

SYNTHETIC STUDIES IN BRIDGED BIPHENYLS

A Thesis submitted to the University of London
for the Degree of Doctor of Philosophy

By

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Bedford College, London,

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ABSTRACT

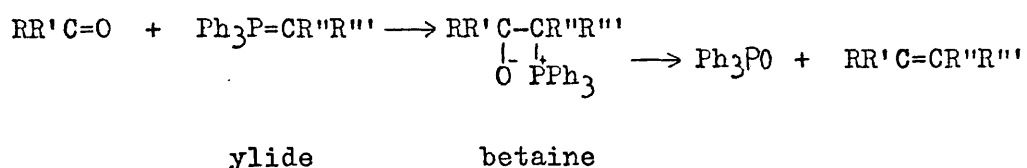
The reaction between 2,2'-bisbromomethylbiphenyl and triphenylphosphine has been found to produce a mixture of the mono- and di-phosponium bromides. The effects involved in the practical work together with the difficulty in separating the mixture seemed to indicate that a pure di-phosponium bromide, the 2,2'-bis(triphenylphosphoniomethyl)biphenyl dibromide, could not be obtained by the various methods described in the experimental section. Attempts to prepare a 2,2'-bridged biphenyl with a larger bridging chain by the reaction between biphenyl-2,2'-dialdehyde and a P(O)-activated reagent such as trimethylene-bis(diphenylphosphine oxide) have been unsuccessful.

A nine-membered ring, the 1-methyl-2,3,8,9-tetrahydro-4,5:6,7-dibenzazonine (m.p. 55-56°) has been synthesized and optically activated by crystallization of its camphorsulphonate (m.p. 201-202°) from acetone. The base liberated from this salt was found to have $[\alpha]_{260}^{21} +614^\circ$ in chloroform, to be optically stable at room temperature and to undergo complete racemization on heating under reflux in cyclohexane for one hour. Its ultra-violet spectrum also reflects a large angle of torsion in the ground state, comparable with that of the 1,2,3,4-dibenzocyclonona-1,3-diene-7-carboxylic acid. Besides the camphorsulphonate, the methiodide, the picrate and the tartrate of this compound have all been prepared and characterized.

A reinvestigation of a series of condensation reactions between biphenyl-2,2'-dialdehyde and several diamines is also included in the present work. The condensation between 2,2'-diaminobiphenyl and *o*-phthalaldehyde has been found to give a red crystalline solid (m.p. 253-254°) as a main product. Spectroscopic studies seem to show that it could not be the cis 10[N-(2''-amino-2'-biphenylyl)1-iscoindol-3-onylidene]isocindolo[2.1-a]dibenzo[d.f]-1,3-diazepine as proposed by Bindra and Elix. A possible structure for this red compound has been tentatively advanced but some of its chemical reactions require further study.

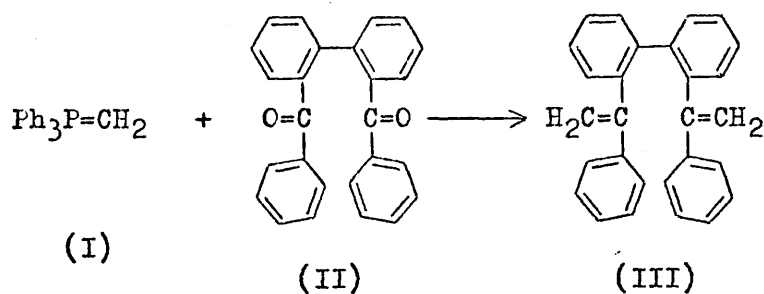
INTRODUCTIONA. A brief account of the application of the Wittig reaction and the use of the P(O)-activated reagents.

The Wittig reaction has been widely used for the synthesis of an olefin from a carbonyl compound since its discovery in 1954. The reaction involves the nucleophilic attack of an ylide on the carbonyl carbon to form a betaine which often spontaneously eliminates the triphenylphosphine oxide to yield the product.

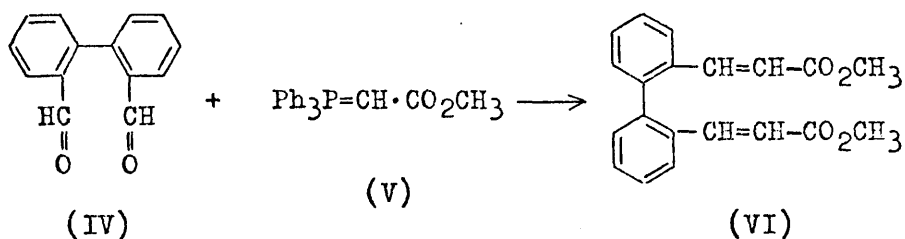


The merit of this reaction is that it can be carried out under mild conditions and that the position of the double bond in the resulting olefin is known with great certainty.

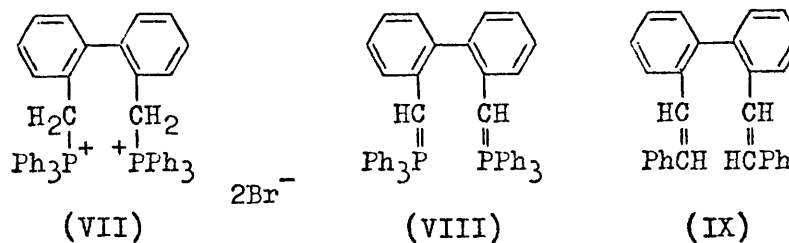
The earliest application of this reaction in the biphenyl series was the treatment of methylenetriphenylphosphorane (I) with 2,2'-dibenzoylbiphenyl (II) to form 2,2'-di(β -phenylvinyl)biphenyl (III) by Wittig and Stilz (1956). Hall and Prakobsantisukh (1965)



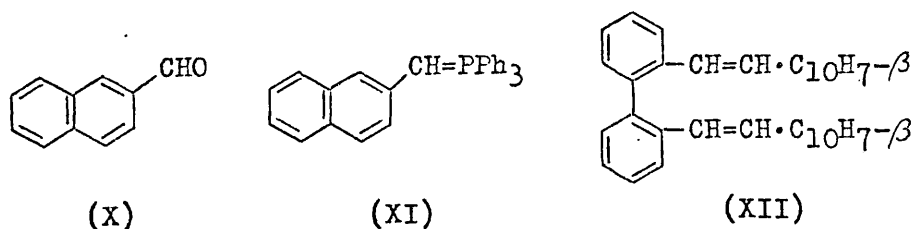
found that the reaction between biphenyl-2,2'-dialdehyde (IV) and the stable phosphorane (V) proceeded satisfactorily to give the methyl ester (VI).



When the diphosphorane (VIII) derived from the bisphosphonium dibromide (VII) was allowed to react with benzaldehyde, it gave 2,2'-di- α -styrylbiphenyl (IX).

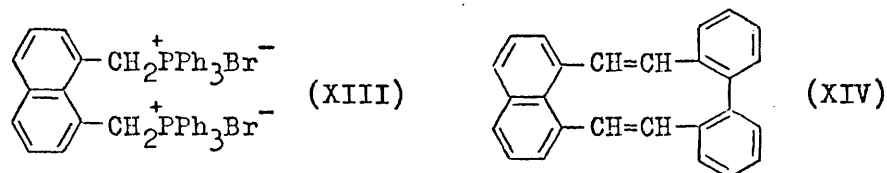


Analogous to the above reaction was the preparation of 2,2'-bis[2-(β -naphthyl)vinyl]biphenyl (XII) from (IV) and (XI) as well as from (VIII) and (X) by Bergmann and his co-workers (1967).

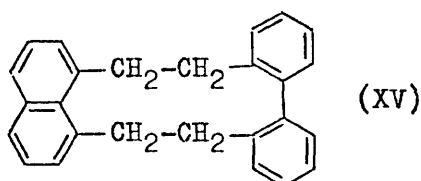


Wittig reaction between the diphosphorane derived from

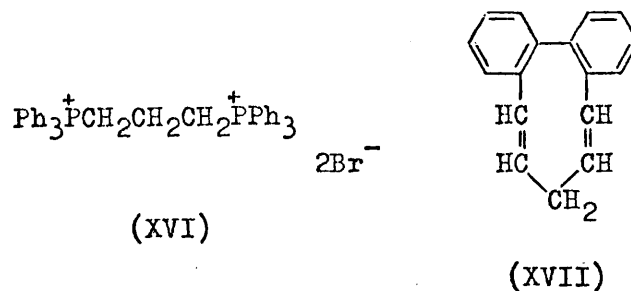
(XIII) and the dialdehyde (IV) by addition of equimolar amounts of (XIII) and (IV) in methanol to a solution of lithium methoxide in methanol at room temperature to give a 58% yield of (XIV) had been



reported by Mitchell and Sondheimer (1968). The naphthalene derivative, an 11-membered ring compound (XV) was obtained in 52% yield by catalytic hydrogenation of (XIV) in ethyl acetate over 5% Pd-CaCO₃ for 30 minutes.



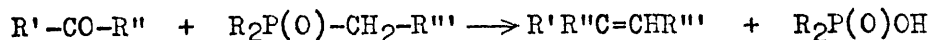
Recently, Rabinovitz and his co-workers (1970) had successfully prepared the 9-membered ring compound (XVII) by the treatment of the dialdehyde (IV) with the diphosphorane derived from bisphosphonium dibromide (XVI). The reaction was carried out under an



argon atmosphere and in the presence of sodium methoxide in DMF at 50° for 3 hours. Although the yield (5%) was very low, it indicated that the reaction was applicable to the preparation of 2,2'-bridged biphenyls where the homocyclic bridge contains only aliphatic carbons.

The Wittig reaction provides a shorter route to the synthesis of biphenyls with a larger bridging ring. The resulting compounds such as (XIV) and (XVII) will be twisted and dissymmetric when saturated in the bridging chain. Optical resolution might perhaps be achieved by means of chromatography on cellulose-2 $\frac{1}{2}$ -acetate or the like.

Another shorter route to the synthesis of 2,2'-bridged biphenyls with a larger bridging ring could perhaps be found by the use of the so called P(O)-activated reagents discovered by Hörner and his co-workers in 1958. These reagents are organophosphorus compounds containing the group P(O)-CH₂. They react readily with aldehydes and ketones with various functional groups to yield olefins and their derivatives as represented by the following reaction:



P(O)-activated olefin synthesis has been reported to possess a number of advantages over the Wittig reaction. In the Wittig reaction, aldehydes with strong electron-donating groups near the

reaction centre are non-reactive. Phosphoranes containing electron-withdrawing groups do not as a rule react with ketones under the usual conditions. Although these difficulties may be avoided by heating the components at high temperatures in sealed tubes for a long duration or by carrying out the reaction in high-boiling solvents, these severe reaction conditions have an unfavourable effect on the yields of unsaturated products and in many cases they are not permissible. Furthermore, perhaps the most important of all is that the reaction involves the difficulty of isolating the olefin so formed in a majority of cases.

On the other hand, P(O)-activated reagents are more reactive towards the carbonyl compounds since they are more nucleophilic than phosphoranes. The isolation of olefins is much simpler because they can be readily separated from the highly water-soluble alkali metal salts of alkylphosphoric acids, whereas in Wittig reaction, the separation of the unsaturated product from triphenylphosphine oxide always involves a special procedure.

Like the Wittig reaction, P(O)-activated olefin synthesis makes it possible to introduce the C=C double bond in a specified position and to increase the length of the carbon chain. The reagents are said to be more readily accessible than the phosphoranes.

The present work includes the preparation of several bi-functional P(O)-activated reagents in an attempt to obtain some 2,2'-bridged biphenyls by the reaction between these reagents and

biphenyl-2,2'-dialdehyde. However, instead of giving any identifiable product, the dialdehyde decomposed under the influence of heating and the effect of the strong base potassium tert-butoxide which was used as a condensation reagent. It was thought that the formation of the unsaturated compounds of this type could probably be achieved by the use of the aprotic solvents such as DMF and carrying out the reaction at lower temperature.

The application of the Wittig reaction and the use of the P(O)-activated reagents are by far the two most important methods for the synthesis of olefins and so for the preparation of 2,2'-bridged biphenyls via a shorter route.

B. The stereochemistry of 2,2'-bridged biphenyls

Historical development

Molecular dissymmetry due to restricted rotation was not known until the successful resolution of optically active 6,6'-dinitrodiphenic acid by Christie and Kenner in 1922. It was at that time generally considered that the two benzene rings in biphenyl and its derivatives had a folded structure and the 1,1'-bond was extended (Figure 1). However, these workers realized that a collinear structure would still be dissymmetric provided the two benzene rings were not coplanar.



Figure 1. An erroneous structure of biphenyl molecule - a folded structure.

The hypotheses that the biphenyl molecule had its two benzene rings collinear and that the introduction of bulky ortho-substituents would make it more difficult for these two rings to pass through the coplanar state by rotating about the 1,1'-bond were almost simultaneously made by Turner and Le Fevre, Bell and Kenyon, and Mills in 1926. On this basis, the two benzene rings in 6,6'-dinitrodiphenic acid cannot be coplanar owing to the obstacle effect of the ortho-substituents and as a result of non-coplanarity, the molecule is dissymmetric and optical resolution is therefore possible (Figure 2). Extensive studies on biphenyl

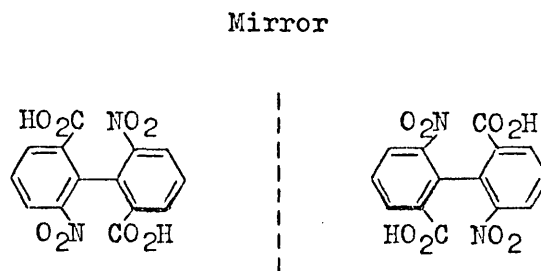
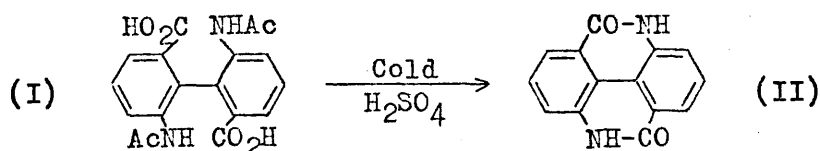


Figure 2. Not superimposable enantiomers:
resolvable 6,6'-dinitrodiphenic acid.

isomerism have proved that the intramolecular steric effect can quite often give rise to molecular dissymmetry and have thus established the obstacle theory of restricted rotation.

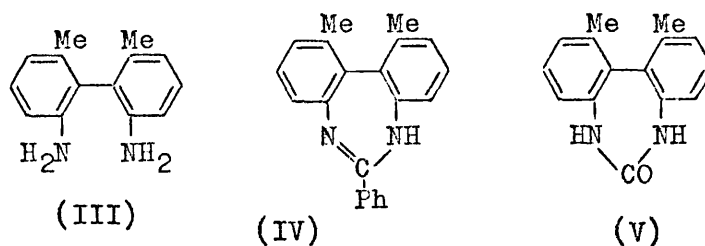
The establishment of this theory has stimulated the interest of many stereochemists in studying the effect of ortho-substituents (in terms of number and size) on optical activity and on the ease of racemization of the biphenyl derivatives. This study also included the effect of the introduction of substituents into the meta and para positions. The results of ring closure between the 2- and 2'- or 6'- substituents in optically active compounds have been investigated only by a few workers.

In 1927, Meisenheimer and Horing found that the dilactam (II) obtained from optically active 6,6'-bis(acetamido)diphenic acid (I) is optically inactive. This has of course to be the case



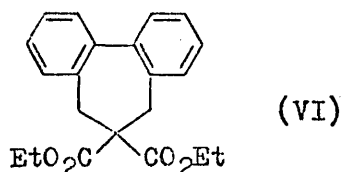
since the molecule is planar and has a centre of symmetry and its tautomeric form would be fully aromatic and planar as well.

However, optical activity is retained in compounds with a larger bridging ring. The two biphenyls (IV) and (V) obtained from (-)-2,2'-diamino-6,6'-dimethylbiphenyl (III) by Sako in 1931



are optically active because the flexibility of the three-atom-bridge allows the ring system to assume a multiplanar structure and the two benzene nuclei to remain non-coplanar.

All attempts to demonstrate multiplanarity without additional hindrance by the 6- and 6'-substituents in such a ring system were in vain and the proof of molecular dissymmetry was not achieved until the successful preparation of optically active 6,6'-dicarbethoxydibenzo-[a,c][1,3]cycloheptadiene (VI) by Iffland and Siegel in 1956.



For roughly the past twenty years, 2,2'-bridged biphenyls have been extensively studied and have yielded much information to

stereochemists for two important reasons: "firstly, they are almost unique among organic molecules of comparable complexity in that they exist, in many cases, in only two conformations which are enantiomerically related; secondly, the energy barrier separating these conformations is frequently high enough to be conveniently measurable" (abstract from a review by D. M. Hall, 1969).

Electronic spectra

The absorption of light in the visible and ultra-violet wavelength regions by organic molecules usually results in electronic transitions involving π -electrons with or without interaction with substituents containing other π -electron or n-electron systems, that is unshared pair of electrons associated with atoms such as nitrogen and oxygen. Empirical correlation between ultra-violet light absorption and molecular structure depends upon the fact that ultra-violet light absorption is characteristic of certain π -electron systems or chromophores rather than that of the molecule as a whole. When two or more chromophores are present in the same molecule without conjugation, the overall absorption is almost additive. When two or more chromophores are in conjugation, the absorption band usually shifts to the longer wavelength region (bathochromic shift) and its intensity is frequently higher than those observed for the two separately.

The ultra-violet spectrum of biphenyl itself exhibits a

broad high-intensity band at 249 nm with a maximal molecular extinction coefficient of 17,300 in 96% ethanol (Beaven and Hall, 1956). This band has been attributed to resonance between the two aromatic nuclei and hence is sometimes termed "the conjugation band". Although the biphenyl molecule was shown by x-ray crystal analysis to be coplanar in the crystalline state (Dhar, 1932) and presumably has an interplanar angle between the two benzene rings of zero to 45° in solution (Braude, 1945), it was generally assumed that a coplanar structure was essential for sufficient overlapping of the π -orbitals of the two benzene rings to produce the typical biphenyl spectrum.

The introduction of only two substituents into the sterically sensitive ortho positions of the biphenyl molecule was found sufficient to prevent the two benzene rings from being coplanar if the substituents are large enough. This was readily reflected by the ultra-violet spectra of a number of ortho-disubstituted biphenyls, e.g., the ultra-violet spectrum of 2,2'-dimethylbiphenyl (Figure 3) failed to show the characteristic intense biphenyl absorption indicating a lack of conjugation between the two benzene rings owing to interference between the two methyl groups and the 2'- and 6'-hydrogen atoms (Williamson and Rodebush, 1941). On the other hand, as the interfering effect of the two hydroxyl groups in 2,2'-dihydroxybiphenyl is comparatively small, the ultra-violet spectrum of this compound showed both the characteristics of a

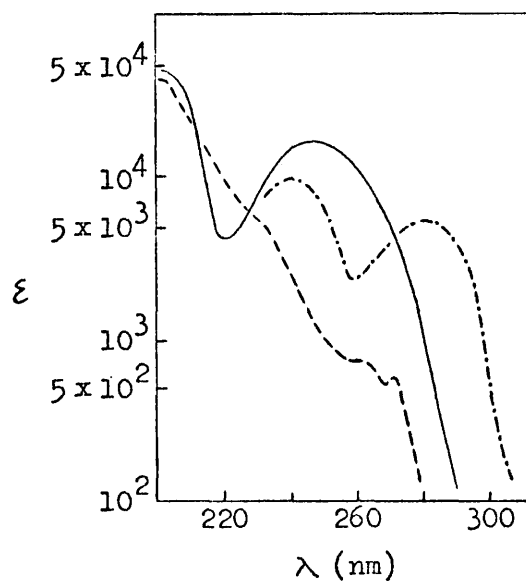


Figure 3.

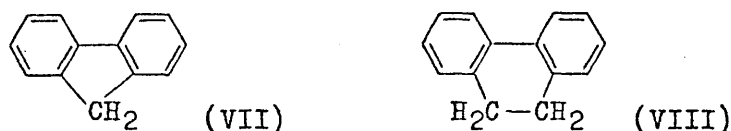
UV spectra of biphenyl (—); 2,2'-dimethylbiphenyl (----) in light petroleum (b.p. 100-120°) (Beaven *et al.*, 1961) and 2,2'-dihydroxybiphenyl (-·-·-) in 95% ethanol (Williamson and Rodebush, 1941).

conjugated biphenyl and of phenyl which could be an intermediate case (Williamson and Rodebush, *loc. cit.*).

By joining the 2,2'-positions in biphenyl with a saturated bridge of two or more atoms, the two benzene rings can also be fixed at an inclined angle and the resulting homocyclic or heterocyclic ring will be nonplanar provided that it retains the normal bond lengths and angles. The interplanar angle θ between the two benzene rings may also be calculated for undistorted structures where the bridge consists of 2, 3 or 4 atoms. When the bridge consists of 5 or more atoms, there can be no possibility of obtaining a fixed angle since the bridging ring is flexible.

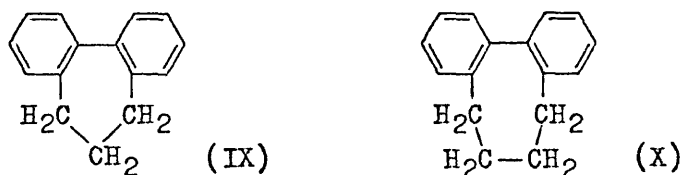
For biphenyls where the bridge has one atom such as fluorene (VII), the above considerations are not applicable since the

molecule is planar and the two benzene rings are not collinear. However, for compounds where the bridge consists of two atoms such as 9,10-dihydrophenanthrene (VIII), the two benzene rings are collinear and, as has been observed by several workers, the ultra-



violet spectrum of 9,10-dihydrophenanthrene exhibits a typical high-intensity biphenyl band at λ_{\max} 264 nm, ϵ_{\max} 18,000 and a broad low-intensity band at the longer wavelength region. The appearance of these bands as absorption contributions from the separate unconjugated phenyl chromophores made it reasonable to think about a lesser angle θ in this compound than in biphenyl itself.

The three-atom-bridge biphenyl (IX) has an ultra-violet spectrum showing a shift of biphenyl conjugation band to shorter wavelength (λ_{\max} 247 nm) accompanied by a reduction in extinction coefficient (ϵ_{\max} 15,700). On increasing the number of bridging carbon atoms to 4, the compound so formed (X) exhibits a further



shift of the conjugation band (λ_{\max} 235 nm, ϵ_{\max} 9,680) (Cope and

Smith, 1956) (Figure 4). The interplanar angle θ increases rapidly

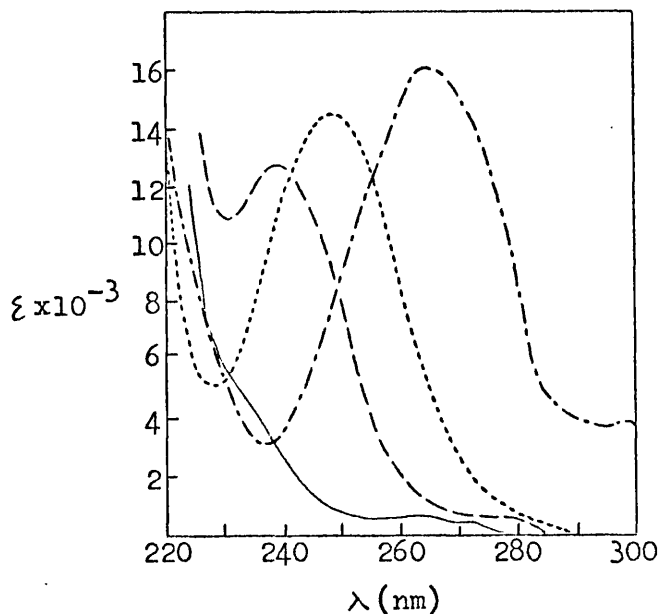
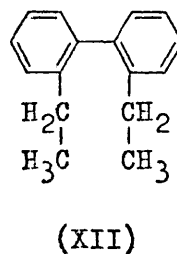
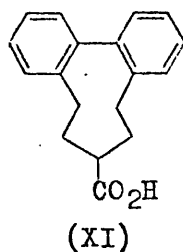


Figure 4.

UV spectra of 2,2'-bridged biphenyls with six-(---), seven-(.....), eight-(----) and nine-(—) membered homocyclic rings in 95% ethanol (Mislow, Hyden and Schaefer, 1962).

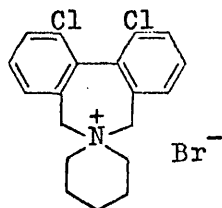
with increasing number of bridging atoms and electronic interaction between the two benzene rings is still sufficient to produce a separated conjugation band even when θ is as large as 59° (for compound X). Complete coplanarity of the benzene rings is evidently not required for the development of a conjugation band.

In biphenyls where the bridge consists of 5 atoms such as the carboxylic acid (XI), the conjugation band is present only as

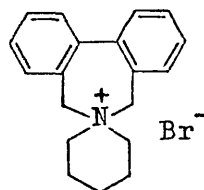


an inflection at short wavelength (λ 231 nm, ϵ 5,550) and its spectrum is nearly superimposable on that of the open-chain analog 2,2'-diethylbiphenyl (XII) (Mislow, Hyden and Schaefer, 1962).

As it has been stated, introduction of two relatively large groups into the ortho positions of biphenyl or its derivatives without a bridging ring could produce a hypsochromic shift and a reduction in intensity of the maximum of the conjugation band. Here the two benzene rings are relatively free to increase the angle of twist so as to accommodate the substituents (Bastiansen, 1950; Littlejohn and Smith, 1954). However, in the case of a bridged biphenyl without a flexible ring, the molecule is constrained and accommodation of two extra ortho substituents was found to be energetically preferable for some atoms or groups largely by their in-plane or out-of-plane deformation. For example, 2,2'-dichlorobiphenyl shows a large hypsochromic shift (ca. 19 nm) of the conjugation band as compared with that of the biphenyl (Figure 5), whereas in the case of dichlorodihydrodibenzazepinium salt (XIII), the presence of two chlorine atoms in the 6- and 6'-positions has only a small effect on the intensity of the absorption maximum and the shift of conjugation



(XIII)



(XIV)

band (λ_{\max} 247 nm) is negligible as compared with that of the dihydrodibenzazepinium salt (XIV) which has λ_{\max} 248 nm (Beaven and Hall, 1956; Ahmed and Hall, 1960).

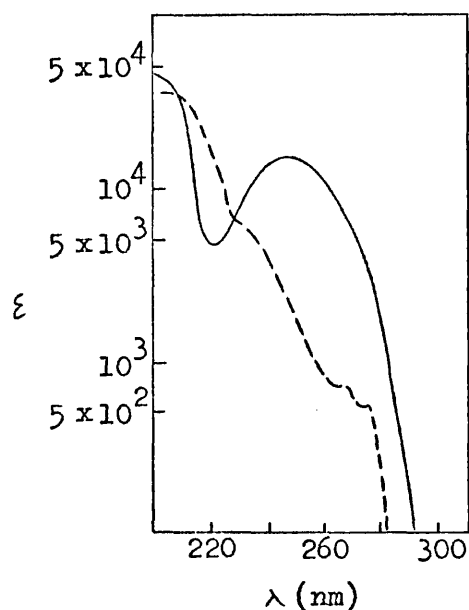


Figure 5.

UV spectra of biphenyl (—) and 2,2'-dichlorobiphenyl (----) in 96% ethanol (Beaven and Hall, 1956).

It is important to note that most substituents would cause a bathochromic shift in the absence of any steric effect, but for a particular substituent, the bathochromic shift will be the same in a bridged biphenyl and an unbridged biphenyl. The conjugation band in a given compound represents a balance between the bathochromic shift which is usually due to interaction between the π and n-electron systems, and the hypsochromic shift which is due to a decrease in electronic interaction across the 1,1'-bond of the two benzene rings. The small hypsochromic shift in the chloro compound (XIII) also indicates that chlorine atoms can be accommodated in

the 6- and 6'-positions with only a small increase in the angle between the planes of the two benzene rings but this is no longer possible when the two chlorine atoms are replaced by larger bromine or iodine atoms. The conjugation band is present only as an inflection in the spectra of both these compounds (Figure 6).

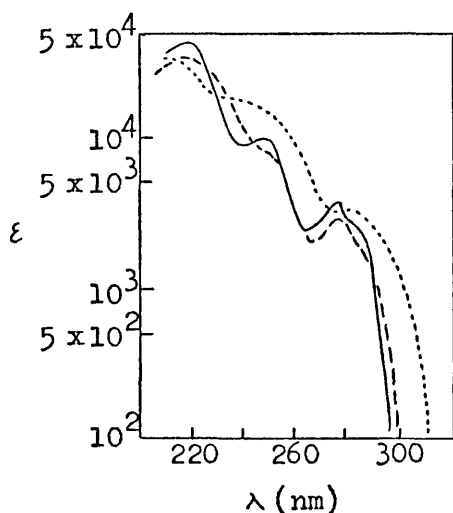


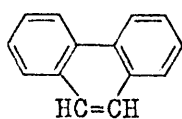
Figure 6.

UV spectra of 4',1''-dichloro- (—), 4',1''-dibromo- (----) and 4',1''-di-iodo-2,7-dihydro-3,4:5,6-dibenzazepinium-1-spiro-1''-piperidinium bromide (.....) in 96% ethanol (Ahmed and Hall, 1960).

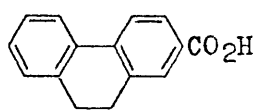
Optical activity and racemization

For a homocyclic 2,2'-bridged biphenyl where the bridge has one atom, i.e., fluorene (VII), there is no possibility of optical isomerism since the molecule is planar and strained (Brown and Bortner; Burns and Iball, 1954). When the bridge consists of two carbon atoms as in phenanthrene (XV), the molecule is also planar, but the saturated compound 9,10-dihydrophenanthrene (VIII) appears to have a twisted biphenyl system and the molecule is dissymmetric. However, attempts to demonstrate optical activity in its derivative

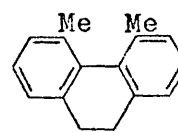
such as (XVI) were unsuccessful (Hall and Turner, 1955) presumably owing to the low energy barrier to inversion (Howlett, 1955). In spite of this failure, the ortho disubstituted dihydrophenanthrene (XVII) was obtained optically active and the (R)-(-)-form obtained was found to have an activation energy for racemization of 23.1 kcal mole⁻¹ (Mislow and Hopps, 1962).



(XV)

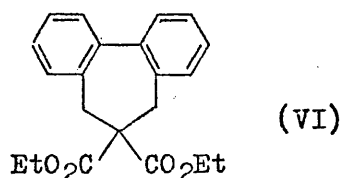


(XVI)



(XVII)

The formation of biphenyl with a three-atom-bridge is particularly easy (Kenner and Turner, 1911; Beaven, Hall and Turner, 1952) but early attempts to resolve such a compound without ortho substituents had failed. However, the diethyl ester (VI) was eventually obtained in the (+)-form by a series of reactions with

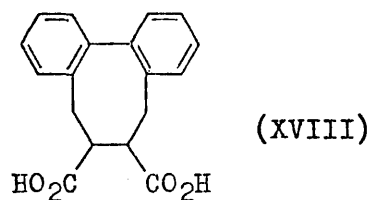


(VI)

(+)-6,6'-dinitrodiphenic acid as a starting material (Iffland and Siegel, 1956). This compound (VI) was optically labile and racemized in cyclohexane solution at 32.5° with a half-life of 80 minutes.

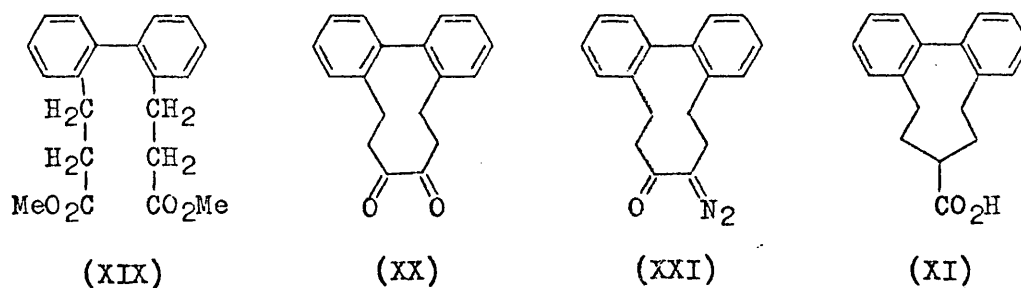
Optically active biphenyls in which four atoms join the

2- and the 2'-position to form part of an eight-membered ring have also been obtained, e.g., the resolution of the dicarboxylic acids (XVIII). This compound exists in cis and trans forms (Beaven et al., 1955; Dvorken et al., 1958). The cis-acid was resolved by



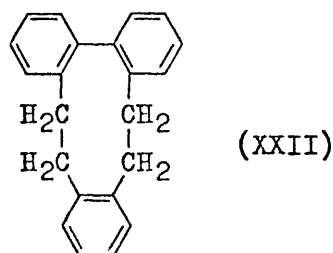
crystallization of the morphine salt from acetone. It racemized in ethanol at 31.5° with a half-life of 85 minutes. The trans-acid was resolved through its brucine salt also from acetone and had a half-life of mutarotation of 12 minutes in ethanol at 31.5° (Dvorken et al., 1958).

The preparation of 2,2'-bridged biphenyls with a nine-membered ring is rather difficult to achieve. However, Mislow and his co-workers (1962) were able to obtain the carboxylic acid (XI) by acyloin ring-closure of the diester (XIX) and direct oxidization of the product to the diketone (XX) followed by ring-contraction of its derivative, the diazoketone (XXI). It was optically activated

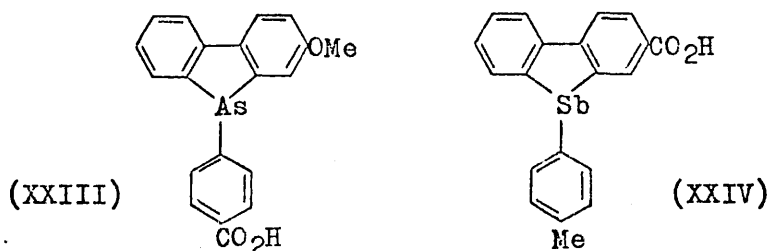


by second-order asymmetric transformation and was found to be optically stable at room temperature. It had $[\alpha]_D = -48.4^\circ$ in benzene and by heating under reflux in benzene for one hour, it underwent complete racemization. As compared with the cis-dicarboxylic acid (XVIII) ($E_{\text{rac}} = 22.8 \text{ kcal mole}^{-1}$), this nine-membered ring compound ($E_{\text{rac}} = 24.0 \text{ kcal mole}^{-1}$) was optically rather more stable.

There are a few compounds with a larger bridging ring. The tribenzocyclodecene (XXII) was obtained by a newer method related to the Wittig reaction (Bestmann and Ruppert, 1968) but its optical activity was not known.

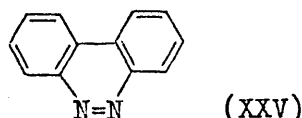


Optical activity has also been demonstrated in biphenyls where the bridge joining the 2- and 2'-position has at least one hetero atom. The 9-arsafluorenes such as (XXIII) and 9-stibiafluorenes such as (XXIV) were both obtained in their enantiomeric

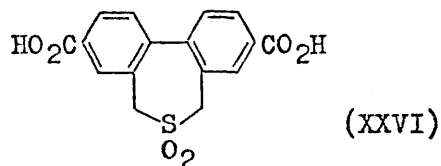


forms but their dissymmetry is due to the pyramidal arrangement of the three dissimilar groups around the hetero atom (Campbell and Morrill, 1955; Campbell and Poller, 1956).

The two-atom-bridge biphenyl benzo[3,4-c]cinnoline (XXV) is planar, and again like phenanthrene, there can be no possibility of optical isomerism.

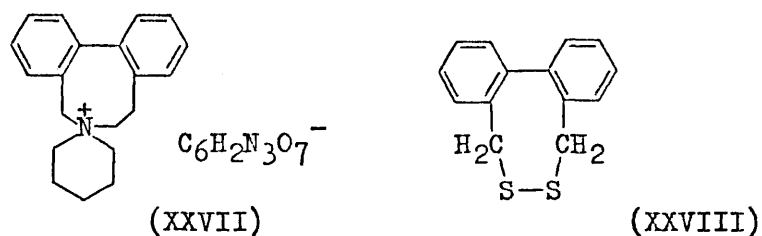


Although many heterocyclic biphenyls where the bridging ring consists of three atoms have been prepared, in the absence of other ortho substituents, only the compound (XXVI), obtained in solution, was found to show (labile) optical activity, having $[\alpha]_D^{25} = 3.1^\circ$ (Truce and Emrick, 1956); presumably the presence of the large hetero atom gives sufficient optical stability for the optical activity to be detectable at room temperature.



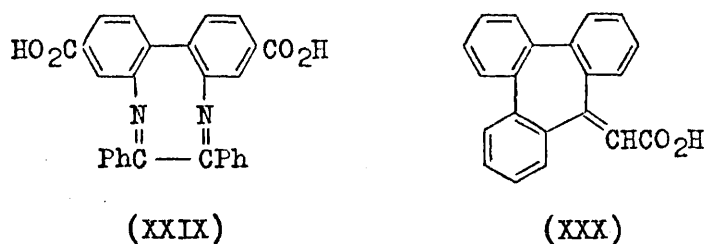
For 2,2'-bridged biphenyls with a heterocyclic bridging ring of four atoms and with only hydrogens occupying the 6- and 6'-position, only a few of them have been found optically active. The tetrahydrodibenzdiazocine (XXVII) was resolved by crystallization of the (+)- and (-)- α -bromocamphor- π -sulphonates. It was

found to have high optical lability with a half life period of racemization of 1.4 minutes at 23° in acetone and has an activation energy of 22.1 kcal mole⁻¹ (Ahmed and Hall, 1959). The dibenzodithiacyclooctadiene (XXVIII) was partially resolved by passing



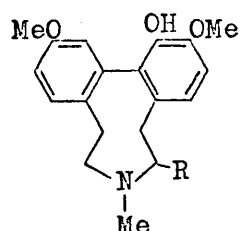
through a column of cellulose-2₁-acetate. The (+)-form has $[\alpha]_{405}^{25} = +66^\circ$ in chloroform and has an energy barrier of 27.3 kcal/mole to racemization. This compound is optically highly stable, presumably owing to the large size of the two sulphur atoms which confers notable rigidity on the molecule (Luttringhaus *et al*, 1967).

A few compounds both homocyclic and heterocyclic where the bridge consists of one or more double bonds are optically highly stable as compared with similar compounds with a saturated bridging ring. Thus the dibenzodiazocine (XXIX) which can be readily resolved by crystallization of the brucine salt (Bell, 1952) is optically stable up to 240° in ethyl benzoate (Hall and Insole, 1964)

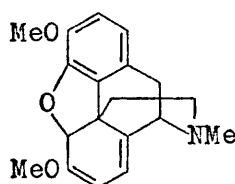


and the tribenzocycloheptatriene (XXX), in which the unsaturation is part of a third benzene ring, racemizes in di(2-methoxyethyl)-ether at 139° (Tochtermann and Kuppers, 1965). The high optical stability can presumably be attributed to the greater rigidity conferred on these compounds by additional double bonds since twisting of the double bonds is an essential deformation for reaching the transition state.

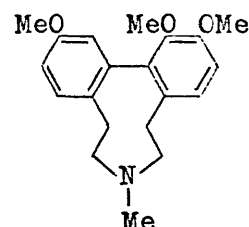
2,2'-Bridged biphenyls with a heterocyclic nine-membered ring are rather inaccessible and for a number of years, only the phenyldihydrothebaine (XXXI; R = Ph) was known to possess optical



(XXXI)



(XXXII)



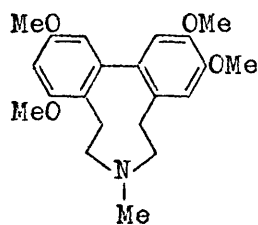
(XXXIII)

activity (Robinson, 1947; Bentley and Robinson, 1950, 1952). This compound has a hydroxyl group in the ortho position which is buttressed by the adjacent methoxy group. The presence of an asymmetric carbon atom on the bridging ring indicates a possibility of its existing as four diastereoisomers and in fact, they were all isolated by Small, Sargent and Bralley (1947). Conformational change resulting from a twist of the biphenyl skeleton was brought about by prolonged heating of any of these isomers at 200° in a

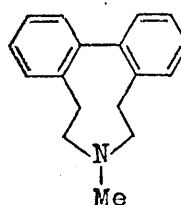
sealed tube, but not the racemization of the asymmetric carbon atom under these conditions.

The action of anhydrous magnesium iodide on thebaine (XXXII) followed by lithium aluminium hydride reduction of the product was shown to give (XXXI; R=H) (Hall and Manser, 1967; Bentley, 1967). By treating (XXXI; R=H) with the reagent $(\text{PhNMe}_3)^+(\text{OEt})^-$ at about 110° it gave the tetrahydrotrimethoxy-N-methyl-dibenzazone (XXXIII) which has no asymmetric carbon atom on the bridging ring. This compound is optically active and has an activation energy to racemization of $31.5 \text{ kcal mole}^{-1}$ (Manser, 1967). As compared with the carboxylic acid (XI), it was more optically stable presumably owing to the effect of the buttressed ortho methoxyl group.

Closely related to the compound (XXXIII) is the alkaloid protostephanine (XXXIV) which has been obtained via a synthesised method (Pecherer and Brossi, 1967) but attempts to bring about optical resolution had failed (Takeda, 1956). Since the carboxylic acid (XI) is optically stable, the replacement of $-\text{CH}-\text{CO}_2\text{H}$ group by $>\text{NCH}_3$ group seemed very unlikely to have a large effect on the ease of racemization. It was thought that the synthesis of a



(XXXIV)

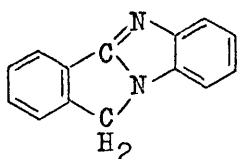


(XXXV)

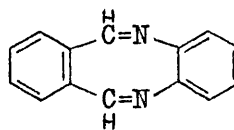
heterocyclic nine-membered ring without any substituent on the phenyl rings (XXXV) would be of great synthetic interest and if optical resolution could be achieved, then a comparison of its ultra-violet spectrum or its racemization data with those of the homocyclic nine-membered ring (XI) would probably provide some informations about biphenyls with a larger heterocyclic bridging ring.

C. Some condensations between aromatic dialdehydes and diamines

For roughly the past ten years, the condensations between aromatic dialdehydes and diamines have been investigated by a number of workers. The reaction product of *o*-phthalaldehyde and *o*-phenylenediamine was confirmed to have the structure (I) rather than (II) (Amos and Gillis, 1964). Similarly, the products obtained

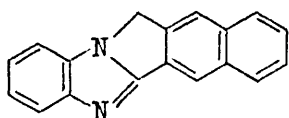


(I)

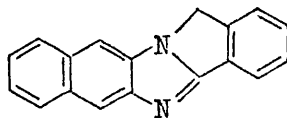


(II)

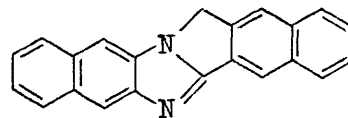
by the treatment of *o*-phenylenediamine with naphthalene-2,3-dialdehyde, 2,3-diaminonaphthalene with *o*-phthalaldehyde, 2,3-diaminonaphthalene with naphthalene-2,3-dialdehyde and 1,2-diaminonaphthalene with naphthalene-2,3-dialdehyde were shown to have the structures (III), (IV), (V) and (VIa or VIb) respectively (Perlmutter and Knapp, 1967).



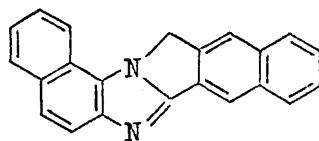
(III)



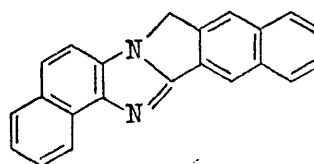
(IV)



(V)

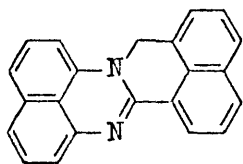


(VIa)

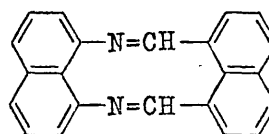


(VIb)

The reaction between 1,8-diaminonaphthalene and naphthalene-1,8-dialdehyde had also been found to give the "hydride shift" product (VII) rather than the bis-Schiff base (VIII). Similar reactions

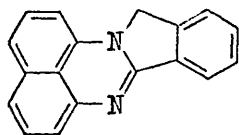


(VII)

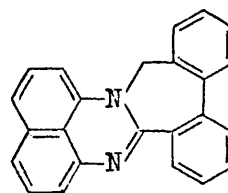


(VIII)

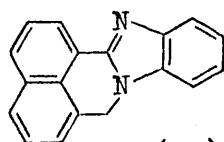
between 1,8-diaminonaphthalene and *o*-phthalaldehyde or biphenyl-2,2'-dialdehyde as well as naphthalene-1,8-dialdehyde and *o*-phenylenediamine or 2,2'-diaminobiphenyl also failed to give a larger ring such as (VIII). The products obtained were reported to have the structures (IX), (X), (XI) and (XII) respectively (Bindra and Elix, 1970).



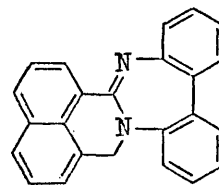
(IX)



(X)



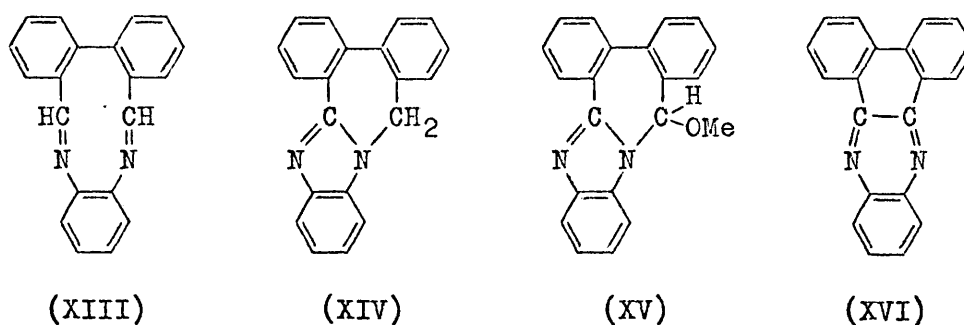
(XI)



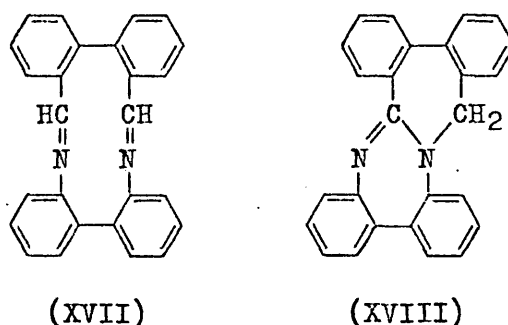
(XII)

Attempts had also been made to prepare the ten-membered ring (XIII) by condensation between biphenyl-2,2'-dialdehyde and *o*-phenylenediamine but the product was found to be (XIV) (Sparatore,

1959; Hawthorne and his co-workers, 1963) and in addition to this compound, some workers also obtained the by-product (XV) when the reaction was carried out in methanol (Bindra and Elix, 1969). The compound (XVI) had also been isolated as a by-product of this condensation reaction although the main product was thought to have



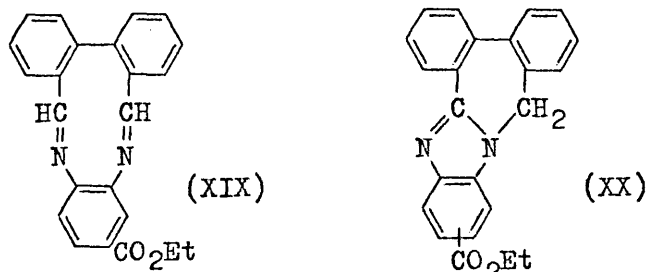
the structure (XIII) by another worker (Prakobsantisukh, 1964). In view of the fact that the condensation between biphenyl-2,2'-di-aldehyde and 2,2'-diaminobiphenyl was shown to give (XVII) rather than (XVIII) (Bergmann and his co-workers, 1966; Bindra and Elix, 1970) and that a comparison of the spectroscopic information about



(XIV) provided by the workers concerned as well as the melting points recorded by them (see page 67) seemed to reveal a distinct

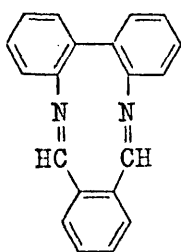
feature of (XIV), a reinvestigation of this condensation reaction was thus of interest.

As we have mentioned in the previous introduction (page 25 2,2'-bridged biphenyls where the bridge consists of one or more double bonds are highly optically stable as compared with similar compounds with a saturated bridging ring. The attachment of an ethyloxycarbonyl group to (XIII) would, after hydrolysis, thus serve as a handle for resolution if (XIII) could be obtained. The previous work of Prakobsantisukh seemed to indicate that the condensation between biphenyl-2,2'-dialdehyde and ethyl 3,4-diaminobenzoate had given (XIX) rather than (XX). Although this was no

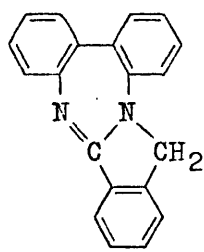


longer considered to be the case, a structure determination of the reaction product is also included in the present work.

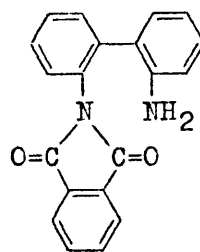
The condensation between 2,2'-diaminobiphenyl and *o*-phthalaldehyde was found to have given neither the expected compound (XXI) nor the one with an alternative structure (XXII) (Blood and Noller, 1957). As the product obtained was reported to be a polymer plus some unidentified red solids, a reinvestigation of this condensation reaction is also of interest. The present work has so far proved that the reaction has given a red crystalline solid (m.p. 253-254°)



(XXI)

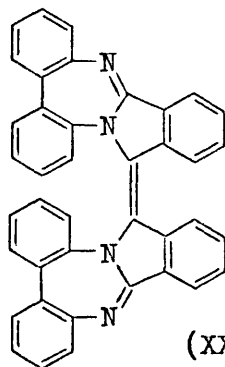


(XXII)

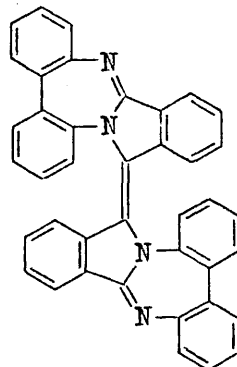


(XXIII)

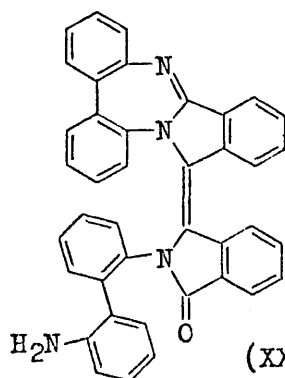
with molecular formula $C_{40}H_{26}N_4O$ and some 2-amino-2'-phthalimido-biphenyl (XXIII) as a by-product. Nevertheless, the recent report of Bindra and Elix (1969) that this condensation gave a polymer seemed to confirm Blood and Noller's experiment. Bindra and Elix also obtained some red to pink coloured compounds with empirical formulae $C_{40}H_{26}N_4O$ and $C_{40}H_{24}N_4$, and according to them, these compounds could have the structural formulae (XXIV), (XXV), (XXVI) and



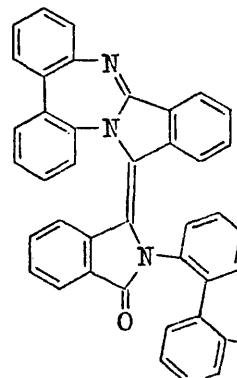
(XXIV)



(XXV)



(XXVI)



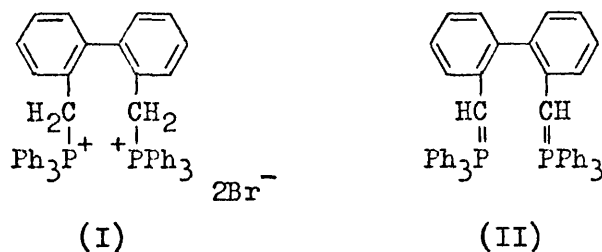
(XXVII)

(XXVII). The compound (XXVI) (m.p. 262°) was found to have ultra-violet spectrum superimposable on that of the red compound (m.p. $253-254^{\circ}$) obtained in the present experiment. Both of them were also found to have similar IR, NMR and mass spectra and hence must have the same structure. As the proposed structure (XXVI) was by no means satisfactory, a further discussion about the structure of the present red compound was advanced.

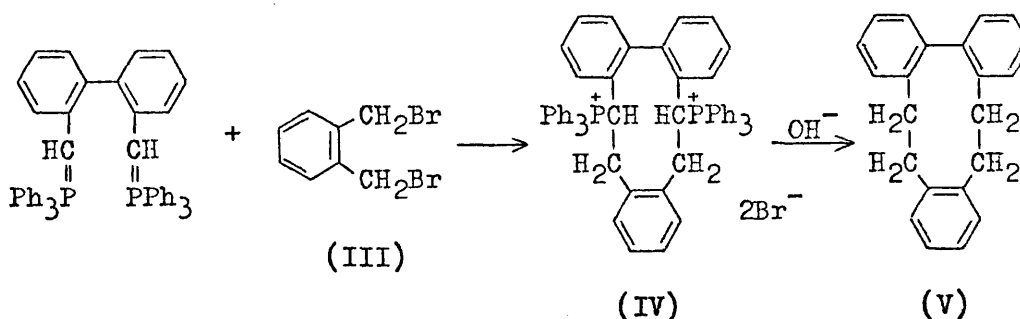
DISCUSSION

A. Attempted preparation of biphenyls with a longer bridging chain

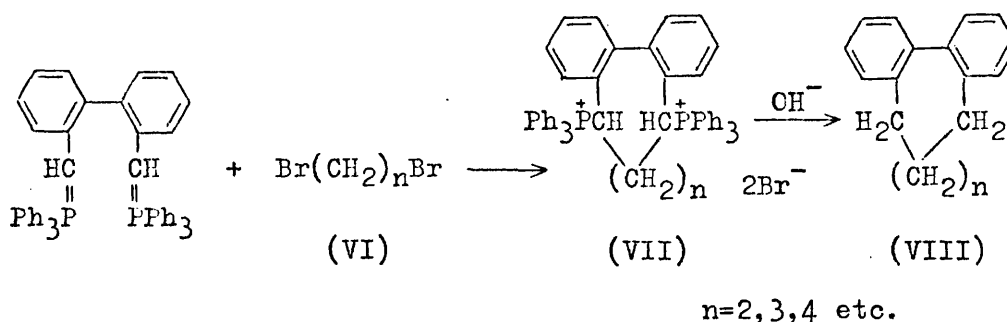
Stable bisphosphoranes such as (II) have been reported to be accessible by heating the bisphosphonium salt (I) for several hours at 160° under reduced pressure in the presence of phosphorus pentoxide (Bestmann and Ruppert, 1966).



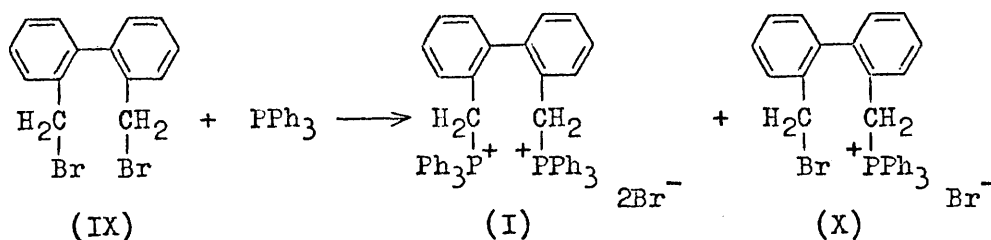
The reaction between the bisphosphorane (II) and *o*-xylenyl dibromide (III) followed by alkaline hydrolysis of the resulting bisphosphonium salt (IV) to give the tribenzocyclodecene (V)



(briefly mentioned on page 23) provides a new possibility for the synthesis of a series of 2,2'-bridged biphenyls. By reaction of (II) with (VI) and treatment of the product with a base under the same condition, the compound (VIII) would probably be obtainable.

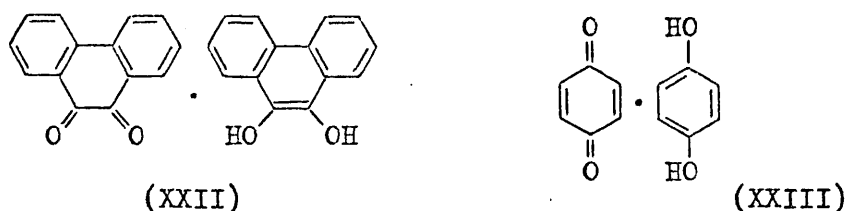


The diposponium salt (I) had been prepared as a dihydrate with m.p. 324–327° in a satisfactory manner by reaction between 2,2'-bisbromomethylbiphenyl (IX) and triphenylphosphine in a high boiling solvent (xylene) or by heating the two reactions together for about 5 minutes at 180° without a solvent (Hall and Prakobsantisukh, 1965). However, when these methods were applied (mesitylene as solvent), both the reactions gave a mixture of the mono- and di-phosponium salts (I and X) which were very difficult to separate. The crystalline solid had m.p. 310–314° after successive crystallization from ethanol-ethyl acetate.



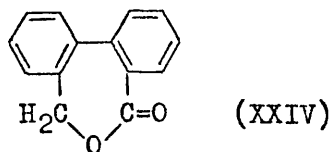
The use of DMF as a solvent had been reported to give a high yield of compound (I) with m.p. >300° when the reaction was carried out under nitrogen (Bergmann, Bracha, Agranat and Kraus, 1967).

The yield was around 65% owing to the formation of a dark green substance, possibly the compound (XXII) since quinhydrone (XXIII)



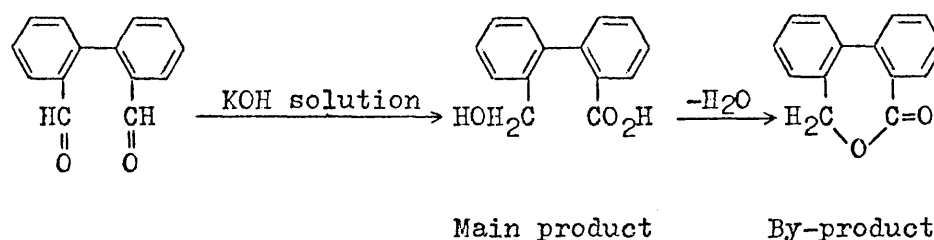
is also dark green in colour. Attempts to improve the yield by using a large excess of reducing agent were unsuccessful.

The oxidation of compound (XII) with lead tetra-acetate in dry benzene to give biphenyl-2,2'-dialdehyde (XIII) (Hall and Prakobsantisukh, 1965) is an excellent method for the preparation of this compound. Reaction proceeded smoothly at room temperature and the crude yield was almost quantitative. The dialdehyde (XIII), obtained as pale yellow crystals from ether-light petroleum (b.p. 40-60°) could also be purified by chromatography on neutral alumina and eluted with a mixture of ether and light petroleum to give colourless crystals. Regrettably, an appreciable amount of the material came down as an ϵ -lactone (XXIV) with m.p. 133-134°. This



compound had been obtained as a by-product when biphenyl-2,2'-dialdehyde was submitted to the action of concentrated potassium

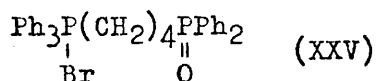
hydroxide solution on the lines of the Cannizzaro reaction (Kenner and Turner, 1911). It was thought that in the present experiment,



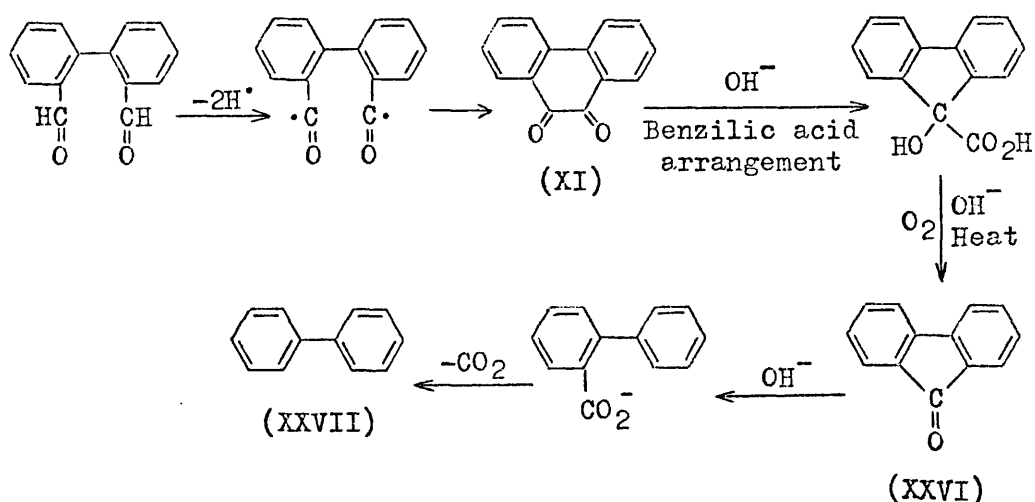
the "neutral alumina" was slightly basic and hence led to the formation of the ϵ -lactone via a similar reaction pathway.

The preparation of trimethylene-1,3-bis(triphenylphosphonium) dibromide (XIV, $n = 3$) by reaction between 1,3-dibromopropane (VI, $n = 3$) and an excess of triphenylphosphine was carried out in DMF (Hörner, Hoffmann, Klink, Ertel and Toscano, 1962) giving a yield of 89%. Reaction between 1,4-dibromobutane (VI, $n = 4$) and excess triphenylphosphine in acetonitrile in an autoclave at 90° afforded the tetramethylene-1,4-bis(triphenylphosphonium) dibromide (XIV, $n = 4$) (Hörner *et al.*, 1962). The yield was up to 95%.

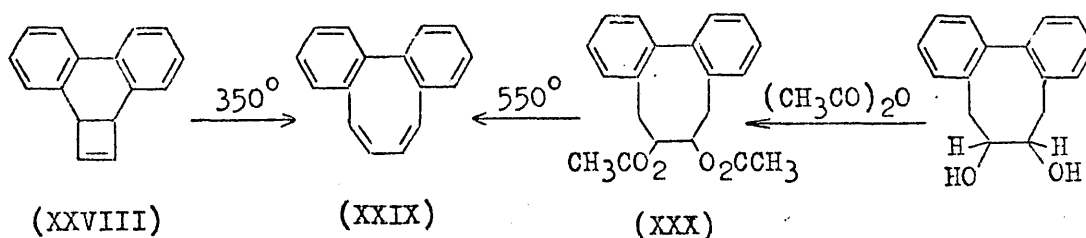
The two phosphine oxide (XV, $n = 3$ and 4) were immediately obtained by alkaline hydrolysis of the two phosphonium salts (XIV, $n = 3$ and 4). Hydrolysis of compound (XIV, $n = 4$) also produced a small amount of the intermediate (XXV) but it could be avoided by longer heating.



Reaction between biphenyl-2,2'-dialdehyde (XIII) and the phosphine oxide (XV, $n = 3$) in dry toluene in the presence of potassium tert-butoxide and under the nitrogen atmosphere failed to give the bridged biphenyl (XVI, $n = 3$). The product was found to be a mixture of 9,10-phenanthrenequinone (XI), fluorenone (XXVI) and biphenyl (XXVII). It seemed that the biphenyl-2,2'-dialdehyde had undergone a series of reactions very rapidly under the influence of the strong base.

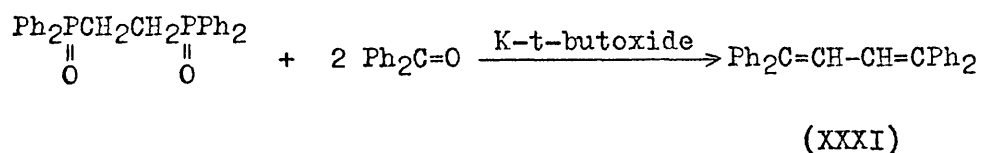


Since the dibenzo-cyclooctatetraene (XXIX) could be obtained from both compound (XXVIII) and (XXX) with m.p. $123-124^\circ$ (Vogel, Frass and Wolpers, 1963), it was hoped that the treatment of



biphenyl-2,2'-dialdehyde with ethylene-bis(diphenylphosphine oxide) (XV, $n = 2$), a by-product obtained from preparation of diphenylvinylphosphine oxide (see page 43), might lead to the formation of such an alkene and provide some reaction conditions for the synthesis of compounds with a larger bridging ring. However, when the reaction was attempted in dry toluene with different quantities of potassium tert-butoxide as condensation reagent, the product remained a mixture of 9,10-phenanthrenequinone and fluorenone.

In order to assure that the failure of these experiments was not due to inefficient technique, it was decided to repeat one of Hörner's experiment: the treatment of ethylene-bis(diphenylphosphine oxide) with benzophenone. As it was expected, 1,1,4,4-tetraphenyl-1,3-butadiene (XXXI) was obtained in 39% yield.

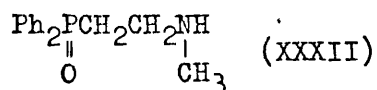


A further attempt was the preparation of dibenzo-cyclodecetetraene (XVI, $n = 4$) by the reaction between biphenyl-2,2'-dialdehyde and tetramethylene-bis(diphenylphosphine oxide) (XV, $n = 4$). However, the product obtained was still a mixture of the familiar 9,10-phenanthrenequinone and fluorenone and some unreacted diphenylphosphine oxide.

Obviously, the above condition used by Hörner and his

co-workers in their preparation of many olefins by the action of P(O)-activated reagents upon carbonyl compounds is not applicable to the synthesis of olefins when biphenyl-2,2'-dialdehyde is included in the reaction. Furthermore, ketones such as 9,10-phenanthrenequinone and fluorenone which appeared to be unreactive towards the P(O)-activated reagents may not be used for the same purpose. The synthesis of 2,2'-bridged biphenyls as indicated in the reaction scheme (I) could possibly be achieved by the use of another condensation reagent and solvent and by varying the reaction time.

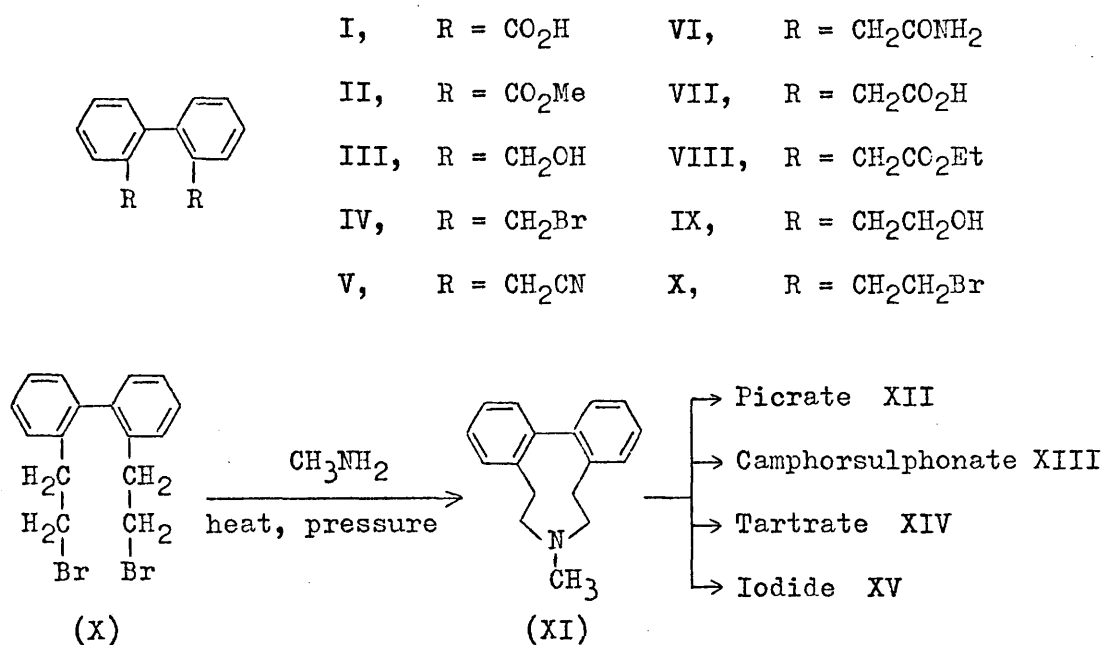
For the second scheme, the compound (XX) was obtained in a two-step process. The reaction between diphenylphosphine chloride (XVII) and ethylene oxide in dry benzene immediately afforded 2-chloroethyl diphenylphosphinite (XVIII) which was heated with triethylamine in an autoclave to give diphenylvinylphosphine oxide (XIX) and the ethylene-bis(diphenylphosphine oxide) (XV, n = 2) as a by-product (Kabachnik, Medved, Polikarpov and Yudina, 1962). The yield were 53.6 and 16.8% respectively. The treatment of the diphenylvinylphosphine oxide with methylamine at room temperature in a close vessel gave [2,2'-(methylimino)diethyl] bis[diphenylphosphine oxide] (XX) (Kabachnik *et al.*, 1962) in 88% yield but it was contaminated with traces of (2-methylaminoethyl)diphenylphosphine oxide (XXXII).



As the use of various P(O)-activated reagents failed to give a bridged biphenyl, no attempt was made at the preparation of compound (XXI).

B. The synthesis of 1-methyl-2,3,8,9-tetrahydro-4,5:6,7-dibenzazonine (XI) and its optical resolution.

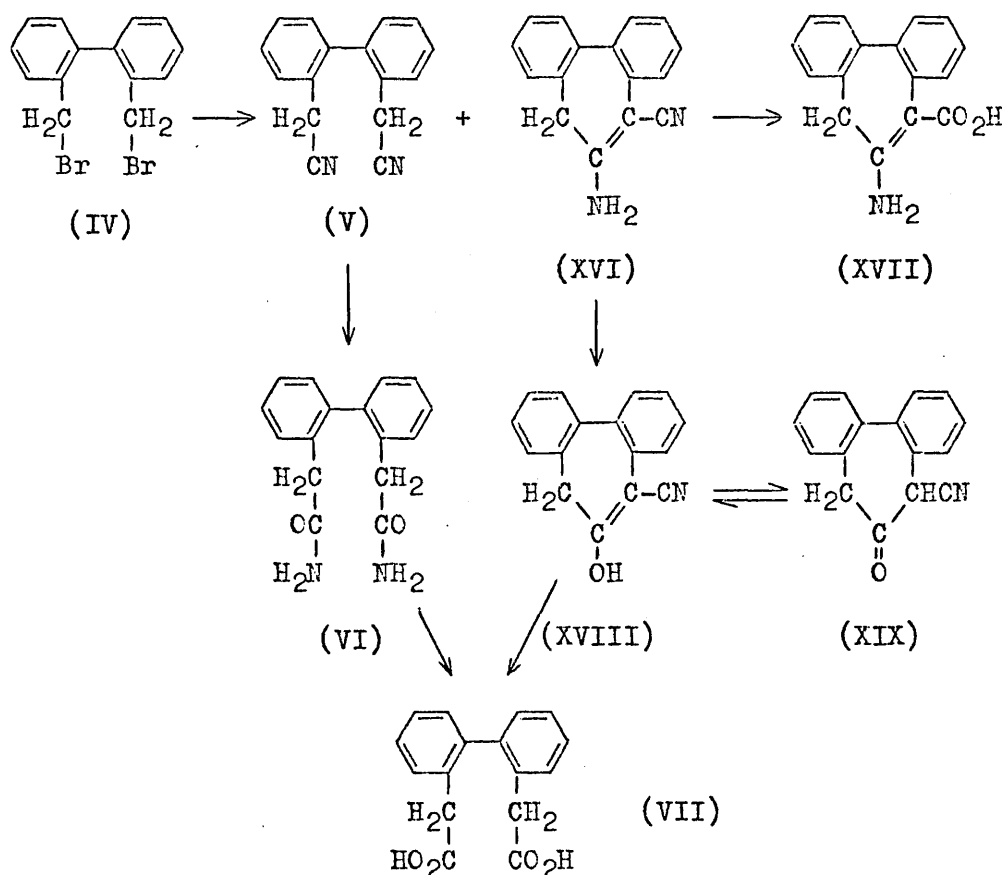
The synthesis of this compound was carried out according to the following reaction scheme:



The readily available diphenic acid (I) was chosen as a starting material and converted into dimethyl 2,2'-diphenate (II) by heating under reflux with methanol in the presence of sulphuric acid in 88% yield. Reduction of the diphenate with lithium aluminum hydride in dry ether (Hall, Lesslie and Turner, 1950) gave an 89% yield of 2,2'-bishydroxymethylbiphenyl (III). Addition of this diol to hydrobromic acid (48-50%) at 90° immediately afforded 2,2'-bis-bromomethylbiphenyl (IV) (Hall *et al.*, 1950). The yield was 85%.

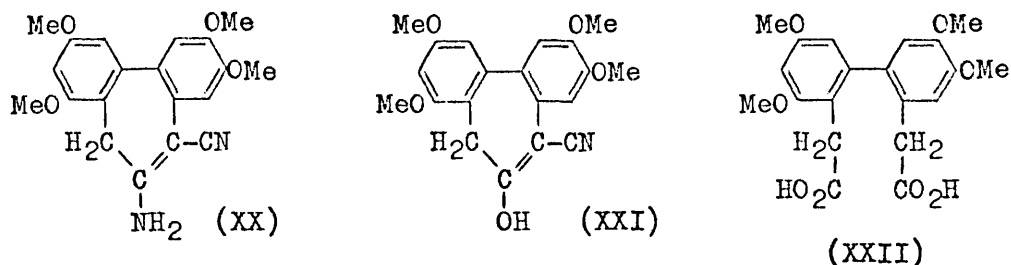
The 2,2'-biphenyldiacetonitrile (V) was obtained from the

dibromide (IV). Reaction of the latter with potassium cyanide in aqueous alcohol (Kenner and Turner, 1911) gave an 80% yield of (V) in the first attempt but in the following preparations, the yield varied from 33 to 61% owing to the formation of a cyclic aminonitrile (XVI). The cyclic aminonitrile could probably be converted



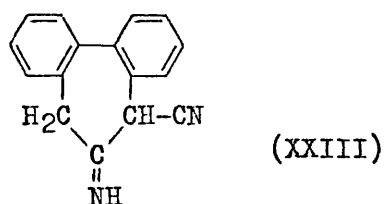
into the desired 2,2'-biphenyldiacetic acid (VII) via acid hydrolysis to (XVIII) and treatment of the product with methanolic sodium hydroxide as in methods used by Fecherer and Brossi (1967) in their preparation of 3,4',5,5'-tetramethoxy-2,2'-biphenyldiacetic acid

(XXII) from (XX) via (XXI). However, in view of the fact that the



use of dimethyl sulphoxide (DMSO) in the preparation of 3,4',5,5'-tetramethoxy-2,2'-biphenyldiacetonitrile from the corresponding dibromide and potassium cyanide (Pecherer *et al.*, 1967) had given a single product in good yield (78%) and the fact that the aprotic solvent DMSO can dissolve both organic and inorganic reagents, it was proposed to carry out the experiment in this solvent. By using DMSO as solvent, the yield of diacetonitrile was brought up to 78% and there was no sign of any side reaction. DMSO is especially useful in dissolving ionic compounds: it solvates the cations most strongly and leaves the anions highly reactive, whereas the protic solvents such as water and ethanol tend to solvate anions particularly firmly and lower their reactivity.

It is worth noting that the above cyclic compound had also been obtained by Kenner and Turner (1911) with m.p. 189° from (V) and was thought by them to be a cyclic iminonitrile (XXIII).



Spectroscopic investigation shows that the imino structure can hardly account for its features. A study of the NMR and IR spectra of this compound is thus of interest. This will be discussed on page 59.

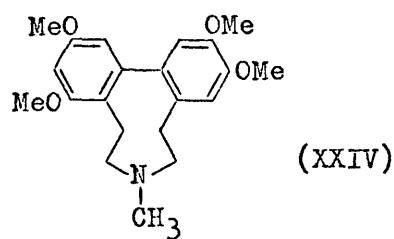
The action of concentrated sulphuric acid on diacetonitrile (V) gave 2,2'-biphenyldiacetamide (VI) (Kenner et al., 1911) in 72% yield. Hydrolysis of this amide with a basic reagent produced 2,2'-biphenyldiacetic acid (VII) (Kenner et al., 1911). The yield was 84%. It melted at 151-152° and turned out to have m.p. 174-175° after a few months' storage. The two melting modifications were also obtained by Mislow, Hyden and Schaefer (1962) in their preparation of this acid.

The direct reduction of diacetic acid (VII) to 2,2'-bis-(2-hydroxyethyl)biphenyl (IX) was carried out in dry ether by means of lithium aluminum hydride (Mislow et al., 1962). Since the yield was up to 78%, there is no point in obtaining this diol via the methyl or ethyl ester (VIII) of the corresponding acid. Moreover, by heating the diacetic acid with ethanol in the presence of concentrated sulphuric acid in the usual manner, the ethyl ester obtained was a viscous oil which did not solidify. Although Kenner (1913) had isolated this compound in large, rhombic crystals from light petroleum (b.p. 60-80°) and determined its melting point (49°), yet attempts to crystallize from the same solvent as well as from other solvents were unsuccessful. It remained as a colourless oil after

standing for over one year. The diol (IX) prepared from this oily ethyl ester using lithium aluminum hydride as reducing agent amounted to an over-all yield of about 48%.

The preparation of 2,2'-bis(2-bromoethyl)biphenyl (X) from the just mentioned diol (IX) involved no difficulty, but the loss due to vacuum distillation was tremendous. Formation of (X) was effected by the action of phosphorus tribromide on the diol in dry benzene (Mislow *et al.*, 1962). The dibromo compound was reported to have m.p. 48-49.5° after purification by chromatography on neutral alumina and recrystallization from methanol. However, after chromatographic purification, attempts to crystallize from methanol were unsuccessful. Further purification by vacuum distillation gave a colourless oil of high viscosity, boiling at 180°/2 mm, in 41% yield.

The method used in the synthesis of the tertiary amine (XI), a nine-membered ring compound, was essentially that applied by Pecherer and Brossi (1967) in the synthesis of protostephanine (XXIV).



The dibromide (X) was dissolved in dry benzene and heated with an excess of methylamine in an autoclave at 140-150° for two hours under fifteen atmospheres of hydrogen. The tertiary amine

formed was worked up in the usual way. After purification by chromatography on alkaline alumina (activity I) using benzene as eluent, it was obtained as a colourless oil. It could not be crystallized from solvents like benzene and light petroleum by scratching, cooling or standing in a refrigerator, nor could it be induced to solidify by leaving the oil in a vacuum desiccator over a drying agent or rubbing with a solvent on a watch glass. However, crystallization was achieved by conversion of this amine into a monopicrate followed by decomposition of the picrate with sodium hydroxide solution; when the regenerated base was stirred with light petroleum (b.p. 60-80°) it was obtained as a colourless crystalline compound, m.p. 55-56°. The yield in the ring-closure stage was rather poor, being only 35.7% calculated from the amount of its monopicrate obtained after recrystallization.

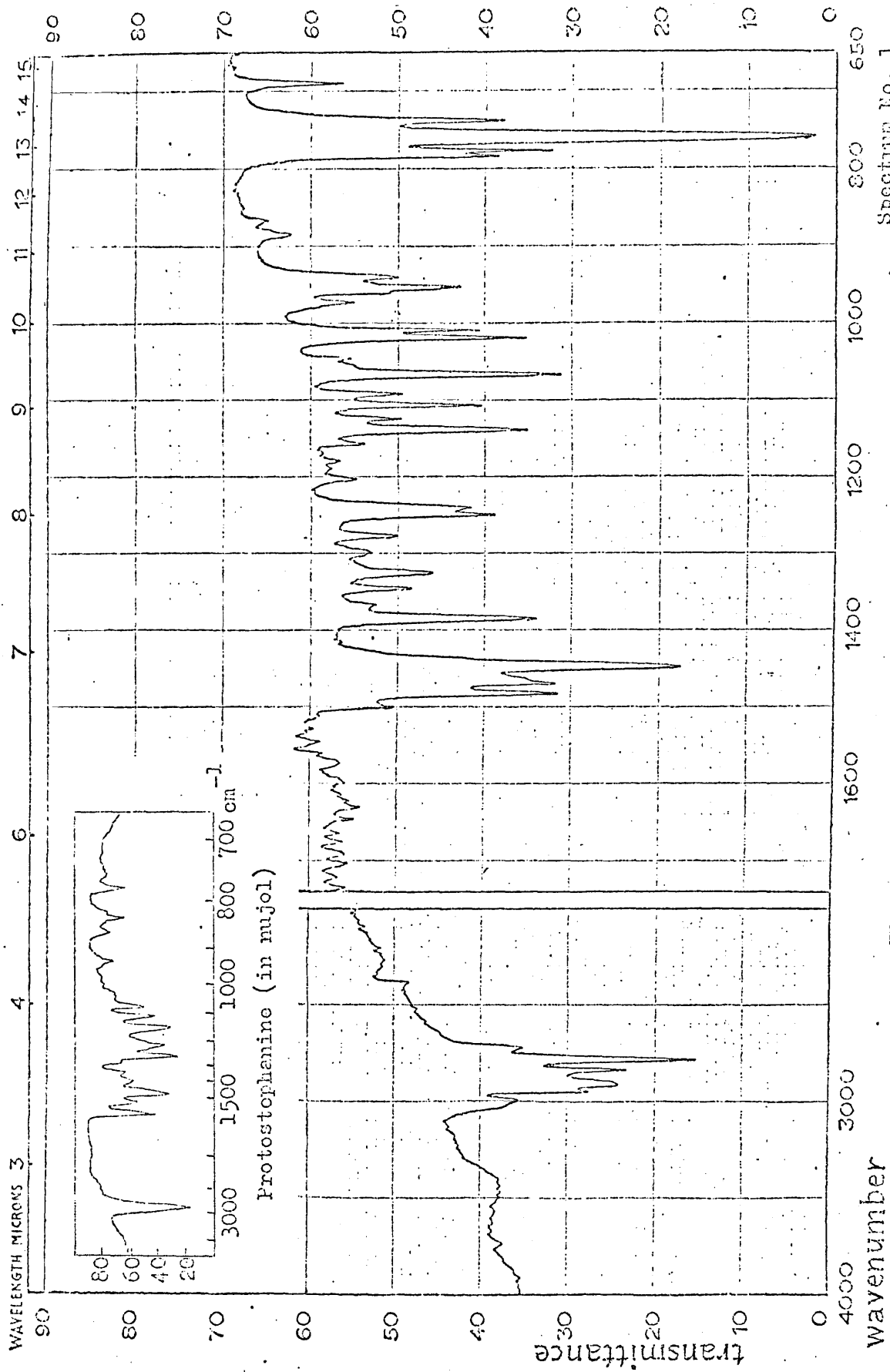
Elemental analysis of compound (XI) gave an acceptable result, although the percentage of carbon was found to be a bit lower than the required value (see page 152).

The molecular weight of this compound can be determined indirectly from molecular weight determination of its monopicrate by a spectroscopic method as described by Cunningham and his co-workers (1951). By using the fact that ethanolic solution of picric acid absorbs strongly between 3500 and 4000 A, whereas only a few colourless organic compounds show appreciable absorption in this region, they determined the absorbances of a number of picrates at an

arbitrary wave length (3800 Å) and having found that the molar absorptivities were very close to an average value 13,440, a value in excellent agreement with the molar absorptivity of picric acid. they assumed that the picrates had $\epsilon_{3800} = 13,440$.

The molecular weight of the monopicrate of compound (XI) determined by this spectroscopy method was in good agreement with the calculated value (error +0.7%). Although the result may be fortuitous, yet this method provided a preliminary estimation of the molecular weight of the tertiary amine. The most accurate value must be sought from mass spectrum.

Comparison of the IR spectrum of the tertiary amine (XI) with that of the protostephanine (Spectrum No. 1) may not be adequate for proof of structure because some of the features of the latter were obscured by the nujol bands. However, the absorptions of the tertiary amine still resembles those of protostephanine except for the presence of a strong band at 760 cm^{-1} and the absence of two strong bands at 1602 cm^{-1} (6.24μ) and 1587 cm^{-1} (6.3μ) which, according to Takeda (1963), might be due to methoxyl-substituted aromatic rings. The strong band at 760 cm^{-1} could probably be attributed to the out-of-plane C-H bending absorption of the two ortho-di-substituted benzene nucleus.¹⁶ The band near 1450 cm^{-1} may be accounted for by the aromatic C=C vibration and the band at 1382 cm^{-1} by the symmetric bending vibration of the methyl group attached to nitrogen.¹⁶ The weak band at 1470 cm^{-1} looks like a



Spectrum No. 1.

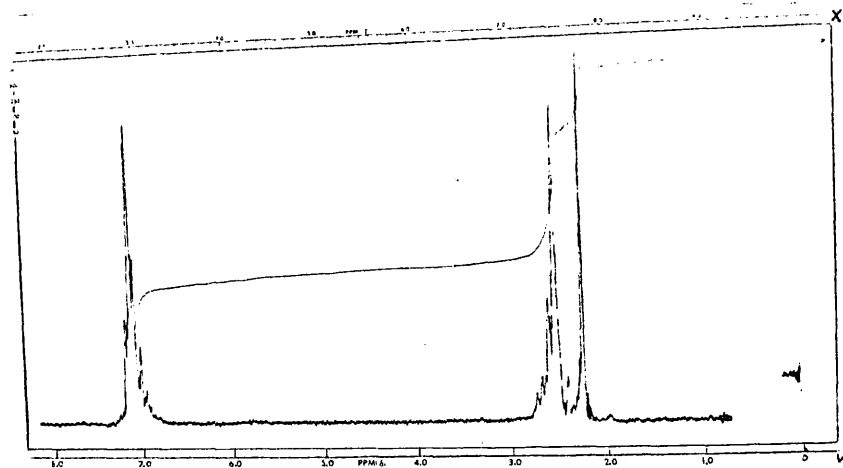
IR spectrum of 1-methyl-2,3,8,9-tetrahydro-

4,5:6,7-dibenzazepine with m.p. 55-56° (in KBr).

combination of asymmetric methyl bending vibration and methyl scissoring vibration. Since all organic compounds have bands between 2750 cm^{-1} and 3100 cm^{-1} due to C-H stretching vibrations, the presence of a group of peaks in the $2700\text{--}3100\text{ cm}^{-1}$ region can only be considered as arising from symmetric and asymmetric methyl stretching vibrations as well as saturated and unsaturated carbon-hydrogen stretching vibrations.

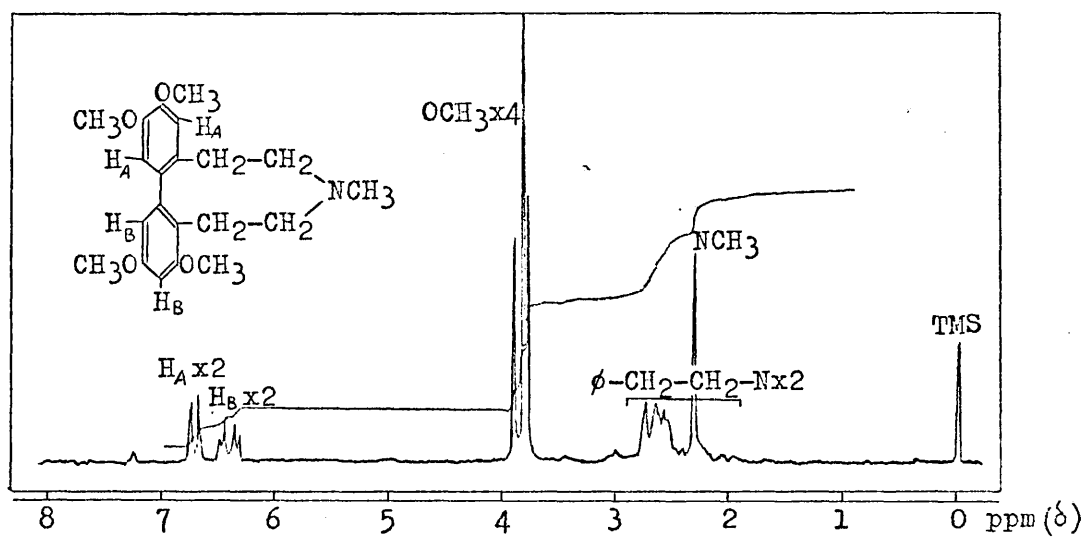
As it is well known that the IR spectrum alone is insufficient to prove the detailed structure of a new compound, a study of its NMR or mass spectrum is a necessity.

The NMR spectrum of the tertiary amine (Spectrum No. 2A) can be well correlated with that of the protostephanine (Spectrum No. 2B). The latter showed two absorption lines centred at δ 6.71, two doublets centred at δ 6.4, probably three lines at δ 3.8-3.95, a multiplet at δ 2.2-2.8 and a singlet near δ 2.3. These signals were assigned respectively for the two protons in the para-position of ring A, two protons in the meta-position of ring B as the AB type, and the protons of O-CH₃, ϕ -CH₂CH₂-N and N-CH₃ groups. In conjunction with the known chemical shifts assigned to the aromatic protons in benzene (δ 7.27), the methylene protons in -CH₂Ph (δ 2.4) or in R-CH₂N-R' (δ 3.3) and the methyl protons in -NCH₃ (about δ 2.16), it is obvious that the signals in Spectrum No. 2A can be assigned as follows: The multiplet at δ 6.95-7.2 must arise from the eight aromatic protons. Those absorption lines at δ 2.4-2.77



Spectrum No. 2A.

NMR spectrum of 1-methyl-2,3,8,9-tetrahydro-4,5:6,7-dibenzazonine with m.p. 55-56°.

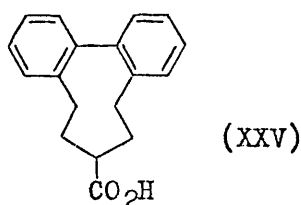


Spectrum No. 2B.

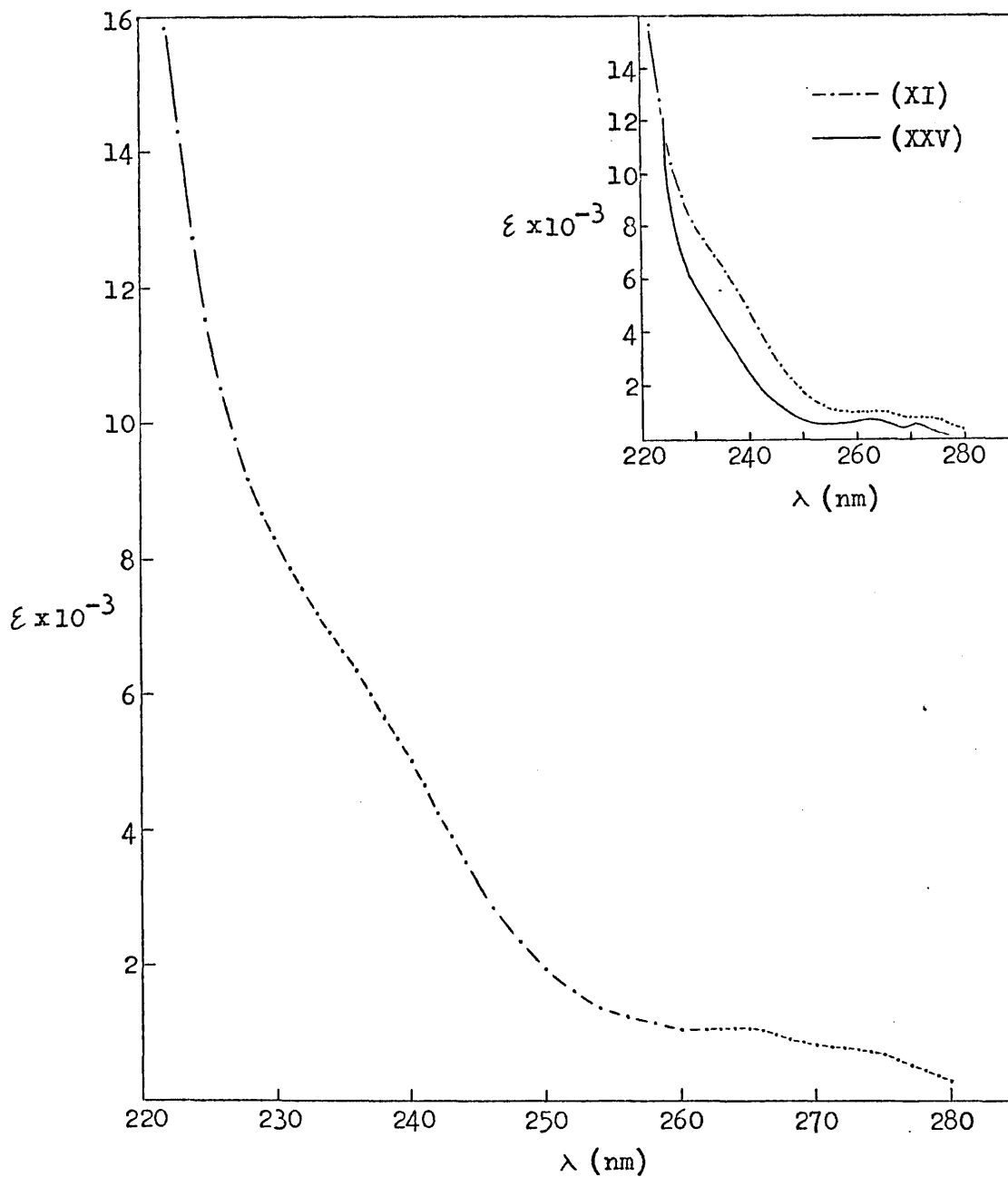
NMR spectrum of protostephanine.

are due to the eight methylene protons and according to Takeda (1963), the splitting pattern must be the A_2B_2 type although the assignment is still not clear. The singlet at δ 2.28 is attributable to the three equivalent protons of the methyl group. Since there are altogether nineteen protons in the formula and the integrated intensities of the three signals are in the ratio 8:8:3 respectively, the structure of this tertiary amine is beyond all doubt.

A comparison of the ultra-violet spectrum of 1-methyl-2,3,8,9-tetrahydro-4,5:6,7-dibenzazonine (XI) with that of 1,2,3,4-dibenzocyclonona-1,3-diene-7-carboxylic acid (XXV) shows that the



compound with a heterocyclic nine-membered ring is spectroscopically almost as conjugated as the one with a homocyclic ring of the same size (Spectrum No. 3 and Table 1). The hypsochromic shift and drop in extinction coefficient of the biphenyl conjugation band exhibited in the spectrum of the latter (inflection at 231 nm, $\epsilon = 5550$) are also observed in that of the former (inflection at ca. 235 nm, $\epsilon = 6,600$). The two inflections at $\lambda = 266$ nm ($\epsilon \approx 1,004$) and $\lambda = 274$ nm ($\epsilon = 716$) in the long wavelength region can be compared with the two bands at $\lambda_{\max} = 265$ nm and $\lambda_{\max} = 273$ nm (ϵ_{\max} , ca. 800 and ca. 600



Spectrum No. 3.

UV spectrum of 1-methyl-2,3,8,9-tetrahydro-4,5:6,7-dibenzazonine with m.p. $55-56^{\circ}$ in 96% ethanol.

Table 1.

Molar absorptivity (ϵ) of 1-methyl-2,3,8,9-tetrahydro-4,5:6,7-dibenzazone in 96% ethanol (concentration: 0.005 mole; cell thickness: 2 mm; instrument: Unicam SP 500; readings of A: ~ 0.2 to 0.7).

λ (nm)	$\epsilon \times 10^{-3}$	λ (nm)	$\epsilon \times 10^{-3}$	λ (nm)	$\epsilon \times 10^{-3}$
280	0.298	263	1.028	237	5.960
279	0.361	262	1.036	236	6.330
278	0.425	260	1.080	235	6.600
277	0.503	258	1.140	234	6.860
276	0.590	256	1.224	233	7.160
275	0.654	254	1.364	232	7.540
274	0.716	252	1.600	231	7.800
273	0.752	250	1.916	230	8.240
272	0.762	248	2.344	229	8.640
271	0.770	246	2.848	228	9.140
270	0.800	244	3.500	227	9.740
269	0.846	243	3.880	226	10.460
268	0.902	242	4.230	225	11.520
267	0.958	241	4.610	224	12.700
266	1.004	240	4.940	223	14.240
265	1.028	239	5.270	222	15.760
264	1.028	238	5.620		

λ_{inf} ca. 235 nm, ϵ_{inf} 6,600;

λ_{inf} 266 nm ϵ_{inf} 1,004;

λ_{inf} 274 nm ϵ_{inf} 716.

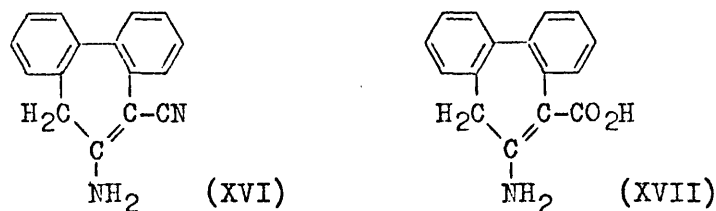
respectively) in compound (XXV).

It is obvious that the conjugation must be slightly less inhibited and the angle of torsion must be smaller in compound (XI) than in compound (XXV). Since for 2,2'-bridged biphenyls where the bridge has five or more atoms, the bridging ring is flexible and many conformations are possible, it seems that an estimation of the value of θ is devoid of significance although according to Suzuki's calculation, compound (XXV) assumed a value of $\theta = 68^\circ$.

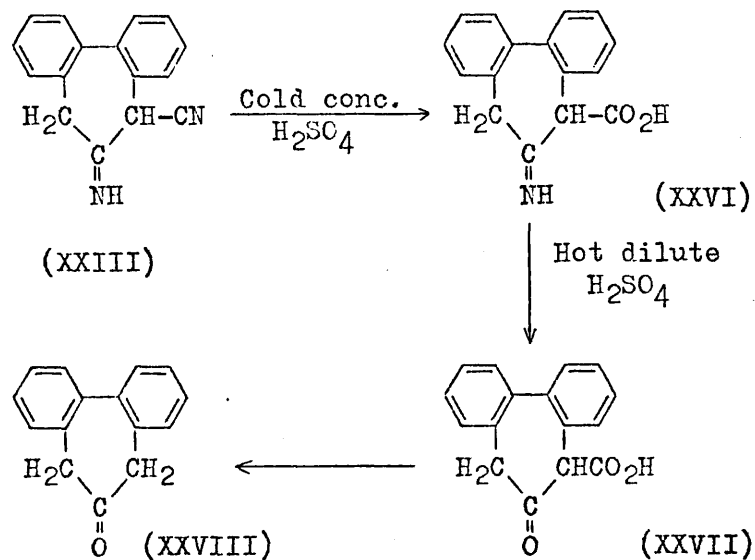
The camphorsulphonate (XIII) and the tartrate (XIV) of the tertiary amine (XI) were obtained in the respective yields of 52% and 35% by allowing the amine to react with (+)-camphor-10-sulphonic acid and (+)-tartaric acid separately in ethanol at room temperature. They were found to have m.p. $201-202^\circ$ and $118-120^\circ$ respectively. The quaternary iodide (XV) had also been obtained in 34% yield by reaction between the amine (XI) and methyl iodide in acetone. Its melting point was $168-170^\circ$.

The tertiary amine (XI) was optically activated by crystallization of its camphorsulphonate (XIII) from acetone. The base liberated from this salt had $[\alpha]_{260}^{21} + 614^\circ$ in chloroform and was optically stable at room temperature. Complete racemization was effected by heating under reflux in cyclohexane for one hour.

In the previous section (page 47), it has been mentioned that the cyclic aminonitrile (XVI) melting at 192-193° had also



been obtained by Kenner and Turner (1911) with m.p. 189° and was thought by them to be a cyclic iminonitrile (XXIII) because this structure could account fairly well for the following sequence of reactions:

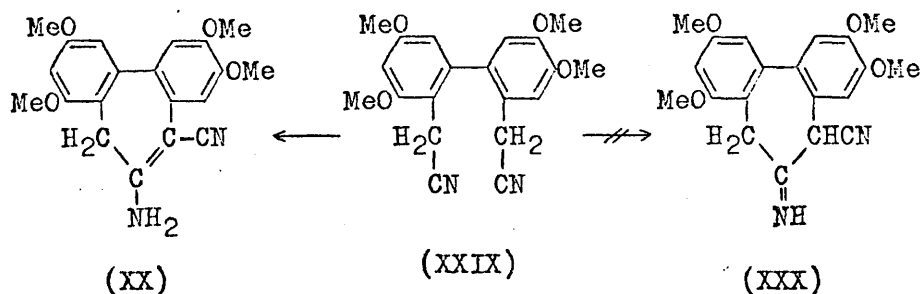


However, when the cyclic aminonitrile (XVI) was treated with cold concentrated sulphuric acid as the method used by Kenner and Turner, the acid obtained was found to have the structure (XVII) and the melting point (179°) was almost the same as that of compound (XXVI)

(m.p. 180°) obtained by Kenner and Turner. Investigation of the detailed structure about compound (XXVII) and (XXVIII) is beyond the scope of this study but the NMR and IR spectra of (XVII) will be mentioned in this section.

Since Kenner and Turner's experiment had also been performed by Bird (1953) who found that the melting point of the two compounds (XXIII) and (XXVI) were $192-193^{\circ}$ and 180° respectively, it is obvious that both the cyclic aminonitrile and the corresponding acid obtained in the present preparations are just the same compounds as those obtained by Kenner and Turner and later by Bird. We are now dealing with the position of tautomeric equilibrium rather than the assignment of an alternative structure to a reaction product. All we want to know is which tautomeric structure is more likely to fit the nitrile and which to fit the acid.

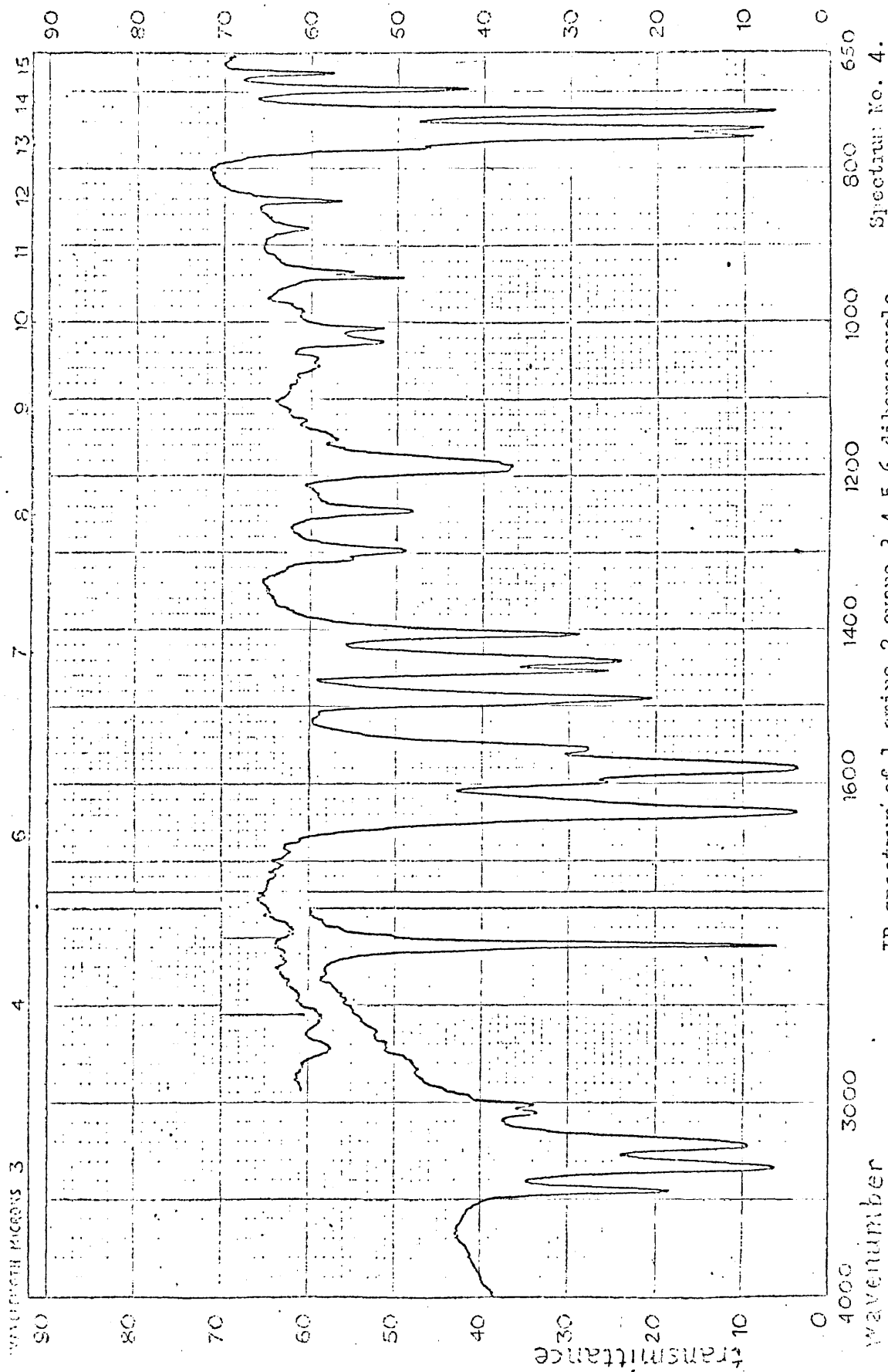
The reaction of 3,4',5,5'-tetramethoxy-2,2'-biphenyldiacetonitrile (XXIX) with a catalytic amount of sodium ethoxide in ethanol giving 6-amino-2,4,9,10-tetramethoxy-5H-dibenzo[a,c]-cycloheptene-7-carbonitrile (XX) and not compound (XXX) (Pecherer and Brossi, 1967) seems to indicate that the existence of a seven-membered



cyclic iminonitrile is open to doubt. In fact, the infra-red spectrum of compound (XX) reported to have absorption bands at 3450, 3350, 3220, 2930, 2828, 2190, 2635, 1590 and 1515 cm^{-1} can be well correlated with the absorption bands of compound (XVI) which are at 3450, 3340, 3220, 3060 (weak), 3010 (weak), 2190, 1638, 1580, 1490, 1455, 1442, 1430, 1190 and in the region 725-760 cm^{-1} (Spectrum No. 4).

Since primary amines show two absorption bands in the 3300-3500 cm^{-1} region arising from the symmetric and asymmetric N-H stretching vibrations, a third band (in some cases) in the same region due to hydrogen bonding effects and an NH_2 deformation absorption near 1650 cm^{-1} , the presence of three medium absorption bands at 3450, 3340 and 3220 cm^{-1} and a strong band at 1638 cm^{-1} in the infra-red spectrum of compound (XVI) must be a strong evidence of the presence of an NH_2 group in this compound. The band at 2190 cm^{-1} is obviously due to $\text{C}\equiv\text{N}$ absorption and the two bands at 1580 and 1590 cm^{-1} must arise from the $\text{C}=\text{C}$ stretching vibrations. The two medium absorptions at about 1455 and 1442 cm^{-1} may be attributed to a third $\text{C}=\text{C}$ absorption band as well as the CH_2 deformation vibration. The band at 1095 cm^{-1} could probably arise from the $\text{C}-\text{N}$ stretching vibration. The strong absorptions in the 725-760 cm^{-1} region must be due to ortho disubstitutions.¹⁶

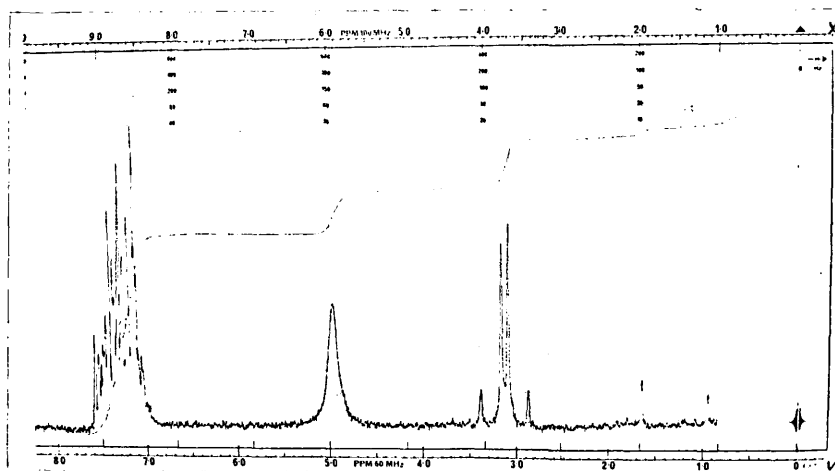
The above structural problem can also be solved on the basis of the number of signals and their relative intensities in



Spectrum No. 4.

IR spectrum of 1-amino-2-cyano-3,4,5,6-dibenzocyclohepta-1,3,5-triene with m.p. 192-193° (in KBr).

the NMR spectrum of this cyclic compound (Spectrum No. 5). As can be seen in structure (XVI), there are two protons attached to a nitrogen atom but there is no proton attached to C₂, whereas in structure (XXIII), there is one proton attached to C₂ and another one to the nitrogen atom. The NMR spectrum showed a multiplet at about δ 7-7.6 arising from the eight aromatic protons, a broad band at δ 4.97 corresponding to the two amino protons and an AB quartet at δ 2.89-3.4 ($J=12.5$ c/s) due to the two chemically equivalent but magnetically non-equivalent protons of the methylene group. The integrated intensity ratio was 8:2:2 respectively. Had the structure (XXIII) been correct, there would have had four groups of signals with an intensity ratio of 8:1:1:2.



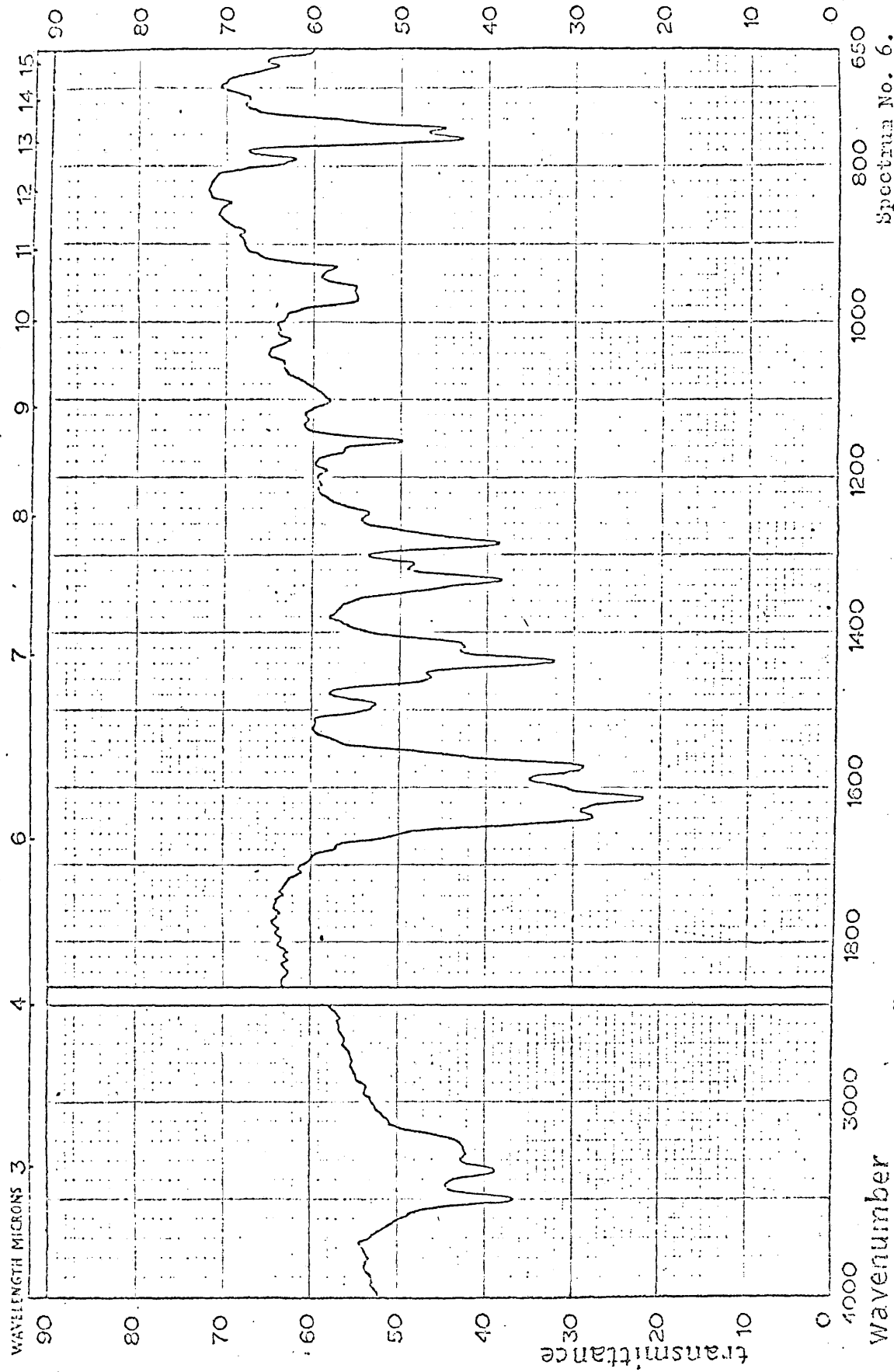
Spectrum No. 5.

NMR spectrum of 1-amino-2-cyano-3,4,5,6-dibenzocyclohepta-1,3,5-triene with m.p. 192-193°.

The infra-red spectrum of the acid (XVII) (Spectrum No. 6) seemed to retain the normal amine absorptions at 3500, 3350 and 1640 cm^{-1} as compared with the infra-red spectrum of the cyclic aminonitrile (Spectrum No. 4), but it did not exhibit the normal acid carbonyl absorption at about 1700 cm^{-1} . The presence of a medium absorption band near 1300 cm^{-1} shown by most amino-acids seemed to indicate that this compound is of the same class and the band at 1575 cm^{-1} may be attributed to the ionic carbonyl absorption, but for an amino-acid, the presence of zwitterion form should give rise to a band near 3070 cm^{-1} due to the NH_3^+ group and no band should appear in the normal 3300-3500 cm^{-1} region.

Since the infra-red spectrum of the acid did not give much evidence about its structure, further informations were sought from its NMR spectrum.

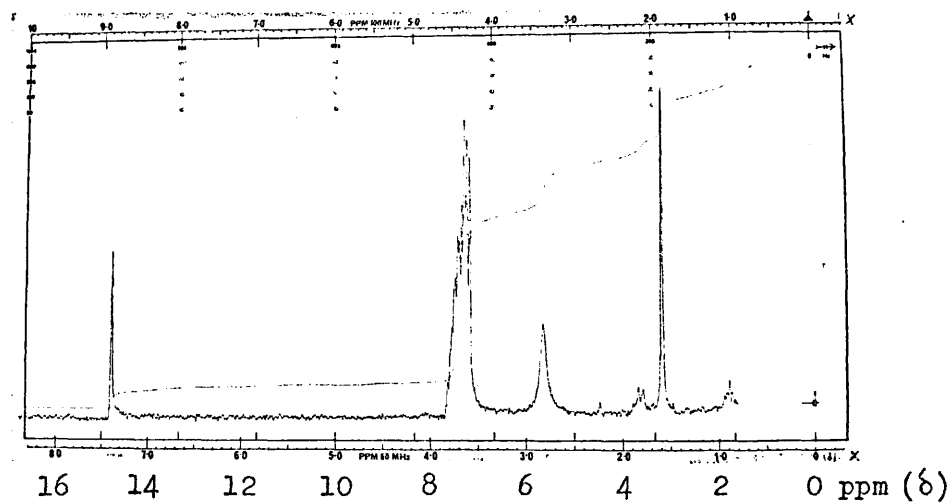
The NMR spectrum of the acid (Spectrum No. 7) revealed the presence of an amino group and an acid group. The singlet at δ 14.76 may be due to the proton of the $-\text{COOH}$ group although it appeared at a lower field position as compared with most acidic protons (δ 10.5-12). The multiplet at δ 7.0-7.63 is obviously due to the eight aromatic protons. The broad band at δ 5.6 can be well attributed to the two protons of the amino group (RNH_2 is at δ 5-9). The singlet at δ 3.13 must come from the rest of the two methylene protons although it also appears at a lower field position (PhCH_2 is at δ 2.4). Since the integrated intensities of the above signals



Spectrum No. 6.

IR spectrum of 1-amino-3,4,5,6-dibenzocyclohepta-1,3,5-triene-2-carboxylic acid with m.p. 179° (in KBr).

are also correct for 1, 8, 2 and 2 protons respectively, this acid must be compound (XVII) and not (XXVI).



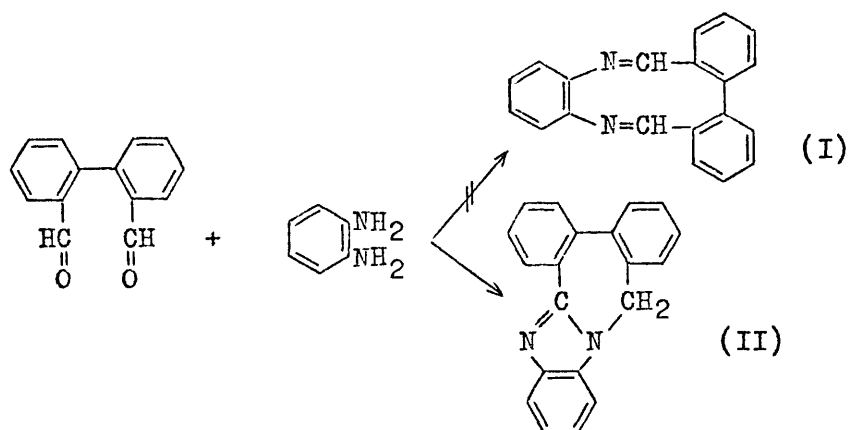
Spectrum No. 7.

NMR spectrum of 1-amino-3,4,5,6-dibenzocyclohepta-
1,3,5-triene-2-carboxylic acid with m.p. 179°
(impurities in the solvent at δ 1.8 and δ 3.7).

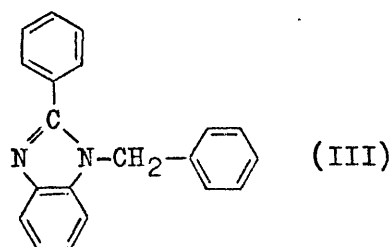
C. Formation of bridged biphenyls by amine-carbonyl condensations

a. Condensation between biphenyl-2,2'-dialdehyde and o-phenylenediamine.

Early in 1959, Sparatore had made an attempt to prepare the heterocyclic bridged biphenyl (I) by reaction between biphenyl-2,2'-dialdehyde and o-phenylenediamine in methanol at room temperature. He obtained a crystalline solid with m.p. 52-57° (could be a misprint for 152-157°) but it was thought to be the azepine (II)

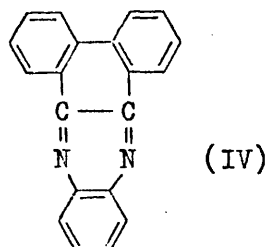


because of its basicity and because the ultra-violet spectra of this compound both in methanol and in hydrochloric acid were similar to those of 1-benzyl-2-phenylbenzimidazole (III) in the same solvents.



A few years later, Hawthorne and his co-workers (1963) reported that the crystalline solid obtained by them from this reaction was thought to exhibit dimorphism because they had isolated two different interconvertible crystal forms (rhomboid, m.p. 188-191^o; needle, m.p. 189-192^o). Their infra-red spectra were different from each other as nujol mulls but identical in carbon disulfide. The compound was proved to have the structure (II) rather than (I) by its NMR spectrum (two aliphatic protons at τ 5.03).

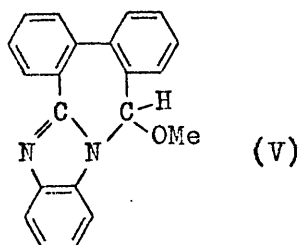
Condensation between biphenyl-2,2'-dialdehyde and *o*-phenylenediamine was also performed by Prakobsantisukh (1964) with ethylene glycol as a solvent at 160^o. She obtained a mixture of two compounds: one was water soluble and melted at 227-230^o but it was insufficient for analysis; another was water insoluble and had m.p. 158-159^o. The ultra-violet spectrum of the latter in methanol (λ_{\max} 298 nm, $\log \epsilon$ 4.164; λ_{\max} 258 nm, $\log \epsilon$ 4.155) was almost identical with that of Sparatore's compound and the picrate (m.p. 279-280^o) prepared from it could be said to have the same melting point as the picrate (m.p. 278-280^o) prepared by Sparatore. However, when the reaction was carried out in methanol, she obtained two solids with m.p. 189-191^o and 216-219^o. The high melting solid was identified as the quinoxaline (IV) by comparison of its infra-red spectrum with that of the known specimen and by mixed melting point (219-221^o). She did not give any comment about the solid with m.p. 189-191^o or come to a conclusion about the structure of

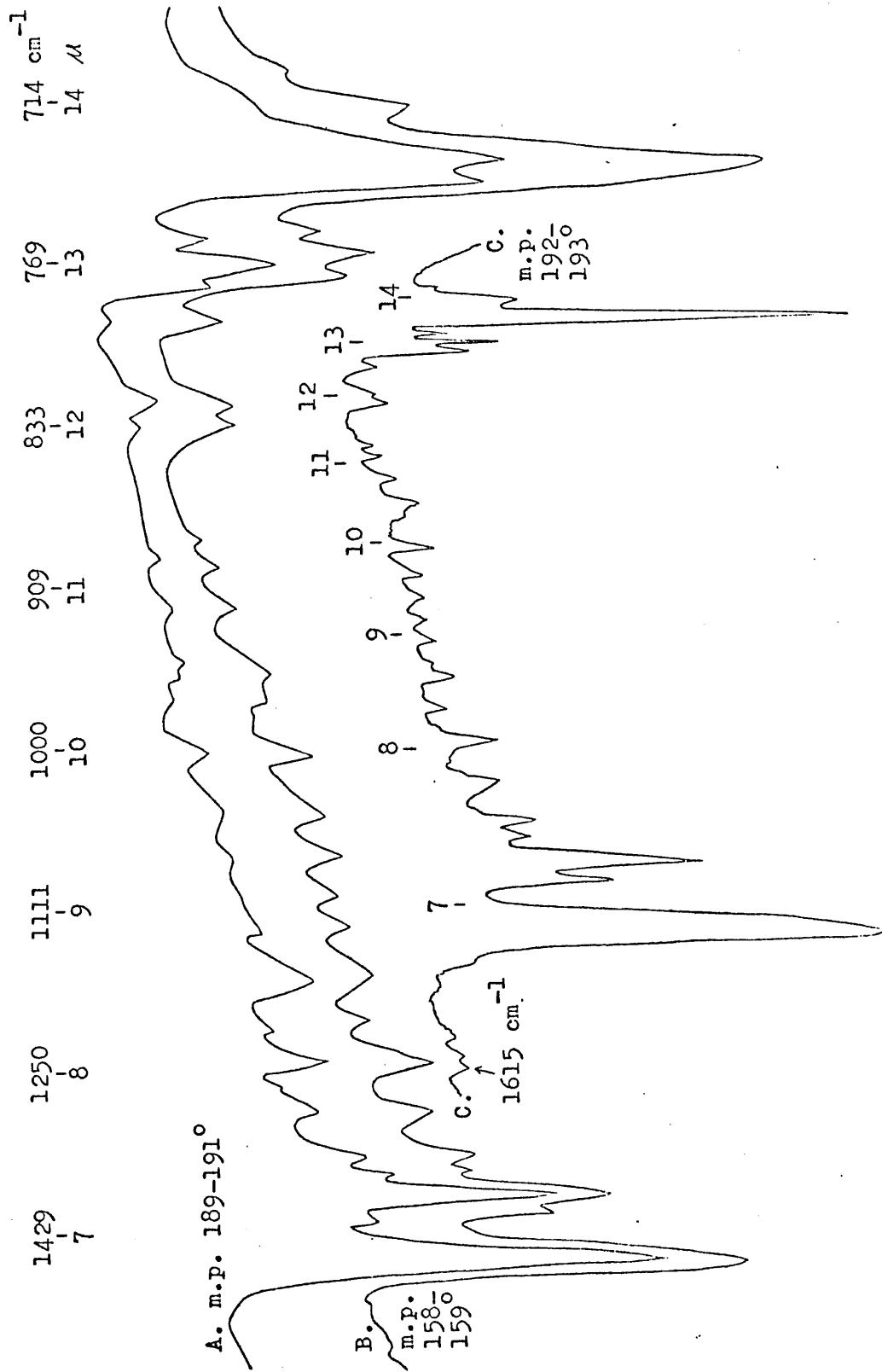


the compound with m.p. 158-159°. She had obtained the infra-red spectra of these two compounds but did not notice that they were almost superimposable (see Spectrum No. 8 A & B).

Bindra and Elix (1969), in an attempt to obtain (I), and in ignorance of Sparatore's and other workers' experiments, also showed that the condensation product was (II) with m.p. 160° when biphenyl-2,2'-dialdehyde and *o*-phenylenediamine were allowed to react in acetic acid or benzene at room temperature. They proved that the reaction involved an intermolecular hydride shift by treatment of *o*-phenylenediamine with equimolar proportions of biphenyl-2,2'-dialdehyde and biphenyl-2,2'-dideuteroaldehyde.

However, when methanol was used as a solvent, they obtained a pale yellow solid with m.p. 155° in 90% yield. It was found to contain approximately 80% of (II) and 20% of (V) which could not be





Spectrum No. 8. IR spectra of 15H-dibenzo[ε,ε]benzimidazo[1,2-a]azepine (in nujol)

separated by preparative TLC. Its NMR spectrum exhibited additional singlets at δ 6.44 (τ 3.56, 1H, methine proton) and δ 3.09 (τ 6.91, 3H, OMe protons) besides the signals corresponding to those of compound (II).

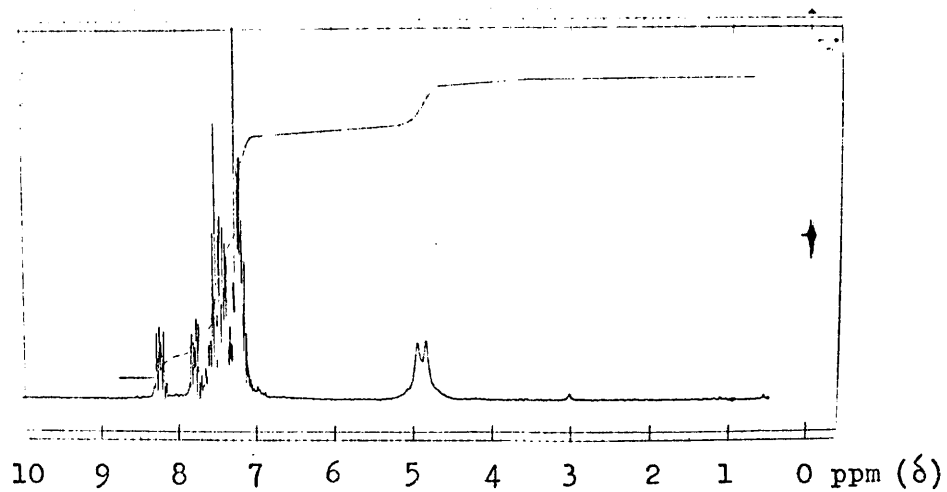
The elimination of (I) as a possible structure for the condensation product left no room for argument. The ultra-violet absorption spectrum of the compound with m.p. 160° obtained in ethanol by Bindra and Elix was found to have λ_{\max} 230 nm, $\log \epsilon$ 4.43; λ_{\max} 260, $\log \epsilon$ 4.3 and λ_{\max} 300, $\log \epsilon$ 4.28 which were very close to the values recorded by Prakobsantisukh and hence by Sparatore. However, when the NMR spectrum of Bindra and Elix's compound (m.p. 160°) was concerned, the chemical shift of the two aliphatic protons was not consistent with the value reported by Hawthorne and his co-workers. According to Bindra and Elix, the spectrum exhibited signals at δ 8.07-8.3 (τ 1.70-1.93, 1H), δ 7.25-8.00 (τ 2.00-2.75, 11H) and "an AB double doublet at δ 6.58, 4.78 (τ 3.42, 5.22; $J = 15$ Hz, 2H)".

In order to confirm the structure of this condensation product and to obtain its NMR spectrum for comparison purpose (see page 76), biphenyl-2,2'-dialdehyde and *o*-phenylenediamine were once and again allowed to react in methanol at room temperature. The product obtained was chromatographed on neutral alumina and then recrystallized from aqueous ethanol to give colourless prisms in 82% yield. Its melting point was $192-193^{\circ}$.

When the reaction was carried out in ethanol and the product recrystallized from aqueous ethanol without a beforehand purification by chromatography, the crystalline solid was obtained in 66% yield and had m.p. 154-157°. A portion of this solid turned out to have m.p. 192-193° when recrystallized from the same solvent and could not be brought back into the low melting form by further crystallization. The other portion also turned out to have m.p. 189-191° on storage for a few weeks.

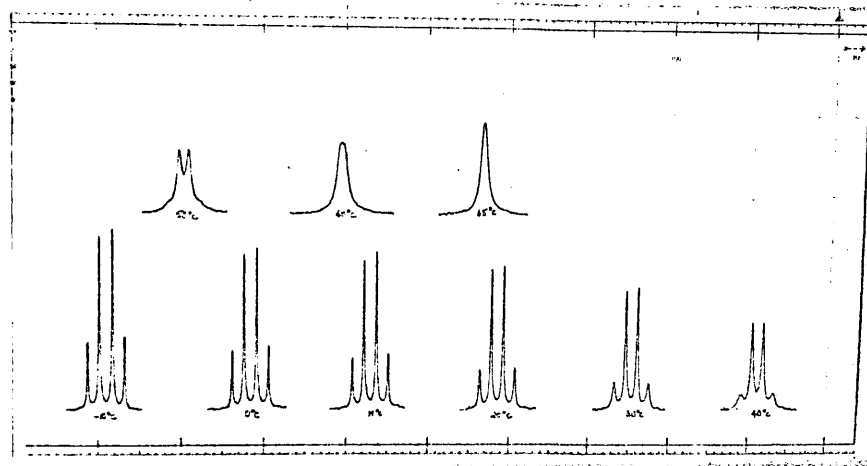
The infra-red spectra of these condensation products obtained both from methanol and ethanol were superimposable on each other irrespective of their difference in melting points. They were also identical with the infra-red spectra of the two solids with m.p. 158-159° and m.p. 189-191° obtained by Prakobsantisukh (see Spectrum No. 8). Hence all condensation products with the molecular formula $C_{20}H_{14}N_2$ ought to have the same structure.

The NMR spectrum of the present compound with m.p. 192-193° (Spectrum No. 9A) was run at 100 Mc/s with $CDCl_3$ as solvent. The two multiplets centred at about δ 7.8 and δ 8.2 could be due to each of the two aromatic protons ortho to nitrogen since their splitting pattern closely resemble each other and are consistent with those of the signals arising from the protons ortho to nitrogen (see Spectrum No. 10B and No. 20B). Their integrated intensities are in the ratio of 1:1 corresponding to a total of two protons. The overlapping lines in the region δ 7.1-7.7 are obviously due to the rest



Spectrum No. 9A.

NMR spectrum of 15H-dibenzo[c,e]benzimidazo-[1,2-a]-azepine with m.p. 192-193° (probed at about 50°C). The signal centred at δ 4.92 becomes a singlet at higher temperatures and an AB quartet at lower temperatures (following spectrum).



Spectrum No. 9B.

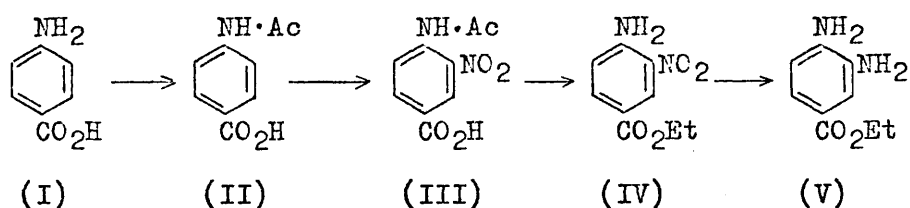
Probe temperatures: 50°, 60°, 65° (top), -10°, 0°, 10°, 20°, 30° and 40°C (bottom, left to right).

of the aromatic protons. They are subdivided into two groups and the integrated intensity is correct for ten protons. The signal centred at δ 4.92 has an intensity ratio corresponding to two protons and must be due to the two methylene protons. On elevation of probe temperature, they gave rise to a singlet. When the temperature was decreased to 30°C or lower, they showed a typical AB quartet ($J_{AB} = 14$ c/s; Spectrum No. 9B). The considerable line broadening feature seems to indicate that the two protons are intermediate between magnetically equivalent and nonequivalent states.

As it can be seen, the chemical shift of the two methylene protons is very close to the value reported by Hawthorne and his co-workers but different from those reported by Bindra and Elix. However, since the present NMR spectrum seems to account fairly well for the structure (II), a summary may be made at this stage: Condensation between biphenyl-2,2'-dialdehyde and *o*-phenylenediamine at room temperature in methanol, ethanol, benzene, acetic acid and at 160° in ethylene glycol gave 15H-dibenzo[c,e]benzimidazo[1,2-a]azepine (II) as a main product with m.p. 192-193°. Its metastable form had m.p. 159-160°. The by-product 15-methoxydibenzo[c,e]benzimidazo[1,2-a]azepine (V) with m.p. 100° had been obtained when methanol was used as a solvent and in the presence of sodium methoxide (5%), it was isolated as a main product in 34% yield (Bindra and Elix's report). The quinoxaline (IV) was once obtained from the reaction mixture by Prakobsantisukh but nothing more is known about her water soluble product with m.p. 227-230°.

b. Condensation between biphenyl-2,2'-dialdehyde and ethyl 3,4-diaminobenzoate.

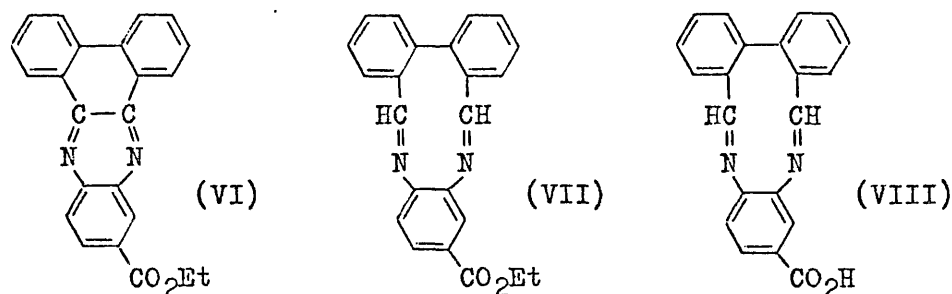
Closely related to the condensation between biphenyl-2,2'-dialdehyde and *o*-phenylenediamine was the condensation between biphenyl-2,2'-dialdehyde and ethyl 3,4-diaminobenzoate (V) which was obtained from *p*-aminobenzoic acid (I) according to the following reaction process:



p-Aminobenzoic acid (I) was converted into *p*-acetamidobenzoic acid (II) in 80% yield by heating under reflux with acetic acid and acetic anhydride. The product was then added to fuming nitric acid at low temperature to give *m*-nitro-*p*-acetamidobenzoic acid (III) in 74% yield. Reaction between the acid (III) and ethanol in the presence of hydrochloric acid gave a 62% yield of ethyl *m*-nitro-*p*-aminobenzoate (IV) which was reduced with stannous chloride in concentrated hydrochloric acid to give the ethyl 3,4-diaminobenzoate (V). The yield was 42%.

The condensation between biphenyl-2,2'-dialdehyde and ethyl 3,4-diaminobenzoate had also been performed by Prakobsantisukh (1964). She allowed the two reactants to react in ethanol at room temperature. The product obtained was a mixture of two compounds

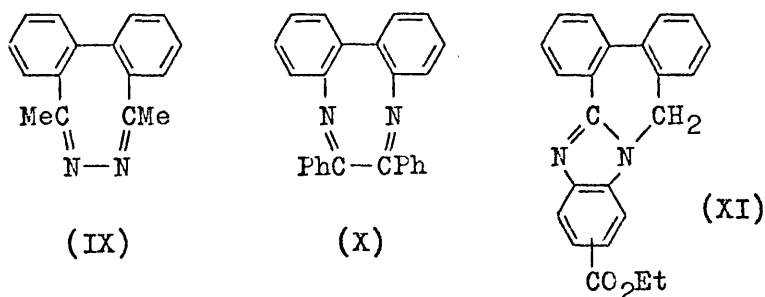
with m.p. 214-215° and 226°. The low melting compound was identified as the quinoxaline (VI) by comparing its infra-red spectrum with that of the authentic sample and by mixed melting point (214-216°). The high melting one was thought by her to be the compound (VII) because of the presence of a "strong" C=N peak at 1613 cm⁻¹ in its infra-red spectrum and on subsequent hydrolysis, it gave an acid with empirical formula C₂₁H₁₄N₂O₂ thought to be the corresponding acid (VIII).



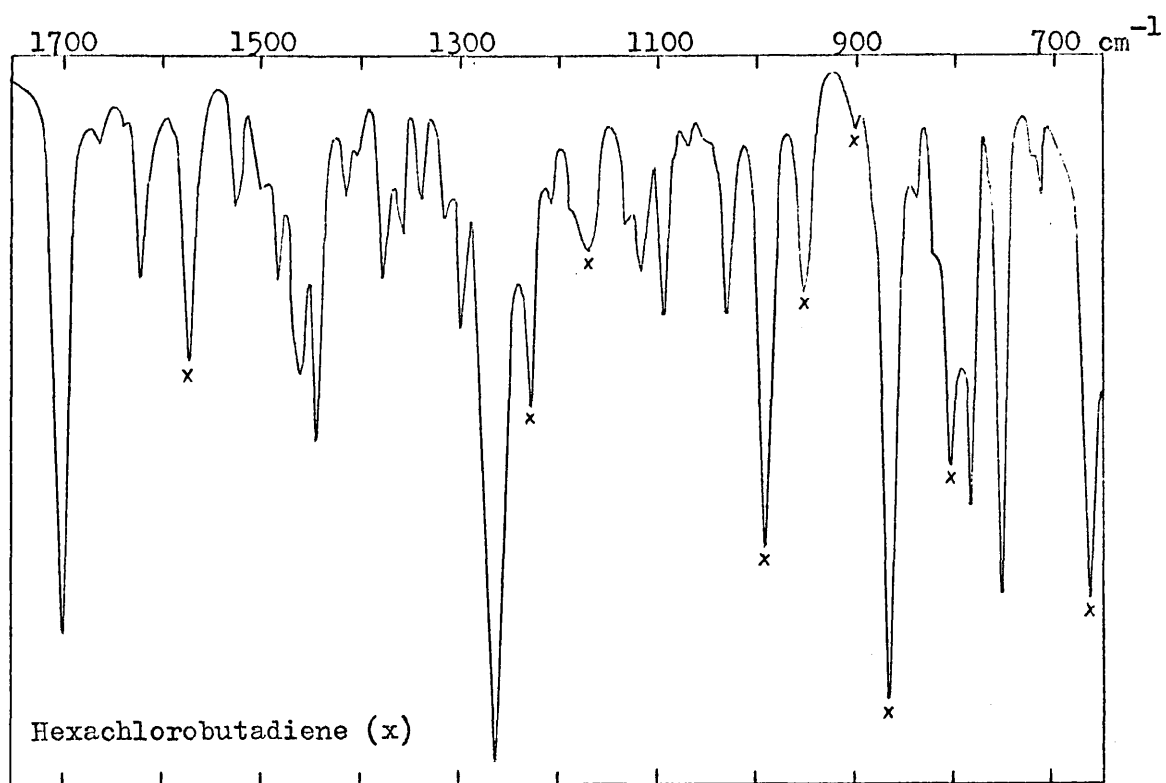
Since Prakobsantisukh did not produce any evidence in support of structure (VIII), it meant that the structure of her condensation product with m.p. 226° remained to be proved. In view of the fact that the condensation between biphenyl-2,2'-dialdehyde and *o*-phenylenediamine had given the azepine (structure II, page 67) as a main product, it was decided to repeat her experiment at the same time and prove the structure of the product by comparison of its spectra with those of the azepine if possible.

As it was expected, the reaction between biphenyl-2,2'-dialdehyde and ethyl 3,4-diaminobenzoate in ethanol at room

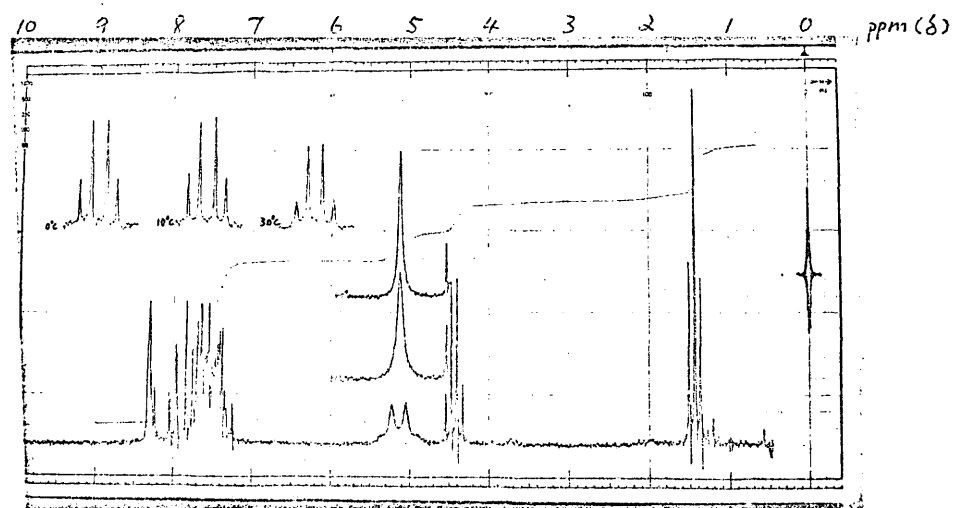
temperature gave a solid with m.p. 228-229°. Its infra-red spectrum was identical with that of the compound with m.p. 226° obtained by Prakobsantisukh. It showed the C=O and C-O stretching frequencies of the ester of an aromatic acid at 1695 cm⁻¹ and 1260 cm⁻¹ respectively and a weak band rather than a strong band at about 1618 cm⁻¹ (Spectrum No. 10A). The presence of this weak band seemed to be indicative of the presence of the C=N group in the condensation product as compared with the C=N stretching absorptions of the 3,8-dimethyl-4,5:6,7-dibenzo-1,2-diazocine (IX) at 1610 cm⁻¹ (Bacon and Lindsay, 1958) and the 5,6:7,8-dibenzo-1,4-diazocine (X) at 1616 cm⁻¹ (Bacon and Bankhead, 1963) although the infra-red spectrum of the azepine (see page 70) showed only a very weak band at about



1615 cm⁻¹. However, the intensity of this band could hardly show whether the compound involves a C=N double bond as in structure (XI) or two C=N double bonds as in structure (VII) because in a variety of aromatic compounds with two C=N groups, this C=N absorption band had been observed to vary from an intense sharp peak to a broad weak hump (Bacon and Lindsay, 1958).



Spectrum No. 10A



Spectrum No. 10 B.

IR (A; in hexachlorobutadiene) and NMR (B) spectra of 12(or 11)-carbethoxy-15H-dibenzo-[c,e]benzimidazo[1,2-a]azepine with m.p. 228-229°.

A comparison of its NMR spectrum (Spectrum No. 10B) with that of the azepine (Structure II, page 67, Spectrum No.9A) provided a clear view about its structure. It showed absorption lines similar to those of the azepine except the presence of two additional signals arising from the protons of the ethyl group and hence it ought to be the 12(or 13)-carbethoxy-15H-dibenzo[c,e]-benzimidazo[1,2-a]azepine (XI) but not the diazecine (VII).

In the NMR spectrum of compound (XI), the triplet and the quartet centred at δ 1.44 and δ 4.43 have a common line separation of 7 c/s. The intensities of these multiplets are in the ratio of 3:2 and those of the individual lines within each multiplet are approximately 1:2:1 and 1:3:3:1 respectively. Since the splitting pattern belongs to A_2X_3 type, these signals must arise from the protons of the ethyl group. The low field shift of the methylene protons can be accounted for by its being attached to a strongly deshielding arylcarbonyloxy group $Ar.CO.O-$ which is expected to shift an attached methylene protons to about δ 4.33.

The multiplet at δ 8.3 may arise from the two protons both ortho to nitrogen. This is consistent with the total shift in position of benzene proton (δ 7.23) caused by the ortho-substituted $-COOR$ (+ δ 0.8) and an ethylenic skeleton $-CH=$ (+ δ 0.2). The integrated intensity is correct for two protons. The two doublets near δ 8.0 could be due to the ring proton ortho to the $-OOC_2H_5$ group since they appeared in a lower field position and the integrated

intensity is correct for one proton.

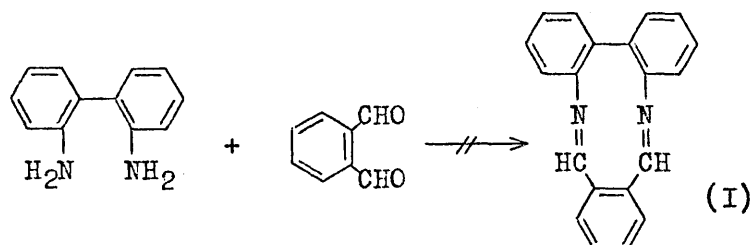
The absorption lines gathered in the region δ 7.3-7.9 must be attributed to the hydrogen atoms in the biphenyl nucleus. They have an intensity ratio corresponding to eight protons.

The two broad peaks at δ 5.23, 5.05 are obviously due to the two methylene protons of the bridging ring. The integrated intensity is correct for two protons. They gave rise to a singlet at 50° (probe temperature) or higher but appeared as a quartet ($J_{AB} = 14$ c/s) at 30° or lower. This is exactly the situation we have seen in the NMR spectrum of the azepine mentioned at page 74).

There was no compound like (VI) or any other by-product obtained in the present condensation reaction. The formation of (VI) seemed to be unlikely since the mother liquor gave only an additional crop of (XI) after passing through a column of neutral alumina.

c. Condensation between 2,2'-diaminobiphenyl and o-phthalaldehyde.

A few years before the report of Sparatore's experiment (page 67), Blood and Noller (1957) had carried out the condensation between 2,2'-diaminobiphenyl and o-phthalaldehyde under a variety of conditions hoping to obtain the 2,3:4,5:8,9-tribenzo-1,6-diazacyclodecapentaene (I). They found that the reaction proceeded



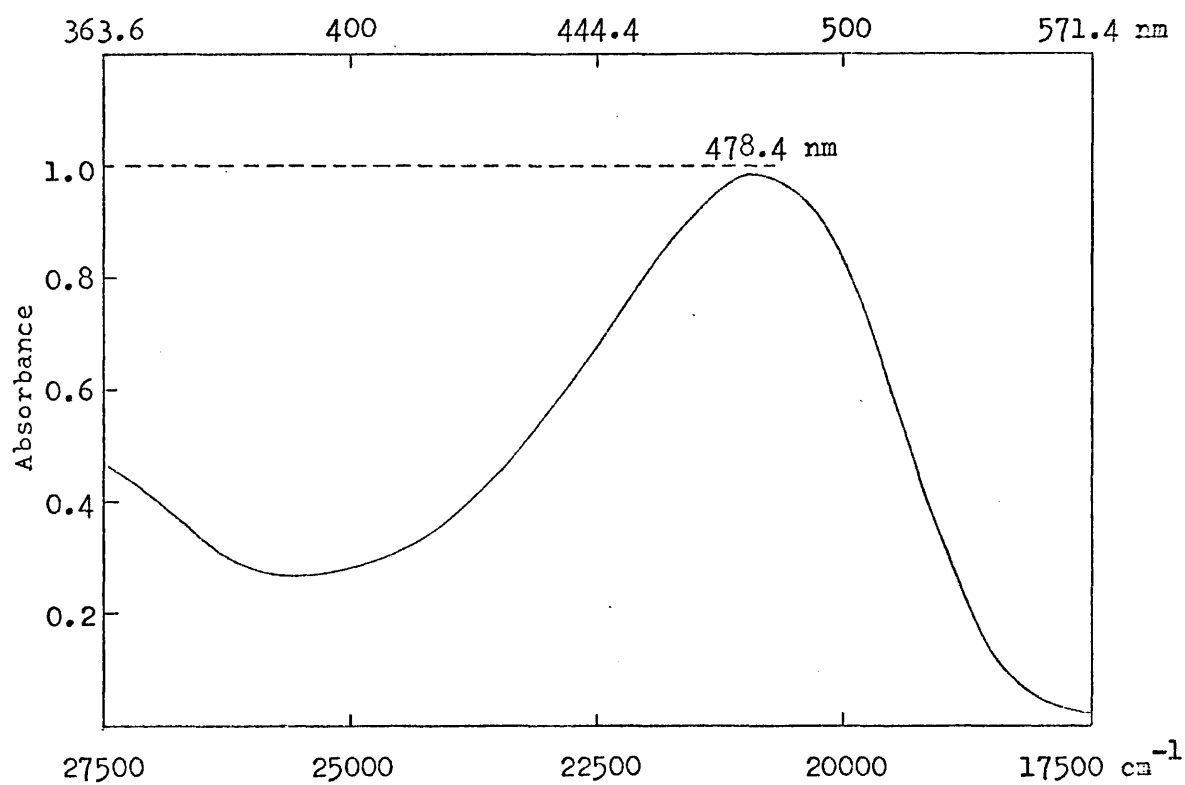
very rapidly in methanol and ethanol but slowed down in 1-butanol and benzene. When a moderately concentrated solution was employed, it gave an amorphous red solid which decomposed over the range 142-160°. When the two reactants (1.2 g of diamine and 0.7 g of dialdehyde) were dissolved separately in ethanol (100 ml for each) and added slowly (0.52 ml per hour) to a large quantity of boiling ethanol (500 ml), the product obtained was a red oil which resisted crystallization after being chromatographed on activated alumina with methylene chloride as an eluent. A further washing of the column with the same solvent gave a small amount (0.006 g) of yellow crystals with m.p. 233-236°. Its infra-red spectrum (in KBr) showed absorptions at 2898, 1658, 1613, 1587, 1527, 1483, 1429,

1364, 1273, 1092, 1018, 950, 943, 885, 864, 840, 823, 800, 743 and 712 cm^{-1} , but attempts to prepare more of this solid proved unsuccessful.

In another preparation, about two times the above quantities of reactants were dissolved separately in equal amounts of ethanol (100 ml for each) and added to 3 l of boiling ethanol at a rate of 0.27 ml per hour. The product was still obtained as an amorphous solid after chromatographic purification and decomposed over the range $123\text{--}205^{\circ}$. Its infra-red spectrum (in KBr) had absorptions at 3390, 2907, 1700, 1634, 1475, 1438, 1300, 1184, 1041, 978, 753 and 694 cm^{-1} .

The above condensation products were thought to be some sort of polymers by Blood and Noller and were not investigated any further.

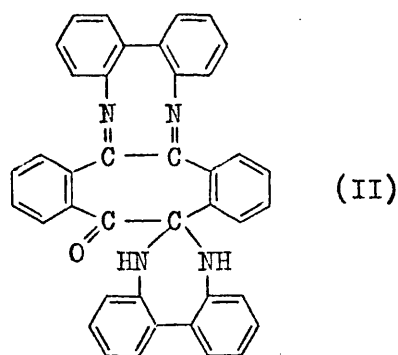
In the present experiment, it was found that a red crystalline solid could be readily obtained in 53% yield if the two reactants were dissolved separately in a minimum amount of ethanol and allowed to react at room temperature. The solid had m.p. $253\text{--}254^{\circ}$ after recrystallization from ethyl acetate and had a strong carbonyl absorption at 1690 cm^{-1} in its infra-red spectrum (see page 93) which was absent from this region of the infra-red spectrum of Blood and Noller's yellow compound with m.p. $233\text{--}236^{\circ}$. Its visible spectrum showed a strong absorption band at $\lambda_{\text{max}} = 478.4\text{ nm}$ with $\log \epsilon_{\text{max}} = 4.17$ in ethanol (Spectrum No. 11). The molecular formula



Spectrum No. 11.

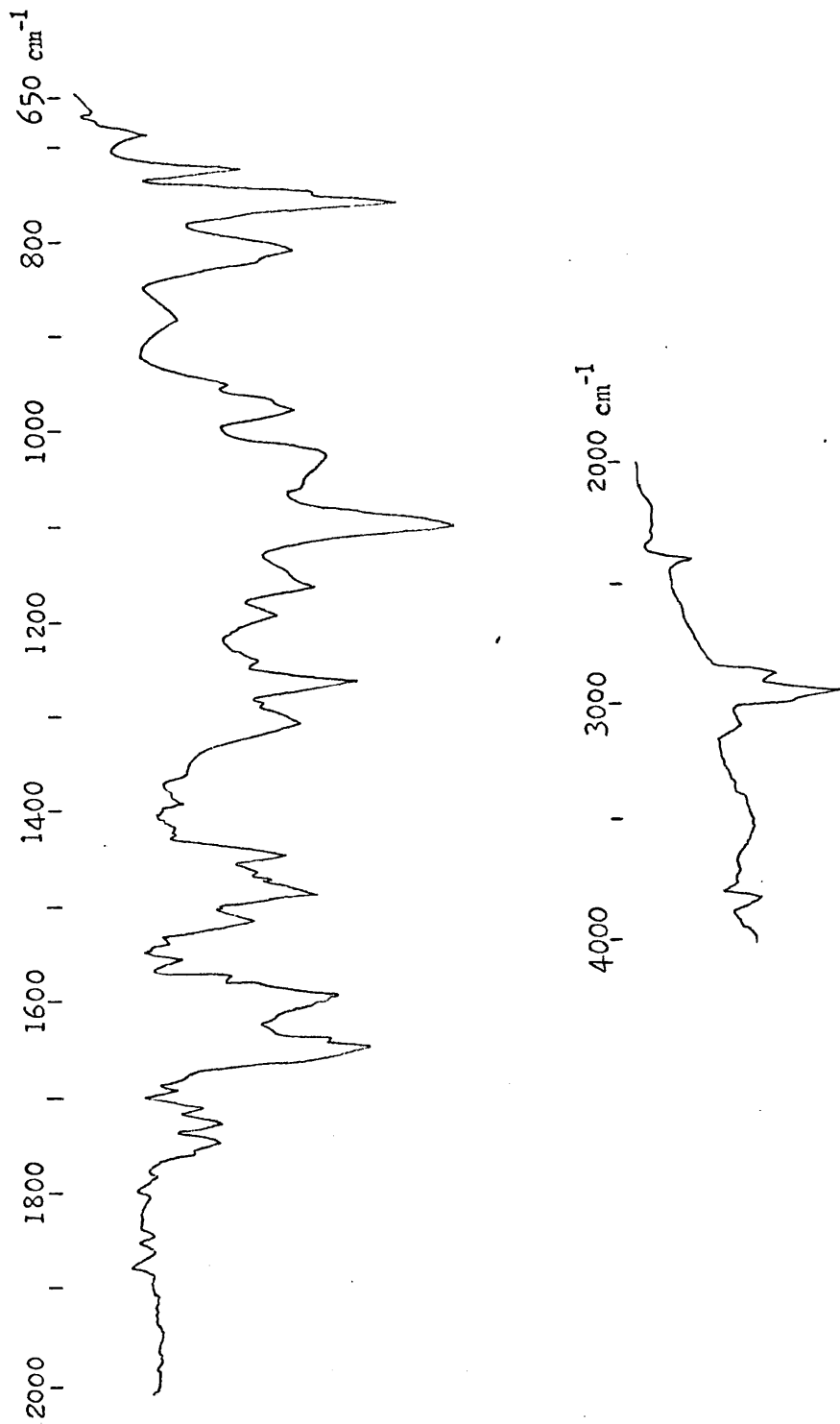
Visible spectrum of the red compound
with m.p. 253-254° (in 95% ethanol).
Cell thickness: 0.2 cm; concentration:
 3.32×10^{-4} mole/l.

of this red compound was found to be $C_{40}H_{26}N_4O$ by exact mass measurement of the molecular ion (measured mass = 578.2096; calculated mass = 578.2108) as well as by calculation from the molecular weight and the result given by quantitative elemental analysis. It was thought to have the structure (II) as discussed on page 92. It



was partially resolved by chromatography on cellulose-2 $\frac{1}{2}$ -acetate and was found to have very high optical stability (see page 165). The treatment of this red compound with a dehydrating agent (p-toluenesulfonic acid) has brought about a complete removal of the carbonyl absorption band from the infra-red spectrum of the reaction product (Spectrum No. 12) but the latter has not yet been investigated.

Condensation between biphenyl-2,2'-dialdehyde and o-phthalaldehyde also gave an amorphous solid as a by-product when the mother liquor was evaporated to dryness and the residue chromatographed on neutral alumina with sodium dried ether as an eluent. It could be recrystallized from ethanol-petroleum ether (b.p. 60-80°) to give yellowish red crystals with m.p. 166-168°. Its IR

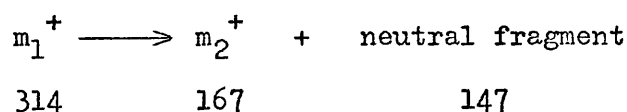


Spectrum No. 12. IR spectrum of the reaction product of the red compound (m.p. 253-254°) and p-toluenesulfonic acid (in KBr).

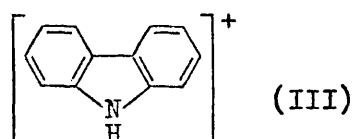
spectrum also showed a carbonyl absorption at about 1700 cm^{-1} (Spectrum No. 13) but the rest of the absorption bands were quite different from those of Blood and Noller's compound with m.p. 123-205°. The presence of two bands in the NH stretching region ($3300\text{--}3500\text{ cm}^{-1}$) seemed to indicate that the compound was a primary rather than a secondary amine.

The mass spectroscopic determination of the molecular weight of this compound had given the possible formula $\text{C}_{20}\text{H}_{14}\text{N}_2\text{O}_2$ (measured mass = 314.1057; calculated mass = 314.1055) which fitted with the results obtained from elemental microanalysis (see page 163).

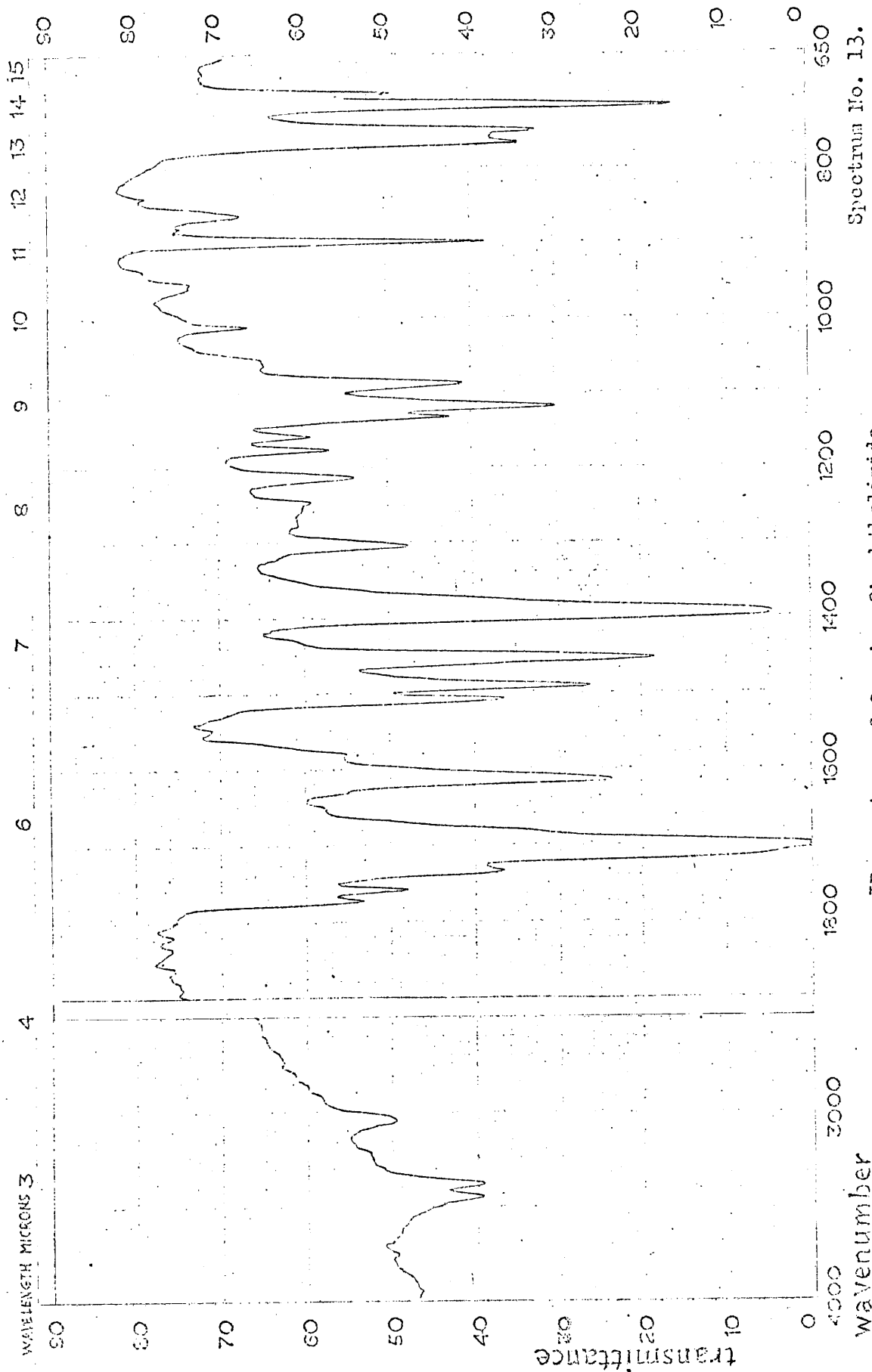
In the mass spectrum of this compound (Spectrum No. 14), the molecular ion peak appeared to be at $m/e = 314$. The prominent metastable peak at $m/e = 88.9$ was evidence for the following transition:



The mass measurement of the ion with $m/e = 167$ gave the formula $\text{C}_{12}\text{H}_9\text{N}$ (measured mass = calculated mass = 167.0735) suggesting that it could be the carbazole ion (III).

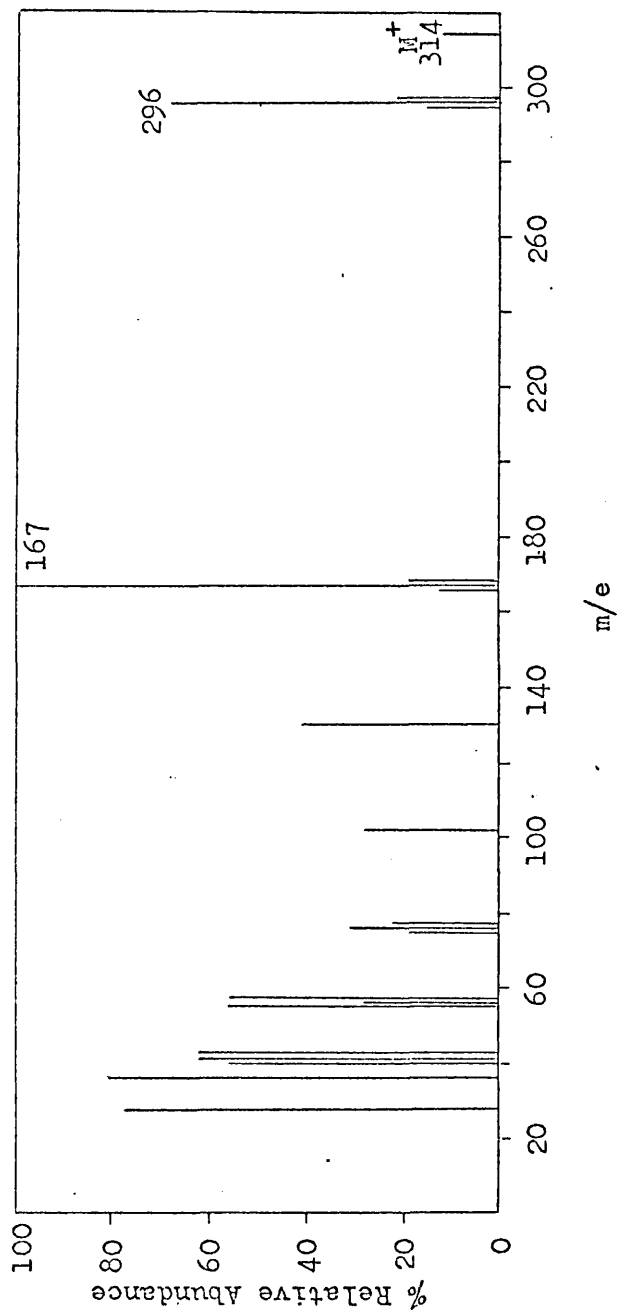


Similarly, the metastable peak at $m/e = 294$ indicated that the ion corresponding to the peak at $m/e = 296$ involved a labile hydrogen atom and that the following transition had occurred:



Spectrum No. 13.

IR spectrum of 2-amino-2'-phthalimido-biphenyl with m.p. 166-168° (in KBr).



Additional peaks arising from traces of air in the instrument: Metastables:

88.9

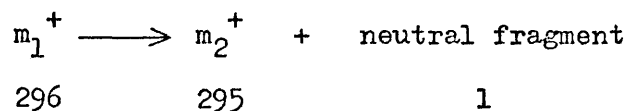
m/e = 18 28 32 44

165

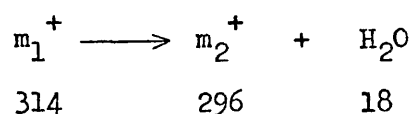
H₂O N₂ O₂ CO₂

294

Spectrum No. 14. Mass spectrum of 2-amino-2'-phthalimidobiphenyl with m.p. 166-168°

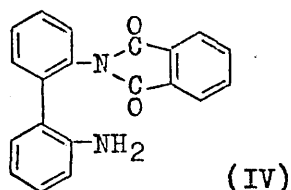


However, the peak at $m/e = 296$ seemed to be arisen from some contaminant because there was no metastable peak corresponding to the following transition and it resulted in differing 314/296 ratio



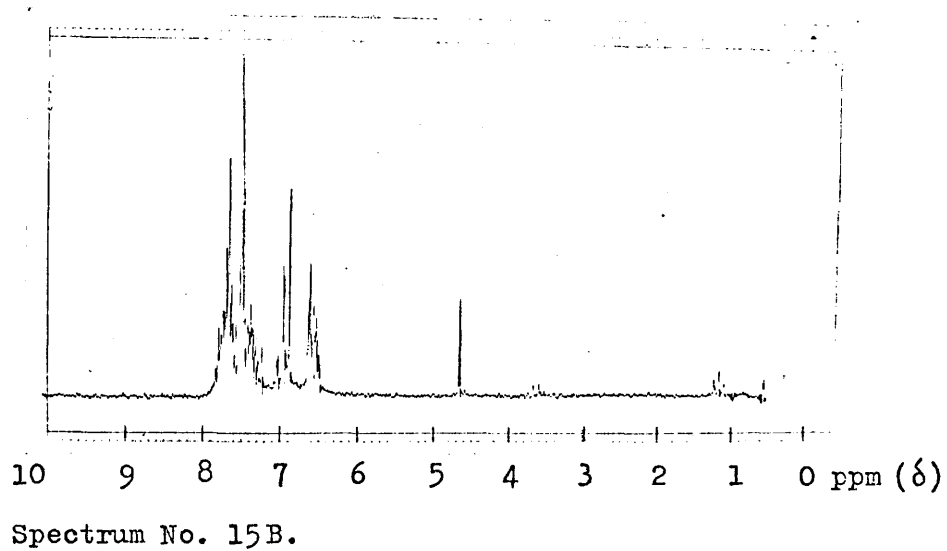
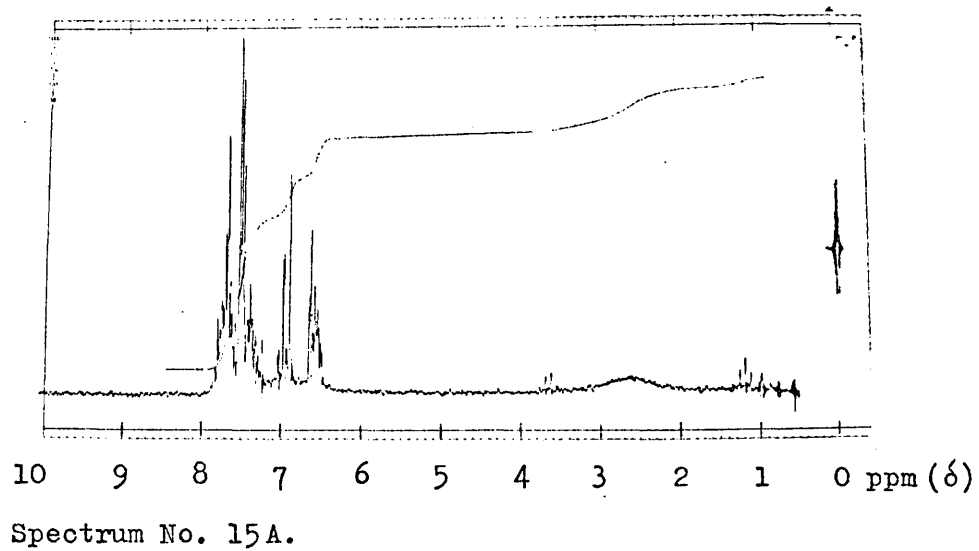
when the sample was run at different temperature.

In conjunction with some of the features in the above infrared spectrum, it was thought that the by-product could be 2-amino-2'-phthalimidobiphenyl (IV).



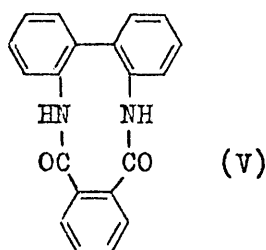
A study of its NMR spectrum proved that the structure (IV) was consistent with the observed feature (Spectrum No. 15 A) as interpreted below. The intensities of the signals in the region δ 2.1-3.1 and at δ 6.5-6.67, 6.9-7.1, 7.2-7.6 and 7.6-7.9 are in the ratio of 1:1:1:2:2 respectively. Since there are altogether 14 protons in the formula, a unit in the ratio should therefore correspond to 2 protons.

The hump at δ 2.1-3.1 was removable by deuteration with



NMR spectra of 2-amino-2'-phthal-
imidobiphenyl with m.p. 166-168°.

D₂O (Spectrum No. 15 B) and was likely to arise from the two -NH₂ protons but not the two -NH protons adjacent to the two carbonyl groups as in structure (V) since the -NH proton in 4-methylbenzanilide is at δ 9.45 (page 108).



The multiplet at δ 6.5-6.67 could be due to the two ring protons ortho and para to the -NH₂ group as the shifts of benzene protons (δ 7.27) in these positions caused by the substituent are about - δ 0.8 (ortho) and - δ 0.4 (para). Similarly, the other multiplet at δ 6.9-7.1 could be due to the two ring protons ortho and para to -N(CO)₂Ar group as compared with the shifts of benzene protons to + δ 0.4 (ortho) and - δ 0.3 (para) caused by the substituted -NH·CO·R group.

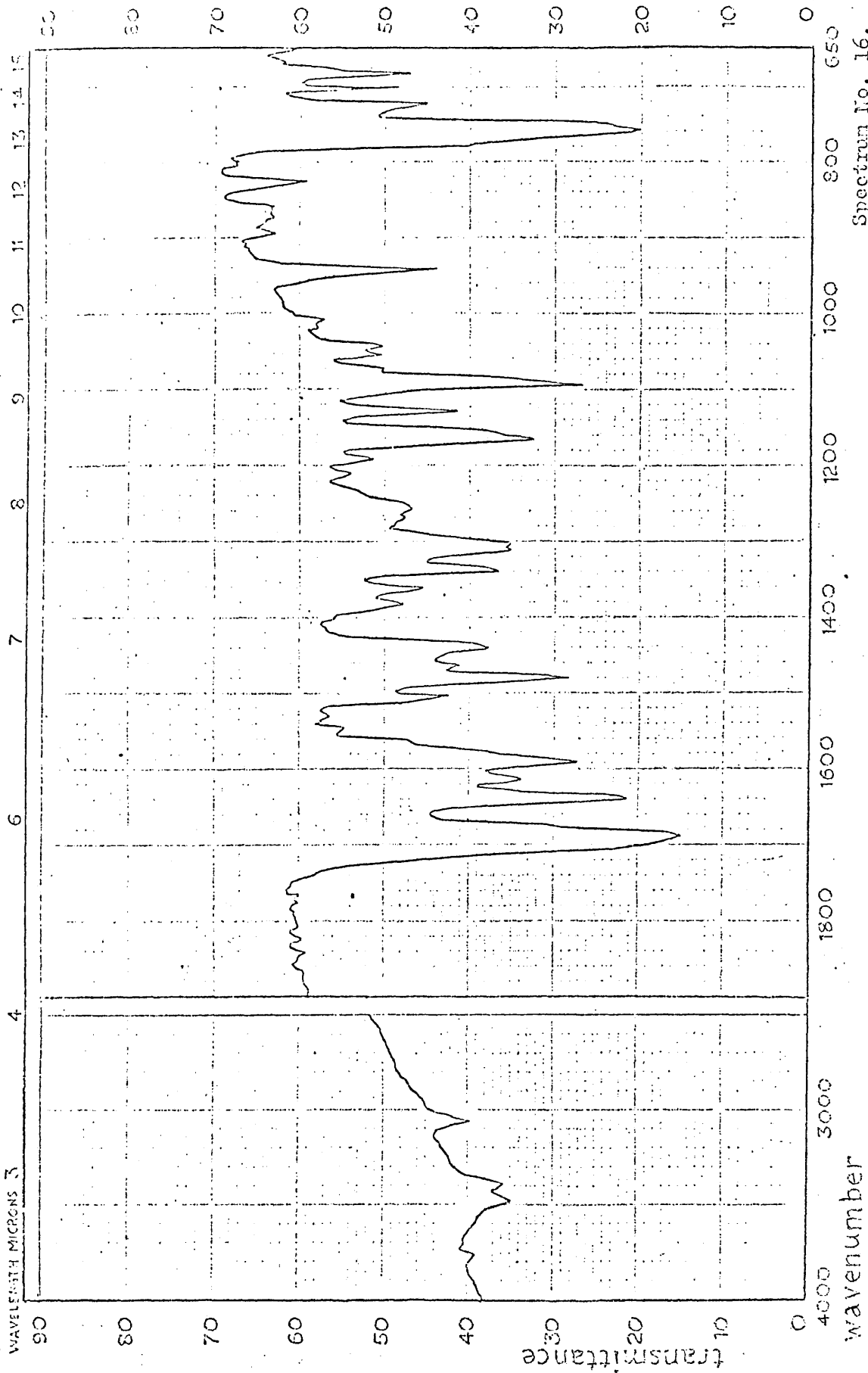
The absorption lines at δ 7.6-7.8 may arise from the four ring protons ortho and para to the two carbonyl groups since the shifts of the two ring protons ortho and para to -CO·R group are about δ 0.6 and δ 0.3 respectively. Those at δ 7.3-7.6 are obviously attributable to the rest of the 4 ring protons.

The route to the formation of the compound (IV) was not known. It was first suspected that this compound could have been

formed from the diamine and phthalic acid if the phthalaldehyde contained some phthalic acid or oxidised to it during the reaction. However, when *o*-phthalaldehyde was used soon after recrystallization, the yield of this by-product was still appreciable. The treatment of biphenyl-2,2'-diamine with phthalic acid under such a condition did not give any product. Recovery of these two reactants was almost quantitative.

The infra-red spectrum of the red compound with m.p. 253-254° (Spectrum No. 16) exhibits a strong carbonyl absorption band at 1690 cm⁻¹ and another strong band at 760 cm⁻¹ which is attributable to ortho-di-substituted aromatic absorption arising from out-of-plane deformation vibrations of the four adjacent hydrogen atoms remaining on the ring.¹⁶ Accompanying the band at 760 cm⁻¹, ortho-di-substitution also gives rise to a series of relatively weak bands in 950-1225 cm⁻¹ region and thus renders the identification of the two medium absorptions at 1095 cm⁻¹ and 1165 cm⁻¹ difficult.

The band at about 1640 cm⁻¹ may be due to C=N stretching. The assignment of this band is also a difficult one although it falls in the aryl conjugated C=N stretching absorption range 1630-1660 cm⁻¹, but it can be confused with the skeletal stretching modes of the C=C double bond which leads to the presence of a group



Spectrum No. 16.

IR spectrum of the red compound with m.p. 253-254° (in KBr).

of four bands in the region 1450-1650 cm^{-1} . The two bands near 1480 cm^{-1} and 1600 cm^{-1} in conjunction with the weak C-H stretching band near 3020 cm^{-1} are characteristic of the aromatic ring itself.

The appearance of two weak bands in the neighbourhood of 3400 cm^{-1} and 3500 cm^{-1} can hardly show whether the compound is a primary or a secondary amine. They may arise from the symmetric and asymmetric stretching vibrations of two hydrogen atoms attached to one nitrogen or from the stretching vibrations of two N-H groups in different chemical environments. Although differentiation can be sought from the region 1590-1650 cm^{-1} in which primary amines may give rise to a strong to medium N-H deformation absorption whereas in the case of secondary amines, only a very weak band is observed, in the present spectrum, this region is obscured by the aromatic ring vibration near 1600 cm^{-1} . The unique indication of its being a secondary rather than a primary amine is the presence of a weak band near 1510 cm^{-1} . This band has been investigated by deuteration techniques as an additional weak absorption arising from the N-H deformation vibration coupled with the lower-frequency C-N stretching vibration in secondary amines (Hadži and Skrblijak, 1957). However, the reliability of such a weak evidence is doubtful.

It may be concluded that the most definite information given by the infra-red spectrum about the molecular structure is that the red compound contains C=O and N-H groups. Instead of indicating the presence of a certain class of amines, it shows that the compound

can be an amide as well since amides also have absorption in the 1600-1640 cm^{-1} region due to N-H deformation.

The deduction of the molecular structure of the red compound depends heavily upon the exact determination of its molecular weight. To ensure that the molecular ion peak in its mass spectrum has been chosen properly is therefore a necessity.

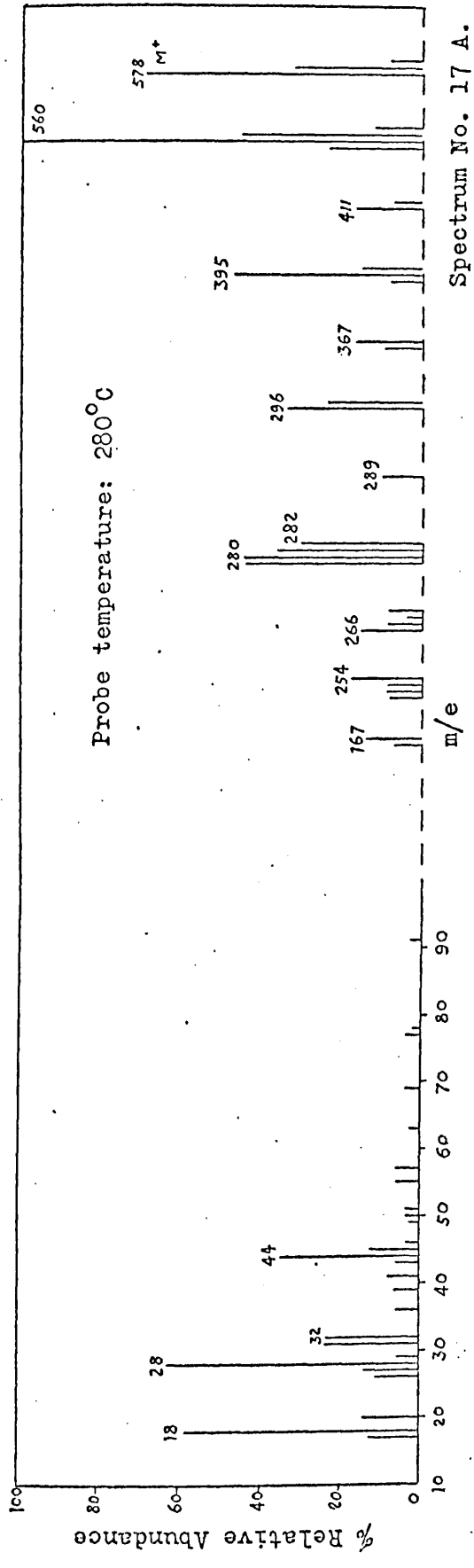
Attention has been drawn to the fact that hydrogen losses can occur prior to ionization but there is no sign of this because when this happens, the spectrum usually exhibits a series of peaks 2 a.m.u. apart from the pseudo molecular ion peak.

Abstraction of a hydrogen atom from a neutral molecule by the molecular ion or fission of molecular ion with the loss of a hydrogen atom can also be the case in the present compound. If ions are produced in significant amount and are very stable whereas the molecular ion has low stability and fragments readily, the substantial peak could be $M+1$ or $M-1$. Fortunately, this confusion is expelled by the Nitrogen Rule which states that the peak corresponding to the molecular ion of a molecule will be of even mass except when an odd number of nitrogen atoms is present. Elemental analysis (see page 163) in connection with the approximate molecular weight given by the mass spectrum shows that the red compound contains 4

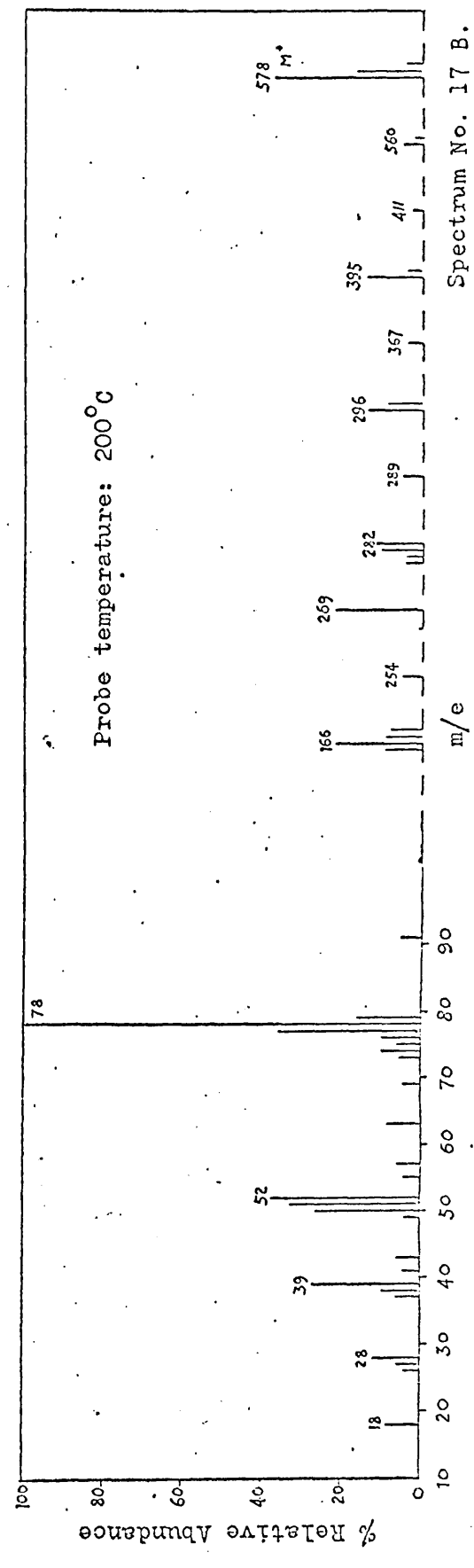
nitrogen atoms and so the molecular ion peak must be either at $m/e = 578$ or 580 . Since the molecule contains 40 carbon atoms and the chance of having one ^{13}C atom is about 44%, there must be a peak at $M+1$ having an intensity of about 44% of that of the molecular ion peak M . As can be seen from Spectrum No. 17A (or 17B), the height of the peak at $m/e = 579$ is about 46% of that of the peak at $m/e = 578$. This indicates that the peak at $m/e = 578$ ought to be the molecular ion peak rather than the one at $m/e = 580$.

However, the difficulty in recognition of the molecular ion peak still exists because the molecular ion may lose a molecule of hydrogen in its fragmentation process as well. When this is the case, the peak at $m/e = 580$ could probably be the molecular ion peak and the one at $m/e = 578$ could be due to the fragment ions. At this point, a careful examination of the NMR spectrum of the red compound is necessary. Calculation of the various integrated intensities shows that there are not more than 28 protons appeared in the NMR spectrum including the proton from CHCl_3 and other impurities of the solvent. If the molecule of the red compound contains 27 protons, its molecular ion will be of odd mass 579, but this is prohibited by the Nitrogen Rule.

It is thus believed that the peak at $m/e = 578$ is a genuine molecular ion peak being compatible with all the other features of the mass spectrum as can be seen in the following discussion.



Spectrum No. 17 A.

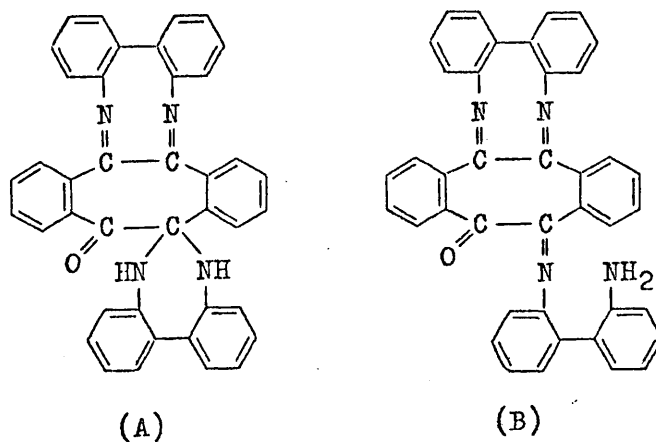


Spectrum No. 17 B.

Mass spectra of the red compound with m.p. 253-254°

Exact mass measurement combined with elemental analysis indicates that the molecular formula of the red compound is $C_{40}H_{26}N_4O$. The possibility of its being an ether is ruled out because there is an M-18 peak in the mass spectrum. The presence of a strong carbonyl absorption band at 1690 cm^{-1} in the infra-red spectrum (see Spectrum No. 16) shows that it could be an aldehyde, a ketone or an amide, but the possibility of its being a keto-enol tautomeric mixture is rejected because there is no signal due to the corresponding proton in the keto-form in the NMR spectrum (see Spectrum No. 18 A and page 107).

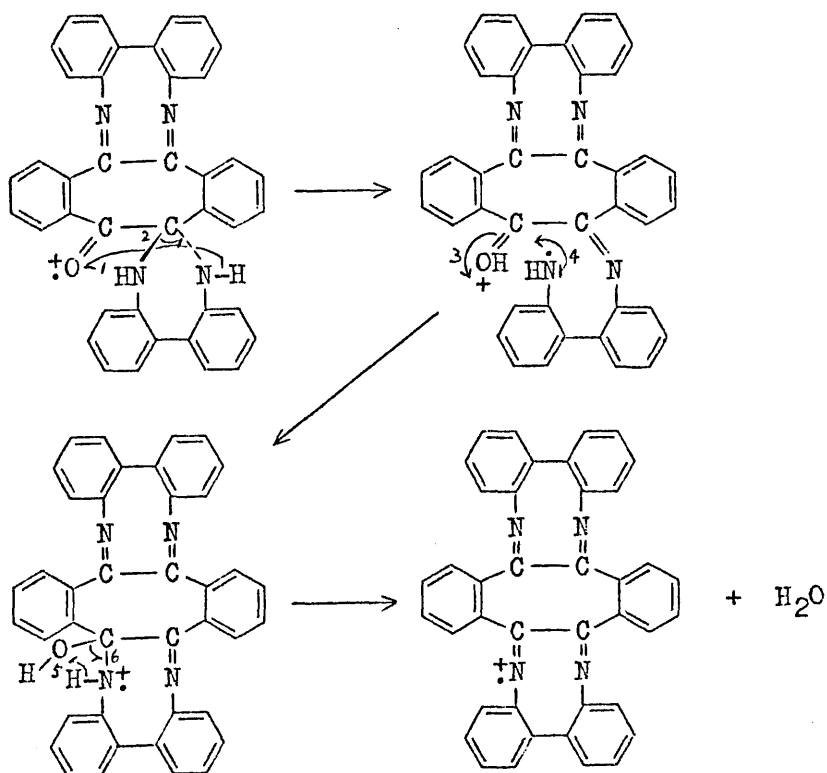
A study of the NMR spectrum also reveals that the red compound is neither an aldehyde nor an amide and besides the two exchangeable protons, only aromatic protons are observed. It must, therefore, be an amino ketone. The relatively low percentage of hydrogen involved in the formula and the colour of the compound itself all lead to the presentation of the following two alternative structures:



Structure (A) is supported by the NMR spectrum and can account fairly well for the features of the two mass spectra probed at 280° and 200° C (Spectrum No. 17A and No. 17B) as described in the following sections.

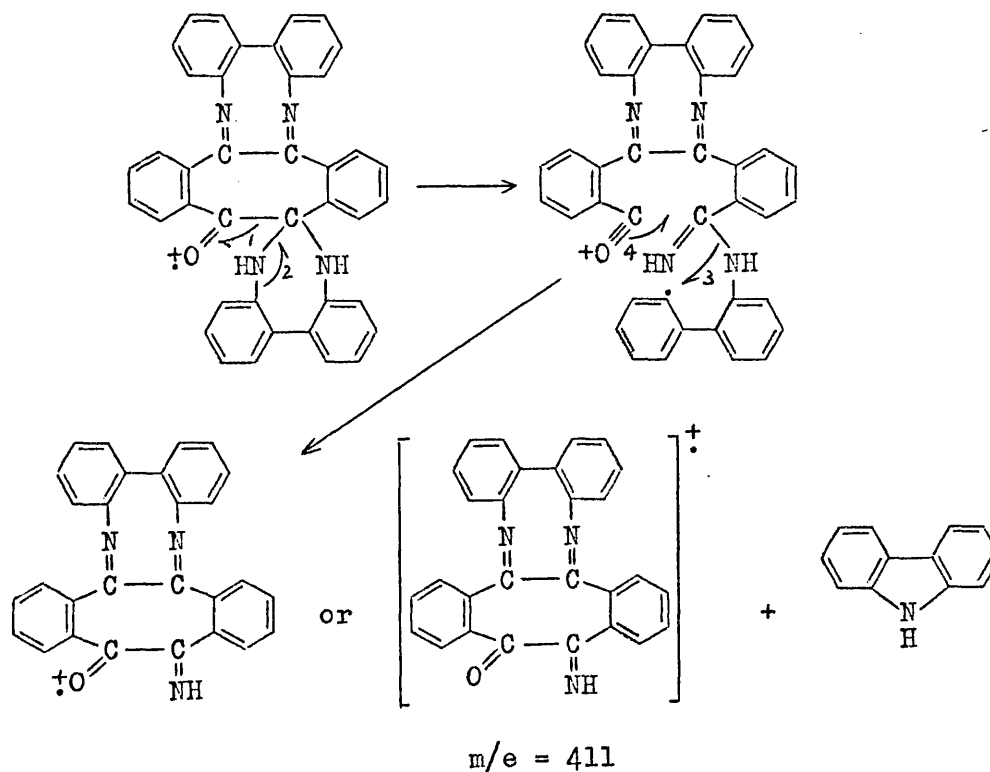
The molecular ion M ($m/e = 578$) may be formed by the loss of a non-bonded electron from oxygen or any nitrogen atom in structure (A). The two peaks at $m/e = 579$ and $m/e = 580$ are the characteristic isotope peaks (M+1) and (M+2).

Elimination of water from the molecular ion M and its two isotopic species (M+1) and (M+2) gives rise to a group of peaks at $m/e = 560$, $m/e = 561$ and $m/e = 562$ respectively. A possible route could be as follows:

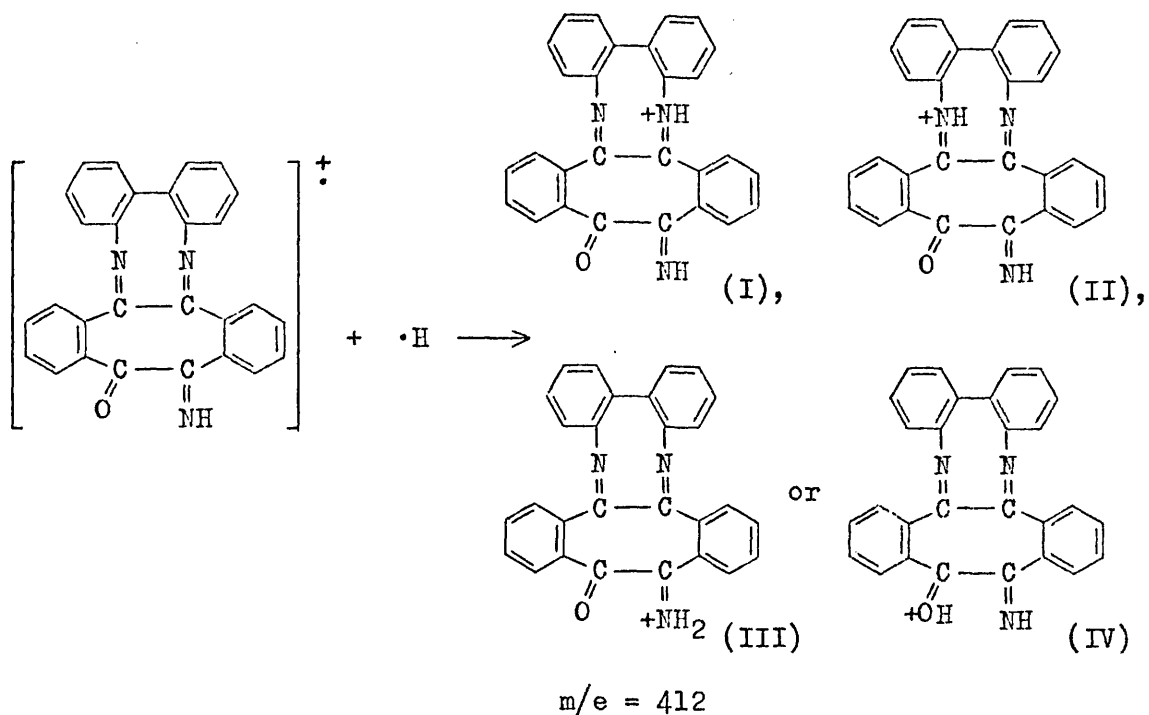


Since odd-electron ions are less stable, elimination of a hydrogen atom from the fragment ion of $m/e = 560$ to produce the most stable even-electron ion corresponding to the peak at $m/e = 559$ is also possible.

Elimination of carbazole as a neutral fragment from the molecular ion leads to the formation of an odd-electron ion of $m/e = 411$.

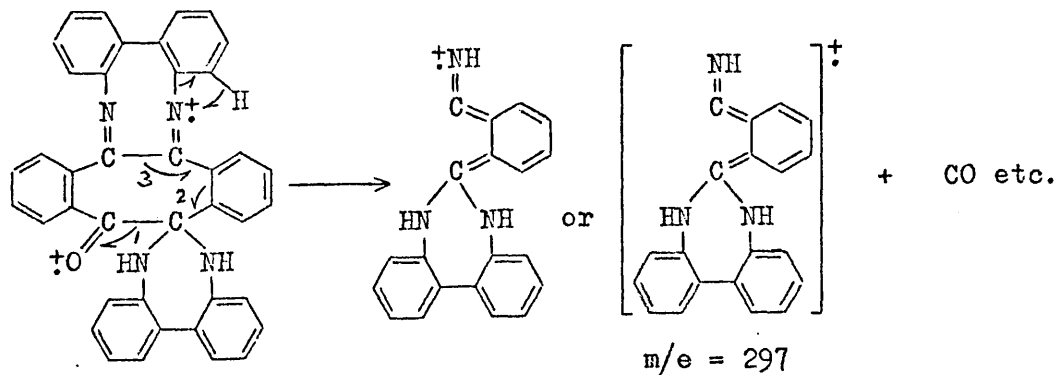


To achieve the most stable electron configuration, this ion may abstract a hydrogen atom from a neutral fragment giving rise to a peak corresponding to $m/e = 412$.

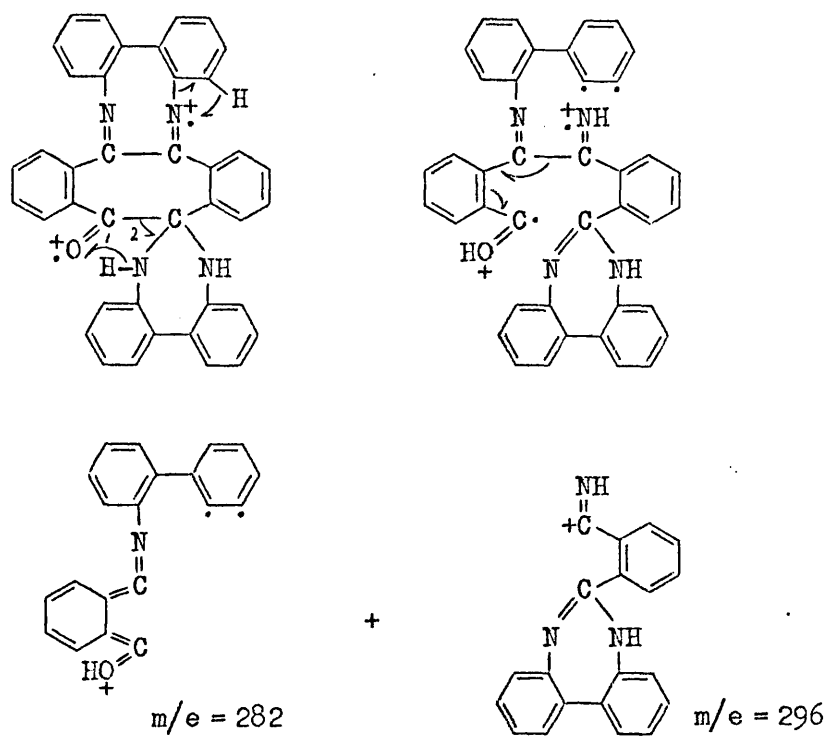


Degradation with loss of ammonia and then carbon monoxide as two stable neutral fragment from the fragment ion of $m/e = 412$ should produce two ions corresponding to the two peaks at $m/e = 395$ and $m/e = 367$ respectively.

The decomposition of the doubly charged molecular ion may yield an ion of $m/e = 297$.

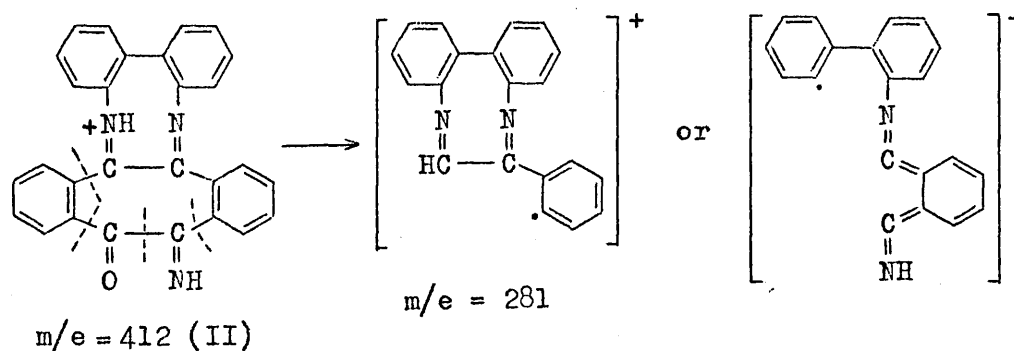


If it proceeded as below, the resulting ion would be of $m/e = 296$ and $m/e = 282$.



The loss of a hydrogen atom from the fragment ion of $m/e = 297$ may also produce the ion of $m/e = 296$.

Successive elimination of a benzene fragment, carbon monoxide and hydrogen cyanide from the ion of $m/e = 412$ (I or II) seems



to give an ion of $m/e = 281$. Although the mechanism is not known, these fragmentations are supported by the facts that this ion and the ion of $m/e = 296$ were found to have the formulae $C_{20}H_{13}N_2$ and $C_{20}H_{14}N_3$ by accurate mass measurement:

Measured mass	Possible formulae	Calculated masses
296.1185	$C_{20}H_{14}N_3$	296.1189
281.1081	$C_{20}H_{13}N_2$	281.1079

Peaks at $m/e = 289$ and $m/e = 280$ are obviously due to the two doubly charged molecular ion M and fragment ion (M-18) respectively.

The derivation of the ion of $m/e = 279$ is rather difficult to imagine. It could have been formed from the fragment ion of $m/e = 411$ by successive elimination of a benzene fragment, carbon monoxide, hydrogen cyanide and a hydrogen atom of the benzene ring.

Elimination of hydrogen cyanide from both ions of $m/e = 296$ and $m/e = 281$ should produce fragment ions of $m/e = 269$ and $m/e = 254$ respectively.

The peak at $m/e = 266$ is negligible in Spectrum No. 17B. The origin of the fragment ion corresponding to this peak is not clear but probably could be related to the ion of $m/e = 281$ if an -NH group should happen to be lost from it.

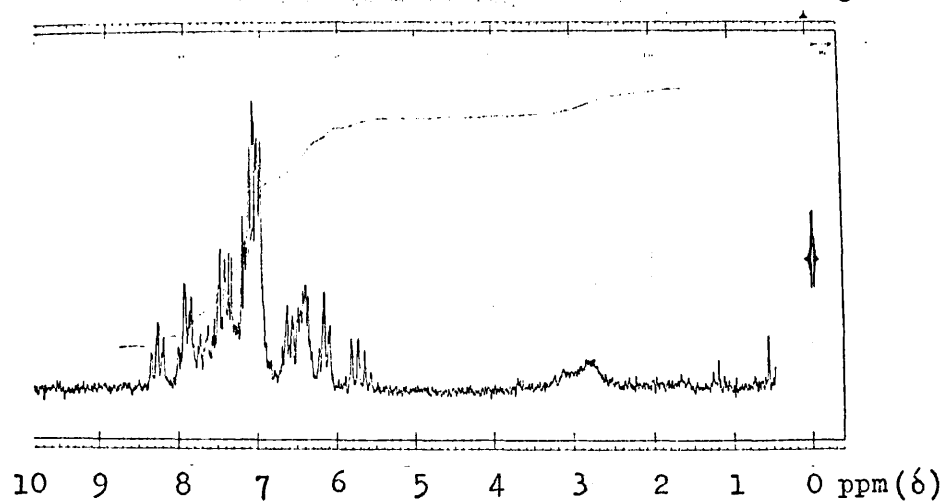
The peak at $m/e = 167$ must be due to the carbazole ion. Loss of a hydrogen atom from this species corresponds to the ion

of $m/e = 166$. Fission of C=N double bond and the 1,1'-bond of the biphenyl nucleus should give rise to ions of $m/e = 91$.

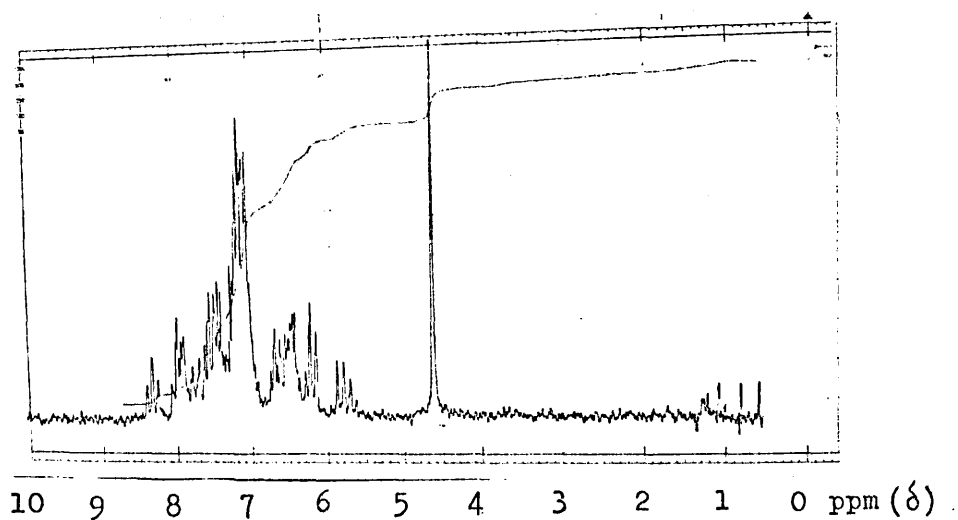
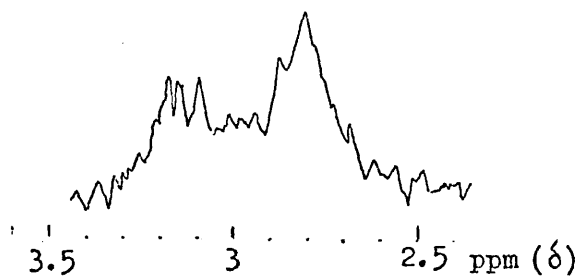
Peaks due to the well known benzene fragment ions are those at m/e equals to 79, 78, 77, 52, 51, 50 and 39. The two peaks at $m/e = 44$ and $m/e = 32$ must be due to CO_2 and O_2 from traces of air in the instrument. Finally, peaks at $m/e = 28$, $m/e = 27$ and $m/e = 18$ are due to carbon monoxide, hydrogen cyanide and water respectively.

A distinct feature in the two mass spectra of this compound probed at 280° and 200° C is that in the first spectrum, the base peak is at $m/e = 560$ whereas in the second spectrum the base peak is at $m/e = 78$. This could be that at lower temperature, elimination of water to give the fragment ion of $m/e = 560$ did not occur so readily and so the other fragmentations occurred and went down to the fragment ion of $m/e = 78$ and other small pieces; i.e., the main fragmentations at 200° C were not through the ion of $m/e = 560$. The breakdown of fragment ion (M-18) with the formation of the benzene fragment $C_6H_6^+$ seems to imply the reality of its structure.

The NMR spectrum of the red compound shows two broad humps in the higher-field position and at least seven groups of signals in the aromatic region (Spectrum No. 18A). The δ values and the



Spectrum No. 18A.



Spectrum No. 18B.

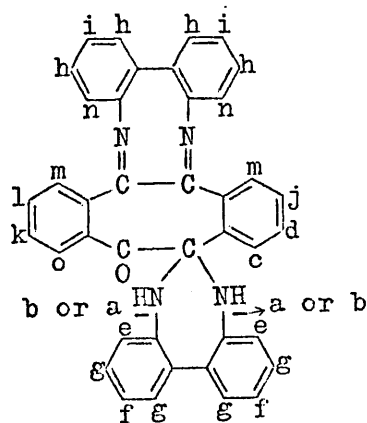
NMR spectra of the red compound with m.p. 253-254 $^{\circ}$.

numbers of protons responsible for the individual signals are listed in Table 2.

Table 2.

Chemical shifts for the protons of
the red compound with m.p. 253-254°

δ	H	Multiplicity	Assignment
2.8	1	Broad hump	a or b
3.1	1	Broad hump	b or a
5.6-5.9	1	5 lines	c
6.2	1	Triplet	d
6.3-6.7	4	Multiplet	e and f
6.9-7.3	10	Multiplet	g,h and i
7.3-7.8	5	Multiplet	j,k,l and m
7.9	2	Multiplet	n
8.3	1	Triplet	o



Structure (A)

The use of the deuteration method immediately reveals that the two broad humps are due to exchangeable protons and are not coupled to any other signals in the aromatic region (Spectrum No. 18B). The problem arises from the fact that the signals in the aromatic region are fine and irregular. Interpretation of the spectrum on the basis of splitting pattern is almost impossible except for those corresponding to one proton.

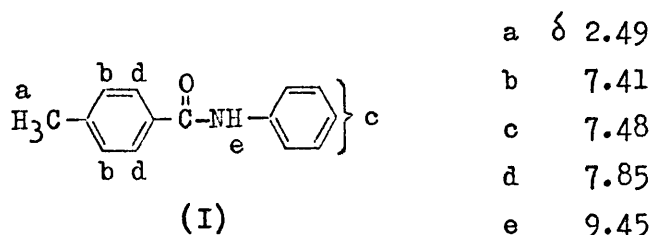
It is obvious that the red compound is not an aldehyde because there is no resonance at δ 9-11 where aldehyde is expected to show a singlet. The presence of two broad humps indicates that the two exchangeable protons are quite different in their environments and so the possibility of its having the structure denoted as (B) on page 98 is readily ruled out.

The two exchangeable protons must be, therefore, either attached to two different nitrogen atoms or one attached to a nitrogen and the other one to an oxygen atom, but the latter case is very unlikely. As it has been shown that the compound contains only one oxygen atom and there is a carbonyl absorption band in its infra-red spectrum, the presence of an OH group is impossible unless this is not a single compound but a keto-enol tautomeric mixture.

For an enolic proton, the chemical shift is about δ 15-17. Although this is beyond the range of the present spectrum, a keto-enol mixture also gives rise to a signal somewhere in the higher-field region due to the corresponding proton in the keto-form, but

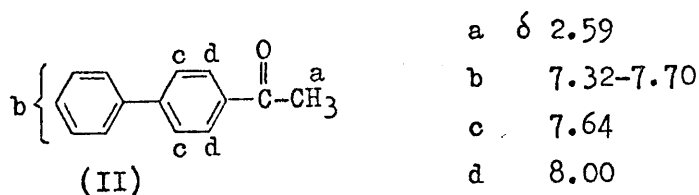
with greatly reduced integrated intensity. In other words, if the two tautomeric forms are present in equal amount, the intensity of this signal should correspond to one half of a proton. However, the integrated intensity of the two humps is correct for two protons. The signal due to a methine proton is also expected to be sharper than these. Hence the presence of an enolic OH is doubtful.

The possibility of its being an amide with the structure unit $-\text{ArCO}-\text{NH}-\text{Ar}-$ is also ruled out because signals arising from the proton attached to nitrogen in aromatic amide should appear in the low-field region. The chemical shift of this proton in 4-methylbenzanilide (I) provides a good example.



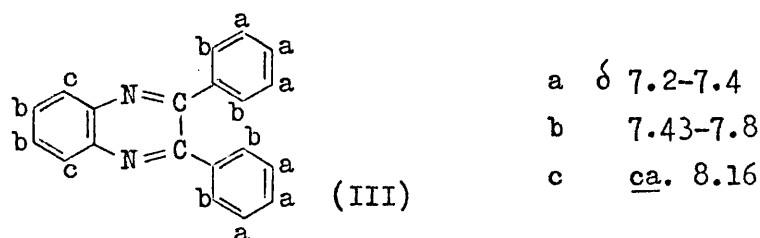
It ought to be quite interesting at this stage to see how far structure (A) is able to account for the features of the NMR spectrum of this red compound.

The triplet at δ 8.3 could be due to the proton adjacent to the carbonyl group. Its chemical shift is compatible with that of the ortho proton in 4'-phenylacetophenone (II).



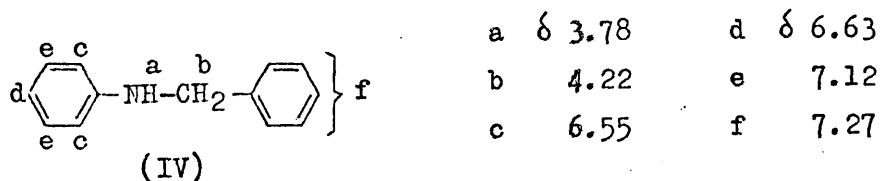
The splitting pattern is not difficult to understand. Since two aromatic protons in the meta-position of each other can give rise to four absorption lines (see Spectrum No. 2B), one should expect to see a group of three lines if this proton was further split by another protons in the meta-position. The integrated intensity is correct for one proton.

The multiplet centred at δ 7.9 may arise from the two aromatic protons ortho to the nitrogen atoms in the eight-membered ring as compared with the chemical shift of the two protons ortho to nitrogen in 2,3-diphenylquinoxaline (III):



Its intensity corresponds to two protons.

The multiplet at δ 6.3-6.7 seems to be subdivided into two groups. The signal centred at δ 6.45 could be due to the two aromatic protons ortho to NH, while the other group centred at δ 6.65 may be attributed to the two protons para to NH. These assignments are based on the fact that aromatic protons ortho and para to NH in N-phenylbenzylamine (IV) are at δ 6.55 and δ 6.63 respectively.



The splitting patterns are irregular but resemble those arising from aromatic protons ortho and para to an amino group. The total integrated intensity is correct for 4 protons.

The signal at δ 6.2 is analogous in splitting pattern to the signal at δ 8.3. It could be arising from the aromatic proton indicated as d in structure (A). The integrated intensity is also correct for one proton.

At δ 5.6-5.9, there appears a group of lines probably 5, and 3 of them are almost of equal intensity. The integrated intensity corresponds to one proton which could be the aromatic proton indicated as c in structure (A). Its feature cannot be accounted for by simple splitting rule.

The total effect of substituents on the chemical shifts of the above two protons indicated as c and d is not known. A construction of the Dreiding model shows that these protons lie over the plane of one of the two benzene rings attached to the NH groups (Figure 7 and 8). It is, therefore, thought that the shifts of these protons to the high-field position of the aromatic region must be due to the long-range shielding effect of the benzene ring. The monobenzo[2,2]paracyclophane (V) provides a good example. The two aromatic protons indicated by the arrows are at δ 5.5 because they lie over the plane of another benzene nucleus. For the same reason, the proton attached to C₈ in [2,2]metacyclophane (VI) is at δ 4.27.

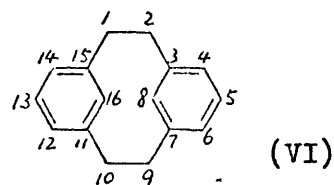
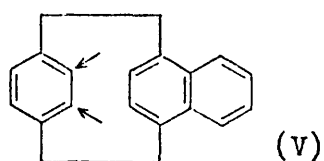


Figure 7.



Figure 8.

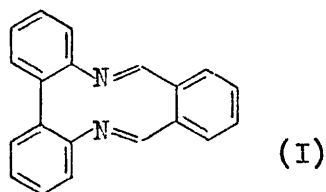
Molecular models showing the two aromatic protons being above the plane of the benzene ring.



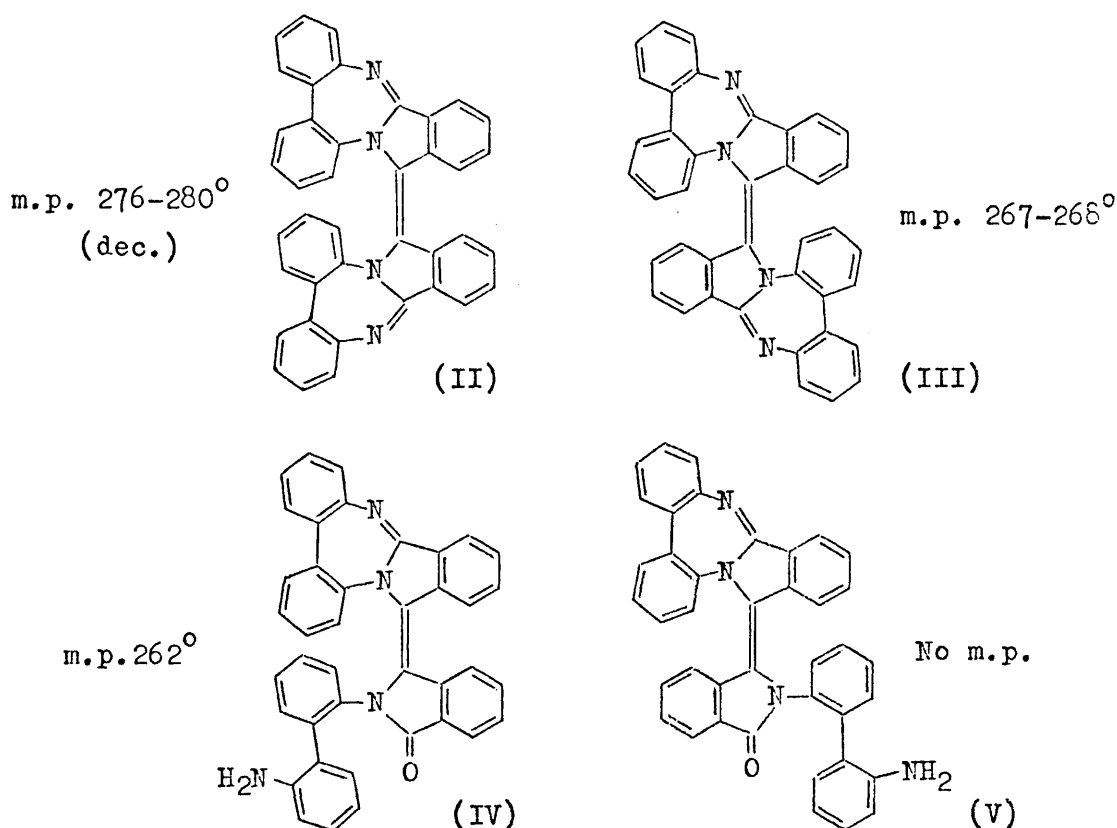
The rest of the aromatic protons must be responsible for the two groups of signals in the region δ 6.9-7.8. Their chemical shifts are also compatible with those of the protons indicated as e in N-phenylbenzylamine, a and b in 2,3-diphenylquinoxaline, c in 4'-phenylacetophenone and b in 4-methylbenzanilide.

Finally, the two broad humps at δ 2.8 and 3.1 are due to the two exchangeable protons as mentioned in the very beginning of this section. Their combined intensity can also be estimated from the intensity of the singlet arising from DHO in Spectrum No. 18B.

Recently, Bindra and Elix (1969) also reinvestigated the condensation between 2,2'-diaminobiphenyl and *o*-phthalaldehyde in an effort to isolate the compound (I). The reaction was carried



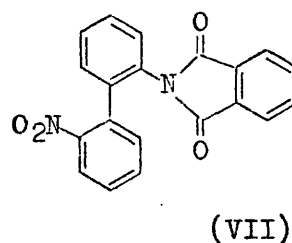
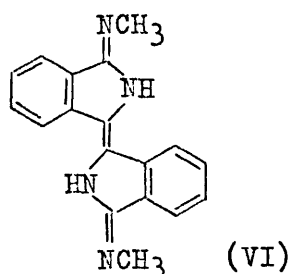
out in methanol at room temperature. They found that the major product was a "linear" polymer as reported by Blood and Noller (1957). The minority afforded four highly coloured compounds which were separated and purified by repeated chromatography on alumina plates and characterized as (II), (III), (IV) and (V). The determination of the structure of these four compounds was based upon



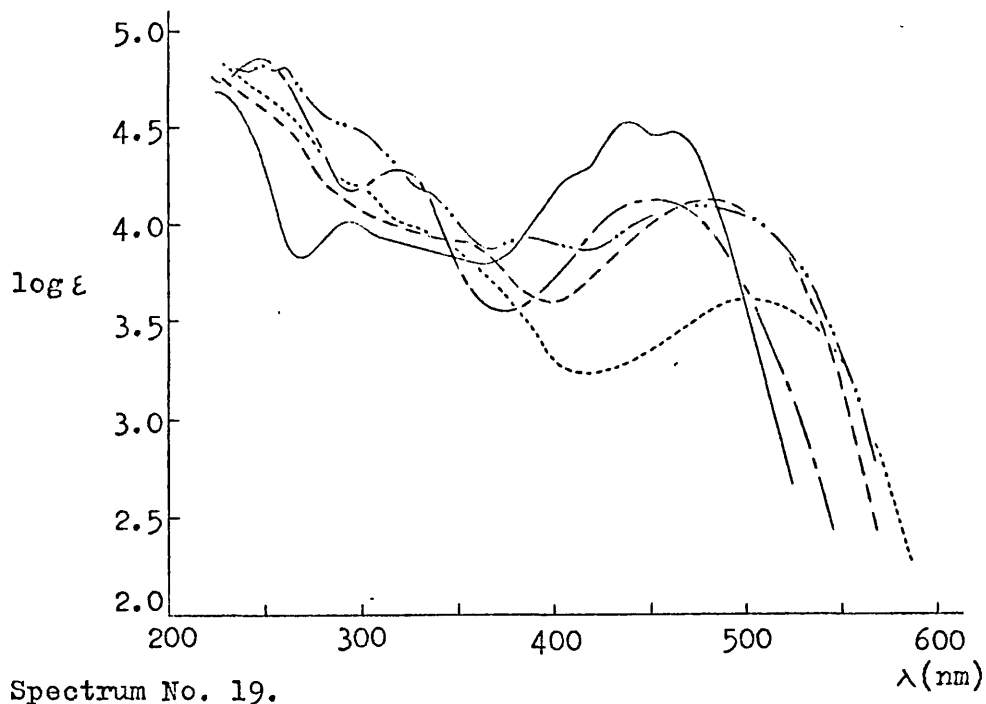
the following spectroscopic data and experimental results:

1. Accurate mass measurement of the respective molecular ions gave the empirical formulae $C_{40}H_{24}N_4$ for (II) and (III) and $C_{40}H_{26}N_4O$ for (IV) and (V).

2. The NMR spectrum of (IV) showed that this compound contained 24 aromatic protons (τ 1.7-3.8, multiplets) and two exchangeable protons (τ 6.9-7.3, broad, exchanged with D_2O).
3. The infra-red spectrum of (IV) exhibited carbonyl absorption at 1690 and 1710 cm^{-1} and two bands at 3360 and 3450 cm^{-1} which were said to confirmed the presence of a primary amino group.
4. The major peaks that appeared in the mass spectrum of (IV) were at m/e 579, 578 (100%), 560, 395, 297, 296, 282, 281 and 254.
5. Both the anhydro-compounds (II) and (III) rapidly hydrolysed when their chloroform solutions were exposed separately to the atmosphere. They both gave a mixture of (IV) and (V).
6. Dehydration of either (IV) or (V) with phosphorus oxychloride and pyridine regenerated a mixture of the anhydro-compounds (II) and (III).
7. The ultra-violet and visible spectra of (II), (III), (IV) and (V) resembled that of the di(3-methylimino-1-isoindolinylidene) (VI) and hence identified the chromophoric groups present in these compounds (Spectrum No. 19).



8. Oxidation of (III) with potassium permanganate in acetic acid gave N-(2'-nitro-2-biphenyl)phthalimide (VII) as the main product.



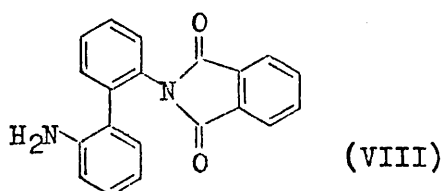
UV and visible spectra of II (-----),
 III (-·-·-·-·-), IV (-----), V (·········)
 and VI (—————).

The mass spectral fragmentation patterns of (II), (III), (IV) and (V) were said to be obscure and of no aid in structure elucidation.

At this report, a careful re-consideration of the assignment of a structural formula to the present red compound with m.p. 253-254° is necessary. The electronic spectrum of this compound was found superimposable on that of (IV) with m.p. 262°. Its

infra-red spectrum also exhibited absorption bands near 3360 and 3450 cm^{-1} and at 1690 cm^{-1} (there could be another one at 1710 cm^{-1}). A comparison of the NMR and mass spectra of these two compounds showed that they have similar spectral features except the absence of some absorption lines at τ 4.4-4.1 (δ 5.6-5.9) in the NMR spectrum of (IV). Despite this dissimilarity and a deviation of melting points, the two compounds can be said to have the same structure. They may have different arrangements of atoms in space (see IX A and IX B) if the absence of those absorption lines at τ 4.4-4.1 is in accordance with the report and not a mistake of printing.

However, the conclusion drawn by Bindra and Elix in the structure determination of their condensation products is open to question. As we have mentioned on page 94, the presence of two absorption bands near 3400 cm^{-1} and 3500 cm^{-1} in the infra-red spectrum cannot show whether the red compound is a primary or a secondary amine. On the other hand, the presence of two separate humps removable by deuteration with D_2O in the NMR spectrum of this red compound (see page 107) seemed to serve as a strong evidence of its being a secondary rather than a primary amine. This point of view may be supported by comparison of its NMR spectrum with that of the 2-amino-2'-phthalimidobiphenyl (VIII) in which the absorption



due to the two amino protons only appeared as a smooth hump (Spectrum No. 15A).

In addition to this argument, one can see that (II) and (III) are diastereomers that owe their existence to hindered rotation about double bonds. Although dehydration of either (IV) or (V) with phosphorus oxychloride and pyridine might cause isomerisation, hydrolysis of (II) or (III) to bring the cleavage of either C=N bond should give only the cis compound (IV) or the trans compound (V) respectively but not a mixture of (IV) and (V).

The electronic spectra of (III) and (V) seem to be quite different from that of the di(3-methylimino-1-isoindolinylidene) (VI) which may not serve as a suitable compound for comparison.

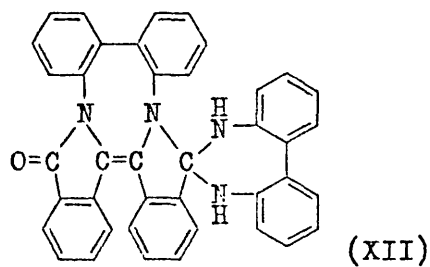
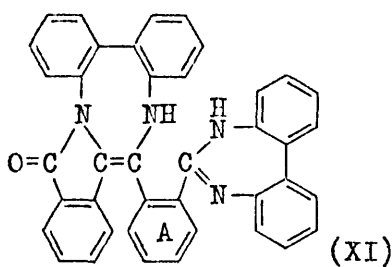
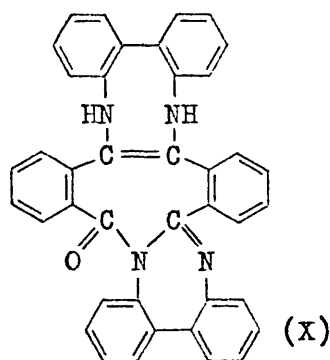
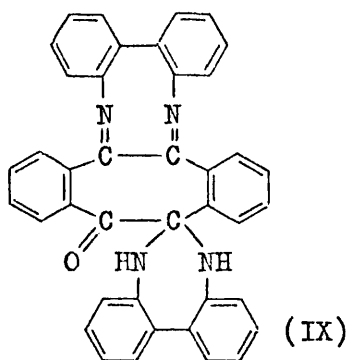
Finally, oxidation of an amine to yield a nitro compound is an extraordinary reaction. Tertiary amines are likely to give an amine oxide on the lines of Cope elimination.

An inspection of the molecular structure of (IV) and (V) seems to give us an impression that the two compounds should lose water very readily to give (II) or (III) as a main product. However, according to Bindra and Elix's report, compound (IV) was obtained in better yield, being 9.2% as compared with a 2% yield of (II) and a 2.3% yield of (III).

The fact that the present red compound (m.p. 253-254°) is (or very likely to be) a secondary amine and that a molecule of water can be removed from it (but not so easily) either by the

action of a dehydrating agent, or by the bombardment of high energy electrons in the ionization chamber of mass spectrometer, is very helpful to structure determination of this compound.

For a secondary amine with the molecular formula $C_{40}H_{26}N_2$, there are only four possible structures that can be drawn with the normal valencies of carbon, hydrogen and nitrogen, namely (IX), (X), (XI) and (XII).

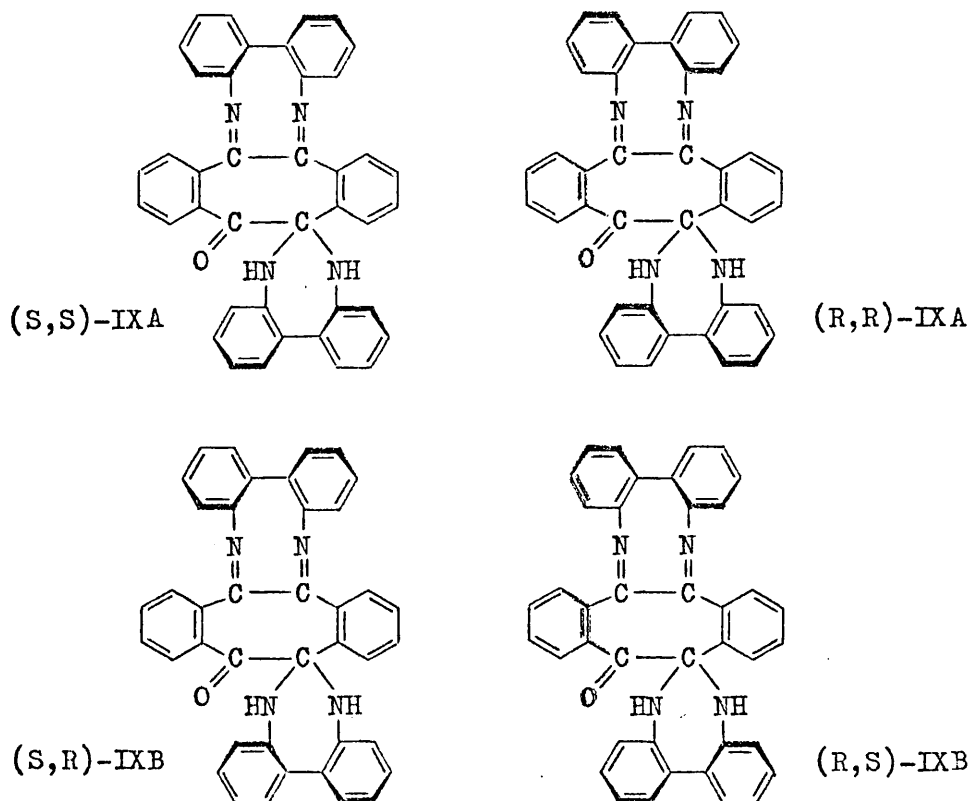


A construction of their molecular models shows that (IX) is likely to lose a molecule of water but there remains no possibility for (X) or (XII) to do so. The two -NH groups in (XI) can get in touch with each other and interaction between these two groups (if this should happen) may lead to the formation of (IV) and (II).

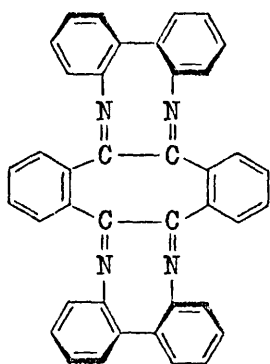
However, this could not be the case for there will be a hindered rotation of the two benzene rings attached to the two -NH groups in the transition state.

The fact that the present red compound is highly optically stable is also in opposition to the assignment of a molecular structure like (XI) which might be optically labile as a result of restricted rotation of ring A about the single bond to the carbon atom of the C=C double bond.

The conclusion that the present red compound could have the structure (IX) seems to obtain a further support by the existence of a total of four configurational isomers as shown below. (R) and (S) refer to the configurations of each bridged biphenyl within the molecule.

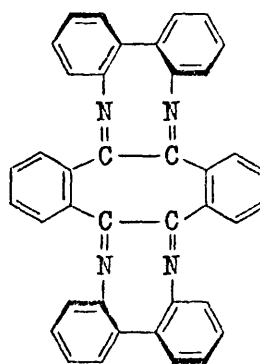


They are indeed two sets of enantiomers. They could be the two compounds obtained by Bindra and Elix with the empirical formula $C_{40}H_{26}N_4O$. The two anhydro-compounds with empirical formula $C_{40}H_{24}N_4$ may well have the following two sets of structures:



(R,S)-XIIIA

Superimposable on
its mirror image
(S,R-configuration)
A meso compound



(R,R)-XIIIB

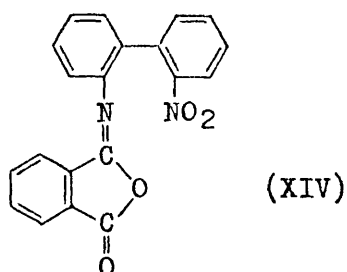
Not superimposable
on its mirror image
(S,S-configuration)

Structure (XIII A) possesses a plane of symmetry and is of course superimposable on its mirror image. It would be optically inactive if it does exist. On the other hand, structure (XIII B) is not superimposable on its mirror image and hence would be obtained as a mixture of two enantiomers.

A construction of molecular models of the above four sets of structures may help us to explain why the dehydration of either one of the two compounds with empirical formula $C_{40}H_{26}N_4O$ should give a mixture of two anhydro-compounds and that the hydrolysis of either anhydro-compound regenerated a mixture of the two compounds

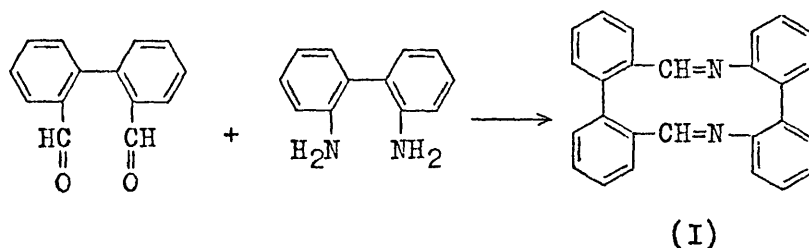
with empirical formula $C_{40}H_{26}N_4O$, but the reality of this experiment is questionable.

The remaining problem is that the oxidation of an amine to give a nitro compound is an unexpected reaction. Although the compound with an empirical formula $C_{20}H_{12}N_2O_4$ was believed by Bindra and Elix to be the *N*-(2'-nitro-2-biphenyl)phthalimide (VII) because its infra-red spectrum showed two absorption bands at 1530 (NO_2) and 1350 cm^{-1} (NO_2) in addition to the carbonyl absorption, a compound like (XIV) may well give rise to similar absorption bands.



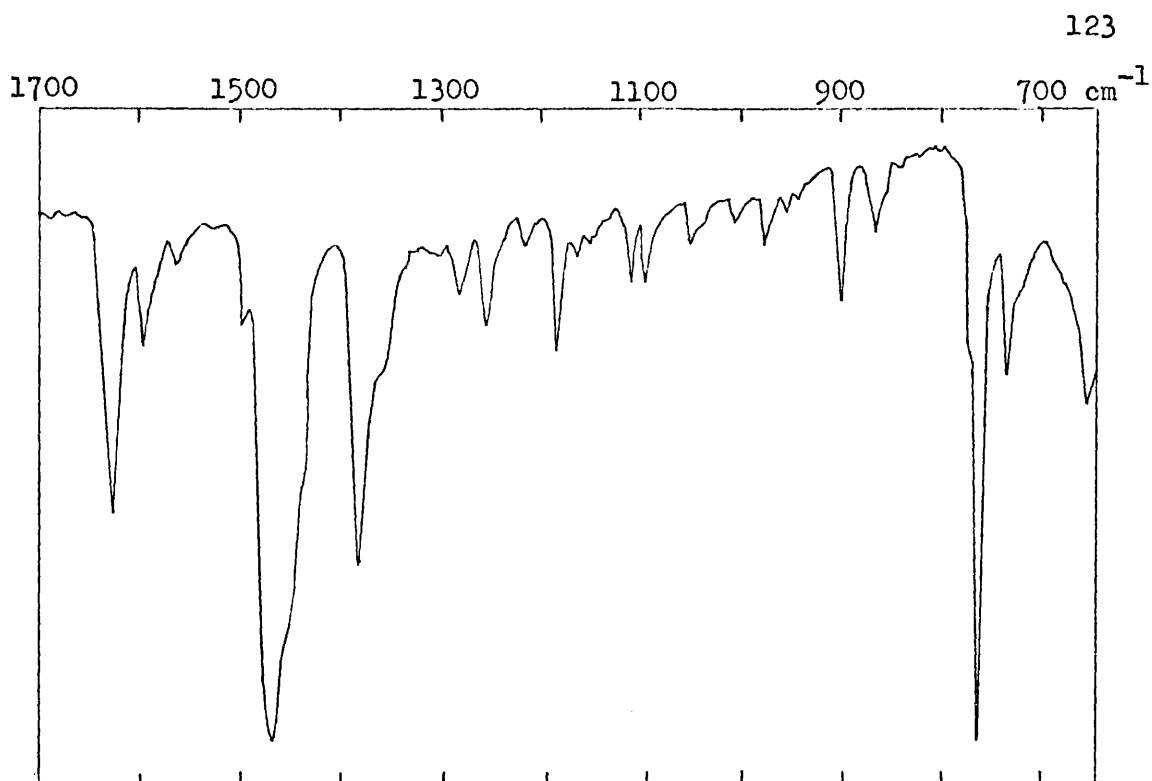
d. Condensation between biphenyl-2,2'-dialdehyde and 2,2'-diaminobiphenyl.

It would be of interest to note that although the condensation between biphenyl-2,2'-dialdehyde and *o*-phenylenediamine and also between 2,2'-diaminobiphenyl and *o*-phthalaldehyde failed to give the expected compounds with a ten-membered ring, the condensation between the two biphenyls had given 9,20-diazatetrabenzo-[a,c,g,i]cyclododecene (I) as a single product with m.p. above 300°

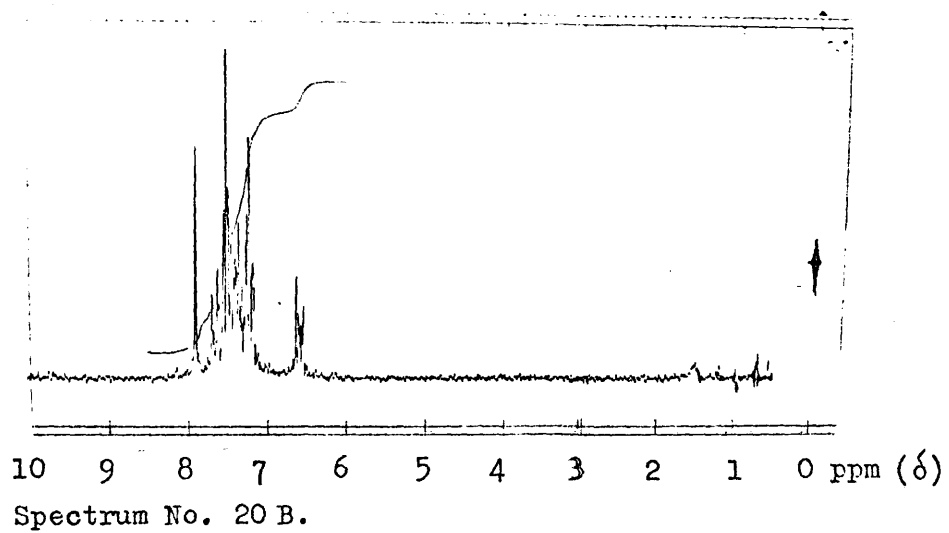


when the reaction was carried out in methanol at room temperature (Bergmann, Agranat and Kraus, 1966). This compound was reported to have infra-red absorption bands at 1625, 1600, 1560, 1475 and 1450 cm^{-1} (in nujol) and NMR absorption singlet at δ 8.05 arising from the two vinylic protons, multiplet at δ 6.60-7.08 due to the two protons ortho to the methine group and another multiplet at δ 7.2-7.75 corresponding to the rest of the 14 aromatic protons.

In order to make a comparison with the present work, biphenyl-2,2'-dialdehyde and 2,2'-diaminobiphenyl were allowed to react in ethanol at room temperature. The solid obtained was recrystallized from benzene giving colourless prisms with m.p. 312-313°



Spectrum No. 20 A.



IR (A) and NMR (B) spectra of 9,20-diazatetra-benzo[a,c,g,i]cyclododecene with m.p. 312-313°.

in 68% yield. Its infra-red spectrum (Spectrum No. 20A) showed absorption bands as indicated above, whereas its NMR spectrum (Spectrum No. 20B) was found to have a singlet at δ 7.93, a multiplet at δ 6.6 and a group of overlapping absorption lines at δ 7.2-7.8. The intensities of these signals are in the ratio of 1:1:7 respectively. The multiplet at δ 6.6 was thought to arise from the two ring protons ortho to nitrogen but not to the methine group since the shift in the position of benzene protons ortho to the substituent $-\text{CH}=\text{}$ is $+\delta$ 0.2 which means that the two aromatic protons ortho to the methine group should appear at a lower-field position. The splitting pattern of this multiplet is consistent with ortho and meta couplings around the ring.

REMARKS

Melting points below 120° were determined in an oil bath. Those above 120° were determined on an Electro-thermal melting point apparatus. All melting points are corrected.

Infra-red spectra were measured on a Unicam SP. 200 spectrophotometer either with a mulling agent or as pressed KBr discs.

Visible spectra were measured on a Unicam SP. 800 automatic recording spectrophotometer. Ultra-violet spectra were measured on a Unicam SP. 500 manual spectrophotometer. Quartz cells were employed throughout.

Mass spectra were measured by the Physico-Chemical Measurements Unit at Harwell, Berks.

NMR spectra were either run at 100 MHz by the Physico-Chemical Measurements Unit at Harwell, Berks or at 60 MHz on a Varian A 60 instrument. Chemical shifts were measured on the δ -scale relative to TMS as internal standard ($\delta = 0$).

Optical rotatory dispersion curves were measured on a Perkin-Elmer P 23 spectrophotometer.

Microanalyses were performed either by Dr. A Bernhardt and his staff in West Germany or by Dr. Strauss at Oxford.

EXPERIMENTALDimethyl 2,2'-diphenate

(B. Prakobsantisukh, Ph.D. Thesis, University of London, 1964)

A solution of diphenic acid (100 g, 0.412 mole) in methanol (1000 g) was heated under reflux with concentrated sulphuric acid (100 g) for 6 hours. It was then poured into approximately 2 l of water with stirring. The white crystalline solid obtained was filtered off and washed with saturated sodium bicarbonate solution then with water. After drying, first at about 60° on a water bath, and then over concentrated sulphuric acid in a vacuum desiccator, the crude product (103 g) had m.p. 72-74°. Recrystallization from methanol gave colourless prisms (98.1 g) in 88% yield, m.p. 73-74° (lit.,⁵⁸ 73-74°). This experiment was performed four times with 380 g of diphenic acid and gave 354 g of dimethyl diphenate.

2,2'-Bishydroxymethylbiphenyl

(D. M. Hall, M. S. Lesslie and E. E. Turner,
J. Chem. Soc., 1950, 711)

Dimethyl diphenate (38 g, 0.14 mole) was dissolved in Na-dried ether (360 ml) and added as fast as refluxing permitted to lithium aluminum hydride (8.5 g, 0.22 mole) in dry ether (300 ml) with stirring. When reaction appeared to be over, wet ether, water and dilute sulphuric acid (>2N) were successively introduced until two clear layers were obtained. The ether was removed by heating on a water bath, and the white solid, after filtration, was washed

with water and dried at about 90° in the oven. It was crystallized from benzene giving white needles (26.7 g, 89%), m.p. $111-112^{\circ}$ (lit., $112-113^{\circ}$). This preparation was repeated several times and altogether 346 g of dimethyl diphenate were converted into 224 g of diol.

2,2'-Bisbromomethylbiphenyl

(D. M. Hall, M. S. Lesslie and E. E. Turner,
J. Chem. Soc., 1950, 711)

2,2'-Bishydroxymethylbiphenyl (30 g, 0.088 mole) was added with stirring to hydrobromic acid (48-50%, 1500 ml) in a wide-necked conical flask at 90° . After the addition, it was boiled for 20 minutes and then left to cool down. The solid was collected on a sintered glass filter, washed with cold water and dried in a vacuum desiccator over sodium hydroxide pellets. When crystallized from light petroleum (b.p. $60-80^{\circ}$), colourless prisms (40.4 g, 85%) were obtained. It melted at $91-92^{\circ}$ (lit., $91-93^{\circ}$; 94%). A total amount of 273 g of dibromide were prepared from 220 g of diol by this method.

2,2'-Bis(triphenylphosphoniomethyl)biphenyl dibromide

A. Without any solvent

(D. M. Hall and B. Prakobsantisukh, J. Chem. Soc., 1965, 6311)

2,2'-Bisbromomethylbiphenyl (3.4 g, 0.01 mole) and triphenylphosphine (9 g, 0.034 mole) were ground together, passed

through a fine sieve and collected as a thin layer in a large beaker. The mixture was then placed in a metal bath (covered with charcoal) at 290° for 5 minutes. As soon as the temperature rose up, the powder melted but readily solidified and could not be well stirred by hand. The solid was left to cool down and ground with benzene. The insoluble material was filtered off, washed with light petroleum (b.p. $60-80^{\circ}$) and dried. It was crystallized from ethanol-ethyl acetate giving white crystals (5.4 g, 60%, supposing the compound was a disubstituted phosphonium salt), m.p. $294-306^{\circ}$. After successive crystallization from the mixed solvents, it melted at $310-314^{\circ}$ (lit., $323-326^{\circ}$ for dibromide dihydrate and between $250-300^{\circ}$ after loss of water; yield: 78%).

B. In dry mesitylene

Mesitylene was dried first with calcium chloride, then distilled through a column and dried again with sodium wire. The dibromo-compound (20.4 g, 0.06 mole) and triphenylphosphine (42 g, 0.16 mole) were dissolved separately in the dry solvent (660 ml in all) and heated together under reflux for 35 hours with vigorous stirring. The white phosphonium salt gradually appeared and when reaction had finished, it was filtered off, washed with light petroleum (b.p. $60-80^{\circ}$) and dried. The crude product obtained (50 g) had m.p. $280-305^{\circ}$. Successive crystallization from ethanol-ethyl acetate gave white crystals, m.p. $313-321^{\circ}$. The filtrate, when evaporated to dryness under reduced pressure and the residue

washed with ether gave another crop of crystals (6.64 g). After recrystallization from ethyl acetate, it melted at 154-155°. This was found to be the triphenylphosphine oxide by its melting point, nuclear magnetic resonance and infrared spectra.

When the reaction was carried out under a slow stream of dry nitrogen (label: "oxygen-free") with a solution of the dibromo-compound (3.4 g) and triphenylphosphine (7.9 g) in dry mesitylene for a duration of 35 hours, triphenylphosphine oxide (0.76 g) was again isolated from the filtrate. The resulting phosphonium salt (6.1 g) melted at 290-305° and increased to 315-323° after many more crystallizations.

C. In dry dimethylformamide

(E. D. Bergmann, P. Bracha, I. Agranat and M. A. Kraus,
J. Chem. Soc., 1967, 328)

Dimethylformamide was boiled with one-tenth of its volume of benzene (dried over calcium chloride) and distilled through a fractionating column. The middle fraction (b.p. 194-195°) was collected and used without further treatment. The dibromo-compound (3.4 g, 0.01 mole) and triphenylphosphine (5.8 g, 0.022 mole) were dissolved in the dry solvent (30 ml) and heated under reflux for 3 hours under dry nitrogen. The reaction mixture was then left to stand overnight and the phosphonium salt obtained was filtered off, washed with ether and dried. It was crystallized from ethanol-ethyl acetate giving white crystals (7.1 g), m.p. 303-311°. After

three more crystallizations, it melted at 312-317° (lit., m.p. above 300°, crude yield: 98%).

Trans-9,10-dihydro-9,10-dihydroxyphenanthrene

(J. Booth, E. Boyland and E. E. Turner, J. Chem. Soc., 1950, 1188)

The lithium aluminum hydride (1 g, 0.025 mole) was suspended in sodium dried ether (200 ml) and the 9,10-phenanthrenequinone (4 g, 0.019 mole), previously dried over phosphorus pentoxide, was put in a Soxhlet thimble and extracted with the ether. A greenish yellow precipitate was formed soon afterwards. Extraction was continued for 6 hours and the reaction mixture treated with water (40 ml) and dilute sulphuric acid (120 ml) after cooling to room temperature. The ether solution was combined with the ethereal extract of the aqueous solution and washed several times with dilute sodium hydroxide solution until free of green substance. When dried over sodium hydroxide pellets, the green substance was again formed and collected at the bottom of the flask. It was filtered off and the ether removed by distillation. The diol obtained was recrystallized from benzene giving white needles (0.36 g), m.p. 186-187°. The yield was 32% based on the amount of quinone consumed in this preparation (lit., needles, m.p. 185-187°, prisms, 194°). A great deal of phenanthrenequinone (0.29 g) was left in the thimble.

The preparation of diol was then repeated without a Soxhlet extractor.⁷⁴ The solid phenanthrenequinone (4 g) was added in

small portions to the stirred suspension of lithium aluminum hydride (1 g) in dry ether (200 ml) and the mixture heated under reflux for $4\frac{1}{2}$ hours. On addition of water (45 ml) and dilute sulphuric acid (60 ml), two clear layers were obtained. The ether layer contained some white needles, and when more ether was added with shaking, green substance was formed. This substance was decomposed with dilute sulphuric acid and the generated yellow solid dissolved in additional ether. The combined ethereal solution, after being washed with dilute sodium hydroxide solution, was again dried over sodium hydroxide pellets. The formation of green substance was still considerable. The product obtained (3.1 g) was recrystallized from benzene giving white needles (2.15 g, 53%), m.p. 186-187°.

It was attempted to carry out the reaction by the use of an ether extractor. The phenanthrenequinone (8 g, 0.038 mole) and sodium dried ether (100 ml) were put into an ether extractor which was joined to a flask (1 liter) containing lithium aluminum hydride (2 g, 0.05 mole) and dry ether (400 ml). Both of the suspensions were stirred with magnetic stirrers. The former was warmed in a water bath and the latter heated under reflux. Extraction was continued until all solid dissolved (5 hours) and the solution in the extractor was poured into the flask. The mixture was heated for one more hour and then worked out as described in the above section. White needles of the diol were obtained (5.3 g) in 65% yield when recrystallized from benzene, m.p. 186-187°. It was

sparingly soluble in hot cyclohexane and recrystallization from this solvent was not satisfactory.

Biphenyl-2,2'-dialdehyde

(D. M. Hall and B. Prakobsantisukh, J. Chem. Soc., 1965,6311)

To a suspension of the dihydrodihydroxyphenanthrene (8.5 g, 0.04 mole) in sodium dried benzene (250 ml), solid lead tetraacetate (18.2 g, 0.41 mole) was added and the mixture stirred at room temperature for 4 hours. After stirring, the white lead diacetate was filtered off and the yellow filtrate was evaporated to dryness under reduced pressure to give an oily substance (8.1 g) which solidified on standing overnight. The solid obtained was recrystallized from dry ether-light petroleum (b.p. 40-60°) giving pale yellow crystals (6.9 g) in 82% yield (lit., 73%), m.p. 57-59°.

In another preparation, the crude dialdehyde (4 g) was purified by chromatography. It was dissolved in a minimum amount of dry ether and passed through neutral alumina (60 g) using a mixture of 30% dry ether and 70% of light petroleum (b.p. 40-60°) as eluent. The first portion of eluate gave colourless prisms (1.92 g) and had m.p. 60-61° (lit., 61-62°) when recrystallized from its crystallization solvent. The second portion of eluate yield white crystals (1.31 g) which were insoluble in ether. When recrystallized from ethyl acetate, the compound melted at 133-134° and was identified as an ϵ -lactone (XXIV; page 39) both by its

melting point and infrared spectrum.

Trimethylene-1,3-bis(triphenylphosphonium)dibromide

(L. Hörner, H. Hoffmann, W. Klink, H. Ertel and V. G. Toscano,
Chem. Ber., 1962, 95, 581)

Triphenylphosphine (38 g, 0.145 mole, an excess of 45%) was dissolved in dimethylformamide (130 ml, dried over molecular sieve and distilled) and heated under reflux with 1,3-dibromopropane (10.1 g, 0.05 mole) for 3 hours. White crystalline solid began to form after about 30 minutes' heating. When reaction had finished, it was left to cool down, collected by filtration and washed with light petroleum (b.p. 60-80°). The filtrate gave a second crop of crystalline solid when concentrated. It was also washed with light petroleum and dried together with the first crop at 110-120°. Recrystallization from ethanol-ether gave white needles (32.4 g, 89%), m.p. 332-334° (lit., 335-336° and 344-345°⁷⁴). Triphenylphosphine (10.7 g, 91% of the excess) was recovered from the filtrate and the light petroleum washings after evaporation and recrystallization.

Trimethylene-bis(diphenylphosphine oxide)

(L. Hörner, H. Hoffmann, W. Klink, H. Ertel and V. G. Toscano,
Chem. Ber., 1962, 95, 581)

Trimethylene-bis(triphenylphosphonium)dibromide (15.8 g, 0.034 mole) was put into sodium hydroxide solution (6.8 g of NaOH

pellets in 80 ml of water) and boiled under reflux for 2 hours with stirring. The oily substance was extracted with chloroform and the solution dried over anhydrous sodium sulphate. After filtration and removal of solvent by distillation, a colourless oil was obtained. The oil solidified when allowed to stand overnight. The solid was washed with ether, sucked to dryness and crystallized from toluene-cyclohexane to give white crystals (10.6 g, 70%), m.p. 140-141° (lit., 142-144°; 63%).

Tetramethylene-1,4-bis(triphenylphosphonium)dibromide

(L. Hörner, H. Hoffmann, W. Klink, H. Ertel and V. G. Toscano, Chem. Ber., 1962, 95, 581)

Triphenylphosphine (65.6 g, 0.25 mole, 25% in excess), 1,4-dibromobutane (21.6 g, 0.1 mole) and acetonitrile (30 ml) were placed altogether in an autoclave and heated at 90° for 36 hours. The resulting crystalline mass was filtered off, dissolved in chloroform and precipitated with ether. When recrystallized from methanol-ether, it gave transparent tetragonal prisms (70.4 g, 95%) which became opaque after storage for a few days, m.p. 295-297° (lit., 296-298°).

Tetramethylene-bis(diphenylphosphine oxide)

(L. Hörner, H. Hoffmann, W. Klink, H. Ertel and V. G. Toscano, Chem. Ber., 1962, 95, 581)

Tetramethylene-bis(triphenylphosphonium)dibromide (37 g,

0.05 mole) was heated under reflux with sodium hydroxide solution (10 g of NaOH pellets in 100 ml of water) for 2 hours. The product was extracted with chloroform and the solution dried over anhydrous sodium sulphate. After drying, the solution was concentrated and treated with ether. The white precipitate obtained was collected on a filter, washed with some ether and sucked to dryness. When boiled with toluene, there was a great deal of insoluble material. It was filtered off and crystallized from ethanol-ether giving white prisms (9.05 g), m.p. 188-190°. The toluene solution was warmed on a hot plate with addition of cyclohexane. It gave tetramethylene-bis(diphenylphosphine oxide) in white crystalline form (9.36 g, 41%), m.p. 260-261° (lit., 259-260°; 100%).

The low melting compound (7.87 g) was once again boiled for 2 hours with sodium hydroxide solution (2.1 g of NaOH pellets in 20 ml of water) and worked up as stated above. The product obtained was all soluble in hot toluene. Addition of cyclohexane gave white crystals (5.81 g, 96%). It melted at 261-262°. The total yield of phosphine dioxide was 70%. The low melting one was obviously the intermediate compound tetramethylene-1-diphenylphosphine oxide-4-triphenylphosphonium bromide (lit.,⁶⁹ m.p. 172° and 187°).

Attempted preparation of 1,2,3,4-dibenzo-cyclonona-1,3,5,8-tetraene
(Adapted from: L. Hörner, H. Hoffmann, W. Klink, H. Ertel and
V. G. Toscano, Chem. Ber., 1962, 95, 581)

A two-necked flask (250 ml) was placed on the balance, flushed with nitrogen (dried with concentrated sulphuric acid) and weighed accurately. Potassium tert-butoxide was poured directly into the flask through a tubulate outlet and weighed to the required amount (4.48 g, 0.04 mole). After weighing, it was soaked with toluene (80 ml, dried over sodium wire and redistilled) and stirred with a glass-sealed magnetic stirrer. Trimethylene-bis(diphenylphosphine oxide) powder (4.444 g, 0.01 mole) was added in small portions. The solution which became pale yellow soon after the addition, was stirred for some time. The flask was fitted with a double surface condenser carrying a calcium chloride tube and the tube for the passage of nitrogen was replaced by a dropping funnel. Biphenyl-2,2'-dialdehyde (2.1 g, 0.01 mole), dissolved in dry toluene (20 ml), was then added slowly and the mixture heated under reflux on the oil bath at 130° for 9 hours. As the temperature rose to 65°, the colour of the solution gradually changed from yellow to pale green and finally to dark brown. When cooled to room temperature, water was added until no more solid was left in the flask. The organic layer was separated, washed with water and dried over anhydrous sodium sulphate. After filtration and removal of solvent under reduced pressure, a yellow solid (1.36 g) was obtained.

Crystallization from benzene gave 9,10-phenanthrenequinone (0.54 g) in 26% yield, m.p. 207-209°. The filtrate was chromatographed on neutral alumina (15 g) and washed down with light petroleum. The low boiling fraction (b.p. 40-60°) afforded a little bit of biphenyl (0.06 g, 4%), m.p. 68-69°. The high boiling fraction (b.p. 80-100°) yielded green oil which solidified on long standing. Recrystallization from light petroleum (b.p. 60-80°) gave fluorenone (0.32 g, 18%) in greenish yellow crystalline form, m.p. 82-83°. All the three compounds obtained were identified both by their melting points and by comparison of their infrared spectra with those of the known specimens.

Attempted preparation of 1,2,3,4-dibenzo-cyclooctatetraene

(Adapted from: L. Hörner, H. Hoffmann, W. Klink, H. Ertel and V. G. Toscano, Chem. Ber., 1962, 95, 581)

Potassium tert-butoxide (2.35 g, 0.021 mole) was introduced into a two-necked flask (250 ml) under dry nitrogen and covered with dry toluene (40 ml) as described in the previous experiment. Ethylene-bis(diphenylphosphine oxide) (2.15 g, 0.005 mole) was added in small portions with stirring and still under nitrogen atmosphere. The solution became pale yellow immediately after the addition of the first portion and the solid potassium tert-butoxide disappeared when all had been added. Stirring was continued for a short time and the solution of biphenyl-2,2'-dialdehyde (1.05 g, 0.005 mole)

in dry toluene (10 ml) was added through a dropping funnel. The mixture turned to dark-red colour during the addition. It was heated under reflux to an oil bath temperature of 130° for 9 hours and then left to cool down. The colour of the solution returned to pale yellow and there was some dark-red solid collected at the bottom of the flask. The solid was destroyed by addition of water and the organic layer, after separation, was washed with water and dried over anhydrous sodium sulphate. The dry solution was distilled off giving a yellow solid (0.72 g). It was recrystallized from benzene and gave 9,10-phenanthrenequinone (0.24 g) in 23% yield, m.p. $208-210^{\circ}$. The filtrate, when passed through neutral alumina (10 g) using light petroleum (b.p. $80-100^{\circ}$) as eluent, afforded some green oil (0.33 g). It solidified on standing for a few days. Recrystallization from light petroleum (b.p. $60-80^{\circ}$) gave fluorenone (0.18 g) in 20% yield, m.p. $83-84^{\circ}$. There was no evidence of the presence of the expected compound.

1,1,4,4-Tetraphenyl-1,3-butadiene

(L. Hörner, H. Hoffmann, W. Klink, H. Ertel and V. G. Toscano, Chem. Ber., 1962, 95, 581)

Potassium tert-butoxide (1.5 g, 0.0135 mole) was weighed in a two-necked flask under dry nitrogen and stirred with sodium dried toluene (20 ml) as described before. When the first portion of ethylene-bis(diphenylphosphine oxide) (1.38 g, 0.0032 mole) was

added, the solution became pale yellow in an instant. After the addition of all solid, a double surface condenser with drying tube was joined to the flask. Nitrogen was disconnected and its inlet fixed with a dropping funnel. The solution of benzophenone (1.25 g, 0.0068 mole) in dry toluene (10 ml) was then added through the funnel and the mixture heated under reflux for 9 hours on an oil bath at 130°. The colour of the solution changed from yellow to orange and to red-orange one after another and became lighter again when a colourless precipitate was separated. When cooled to room temperature, water was added to dissolve the solid formed. The water layer was removed and the organic solution washed with some water and dried over anhydrous sodium sulphate. After filtration and distillation, a green solid (0.51 g) was obtained. Recrystallization twice from glacial acetic acid gave pale green fluorescent needles (0.44 g) in 39% yield, m.p. 196-197° (lit., 195-196°; 41%).

Attempted preparation of 1,2,3,4-dibenzo-cyclodeca-1,3,5,9-tetraene
(Adapted from: L. Hörner, H. Hoffmann, W. Klink, H. Ertel and
V. G. Toscano, Chem Ber., 1962, 95, 581)

To a stirred suspension of potassium tert-butoxide (3.37 g, 0.03 mole) in dry toluene (40 ml) in a two-necked flask under dry nitrogen, tetramethylene-bis(diphenylphosphine oxide) powder (2.29 g, 0.005 mole) was added. The solution remained colourless after 2 hours' stirring although pale yellow colour had appeared

for a short time. It was gradually heated to 130° on an oil bath and kept at this temperature for another 2 hours. The solution changed to pale yellow, egg yellow and finally to pure tea colour with increase in temperature. The two solids dissolved in the hot solution but when the solution was cooled down, some white precipitate appeared again. The solution of biphenyl-2,2'-dialdehyde (1.05 g, 0.005 mole) in dry toluene (10 ml) was added dropwise at room temperature. The reaction mixture suddenly changed to red-orange colour. It was heated under reflux for 8 hours. During the heating, a colourless precipitate separated and some brown solid was formed. The solid was dissolved in water after cooling. The water solution was discarded and the organic solution washed with water and dried over anhydrous sodium sulphate. Removal of solvent gave yellow solid (0.84 g). When warmed with benzene, there appeared a small amount of white solid. It was filtered off and dried. The solid obtained (0.12 g) had m.p. $258-260^{\circ}$ and its infra-red spectrum was identical with that of the phosphine dioxide (5% recovery). The benzene solution gave 9,10-phenanthrenequinone (0.32 g) in 31% yield, m.p. $206-208^{\circ}$. Its mother liquor yielded fluorenone (0.13 g, 15%, m.p. $82-83^{\circ}$) and some more quinone (0.02 g) after chromatographic separation (neutral alumina, 10 g), first with light petroleum (b.p. $80-100^{\circ}$) and then with benzene as eluent.

Diphenylvinylphosphine oxide

(M. I. Kabachnik, T. Ya. Medved', Yu. M. Polikarpov and K. S. Yudina, Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk 1962, 9, 1584)

Ethylene oxide was first cooled to 0° , then evaporated at room temperature, and passed through soda lime into a solution of diphenylphosphine chloride (77.2 g, 0.35 mole) in sodium dried benzene (140 ml). The reaction flask (500 ml) was equipped with a dry ice condenser carrying an U-tube filled with paraffin oil. The reaction mixture was stirred with a magnetic stirrer and ethylene oxide was added at such a rate that the temperature did not rise above 60° . Addition was continued for a further period of 1 hour when the exothermic reaction had finished. The colourless solution obtained was distilled under reduced pressure to remove the solvent. The residual product was poured into an autoclave together with triethylamine (54 g, 0.53 mole) which had previously been dried over potassium hydroxide pellets and distilled through a fractionating column. The autoclave was heated for 1 hour at 120° then for 3 hours at 160° . The resulting crystalline solid was filtered off (130 g), dried over concentrated hydrochloric acid in a desiccator and extracted with 350 ml of hot benzene. The undissolved white precipitate was collected on a sintered glass filter and washed with water to remove triethylamine hydrochloride. Recrystallization from 50% ethanol gave ethylene-bis(diphenylphosphine oxide) as a by-product (12.7 g, 16.8%), m.p. $269-270^{\circ}$ (lit., $269-270^{\circ}$; 18%).

The benzene solution was washed with water, dried over anhydrous sodium sulphate and evaporated to dryness. The white solid obtained was crystallized from benzene giving the diphenylvinylphosphine oxide (42.84 g) in 53.6% yield, m.p. 116-117° (lit., 116-117°; 55%).

[2,2'-(methylimino)diethyl]bis[diphenylphosphine oxide]

(Adapted from: M. I. Kabachnik, T. Ya. Medved', Yu. M. Polikarpov and K. S. Yudina, Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk 1962, 9, 1584)

Diphenylvinylphosphine oxide (2.05 g, 0.009 mole) was put into a small Parr bomb provided with a stopper carrying a calcium chloride tube, and cooled in a dry ice-ethanol mixture to about -10°. Methylamine (1.4 g, 0.045 mole) was also cooled to the same temperature and added to the solid. The stopper was replaced by the original equipment and the reaction mixture allowed to stand at room temperature for one day. It was then dried under reduced pressure to remove the excess of methylamine. The product obtained was crystallized from benzene-ether giving methyldi(2-diphenylphosphinylethyl)amine (1.93 g, 88%) in white crystalline form, m.p. 166-167°. Found: C, 71.9; H, 6.6; N, 3.04; P, 11.9, M = 487.1837 (from mass spectrum). $C_{29}H_{31}NO_2P_2$ requires C, 71.4; H, 6.4; N, 2.9; P, 12.7%, M = 487.1830. The mass spectrum revealed that the sample contained traces of (2-methylaminoethyl)diphenylphosphine oxide.

2,2'-BiphenyldiacetonitrileA. In absolute alcohol

(J. Kenner and E. G. Turner, J. Chem. Soc., 1911, 99, 2101)

A saturated aqueous solution of potassium cyanide (1.47 g, 0.022 mole) was boiled with about 3 times its volume of absolute alcohol (20 ml), and to this boiling mixture, finely powdered 2,2'-bisbromomethylbiphenyl (3.4 g, 0.01 mole) was added in small portions. The reacting solution was maintained at 50-60° for 4 hours and then treated with water. The diacetonitrile came down as an oil but readily solidified. It was filtered off, washed with water, and dried over calcium chloride under vacuum. Crystallization from ethanol gave pale yellow crystals (1.85 g, 80%), m.p. 77-78° (lit., 77°; 90%). This preparation was repeated four times, some on a larger scale, and in the subsequent reactions, a mixture of two products was obtained: the diacetonitrile and a pale yellow solid, which was less soluble in ethanol, was separated and recrystallized twice from ethanol giving pale yellow needles, m.p. 192-193°. This solid was later proved to be the cyclic compound 1-amino-2-cyano-3,4,5,6-dibenzocyclohepta-1,3,5-triene (XVI; page 46). It had also been obtained by Kenner and Turner with m.p. 189° but was thought by them to be a cyclic iminonitrile (XXIII; page 47). When the cyclic compound was obtained, the yield of diacetonitrile was reduced to 33%.

B. In dimethyl sulfoxide

(Adapted from: B. Pecherer and A. Brossi,
J. Org. Chem., 1967, 32, 1053)

A saturated solution of 2,2'-bisbromomethylbiphenyl (20.4 g, 0.06 mole) in dimethyl sulfoxide (180 ml, dried over zeolite molecular sieve) was added gradually to a stirred suspension of potassium cyanide (9.76 g, 0.15 mole) in the same solvent (60 ml). The solution became yellow within a short time and its temperature rose to 35° at the end of the addition. After keeping at 30-35° for 2 hours, water was added and the pale yellow precipitate obtained was filtered off, washed with water and dried. The crude product (12 g) was crystallized from ethanol giving pale yellow rectangular blocks (10.8 g, 78%), m.p. 77-78°. This preparation had been repeated seven times with 142.8 g of dibromide. The diacetonitrile obtained was 71.2 g in all.

1-amino-3,4,5,6-dibenzocyclohepta-1,3,5-triene-2-carboxylic acid

(Adapted from: J. Kenner and E. G. Turner,
J. Chem. Soc., 1911, 99, 2101)

The unknown (1 g, m.p. 192-193°; supposing it was an aminonitrile) obtained from preparation of 2,2'-biphenyldiacetonitrile was dissolved in cold concentrated sulphuric acid (10 ml) and allowed to stand overnight. The resulting solution was poured on to crushed ice with stirring. The white precipitate obtained was filtered off, washed with cold water and dissolved in dilute sodium

hydroxide solution. After filtration, the filtrate was acidified with dilute sulphuric acid. The regenerated solid was collected on a filter, washed with water, dried and crystallized from ethanol giving white, fine crystals (0.67 g, 62%), m.p. 179° (lit., 180° , for the acid obtained from the supposed cyclic iminonitrile).

2,2'-Biphenyldiacetamide

(J. Kenner and E. G. Turner, J. Chem. Soc., 1911, 99, 2101)

2,2'-Biphenyldiacetonitrile (13.93 g, 0.06 mole) was dissolved in five times its weight of concentrated sulphuric acid and the solution allowed to stand for 24 hours. It was then poured slowly into approximately 250 ml of water and made alkaline with ammonia solution (S.G. 0.88, 90 ml). The yellow precipitate obtained was collected on a filter, washed with cold water and dried in the oven. Crystallization from ethanol gave pale yellow needles (11.6 g, 72%), m.p. $209-211^{\circ}$. When recrystallized twice from the same solvent, it had m.p. $217-218^{\circ}$ (lit., $210-211^{\circ}$). This procedure was performed six times, consuming 80.1 g of diacetonitrile to obtain 55.6 g of diacetoamide.

2,2'-Biphenyldiacetic acid

(J. Kenner and E. G. Turner, J. Chem. Soc., 1911, 99, 2101)

2,2'-Biphenyldiacetamide (5.8 g, 0.0216 mole) was boiled under reflux with sodium hydroxide solution (10%, 60 ml) until no

more ammonia gas could be detected (16 hours). The mixture was then acidified with dilute sulphuric acid and the diacetic acid, which came down as a pale yellow precipitate, was filtered off. It was washed with some icy water and crystallized from water (with addition of charcoal) giving colourless prisms (4.9 g, 84%). m.p. 151-152° (lit., 153-154°). In another preparation, the acid obtained had m.p. 174-175° and since then all preparations of this acid have given the high melting product. The low melting one turned out to have m.p. 174-175° (lit.,⁶⁶ 174-174.5°) after storage for a few months. Altogether 41.6 g of the diacetic acid were obtained by this method, some on a larger scale, the consumption of diacetamide being 52.1 g.

Diethyl 2,2'-biphenyldiacetate

(J. Kenner, J. Chem. Soc., 1913, 613)

2,2'-Biphenyldiacetic acid (2.7 g, 0.01 mole) was dissolved in ethanol (40 g) and heated under reflux with its own weight of concentrated sulphuric acid for 5 hours. The reaction mixture was poured into water (~400 ml) with stirring and the oily substance extracted with ether. The ethereal solution was washed with sodium bicarbonate solution and dried over anhydrous sodium sulphate. After drying and removal of solvent, it gave colourless oil which did not solidify on long standing. It was then dissolved in sodium dried ether and two-thirds of the solution (100 ml) was

added to a stirred suspension of lithium aluminum hydride (1 g) in dry ether (50 ml) as stated in the following preparation. The product obtained was crystallized from benzene-n-hexane giving the 2,2'-bis(2-hydroxyethyl)biphenyl (0.77 g, m.p. 87-88°) in an overall yield of 48%. The remaining one-third of the solution was evaporated and attempts to crystallize from ethanol or light petroleum (b.p. 60-80°) were unsuccessful (lit., m.p. 49° from light petroleum).

2,2'-Bis(2-hydroxyethyl)biphenyl

(K. Mislw, S. Hyden and H. Schaefer,
J. Amer. Chem. Soc., 1962, 84, 1449)

To a stirred suspension of lithium aluminum hydride (1.75 g, 0.046 mole) in sodium dried ether (50 ml), a solution of 2,2'-biphenyldiacetic acid (5 g, 0.0184 mole) in dry ether (400 ml) was added at such a rate that the solution boiled gently. When reaction was over, wet ether, water and 2 N sulphuric acid were added one after another until two clear layers were obtained. The ether layer and the ethereal abstract of the aqueous layer were combined, washed with sodium bicarbonate solution and dried over anhydrous sodium sulfate. Removal of most of the ether afforded a colourless oil which crystallized on standing overnight. The product (3.9 g) had m.p. 77-79°. Recrystallization from benzene-n-hexane gave colourless prisms (3.5 g) in 78% yield, m.p. 88-89° (lit., 88-89°). The

reduction of diacetic acid was repeated six times and 20.4 g of diol were obtained.

2,2'-Bis(2-bromoethyl)biphenyl

(K. Mislow, S. Hyden and H. Schaefer,
J. Amer. Chem. Soc., 1962, 84, 1449)

A solution of 2,2'-bis(2-hydroxyethyl)biphenyl (5 g, 0.0206 mole) in sodium dried benzene (50 ml) in a two-necked flask was cooled to 10°. The flask was loosely stoppered and phosphorus tri-bromide (5.6 g, 0.0206 mole) was added dropwise through a separatory funnel. A viscous material appeared immediately after each addition. It was stirred until all dissolved and then heated under reflux for 2 hours. The clear resulting solution was poured out, washed with cold water, and dried over anhydrous sodium sulfate. After filtration and removal of benzene under reduced pressure, it gave a pale brown syrup (6.9 g). The syrup was dissolved in n-hexane, passed through 140 g of neutral alumina (activity II) and eluted with n-hexane. Evaporation of the solvent from the combined eluates gave a colourless oil (4.86 g). Attempts to crystallize from methanol were unsuccessful. It was then purified by vacuum distillation. The dibromide obtained (2.49 g, 41%) had b.p. 180°/2 mm (lit., m.p. 48-49.5° from methanol). Altogether 19.68 g of diol were used in this preparation to give a total yield of 12.29 g.

1-Methyl-2,3,8,9-tetrahydro-4,5:6,7-dibenzazone

(Adapted from: B. Pecherer and A. Brosi,
J. Org. Chem., 1967, 32, 1053)

A solution of 2,2'-bis(2-bromoethyl)biphenyl (1.84 g, 0.005 mole) in sodium dried benzene (70 ml) was poured into an autoclave accommodated with a stopper carrying a calcium chloride tube, and cooled to about -10° in a mixture of dry ice and ethanol. The methylamine, available in a sealed tube, was also cooled to -10° and added to the solution as soon as the sealed tube was opened. The autoclave was then immediately fitted with its original equipment and the mixture heated for 2 hours at $140-150^{\circ}$ under fifteen atmospheres of hydrogen. When reaction had finished, the benzene solution was washed with cold water and extracted 3 times with hydrochloric acid (10%, 25 ml in all). On addition of an excess of potassium hydroxide solution (10%, 28 ml), the liberated amine was taken up with ether (100 ml) and dried over anhydrous sodium sulfate. After filtration and removal of ether by fractional distillation, a slightly coloured syrup (1.15 g) was obtained. It was dissolved in benzene (12 ml), passed through 30 g of "Camag" alkaline alumina (activity I) and eluted with benzene. The eluate, when evaporated to dryness under reduced pressure, gave a clear, oily substance (0.92 g) which did not solidify on long standing. Attempts to recrystallize from solvents such as benzene and light petroleum were unsuccessful. It was thereafter converted into its monopicrate

(0.83 g) as described in the following preparation. The synthesis of this tertiary amine was performed 3 times with different quantities of dibromide to afford 5.62 g of the neat base as a syrup. The yield in the ring-closure stage was 35.7% based on the amount of picrate obtained.

1-Methyl-2,3,8,9-tetrahydro-4,5:6,7-dibenzazonine monopicrate

A. Preparation

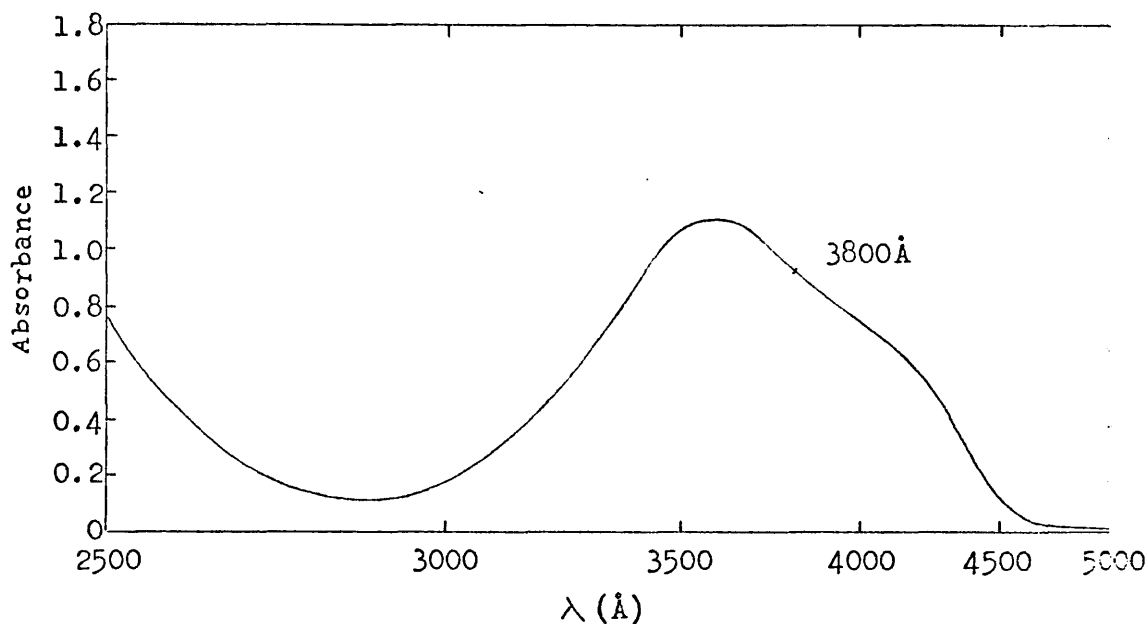
A concentrated ethanolic solution of the tertiary amine (syrup, 0.92 g, ≤ 0.0038 mole) was added dropwise with shaking to a saturated solution of picric acid (0.87 g, 0.0038 mole) in ethanol. The yellow picrate was obtained at once. It was filtered off and dried under vacuum. Recrystallization twice from benzene gave flat yellow crystals, m.p. 176-177°. The yield (0.83 g) was 46%, calculated as if the syrup were a pure compound. Altogether 5.51 g of the tertiary amine were converted into the monopicrate giving a total yield of 4.22 g. Found: C, 59.0, 59.2; H, 4.7, 4.8; N, 12.2, 12.0. $C_{23}H_{22}N_4O_7$ requires C, 59.3; H, 4.9; N, 11.9%.

B. Spectrophotometric determination of the molecular weight

(K. G. Cunningham, W. Dawson and F. S. Spring,
J. Chem. Soc., 1957, 3, 2305)

A few pieces of the picrate being weighed accurately (3.25 mg) were dissolved in ethanol (96%) in a volumetric flask and the solution diluted to 100 ml. The ultra-violet spectrum recorded

with this concentration by the use of a Unicam SP 800 spectrophotometer and a pair of matched quartz cells of 1 cm thickness was shown below:



By assuming the picrate ion has a value of 13,440 for ϵ_{3800} , the molecular weight M was determined from the relationship

$$M = 13,440 Cn / \log \left(\frac{I_0}{I} \right)$$

where n is the molar ratio of the picric acid to bases or picric acid to hydrocarbons in the picrate and C is measured in grams per litre of solution. The value calculated and found for the mono-picrate were listed in Table 3.

Table 3.

Picrate	C (mg/100 ml)	$\log \left(\frac{I_0}{I} \right)_{3800}$	M_{found}	$M_{\text{calc.}}$	Error. %
1-Methyl-2,3,8,9-tetrahydro-4,5:6,7-dibenzazonine	3.250	0.93	469.6	466.4	+ 0.7

C. Decomposition

The monopicrate (0.83 g, 0.00178 mole) was put into sodium hydroxide solution (10%, 7 ml) and well stirred with addition of water (15 ml) and ether (20 ml) to bring all solid dissolved. The alkaline solution was repeatedly extracted with ether and the combined ethereal solution dried over potassium hydroxide pellets. After filtration, ether was removed by careful fractional distillation and the liberated amine dried in a vacuum desiccator. Crystallization from light petroleum (b.p. 60-80°) gave colourless, rectangular crystals (0.32 g) in 76% yield, m.p. 55-56°. Found: C, 85.3; H, 8.3; N, 6.3. $C_{17}H_{19}N$ requires C, 86.0; H, 8.0; N, 5.9.

1-Methyl-2,3,8,9-tetrahydro-4,5:6,7-dibenzazonine camphorsulphonate

The tertiary amine (0.23 g, 0.00097 mole) was dissolved in a minimum amount of ethanol in a conical flask (10 ml) and a saturated solution of (+)-camphor-10-sulphonic acid (0.225 g, 0.00097 mole) in ethanol was added dropwise. The flask was loosely stoppered with a cork and left to stand at room temperature. The solution remained clear after many days. When evaporated to dryness in the air, it gave an oily substance which did not solidify. It was then warmed with a few milliliters of acetone and on scratching and standing, white crystalline solid (0.4334 g) was obtained. Recrystallization from acetone yielded transparent crystals which became opaque after keeping in the vacuum desiccator

for one day. Both the first crop (0.084 g) and the second crop (0.1526 g) had m.p. 201-202°. Yield: 52%.

(+)-1-Methyl-2,3,8,9-tetrahydro-4,5:6,7-dibenzazone

The azonine camphorsulphonate (2nd crop; 120 mg; 0.000255 mole) was placed in a small conical flask followed by addition of water (8 ml) and sodium hydroxide solution (4 ml; 0.01 mole) with stirring. The milky mixture was then extracted with chloroform (4 ml) and the organic solution pipetted off, washed twice with water (4 ml in all) and dried over a little bit of potassium carbonate for a short while in a small glass pot with sintered filter. After filtration under pressure, a portion of solution was transferred to a polarimeter tube and observed with a Perkin-Elmer P 23 spectropolarimeter and the rest was kept in a refrigerator. The liberated azonine was found to be dextrorotatory and optically stable at room temperature. It racemized after heating under reflux in cyclohexane for one hour. The results obtained were listed in Table 4A and 4B and a plot of specific rotation against wavelength is shown in Figure 9.

Table 4A.

Optical rotations of (+)-1-methyl-2,3,8,9-tetrahydro-4,5:6,7-dibenzazonine in chloroform (concentration of solution: 0.00505 g/ml, being calculated from the amount of its camphorsulphonate employed in this determination; cell length: 0.01 dm).

A. At 21°.

λ (nm)	α_{λ}^{21}	$[\alpha]_{\lambda}^{21}$	λ (nm)	α_{λ}^{21}	$[\alpha]_{\lambda}^{21}$
258	+0.034°	+673°	278	+0.015°	+297°
260	0.031	614	282	0.013	257
262	0.029	574	286	0.010	198
264	0.027	535	290	0.010	198
266	0.024	475	294	0.008	158
268	0.022	435	298	0.009	178
270	0.020	396	302	0.009	178
272	0.019	376	306	0.008	158
274	0.018	356	310	0.007	138
276	0.017	336			

B. At 57°.

λ (nm)	α_{λ}^{57}	$[\alpha]_{\lambda}^{57}$
254	+0.025°	+495°
256	0.024	475
258	0.023	455
260	0.022	436
262	0.019	376
264	0.014	277
266	0.012	238
268	0.008	158
270	0.009	178

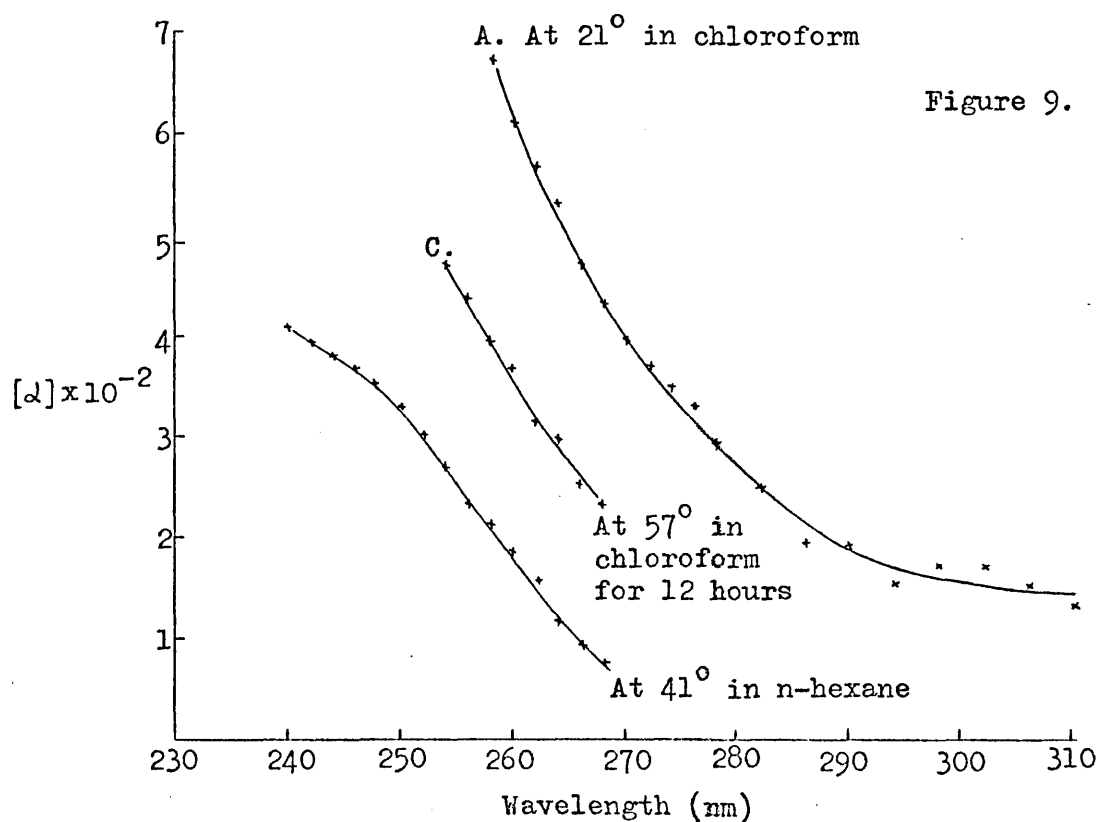
C. After keeping at 57° for 12 hrs.

λ (nm)	α_{λ}^{57}	$[\alpha]_{\lambda}^{57}$
254	+0.024°	+475°
256	0.022	436
258	0.020	396
260	0.019	376
262	0.016	317
264	0.015	297
266	0.013	257
268	0.012	238
270	0.007	138

Table 4 B.

Optical rotations of (+)-1-methyl-2,3,8,9-tetrahydro-4,5:6,7-dibenzazonine in n-hexane (concentration of solution: 0.00758 g/ml, being calculated from the amount of its camphorsulphonate employed in this determination; cell length: 0.01 dm) at 41°.

λ (nm)	α_{λ}^{41}	$[\alpha]_{\lambda}^{41}$	λ (nm)	α_{λ}^{41}	$[\alpha]_{\lambda}^{41}$
240	+0.031°	+409°	256	+0.017°	+224°
242	0.030	395	258	0.016	211
244	0.029	382	260	0.015	198
246	0.028	369	262	0.012	158
248	0.027	356	264	0.009	119
250	0.025	330	266	0.007	92
252	0.023	303	268	0.006	79
254	0.020	264			



1-Methyl-2,3,8,9-tetrahydro-4,5:6,7-dibenzazonine tartrate

To a concentrated solution of the tertiary amine (0.05 g, 0.00021 mole) in ethanol in a conical flask (5 ml), a saturated solution of (+)-tartaric acid (0.0158 g, 0.000105 mole) in ethanol was added. The flask was loosely stoppered and stood at room temperature for a few days. No solid separated from the solution. It was therefore evaporated under vacuum to dryness and the resulting oil warmed with acetone. On scratching with a glass rod and standing overnight, white solid was obtained. Recrystallization from acetone gave tiny crystals (0.023 g, 35%), m.p. 118-120°.

1,1-Dimethyl-2,3,8,9-tetrahydro-4,5:6,7-dibenzazoninium iodide

A mixture of methyl iodide (0.082 g, 0.0006 mole) and the tertiary amine (syrup, 0.095 g, 0.0004 mole) in acetone (dried over anhydrous potassium carbonate and then distilled through a fractionating column) was heated under reflux for one hour. The resulting solution was red in colour, and when evaporated to dryness gave an oily substance which solidified on standing overnight. The solid (0.14 g) was washed with ethyl acetate and recrystallized from ethanol-ether giving pale red prisms, m.p. 168-170°. The yield of the quaternary iodide (0.052 g) was 34%, assuming that the syrup was a pure compound. Found: C, 57.1; H, 5.3; N, 3.6; I, 33.4. $C_{18}H_{22}NI$ requires C, 57.0; H, 5.8; N, 3.7; I, 33.5%.

Condensation between biphenyl-2,2'-dialdehyde
and o-phenylenediamine

(F. Sparatore, Ann. Chim. (Italy), 1959, 49, 2102)

Biphenyl-2,2'-dialdehyde (1.05 g, 0.005 mole) and o-phenylenediamine (0.54 g, 0.005 mole) were dissolved separately in a minimum amount of methanol (10 ml in all) at room temperature. The two solutions were mixed up and left to stand for one day. The mixed solution remained very clear after standing. It was then treated with water and a great deal of pale yellow solid was obtained. After filtration and drying, the solid (1.39 g) was dissolved in some benzene, passed through neutral alumina (20 g) and eluted with sodium dried ether. The eluate, when evaporated to dryness, gave nearly colourless crystals (1.27 g, m.p. 190-193°). It was recrystallized from aqueous ethanol (35% of water) giving colourless crystals (1.15 g) with m.p. 192-193° (lit.,⁴⁷ 189-190°) in 82% yield and was shown to have the structure (II) as discussed on page 67.

The dialdehyde (1.05 g) and the diamine (0.54 g), when dissolved in ethanol (25 ml in all) and the mixture scratched with a glass rod, produced pale yellow solid almost instantaneously. The solid obtained was crystallized from aqueous ethanol (35% of water) giving colourless prisms (0.55 g, m.p. 157-158°). The filtrate was poured into water (20 ml), digested with benzene and dried over anhydrous sodium sulphate. After drying, most of the benzene was

removed and the concentrated solution purified by chromatography on neutral alumina (15 g) using sodium dried ether as eluent. The eluate gave some more crystals (0.38 g, m.p. 154-157°). Total yield: 66%. When recrystallized from ethanol or aqueous ethanol, the compound turned out to have m.p. 192-193° and could not be got back into m.p. 154-157° by recrystallization from the same solvent. It was thought to be the same compound of higher melting modification because its infra-red spectrum was identical with that of the lower melting form which had gradually turned out to have m.p. 192-193° on storage for a few weeks.

p-Acetamidobenzoic acid

(E. Ritsert and W. Epstein, Chem. Zentr., 1904, 1, 1587, Deutsch R. P. 151725)

p-Aminobenzoic acid (50 g, 0.364 mole) was added to a warm mixture of glacial acetic acid (200 ml) and acetic anhydride (200 ml) with shaking and then heated under reflux for 6 hours. The resulting solution was allowed to stand overnight and the crystalline solid obtained was filtered off, washed with water and dried. The crude product (33.6 g) had m.p. 254-256°. The filtrate was concentrated to give another crop of crystalline solid (21.5 g, m.p. 253-256°) and then poured into water (200 ml including washings) giving the last crop (1.4 g, m.p. 250-255°). Recrystallization from ethanol gave white prisms (altogether 52.2 g) in 80% yield, m.p. 255-257° (lit., 250-251° and 260-262°; 55%⁷⁴).

m-Nitro-p-acetamidobenzoic acid(A. Kaiser, Chem. Ber., 1885, 18, 2942)

Fuming nitric acid (d. 1.51, 96 ml) was stirred with a glass-sealed magnetic stirrer and cooled in an ice-salt mixture to a temperature between 0° and -10°. p-Acetamidobenzoic acid (50 g, 0.288 mole) was added to it at such a rate that the temperature did not rise above 7°. After the addition, the greenish yellow solution was stood in the freezing mixture for one hour and then poured on to crushed ice with stirring. The yellow solid obtained was collected on a filter, washed with water and dried. The crude product (53.3 g) melted at 215-218°. Crystallization from ethanol gave yellow solid (46.5 g, 74%), m.p. 217-220° (lit., 220-221°).

Ethyl m-nitro-p-aminobenzoate

(B. Prakobsantisukh, Ph.D. Thesis, University of London, 1964)

m-Nitro-p-acetamidobenzoic acid (20 g, 0.089 mole) was dissolved in ethanol (400 ml) and the solution heated under reflux with concentrated hydrochloric acid (120 ml, d. 1.18) for 5 hours. The reaction mixture was then transferred to a large beaker and water (~400 ml) was added with stirring until no more turbidity appeared. The yellow solid obtained was filtered off, washed with some water and dried. The crude product had m.p. 128-131°. Recrystallization twice from ethanol gave yellow crystalline solid (11.6 g, 62%). It melted at 135-138° (lit.,⁸⁰ m.p. 140-142°).

Ethyl 3,4-diaminobenzoate

(E. Ritsert and W. Epstein, Chem. Zentr., 1904, 1, 1587,
Deutsch R. P. 151725)

Stannous chloride (37.5 g, 0.166 mole) was stirred with concentrated hydrochloric acid (47 ml) in a two necked flask fitted with a dropping funnel and a distillation condenser. The mixture was heated to boiling and a saturated solution of ethyl m-nitro-p-aminobenzoate (10 g, 0.0475 mole) in ethanol was added dropwise. As soon as the nitro compound touched the hot mixture, its yellow colour faded away. A great portion of the solvent was distilled off during the addition. The resulting solution was pale green in colour, and when cooled to room temperature, it was treated with an excess of sodium hydroxide solution (30%). The white cake-like precipitate obtained was filtered off, washed with icy water and extracted with hot water. Successive evaporation of water gave three crops of pale brown needles (2.5 g, 0.9 g and 0.2 g) in 42% yield. They melted at 108-110°, 107-109° and 105-108° respectively. When recrystallized from hot water, the compound had m.p. 109-110° (lit., 110-111°; 30% yield). The crystals obtained were nearly colourless.

Condensation between biphenyl-2,2'-dialdehyde
and ethyl 3,4-diaminobenzoate

(B. Prakobsnatisukh, Ph.D. Thesis, University of London, 1964)

A saturated ethanolic solution of biphenyl-2,2'-dialdehyde (0.84 g, 0.004 mole) was mixed up with that of ethyl 3,4-diaminobenzoate (0.72 g, 0.004 mole) at room temperature. No solid was formed after three days' standing. On scratching with a glass rod, a fairly pure yellow precipitate was obtained. It was filtered off and dried. The crude product (0.76 g) melted at 220-224°. The mother liquor was left to stand for one day giving some more crystals (0.11 g) which also melted at 220-224°. The remainder was evaporated to dryness, dissolved in some benzene and passed over a column of neutral alumina (10 g). When eluted with light petroleum (b.p. 60-80°), it gave nearly colourless solid (0.14 g), m.p. 221-224°. The three lots of product were combined and recrystallized from ethanol giving white prisms (0.82 g, 58%), m.p. 223-225°. After two more crystallization from ethanol, its m.p. rose to 228-229° (Thesis, m.p. 226°; yield: 47%; analysis fits $C_{23}H_{18}N_2O_2$). This compound was proved to have the structure (XI) as discussed on page 77.

2,2'-Diaminobiphenyl

(W. L. Mosby, *J. Org. Chem.*, 1957, 22, 671)

A mixture of iron powder (60 g), water (30 ml) and glacial acetic acid (2 ml) were stirred mechanically in a two-necked flask

(500 ml) and boiled under reflux for 15 minutes. 2,2'-Dinitrobi-phenyl (24.4 g, 0.1 mole) was added in small portions occasionally washed down with ethanol (10 ml). It was again boiled for 5 hours and then abstracted with hot benzene (200 ml). The benzene solution was decanted and dried over anhydrous potassium carbonate. After filtration and removal of solvent, the product obtained (17.5 g) was crystallized from a mixed solvent containing 80% of ethanol and 20% of light petroleum (b.p. 60-80°) giving slightly coloured, transparent prisms (16.9 g, 92%), m.p. 79-80° (lit., 80-81°, 97.8%).

Condensation between 2,2'-diaminobiphenyl and o-phthalaldehyde

2,2'-Diaminobiphenyl (2.76 g, 0.015 mole) and o-phthalaldehyde (2.01 g, 0.015 mole) were dissolved separately in a minimum amount of ethanol (52 and 28 ml respectively) at room temperature. The solutions were gradually mixed up and the mixture was found to have a red colour. After one day's standing, there appeared a red crystalline solid and it was scratched from time to time. When more solid was formed, it was filtered off and washed with ether. The crude product (1.82 g) had m.p. 225-230° and after recrystallization from benzene, it gave red tiny crystals (1.58 g) with m.p. 246-248°. When recrystallized from ethanol, it melted at 249-250° and further crystallization from ethyl acetate, the melting point raised to 253-254°.

The filtrate was combined with the ether washings and evaporated to dryness. The dark-red gum obtained (3.1 g) was dissolved in some benzene, passed through a column of neutral alumina (60 g) and eluted with sodium dried ether. Removal of solvent yielded an amorphous red solid (1.2 g, m.p. 90-95°) which was recrystallized from ethanol/petroleum ether (b.p. 60-80°) giving yellowish red crystals (0.84 g, 18%) with m.p. 166-168°. The column was then washed with chloroform giving another crop of red solid which also had m.p. 246-248° (0.72 g) after recrystallization from benzene. The total yield of this compound (2.3 g) was 53%.

Thus the condensation between 2,2'-diaminobiphenyl and *o*-phthalaldehyde gave two products. The one with m.p. 253-254° was believed to have the structure A (see page 98). Found: C, 82.0, 83.4; H, 4.55, 4.77; N, 10.1, 9.8; O, 3.11. $C_{40}H_{26}N_4O$ requires C, 83.0; H, 4.53; N, 9.7; O, 2.77%. The other one with m.p. 166-168° was proved to be 2-amino-2'-phthalimidobiphenyl (see page 89 Found: C, 75.3; H, 4.6; N, 9.4; O, 10.5. Calc. for $C_{20}H_{14}N_2O_2$: C, 76.4; H, 4.5; N, 8.9; O, 10.2% (lit.,³⁹ m.p. 174-176°).

Treatment of 2,2'-diaminobiphenyl with *o*-phthalic acid

2,2'-Diaminobiphenyl (0.92 g, 0.005 mole) and *o*-phthalic acid (0.83 g, 0.005 mole) were dissolved separately in ethanol (40 ml in all) at room temperature. The two solutions were well mixed and allowed to stand for one week and then distilled under

reduced pressure. The residue was washed with chloroform and the insoluble solid filtered off, dried and crystallized from ethanol-chloroform giving white crystalline phthalic acid (0.73 g, 88% recovery), m.p. 192-194°. The chloroform solution was evaporated to dryness and the solid obtained was crystallized from ethanol-light petroleum (b.p. 60-80°) to give the diamine (0.79 g, 86% recovery), m.p. 78-80°. There was no reaction between the two reactants under the above conditions.

Dehydration of the red compound

The red compound (0.1 g, m.p. 253-254°) was dissolved in sodium dried xylene (60 ml) and heated under reflux with p-toluene-sulfonic acid (0.04 g) for one hour. When cooled to room temperature, the resulting solution was washed with some sodium bicarbonate solution then with water and dried over anhydrous sodium sulphate. After drying, the solvent was distilled off under reduced pressure giving a dark red gum which was washed with a little ethanol then dissolved in chloroform and allowed to evaporated on a watch glass. A small piece of red solid was deposited and this was collected and washed again with ethanol. Its infra-red spectrum was recorded (see page 85) but the solid obtained was insufficient for determination of its melting point.

Partial optical resolution of the red compound (m.p. 253-254°)

(A method adapted from resolution of optically active 4,5,6,7-dibenzo-1,2-dithiocyclooctadiene. A. Lüttringhaus, U. Hess and H. J. Rosenbaum, Z. Naturf., 1967, 22b, 1296)

Technical "cellulose-2 $\frac{1}{2}$ -acetate" (110 g) was finely ground, passed through a sieve to remove the coarse particles and boiled with cyclohexane for 6 hours. After filtration, it was dried at 80° under vacuum and then soaked with thiophene-free dry benzene for one day. The mixture was then poured directly into a vibrated column (height: 100 cm, ϕ 1.8 cm) and the solution of the red compound (0.4 g, m.p. 249-250°) in dry benzene (28 ml) was run through the acetate using sodium dried ether as eluent. The eluate was collected in some accurately weighed bottles at 10 ml-fraction with a fraction collector. When evaporated to dryness, the fine red crystals obtained in different bottles were dried in a vacuum desiccator. The various optical rotations of different fractions were determined with a sodium D line polarimeter (tube length = 2 dm) and the results are listed in Table 5.

Table 5.

Fraction No	Eluate (ml)	Obtained (mg)	Concentration (mg/20ml CHCl ₃)	α_D^t	t (°C)	$[\alpha]_D^t$
1-7	70	2.14				
8-9	20	21.21	21.21	+0.24	22	+113.1
10-11	20	29.27	27.36	+0.28	22.5	+102.3
12-13	20	26.16	23.54	+0.17	21	+72.2
14-17	40	32.30	25.32	Nil		
18-21	40	27.09	27.09	-0.11	23	-40.6
22-29	80	17.78	17.78	-0.1	23	-56.2
30-40	110	11.21				

The (+) red compound obtained from fraction 10-11 also had m.p. 249-250°. Its solution (27.36 mg/20 ml CHCl₃) on standing at room temperature for 5 days was observed to have $\alpha_D^{22} = +0.27^\circ$; $[\alpha]_D^{22} = +98.7^\circ$. This specific rotation did not change when the solution in chloroform was boiled under reflux for 1½ hours.

Preparation of 9,20-diazatetrabenzo[a,c,g,i]cyclododecene (I; p. 122)

(E. D. Bergmann, I. Agranat and M. A. Kraus,
J. Org. Chem., 1967, 33, 600)

Biphenyl-2,2'-dialdehyde (1.05 g, 0.005 mole) and 2,2'-diaminobiphenyl (0.92 g, 0.005 mole) were dissolved separately in a minimum amount of ethanol (20 ml for each) at room temperature and then mixed. White crystalline solid was observed soon afterwards. The solution was left to stand overnight and the solid obtained was filtered off and dried. It was crystallized from benzene giving white prisms (1.22 g, 68%), m.p. 306-309°. After recrystallization twice from the same solvent it melted at 312-313° (lit., above 300° from butanol).

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