistillation this gave 2 g. of colourless oil b.p. $174^{\circ}/^{\circ}\text{m.m.}$ which did not give a phenylhydrazone or semicarbazone.

Found: C 68.6; H 5.1.

$\text{C}_{16}\text{H}_{14}\text{O}_2$ requires: C 80.7; H 5.88.

A little was reduced with lithium aluminium hydride when a definite reaction occurred. After decomposition with water and acidification, the ether layer was separated and

on evaporation yielded colourless rectangular plates. On recrystallization from 60-80° petroleum ether clusters of colourless needles m.p. 84-5° were obtained.

Found: C 84.3; H 6.86.

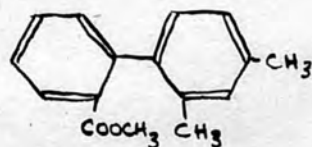
C₁₆H₁₆O₂ requires: C 80.0; H 6.67.

(ii) The method of Long and Heuze [ibid., 1941, 63, 1939] for preparing derivatives of diphenyl was followed.

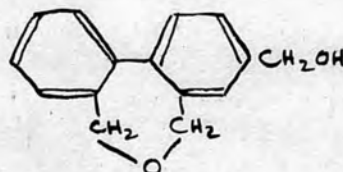
11 g. of powdered anhydrous aluminium chloride were suspended in about 80 c.c. of pure dry carbon disulphide. The suspension was mechanically stirred, and a solution of 14.5 g. of oxepin and 6.5 g. of acetyl chloride in 80 c.c. of dry carbon disulphide was run in over about 20 minutes. Some evolution of hydrogen chloride occurred, and a considerable amount of a dark, tarry substance separated. Stirring was continued for half an hour after the addition was completed, and the mixture was refluxed on a water bath for four hours. The carbon disulphide was distilled off and as the contents of the flask were too viscous to pour, the flask was cooled and ice-water was added. An orange-brown semi-solid and some oil separated. The aqueous mixture was worked up as before, and about 10.5 g. of orange oil was obtained. This was vacuum distilled, when much decomposition occurred, and a few grams of colourless oil

b.p. $180^{\circ}/"0"$ m.m. was obtained. This was identical with the product obtained before, as it gave the same product with m.p. $84-5^{\circ}$ on reduction with lithium aluminium hydride.

8. An attempt was made to prepare the compound (XX) from



(XX)



(XXI)

methyl anthranilate and m-xylene using the Gomberg reaction. It was hoped by subsequent oxidation, reduction and cyclization to prepare the compound (XXI) which should be capable of resolution. The reaction failed, the only product isolated being salicylic acid.

EXPERIMENTAL

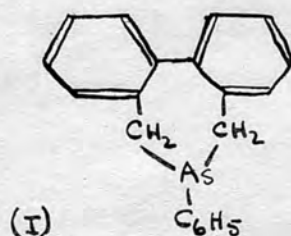
76 g. of methyl anthranilate were warmed with 40 c.c. of water and 100 c.c. of concentrated hydrochloric acid were added with stirring. On cooling, a thick mass of hydrochloride was obtained which was cooled in a freezing-mixture. A solution of 36 g. of sodium nitrite in 72 c.c. of water was added at $0-5^{\circ}$, and the diazo solution was transferred to a 3-litre flask equipped with a mechanical stirrer and surrounded by ice and salt. 500 g. of cold m-xylene were added, and the mixture was vigorously stirred,

and 116 c.c. of 5N caustic soda were added dropwise during the course of one hour, the temperature being maintained between 0° and 5°. Stirring was continued for about 12 hours, the reaction mixture being allowed to warm up to room temperature. The dark red xylene layer was separated, washed with water and dried. The xylene was distilled off, and a dark red oil remained. This was steam-distilled, to remove the last traces of xylene, Needles mixed with tar remained, and by crystallizing three times from benzene, 12 g. of peach needles m.p. 158° were obtained. The product was entirely soluble with effervescence in cold sodium bicarbonate solution, and proved to be salicylic acid.

E. Section IV.

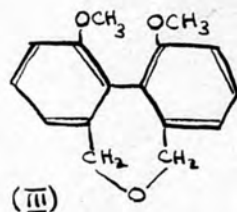
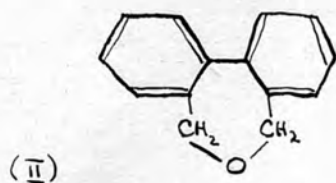
The ultraviolet absorption spectra of various derivatives of diphenyl containing the 7-membered ring bridge were examined in order to show to what extent reliance could be placed on the previous assumption (see introduction) that the type of spectrum gives a valuable guide to molecular configuration. All the compounds studied must of necessity be non-coplanar, with the angle between the ring planes of the order of 50° . These would be expected to have ultraviolet absorption spectra in which the characteristic diphenyl absorption band is either absent or very much reduced in intensity.

Beeby, Mann and Turner [J., 1950, 1923] showed that in 6-phenyl-6-arsa-1:2-3:4-dibenzcyclohepta-1:3-diene (I) the

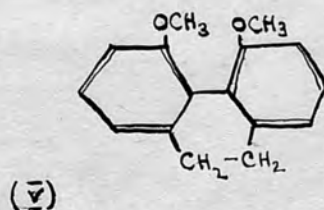
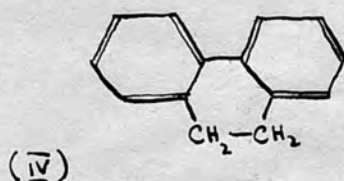


benzene rings subtend an angle of 63° and that this is little altered in the methiodide. As was expected, the ultraviolet absorption spectrum of the latter showed no sign of the diphenyl absorption band.

Beaven, Hall, Lesslie and Turner [J., 1952, 854] compared the ultraviolet absorption spectra of the two oxepins (II) and (III). In the simple oxepin (II) the diphenyl bond is merely slightly shifted to longer wavelengths and



slightly decreased in intensity (Fig. II). (λ_{max} . diphenyl 2475, ϵ_{max} . diphenyl 19,000; λ_{max} . oxepin 2500, ϵ_{max} . oxepin 16,500; both in hexane). This would imply that conjugation is little decreased, and yet the molecule is certainly non-coplanar. The spectrum of the dimethoxy compound (Fig. II) would previously have been interpreted as showing a large departure from coplanarity compared with the parent compound (II), but this view is untenable. The angle between the ring planes in (II) allows introduction of the methoxy groups in (III) without distortion of the molecule. Thus if steric factors alone determine the type of spectrum in diphenyls, (II) and (III) should exhibit similar spectra: the two spectra are however widely different. A similar effect was observed by Beaven, Hall, Lesslie and Turner in comparing the ultra-violet absorption spectra of the two dihydrophenanthrenes (IV) and (V), and the two azepinium salts (VI) and (VII), (Figs. I and III).



Ultraviolet Absorption Spectra of 9:10-dihydrophenanthrene, 9:10-dihydro-4:5-dimethoxyphenanthrene; 2:7-dihydro-3:4-5:6-dibenzoxepin, 2:7-dihydro-4':1''-dimethoxy-3:4-5:6-dibenzoxepin; 2:7-dihydro-3:4-5:6-dibenzazepinium-1-spiro-1''-piperidinium bromide and 2:7-dihydro-4':1''-dimethoxy-3:4-5:6-dibenzazepinium-1-spiro-1''-piperidinium bromide.

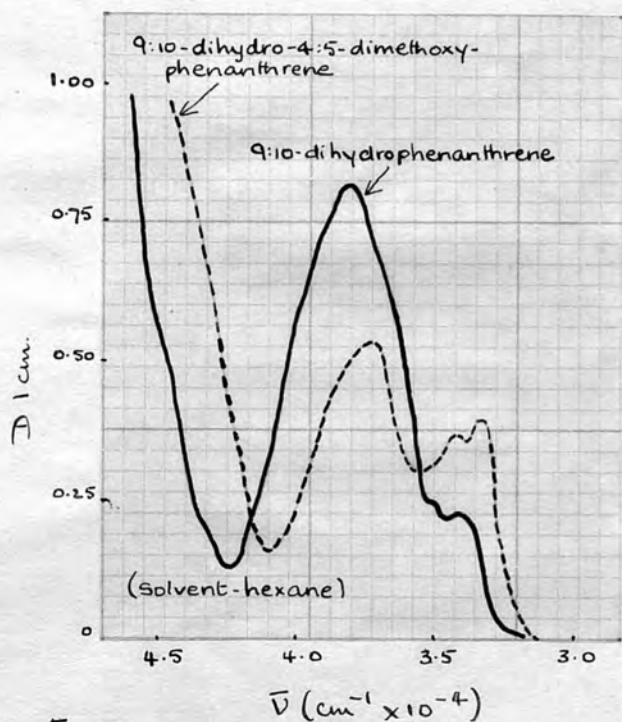


Fig. I.

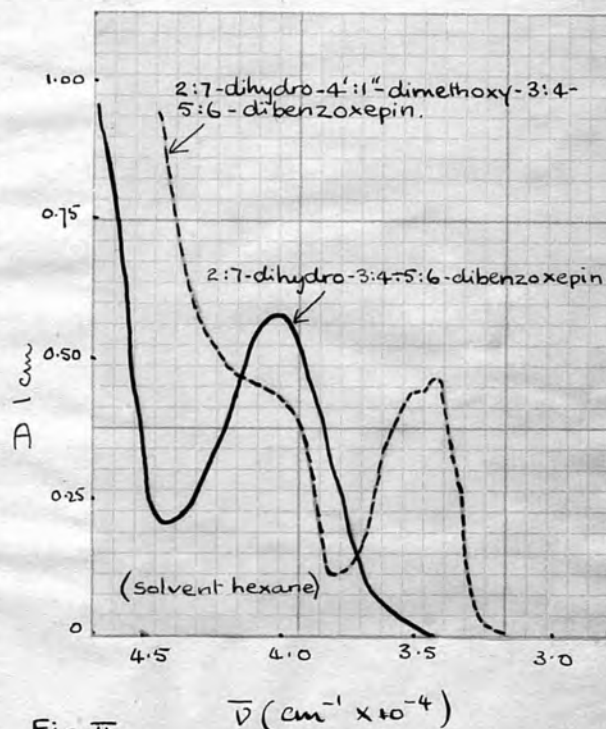


Fig. II.

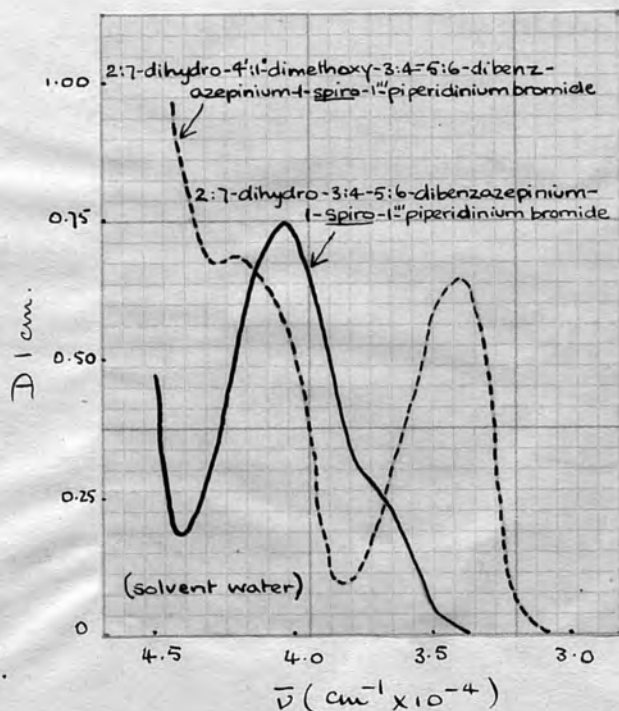
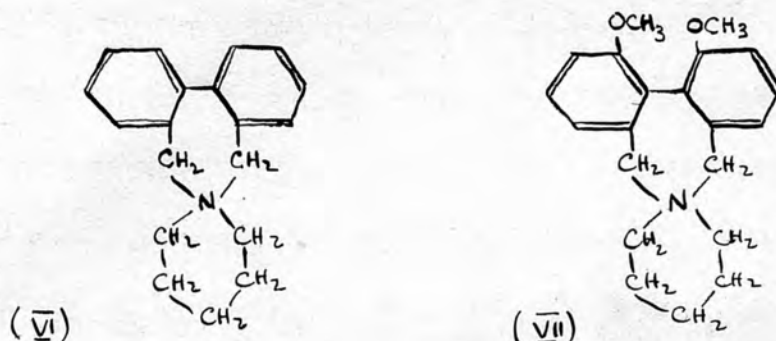
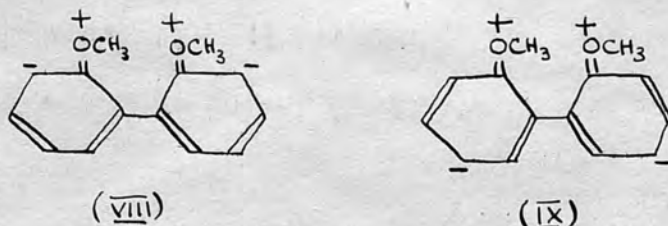


Fig. III.



The authors point out that these unexpected results may be accounted for by two hypotheses. "These are (a) that coplanarity of the two benzene rings is not essential for the appearance of the conjugation band in O:O'-substituted diphenyls, and large departures from coplanarity may be accommodated without complete loss of conjugation; and (b) that in diphenyls which show a conjugation band the introduction of additional groups may reduce the intensity of the band, even when their presence is without steric effect on the configuration."

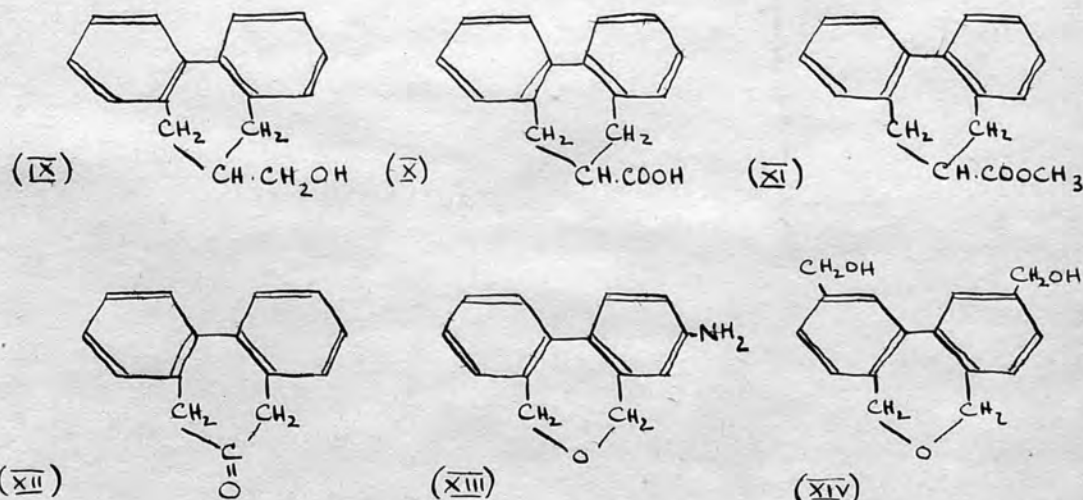
The authors maintain that the loss of the diphenyl band is due to the interaction of the methoxyl groups with the aromatic ring leading to decreased conjugation across the pivot bond. Structures such as (VIII) and (IX) would have precisely this effect.



In the case of the two dihydrophenanthrenes (IV) and (V), the authors point out that ring closure is not so easy in

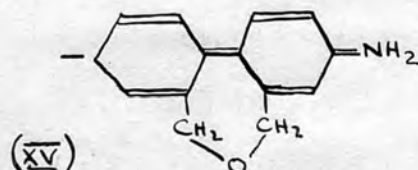
the dimethoxy derivative (V), as the angle between the ring planes in (IV) is about 20° , so that some distortion of the molecule occurs if the two methoxyl groups are introduced. This distortion might cause a further departure from coplanarity, or out-of-plane bending of the methoxyl groups themselves. The first effect is not likely to affect the conjugation band to a great extent, but the methoxyl groups would be able to exert the same effect as in the spectra of the oxepins and azepinium salts. If however the methoxyl groups are bent out of the plane of the rings so that the resonance interaction will be decreased, the diphenyl band should not be so greatly decreased in intensity as in the other cases. This was found to be so.

The ultraviolet absorption spectra of the following six diphenyl derivatives were determined for the present writer by Dr. G. H. Beaven.



It was felt that the determination of the spectra might be of use for two main reasons. Firstly, they might afford

confirmation of the generally accepted rule that the presence of alicyclic rings does not greatly alter the spectrum of an aromatic hydrocarbon system. Secondly as all these compounds are definitely non-coplanar, it was considered worth while to find out whether or not these also showed the diphenyl absorption band. In the case of (XIII) it was thought that the interaction of the amino group with the aromatic ring would increase the conjugation across the pivot bond owing to the contribution of structures such as (XV). This might be expected to show itself as an increased intensity of the diphenyl absorption band. The results



obtained are shown in table 1, and in figures (IV), (V) and (VI).

The report drawn up by Dr. Beaven follows:

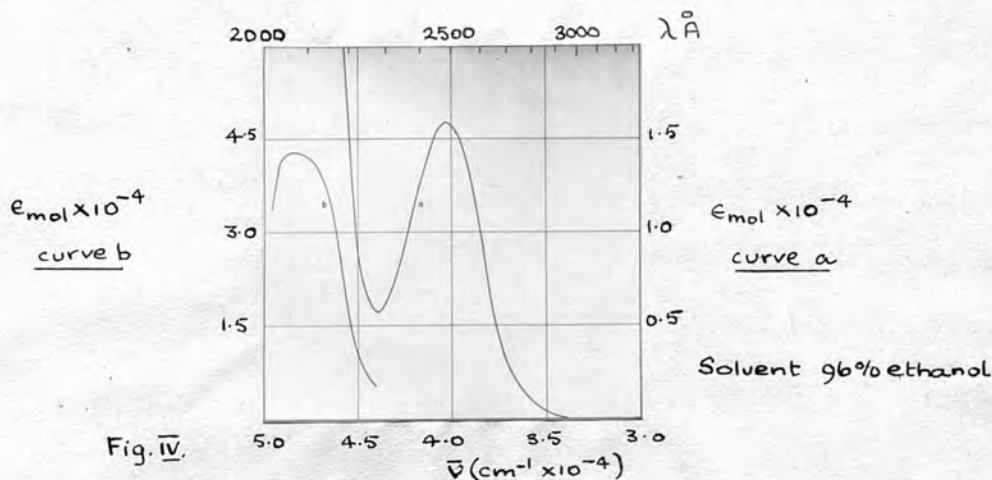
"Experimental. The spectra were measured on an automatic-recording twin-beam spectrophotometer designed and built by Holiday and Sutton^(a) [Trans. Soc. Instrument Technology, 1951, 3, 157 and 166]^(b). The records made by this instrument are linear in optical density as ordinate against wave number as abscissa, and the spectrograms (figs. (IV)-(VI)) are direct tracings of such records, after correction for instrumental zero errors. Important features of the spectra were checked on a Unicam manual single-beam spectrophotometer. With one exception

Table 1. Ultraviolet Absorption Spectra of 2:2'-bridged diphenyls.

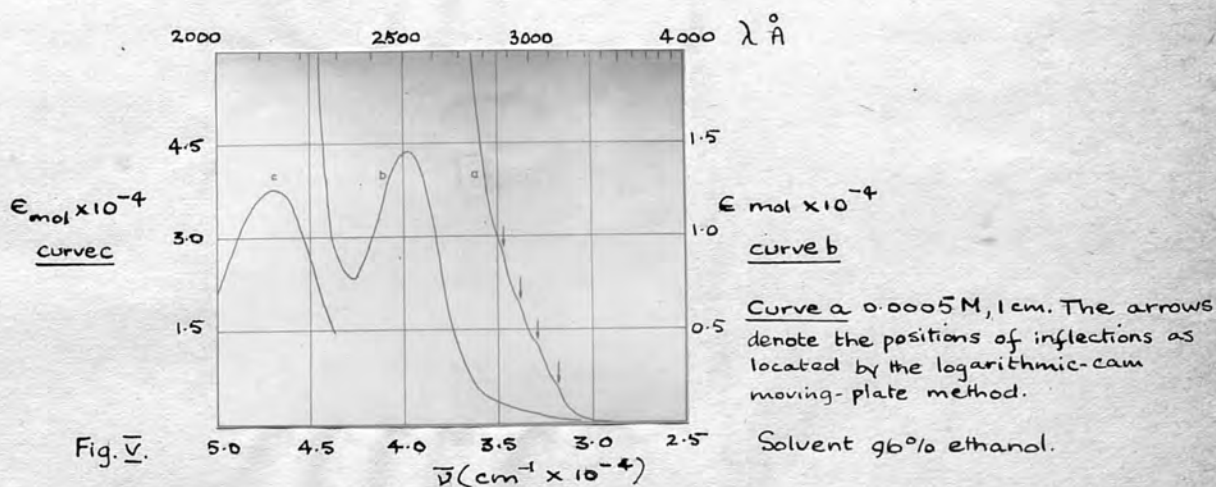
Compound	CONTIGUATION BAND				$\lambda_{\text{infl}} \in \text{infl}$			
	λ_{max}	ϵ_{max}	$\lambda_{\text{min}} \in \text{min}$	$\lambda_{\text{max}} \in \text{max}$				
(IX) 3:4-5:6-dibenzo-1-hydroxy-methylcyclohepta-3:5-diene.	(2080)	(49,000)	2275	5,400	2485	15,500	-	-
(X) 3:4-5:6-dibenzocyclohepta-3:5-diene-1-carboxylic acid.	2060	49,000	2290	6,000	2490	15,500	-	-
(XI) methyl 3:4-5:6-dibenzocyclohepta-3:5-diene-1-carboxylate.	2070	43,000	2275	5,800	2485	16,000	-	-
(XII) 3:4-5:6-dibenzo-1-ketocyclohepta-3:5-diene	2135	37,000	2345	7,800	2515	14,500	{ 3153 } { 3045 } { 2954 } { 2880 }	{ (130) } { (420) } { (660) } { (820) }
(XIII) 2:7-dihydro-2'-amino-3:4-5:6-dibenzoxepin in neutral solution	2060	36,000	2460	3,400	2845	18,500	-	-
(XIII) 2:7-dihydro-2'-amino-3:4-5:6-dibenzoxepin in 0.01M HCl (96% EtOH)	2070	43,000	2300	8,400	2520	18,500	-	-
(XIV) 2:7-dihydro-3':2"-hydroxy-methyl-3:4-5:6-dibenzoxepin.	2150	44,000	2340	6,400	2540	14,500	-	-

Values in parentheses refer to unresolved inflections.

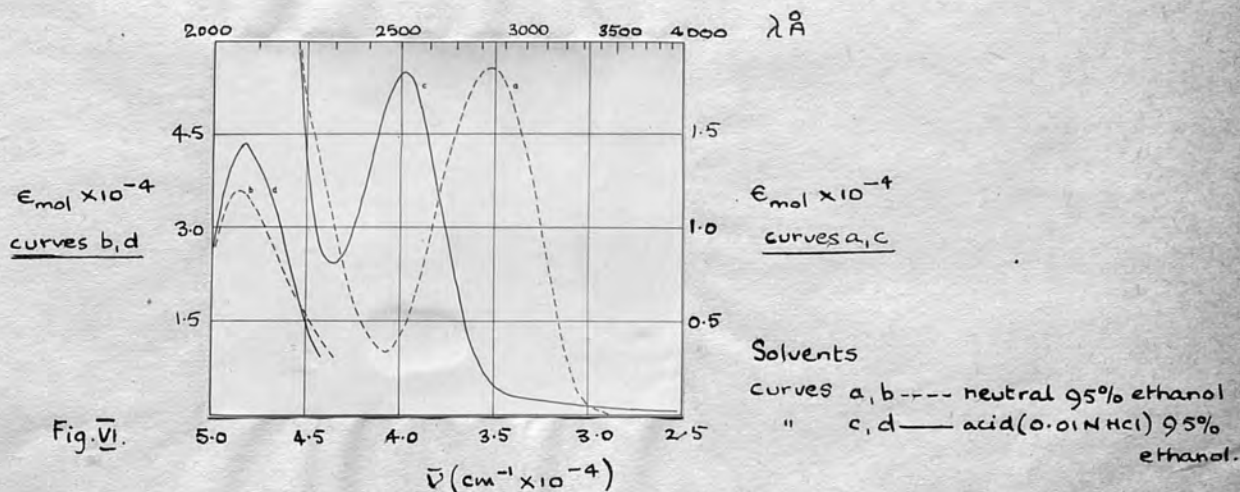
Ultraviolet Absorption Spectrum of methyl 3:4-5:6-dibenzocyclohepta-3:5-diene-1-carboxylate.



Ultraviolet Absorption Spectrum of 3:4-5:6-dibenzo-1-ketocyclohepta-3:5-diene.



Ultraviolet Absorption Spectrum of 2:7-dihydro-2'-amino-3:4-5:6-dibenzoxepin.



(compound XII)) all the compounds were examined at a concentration of 0.50×10^{-4} molar only, so that the ordinate scales have been given in terms of the molecular extinction coefficient (ϵ), by taking the cell length and common concentration into account. Attempts were made to obtain reliable results at wavelengths shorter than ca. 2300\AA by using 0.33 and 0.10 cm. cells. Solvent absorption was thus reduced and stray light errors (cf. Holiday and Beaven [P.S.G. Bulletin, 1950, 3, 53]; Saidel, Goldfarb and Kalt, [Science, 1951, 113, 683]) shown to be substantially absent by showing that Lambert's law was reasonably well followed for these two cell lengths, at least down to 2050\AA . All the compounds were also examined by the logarithmic-cam moving-plate technique (Holiday [J. Sci. Inst., 1937, 14, 166]). No definite indications of long-wave inflections were found, except for compound (XII) for which the four inflections listed in Table 1. were easy to locate with precision by this method.

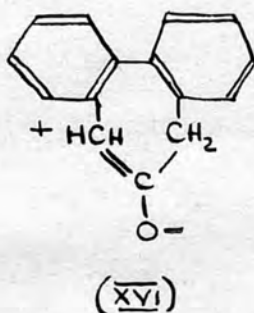
The wavelengths of the various maxima and minima are given to the nearest 5 or 10\AA and extinction coefficients have been rounded off to 5 in the third significant figure.

Results and Discussion. The spectra of compounds (IX), (X) and (XI) require little comment. Both the intensities of the bands and their location are consistent with the expected absorption characteristics of a diphenyl, not containing any

auxochromic substituents, in which conjugation between the two benzene rings has been reduced but not abolished as a result of departure from coplanarity imposed by the 3-carbon chain joining the 2:2'-positions (numbering referred here to a diphenyl structure). Since the 3-carbon chain is saturated, the substituents on the middle atom of the 3-carbon chain (i.e. position 1 when referred to the numbering of the systematic name) would be expected to have little effect on the absorption spectrum of the conjugated system. Further evidence in support of this view is provided by the observation that the spectrum of (X) is essentially identical in neutral and alkaline (0.01N KOH) ethanol, showing that ionization of the carboxyl group does not alter the extent to which the 3-carbon ring determines the absorption spectrum, and suggesting that the carboxyl group is not involved as such in this effect". It is evident that the spectrum of (XIV) does not call for any special comment either.

"The absorption spectrum of compound (XII) is quite remarkable in showing a set of four inflections of low intensity in the 2850-3200^oÅ region. It was at first suspected that the sample might be contaminated with some aromatic material e.g. a naphthalene derivative, but this explanation seems most unlikely in view of the method of preparation, and the fact that there is no sign of the more intense shortwave bands of dicyclic aromatics in the spectrum. If impurities

are ruled out, it seems necessary to consider the possibility that the keto group is involved in some way in the overall conjugation between the two benzene rings, and it is in fact possible to write structures in which hyperconjugation of the adjacent CH_2 group occurs, e.g. (XVI).



The result of such hyperconjugation would be to give the molecule a small proportion of 'strained polycyclic' character, formally analogous to the phenanthrene structure. By analogy with the absorption spectra of polycyclic aromatics containing fused strained alicyclic rings in which there is often an enhancement of fine structure (see Jones [Chem.Rev., 1943, 32, 1] for references), it is not unreasonable to suggest that the fine-structure in the spectrum of (XII) has a similar origin. The position and intensity of the conjugation band indicates that the diphenyl-type conjugation is not greatly reduced, which is consistent with the suggestion that the 3-carbon ring interacts with the remainder of the molecule by second-order or hyper-conjugation, as envisaged in structure (XVI).

The spectrum of (XIII) is of interest. In neutral

ethanol the longwave shift of the conjugation band, when compared with the parent oxepin lacking the amino group (Beaven, Hall, Lesslie and Turner [loc.cit.]), indicates that this group is exerting its expected bathochromic effect, although the small increase in intensity suggests that increased conjugation due to structures of type (XV), involving a central double bond, is not an important effect. In acid solution, in which the nitrogen acquires a proton and becomes positively charged, the unshared electrons of the amino group are unable to interact with the benzene ring, and structures of type (XV) are eliminated. The bathochromic effect of the amino group and the conjugation band move to a shorter wavelength, not very different from that of the parent oxepin, though with little change in intensity. It is of interest to note that this effect of acid is confined to the conjugation band and does not effect the shortwave band of high intensity. The effect of acid on the absorption spectra of aromatic amino compounds has frequently been reported (see Jones [loc.cit.] for references), and it is well-known that the bathochromic shift brought about by an $-NH_3^+$ substituent is always much less than that of the corresponding uncharged amino group, and comparable in fact, to the change produced by a methyl group in the same position. A further point of interest in the spectrum of (XIII) in acid solution is the low but significant absorption extending from about $4000\overset{\circ}{\text{A}}$ to the conjugation band proper. This broad

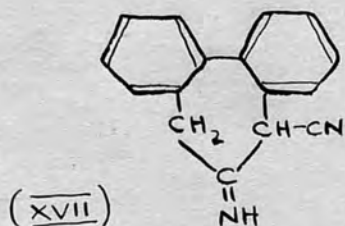
region is thought to be real and not an experimental artefact, but has not yet been examined at higher concentration for selective absorption features. In this connection all the compounds examined, with the exception of (XII) which has been discussed above, showed no inflections on the longwave sides of their conjugation bands and thus resemble the parent unsubstituted oxepin corresponding to (XIII) and (XIV) in possessing no sign of any absorption contributions arising from the benzene rings acting as independent partial chromophores. The dibenzocycloheptadiene structure contained in compounds (IX)-(XII) thus resembles the oxepin and azepinium structures previously examined (Beaven et alia, [loc.cit.]) in that the diphenyl-type conjugation between the two benzene rings is not greatly inhibited by the loss of coplanarity imposed by the 3-carbon bridge."

It is certain that none of the six compounds (IX) to (XIV) has a coplanar structure, and yet each exhibits a spectrum showing the typical diphenyl absorption band. Thus the view that the ultraviolet absorption spectrum of a diphenyl is a valuable guide to configuration must be accepted with reserve, although there is no doubt that it has proved a valuable hypothesis in the past. Evidently an angle of about 50° between the planes of the two benzene rings does not greatly diminish the degree of overlap of the orbitals of the π -electrons of the pivot bond.

EXPERIMENTAL

1. (a) 2:2'-di(cyanomethyl)diphenyl was prepared according to the method of Kenner and Turner [J., 1911, 99, 2109]. 5.2 g. of potassium cyanide were dissolved in as little water as possible, and the solution was mixed with about three times its volume of ethanol. The mixture was brought to the boil and 12 g. of ^{2:2'}bisbromomethyldiphenyl were added gradually. The mixture was maintained at about 50-60° on a hot-plate for four hours, and was then poured into water when an oil separated which gradually solidified. After filtration the solid was crystallized from ethanol, and square or rectangular plates m.p. 77-8° were obtained. Yield about 90%.

(b) 7 g. of dinitrile were dissolved in 30 g. of ethanol, and a gentle current of hydrogen was passed into the flask. About 2 c.c. of 10% sodium ethoxide in ethanol solution were added down the condenser, and the mixture was boiled for one hour. On cooling, colourless crystals of 3:4-5:6-dibenzo-2-cyano-1-imino-cyclohepta-3:5-diene (XVII) separated out m.p. 192-3° (Kenner and Turner [loc. cit.] give m.p. 180°). Yield 6 g.



(c) 3:4-5:6-dibenzo-1-imino-cyclohepta-3:5-diene-2-carboxylic acid was prepared from the iminocyano compound by dissolving the latter in 60 c.c. of concentrated sulphuric acid and leaving overnight. On pouring on to ice, a white solid separated which was left for about 2 hours, after which time a test portion was found to be completely soluble in caustic soda solution showing that no amide was present. The precipitate was filtered off and crystallized from ethanol. 4 g. of colourless needles m.p. 180° were obtained.

(d) 3 g. of the above acid were boiled under reflux with 100 g. of 50% sulphuric acid until no more solid was apparent. The liquid was steam-distilled, and the substance which solidified in the aqueous distillate was filtered off and crystallized from ethanol. The 3:4-5:6-dibenzocyclohepta-3:5-dien-1-one was obtained as large, pale yellow hexagonal prisms. On recrystallization using a little charcoal, it was obtained colourless, m.p. 78-9°, yield 1 g.

2. (a) Phenanthraquinone was prepared from commercial phenanthrene according to the method of Moore and Huntress [J. Amer. Chem. Soc., 1927, 49, 1328]. 600 g. of potassium dichromate were dissolved in 1.5 litres of water and 500 c.c. of concentrated sulphuric acid. The solution was heated to

100° in a large evaporating basin, and 100 g. of finely powdered phenanthrene were added during the course of an hour. When the initially violent reaction was over, the mixture was kept at 110° for half an hour, after which time it was cooled and poured into excess ice-water. The precipitated crude phenanthraquinone was filtered and washed free from chromium salts. It was then powdered into an evaporating basin containing 228.5 g. of sodium metabisulphite in 1,250 c.c. of water, and the mixture was maintained at 50-60° for half an hour. It was filtered free from the red cake-like residue and acidified with 50% sulphuric acid to which a little potassium dichromate had been added. The precipitated phenanthraquinone was filtered, washed and dried, whence it was obtained in 42% yield as a yellow powder m.p. 202-3°.

(b) The quinone was converted into a mixture of 2- and 4-nitrophenanthraquinone by the method of Schmidt and Spoun [Ber., 1922, 55, 1194]. 30 g. of phenanthraquinone were placed in a 3 litre open flask and covered with 900 c.c. of concentrated nitric acid, when a red solution was obtained. The acid mixture was heated to boiling to dissolve all the quinone and boiled for 20 minutes. It was then poured into 2 litres of water, when a flocculent yellow precipitate came out. When it was cold it was filtered and washed

well with water. When it was dry, it was boiled with 700 c.c. of ethanol for about an hour to dissolve the 4-nitrophenanthraquinone. When cool, the undissolved 2-nitrophenanthraquinone was filtered off and crystallized from a large quantity (about 1 litre) of glacial acetic acid. Shining orange rhombs were obtained m.p. $260-0.5^{\circ}$. Yield 16g. A second preparation gave an apparently identical product but with m.p. $270-1^{\circ}$. Both specimens gave an identical nitrodiphenic acid on oxidation (vide infra).

(c) 10 g. of 2-nitrophenanthraquinone were dissolved in 30 c.c. of concentrated sulphuric acid. The almost black viscous solution was run into 100 c.c. of water with vigorous stirring. Next a hot solution of 40 g. of potassium dichromate in 400 c.c. of water was run in, and the mixture was stirred at the boiling point for $2\frac{1}{2}$ hours. After standing overnight, the mixture was filtered and the residue washed. It was dissolved in sodium bicarbonate solution and filtered to remove unchanged quinone. On acidification 4-nitrodiphenic acid was obtained as a very pale lemon crystalline powder m.p. $217-19^{\circ}$, Yield 8.7 g.

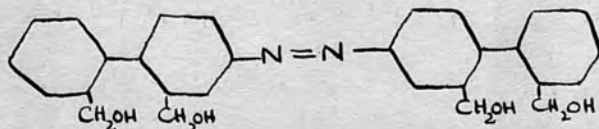
(d) The acid was heated for about 7 hours with its own weight of sulphuric acid and 87 g. of methanol. On pouring into water a very viscous oil was obtained. Solid sodium bicarbonate was added until the liquid was just

alkaline and the ester was extracted with ether. On removal of the ether, a whitish solid was obtained which was crystallized from methanol. Very pale yellow prisms m.p. $95-6^{\circ}$ were obtained in 85% yield.

(e) The dimethyl 4-nitrodiphenate was reduced with lithium aluminium hydride, sufficient being used to reduce both the ester and the nitro groups. 10 g. of dimethyl ester were dissolved in anhydrous ether, and the solution was run into 3.3 g. of lithium aluminium hydride in 200 c.c. of anhydrous ether. A vigorous reaction took place, and the contents of the flask developed an orange-yellow colour. On adding water and dilute acid, the ether layer was orange, and some orange solid was suspended in the aqueous layer. On removing the ether, 6 g. of orange powder were obtained. This was purified by dissolving in acetone, filtering and adding water, m.p. $242-3^{\circ}$.

Found: C 73.33; H 5.78; N 6.20.

$C_{16}H_{26}O_4N_2$ (XVIII) requires: C 73.99; H 5.73; N 6.17.



(XVIII)

The azo compound was dissolved in hot alcohol, and a solution of stannous chloride in concentrated hydrochloric acid was added. The colour changed from deep orange to a dull pale red, and on cooling some brown gum was obtained which was filtered from the now almost colourless solution. On making the solution strongly alkaline, a white precipitate was obtained which diazotized and coupled with β -naphthol. It was not found possible to crystallize it easily, but on boiling with benzene and charcoal and evaporating to small bulk, a white powder m.p. $150-2^{\circ}$ was obtained. It was recovered unchanged after boiling for some time with 50% sulphuric acid, and was presumed therefore to have cyclized during the acid reduction to give 2:7-dihydro-2'-amino-3:4-5:6-dibenzoxepin.

Found: C 79.32; H 6.17; N 6.65.

$C_{14}H_{13}O N$ requires: C 80.00; H 6.19; N 6.67.

The yield from the stannous chloride reduction was very poor, and an alternative method using sodium hyposulphite was employed, but only a small amount of a brownish solid was obtained which, although it gave a good diazo reaction, could not be obtained pure. Reduction with zinc dust and hydrochloric acid gave an intractable gum, and the amine was

Xxd.

unfortunately not volatile in steam.

NOTE: Melting points throughout are uncorrected. The analyses were carried out by Dr. Weiler and Dr. Strauss of Oxford.