TO MY PARENTS

and

PATRICIA.

STUDIES IN THE DIBENZOBIPHENYLENE SERIES

by

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of the University of Edinburgh

in the Faculty of Science.

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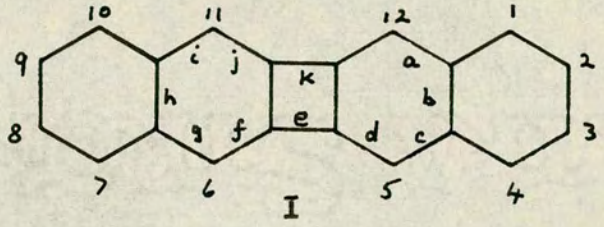
Nomenclature

The names and numbering of the five isomeric dibenzobiphenylenes are given below. In the literature, these compounds have occasionally been named differently and these other names are given below the accepted (underlined,) names.

DIBENZO [b, h] BIPHENYLENE

2, 3: 6, 7 - DIBENZOBIPHENYLENE

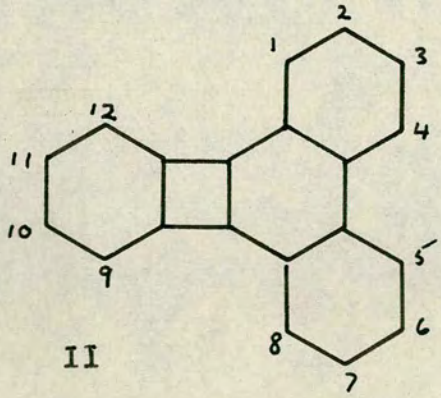
2, 3 - BINAPHTHYLENE



I

DIBENZO [a, c] BIPHENYLENE

1, 2: 3, 4 - DIBENZOBIPHENYLENE

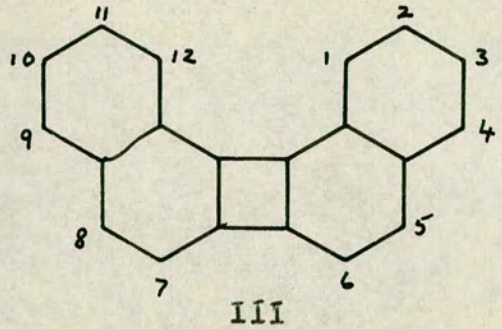


II

DIBENZO [a, i] BIPHENYLENE

1, 2: 7, 8 - DIBENZOBIPHENYLENE

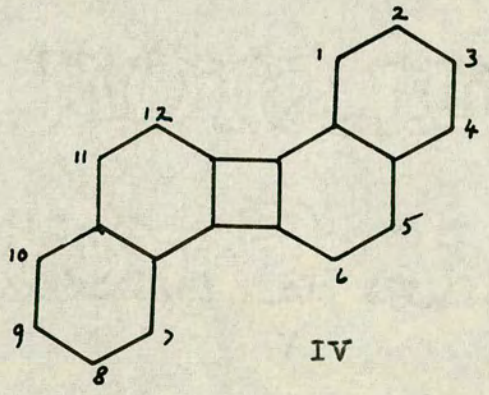
1, 2 - BINAPHTHYLENE.



III

DIBENZO [a, g] BIPHENYLENE

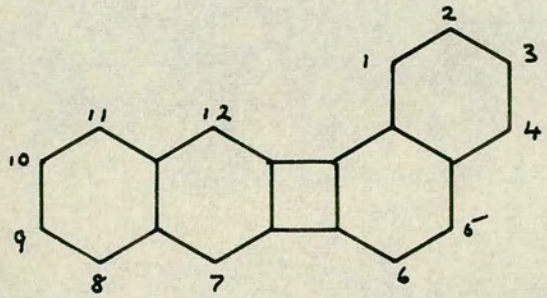
1, 2: 5, 6 - DIBENZOBIPHENYLENE



IV

DIBENZO [a, h] BIPHENYLENE

1, 2: 6, 7 - DIBENZOBIPHENYLENE



V

INTRODUCTION

Just over a century ago Kekule put forward the hypothesis of a cyclic structure containing alternate single and double bonds for benzene. This concept with certain modifications was gradually accepted and chemists came to attribute the stability of benzene and its derivatives to the presence of a cyclic, fully conjugated system of single and double bonds. It then became of great interest to prepare the related compounds cyclooctatetraene and cyclobutadiene to see whether they would exhibit aromatic properties.

In 1911, Willstätter and Waser (1) succeeded in preparing cyclooctatetraene and demonstrated that it behaved as a typical polyolefin. Willstätter and his collaborators tried to prepare cyclobutadiene as well, but they were unsuccessful. Later workers were also unsuccessful in their efforts to isolate the hydrocarbon until 1965, when a note appeared in the literature by Fitzpatrick et al. (82) reporting its isolation and reactions. It was shown by them that although it was an extremely reactive diene, it nonetheless possessed a finite lifetime.

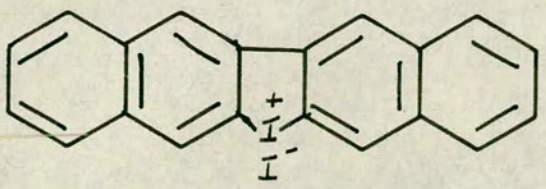
However, derivatives of this system have been prepared and recently there has been a great revival of interest in the subject. The best known derivative is biphenylene and this thesis deals with the dibenzo derivatives of biphenylene, which may also be considered as dinaphtho derivatives of cyclobutadiene. The dibenzobiphenylenes

exist in five stereoisomeric forms (I - V), all but one of which (V), have been synthesised.

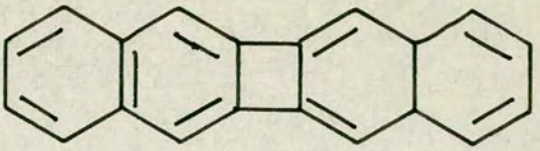
Prior to the first successful synthesis of a dibenzobiphenylene nucleus in 1954 many authors had erroneously claimed to have formed these hydrocarbons and a paper describing these attempts and demonstrating which compounds had actually been formed was published in 1950 by Bell & Hunter (2).

DIBENZO [b, h] BIPHENYLENE (I)

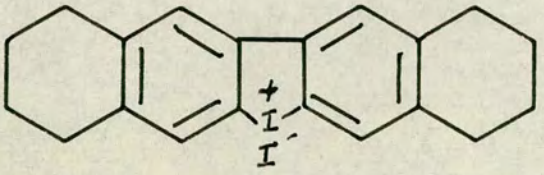
The first successful synthesis was that of dibenzo [b, h] biphenylene (I) by Curtis & Viswanath (3) in 1954 who obtained the compound in 3% yield by tetrazotisation and treatment of 3, 3' - diamino - 2, 2' - binaphthyl with potassium iodide to give an iodinium iodide (VI) which was pyrolysed with cuprous oxide under reduced pressure giving dibenzo [b, h] biphenylene (I). This method has been used with somewhat greater success in the synthesis of biphenylene (4). The hydrocarbon (I) has also been synthesised by these authors by pyrolysis of 5, 6, 7, 8, 5', 6', 7', 8' - octahydro - 2, 2' - binaphthyl - 3, 3' - iodinium iodide (VII). When this synthesis was carried out by Ward & Pearson (5), they also obtained the dibenzo [b, h] biphenylene, but found it was accompanied by two other products which appeared to be hydrogenated derivatives of the dibenzobiphenylene.



VI

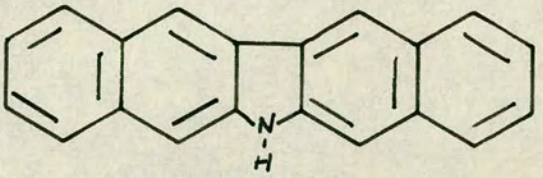


I

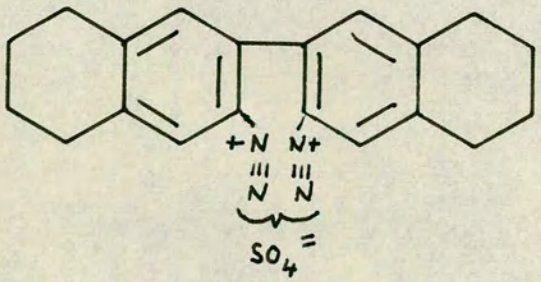


VII

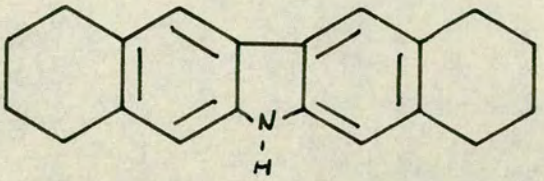
An attempt (5) to form the dibenzobiphenylene by pyrolysis of 5, 6, 7, 8, 5', 6', 7', 8' - octahydro - 2, 2' - binaphthyl - 3, 3' - tetrazonium sulphate (VIII) with cuprous oxide, failed but two apparently pure crystalline products were obtained, one possibly (from the ultraviolet spectral and analytical evidence) 2: 3, 6:7 dibenzocarbazole (IX) and the other an octahydrodibenzocarbazole (X).



IX



VIII

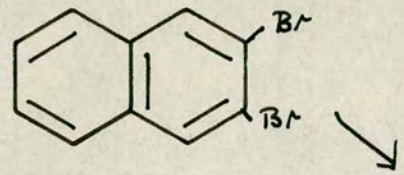


X

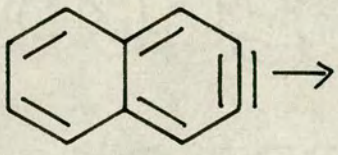
In 1960, two much simpler methods of synthesising (I) were reported by Pearson (6) :-

(a) The reaction of 2, 3 - dibromonaphthalene (XI) with lithium amalgam in ether giving the product in 0.2% yield.

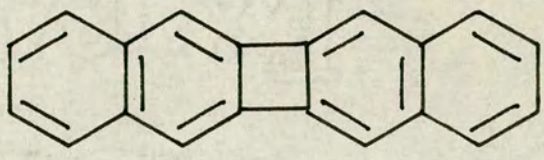
(b) The reaction of 2 - bromo - 3-iodonaphthalene (XII) with copper bronze in dimethylformamide giving a 0.9% yield.



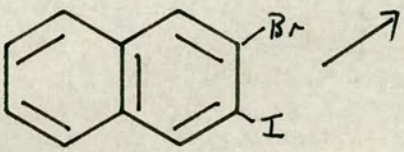
XI



XIII



I



XII

Method (b) is a completely new type of synthesis for aromatic derivatives of cyclobutadiene. Both reactions are postulated by their author as proceeding via dimerisation of a β - naphthalyne (XIII) intermediate, the first by analogy with a reaction carried out by Wittig & Pohmer (7) who showed that biphenylene could be formed from the reaction of o - bromofluorobenzene or o - dibromobenzene in

which the formation of biphenylene was ascribed to dimerisation of a benzyne intermediate. In the case of reaction (b), the β - naphthalyne intermediate (XIII) is possibly stabilised by the highly polar solvent dimethylformamide and since a similar reaction with o - bromoiodobenzene yielded only biphenyl, the success recorded may be due to the exceptional stability of the linear dibenzobiphenylene (I).

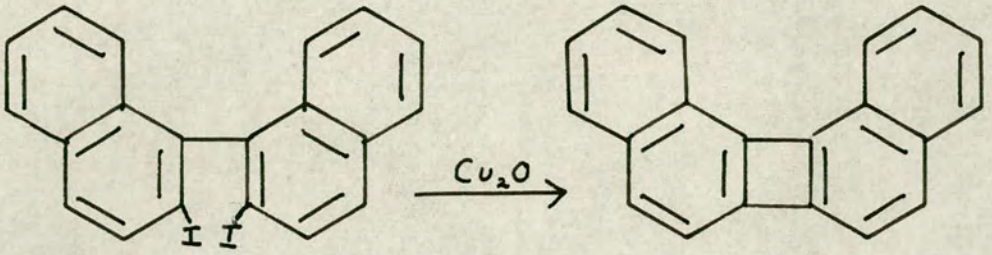
An attempt by Ward & Marriott (8) to isolate the β - naphthalyne intermediate (XIII) by virtue of its dienophilic attack on furan, failed to give any adduct. It seems unlikely (6) that reaction (b) takes place through the initial formation of 3, 3' - dibromo - 2, 2' - binaphthyl for Lothrop (4) showed that 2, 2' - dibromobiphenyl only formed biphenylene when heated with cuprous oxide and not with copper bronze.

Dibenzo [b, h] biphenylene has a high m.p. 376 ± 2° and great stability. Reduction with freshly prepared Raney nickel in ethanolic solution gives 2, 2' - binaphthyl.

DIBENZO [a, i] BIPHENYLENE (III)

Pyrolysis of 2, 2' - diiodo - 1, 1' - binaphthyl (XIV) with cuprous oxide by Cava & Stucker (9) gave this dibenzobiphenylene in 5.5% yield as deep red needles m.p. 136.8 - 138.9°.

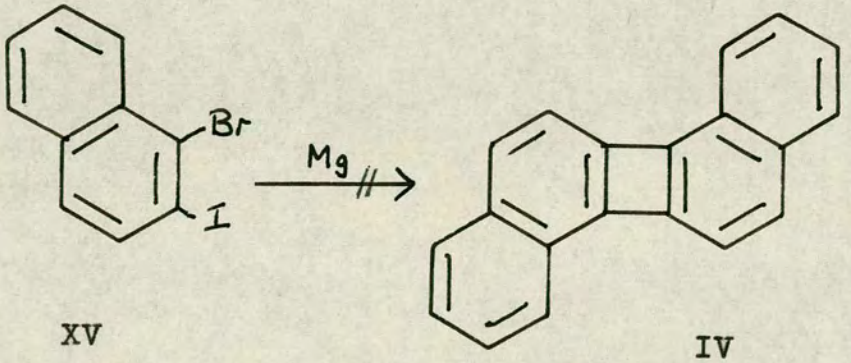
Raney nickel reduction of it gave 2, 2' - binaphthyl confirming its structure since it was prepared from known derivatives of the isomeric 1, 1' - binaphthyl.



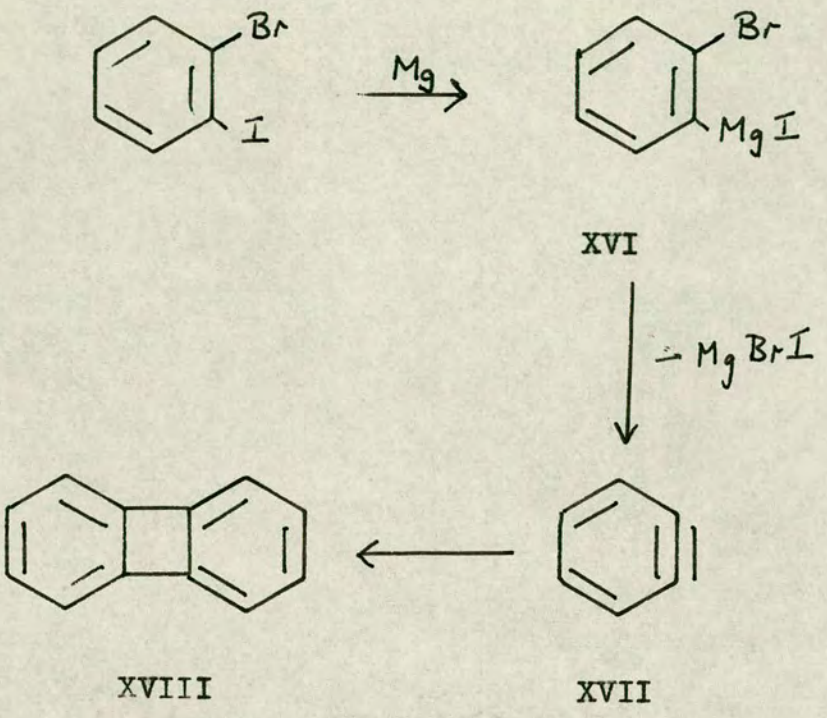
XIV III

DIBENZO [a, g] BIPHENYLENE (IV)

It was found (10) that ethereal 1 - bromo - 2 - iodonaphthalene (XV) reacted with ca. one equivalent of magnesium. After carboxylation, a solid product was isolated and fractional crystallisation gave 2, 2' - binaphthyl and a small amount of orange plates whose U.V. spectrum suggested that they might be 1: 2, 5: 6 dibenzobiphenylene since it strongly resembled that of the [b, h] and [a, i] dibenzobiphenylenes. Its m.p. was 271°. This method has been used to synthesise biphenylene (11) in 3.5% yield and the mechanism is of interest in that it is probable that the o - bromophenylmagnesium iodide (XVI) loses magnesium halide to form benzyne (XVII) which would readily dimerise to biphenylene (XVIII).



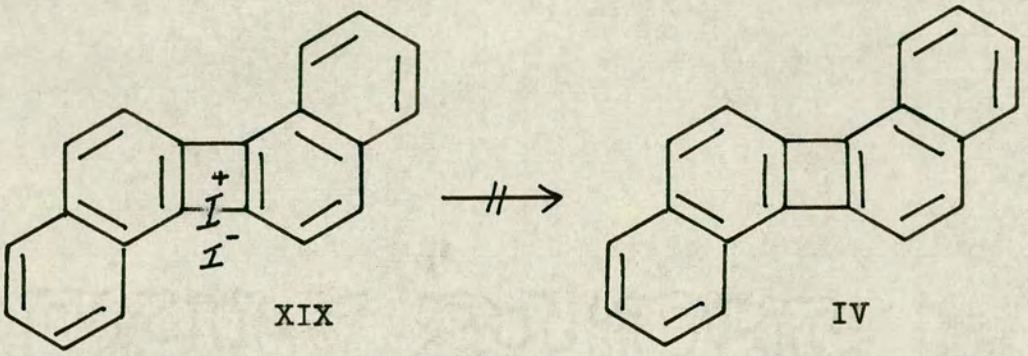
XV IV



It is also possible that the magnesium brings about a Fittig reaction to a small extent with o - bromoiodobenzene to form 2, 2' - dibromodiphenyl which then undergoes an intramolecular Fittig reaction to form biphenylene. It is highly improbable, however, that 2, 2' - dibromodiphenyl is an intermediate, for other workers (12) have shown that this compound in ether reacts very incompletely with magnesium even on prolonged heating and that the Grignard reagent so formed, when heated with cupric chloride (Krizewski - Turner reaction) yielded biphenylene (4% based on the magnesium reacted), tetraphenylene (16%) and diphenyl. The yields of these hydrocarbons,

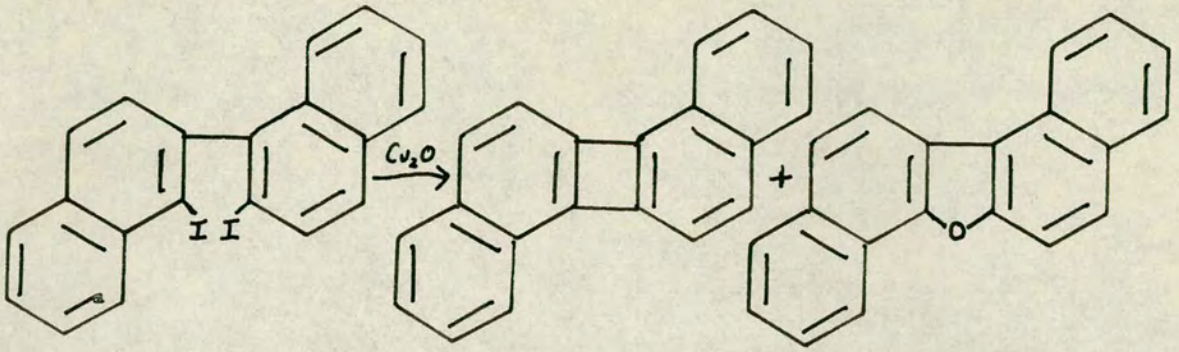
calculated on the total dihalide employed, are of course exceedingly small.

Ward & Pearson (13) attempted to form dibenzo [a, g] biphenylene by pyrolysis of 1, 2' - binaphthyl - 1', 2 - iodinium iodide (XIX) under varying conditions without success.



XIX IV

This failure was attributed by a later author, Barton (34), to the compound assumed to be the iodinium iodide (XIX) by Ward & Pearson being polymeric material since it was somewhat soluble in organic solvents and gave no 1, 2' - diiodo - 1', 2 - binaphthyl on thermal decomposition. Barton formed (IV) by low pressure pyrolysis of 1, 2' - diiodo - 1', 2 - binaphthyl (XX) with cuprous oxide at 250° - 350° in very low yields accompanied by varying amounts of dinaphtho [1, 2 - b: 1', 2' - d] furan (XXI)

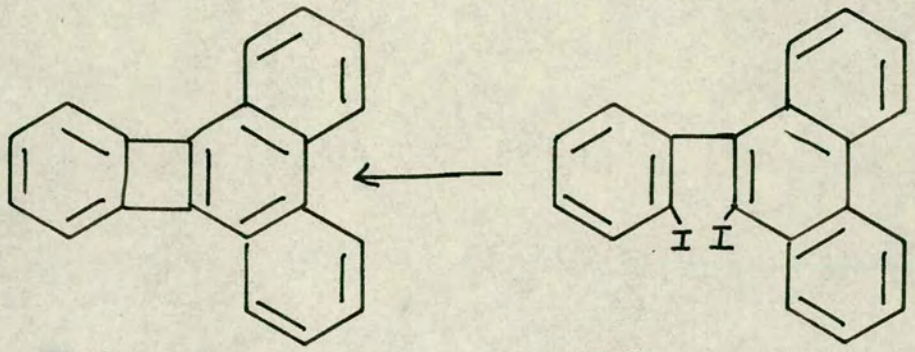


XX IV XXI

The hydrocarbon (IV) forms orange red plates which decompose at their melting point 146 - 147° to become almost colourless. Reduction with Raney nickel in benzene - ethanol resulted in the usual rupture of the four membered ring with the formation of 1, 2' - binaphthyl.

DIBENZO[a, c] BIPHENYLENE (II)

Pyrolysis of 9 - iodo - 10 - (2 - iodophenyl)phenanthrene (XXII) with cuprous oxide at 15 mm. pressure and between 240 - 340° gave a 21% yield of (II). The compound crystallises from hexane as orange red, fluffy needles m.p. 183 - 184° (31). It undergoes the reductive ring opening normal for biphenylene derivatives. Thus, when it was warmed with Raney nickel in ethanolic solution, 9 - phenylphenanthrene was produced in high yield.

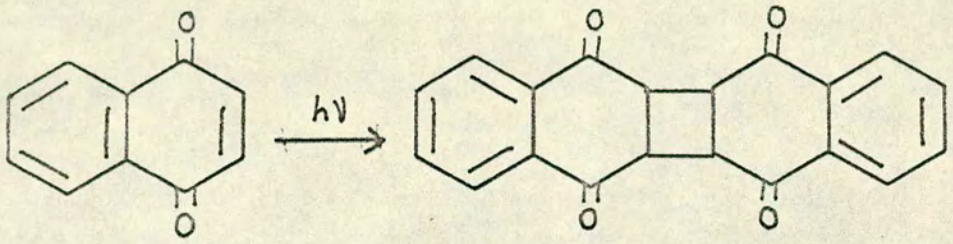


II XXII

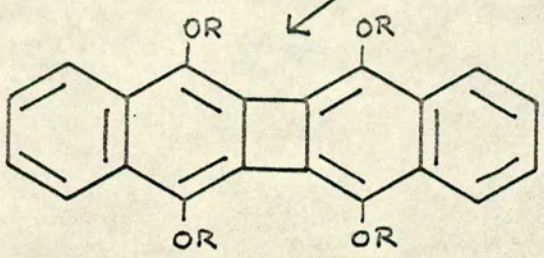
The synthesis of dibenzo [a, h] biphenylene (V) has not yet been reported but there is no reason to suspect it cannot be synthesised since by comparison of its structure with the structures of the known dibenzobiphenylenes, it should be intermediate in stability between [b, h] and [a, i] dibenzobiphenylenes.

SUBSTITUTED DIBENZOBIPHENYLENES

Due to obvious difficulties in obtaining these hydrocarbons (I - IV) in reasonable quantities, few reactions have actually been carried out on the parent compounds and substituted derivatives have been formed largely by synthesis. As has been previously mentioned, reduction leads invariably to rupture of the four membered ring in all the synthesised nuclei. Ward & Marriott (8) converted 2, 3 - dibromo - 1 - nitronaphthalene (XXIII) into a product which must be either 5, 11 (XXIV) or 5, 6 - dinitro dibenzo [b, h] biphenylene (XXV).



XXVI XXVII

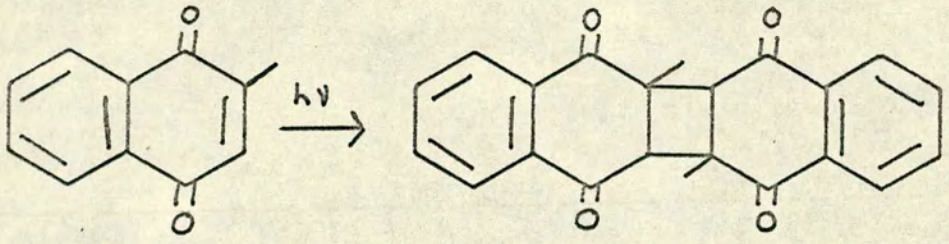


a) R = H

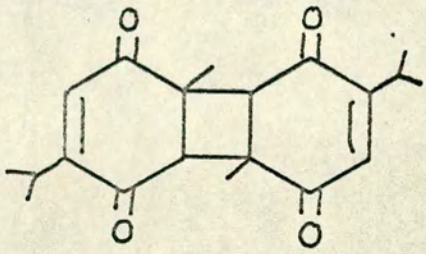
b) R = CH_3

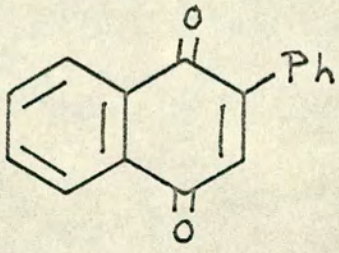
c) R = CH_3;CO

XXVIII

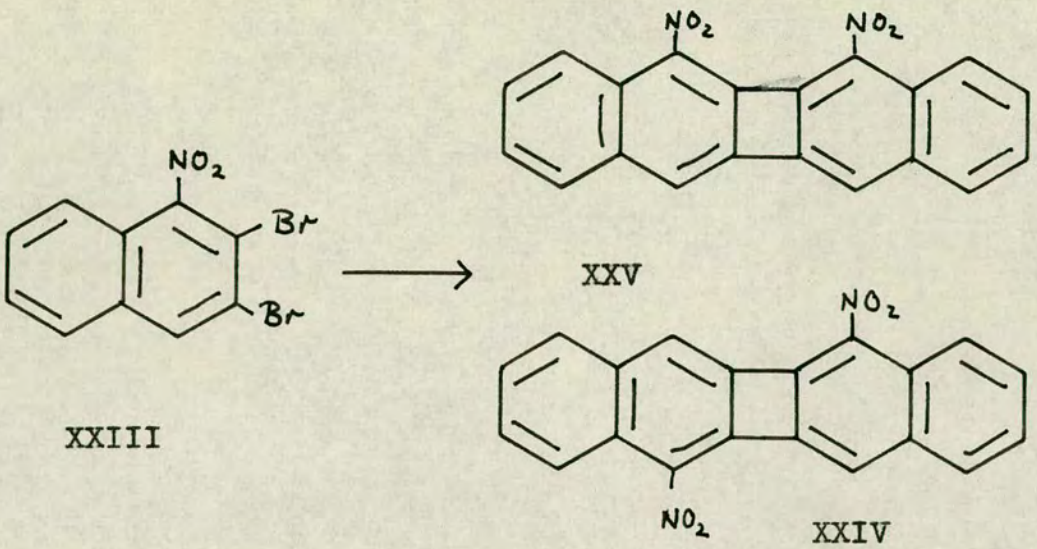


XXIX XXX





XXXI XXXII



The product was not identical with a product obtained on attempted dinitration of the parent compound.

In 1948 Schonberg et al. (14) reported the dimerisation of 1, 4 - naphthoquinone (XXVI), when its solution in benzene was exposed to sunlight. The constitution of the dimer (XXVII) is based on the following facts. The compound is colourless and this makes a quinonoid structure improbable. The substance is not phenolic, for it is insoluble in alkali and does not react with diazomethane. It decomposes on heating at 270°, quantitatively or nearly so, with regeneration of 1, 4 - naphthoquinone. The assignment of a dimeric structure is based on the observation (15) of Madinaveitia that 2 - methyl - 1, 4 - naphthoquinone (XXIX) gives in sunlight, a photo - dimer (XXX) which is soluble enough to allow a molecular weight determination. As the dimer of 1, 4 - naphthoquinone is difficultly soluble, no molecular weight determination could be carried out on it.

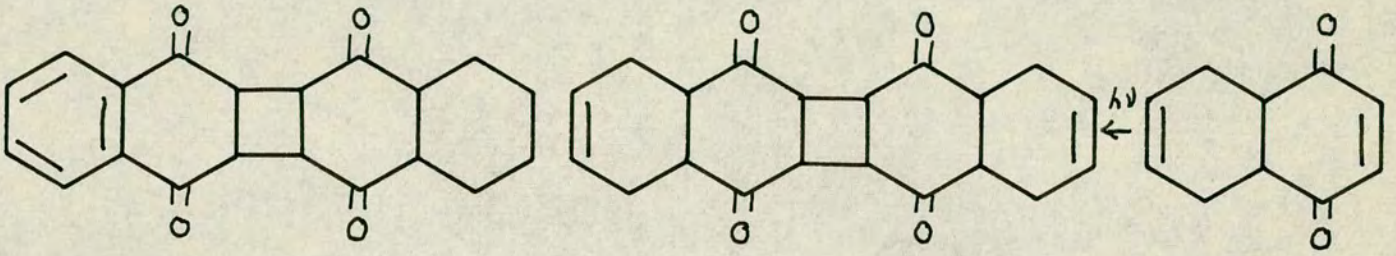
Treatment of the dimer (XXVII) by Bruce (16) with sodium hydroxide in aqueous dioxan gave tetrahydroxydibenzobiphenylene (XXVIIIa) on acidification.

The tetramethyl ether (XXVIIIb) was prepared by reaction of the alkaline solution with dimethyl sulphate and the tetra - acetate (XXVIIIc) by acetylation of either the phenol or the dimer (XXVII) with acetic anhydride and sodium acetate.

The structure of the photodimer prepared by Madinaveitia (15) is considered by Zavarin (17) to be (XXX) by comparison of ultraviolet and infrared data with similar data from the dimer of dithymoquinone which has the structure (XXXI) Zavarin also considers that the colourless polymeric substance formed by Z nicke et al. (18) upon exposure of 2 - phenyl - 1, 4 - naphthoquinone (XXXII) to daylight is probably parallel in structure to the photodimers (XXX) and (XXXI). Unfortunately, all these dimers carry angular groups which prevent aromatisation to biphenylenes.

Cookson et al. (19) irradiated solutions in ethyl acetate of the adduct (XXXIII) of butadiene and p - benzoquinone in sunlight to obtain what is believed to be the dimer (XXXIV). Its infrared spectrum and the fact that it absorbed two equivalents of hydrogen over palladium, leave little doubt that it is this dimer. Dehydrogenation over palladium/charcoal however did not yield a cyclobutane dimer of naphthoquinone, one isomer (XXVII) of which is known. Although the infrared spectrum of the white sparingly soluble product greatly resembled that of the known naphthoquinone dimer, it did not melt, but slowly decomposed between 240 - 300°. Furthermore, it gave an analysis for the dimer (XXXIV) less one molecule of hydrogen, which suggested internal oxidation reduction had taken place. If the dimer has a cis configuration about the

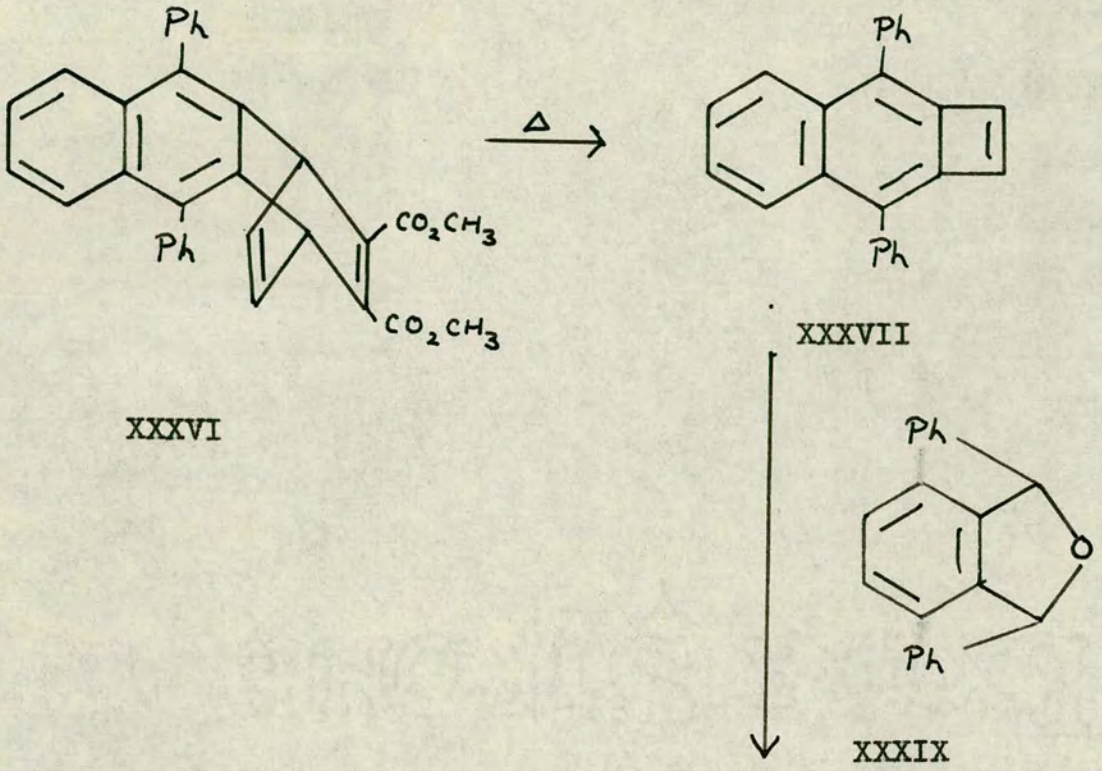
four membered ring then initial oxidation by palladium of one of the cyclohexene rings to a cyclohexadiene could be followed by comparatively easy aromatisation, intramolecularly, whereby the other cyclohexene ring of the molecule is reduced, giving 1, 2, 3, 4, 4a, 5a, 5b, 11s, 11b, 12a - decahydro - dibenzo [b, h] biphenylene - 5, 6, 11, 12 - tetrone (XXXV).



XXXV XXXIV XXXIII

In 1962 Nenitzescu et al. (20) reported the preparation in good yield of 5, 6, 11, 12 - tetraphenyl - 5, 5a, 11b, 12 - tetrahydro, 5, 12 - diepoxy-dibenzo [b, h] biphenylene (XXXVIII) by the thermal decomposition of the adduct (XXXVI) in the presence of excess 2, 5 - diphenyl - 3, 4 - benzofuran (XXXIX).

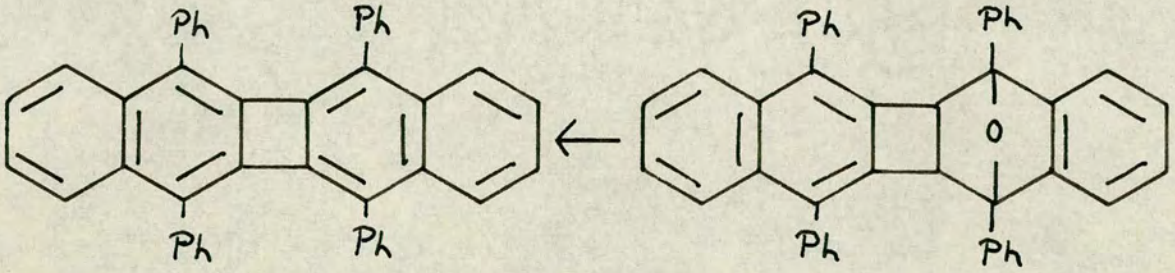
The reaction is postulated as proceeding via a Diels Alder reaction between 3, 8 - diphenyl - cyclobuta[b] naphthalene (XXXVII), the unstable product of the thermal decomposition of the adduct (XXXVI), and the diphenylbenzofuran. Compound (XXXVIII) loses one mole of water on warming, giving a yellow, high melting and difficultly soluble hydrocarbon 5, 6, 11, 12 - tetraphenyl - dibenzo [b, h] biphenylene (XL).



XXXVI

XXXVII

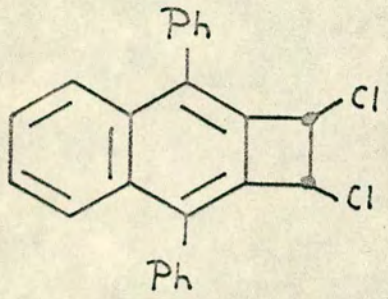
XXXIX



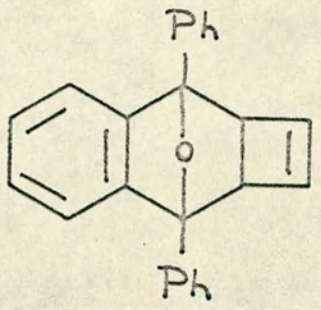
XL

XXXVIII

Later in 1964, Nenitzescu et al. arrived at similar products by slightly different methods. Equimolecular amounts of 2, 5 - diphenyl - 3, 4 - benzofuran (XXXIX) and cis 1, 2 - dichloro - 3, 8 - diphenyl - 1, 2 dihydro - cyclobuta [b] naphthalene (XLI) were shaken in ether with 0.5% lithium amalgam and the precipitate so formed was treated with maleic anhydride and the product

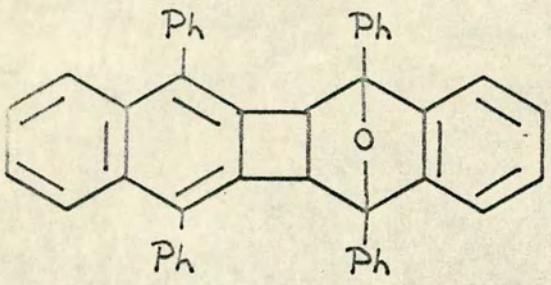


XLI



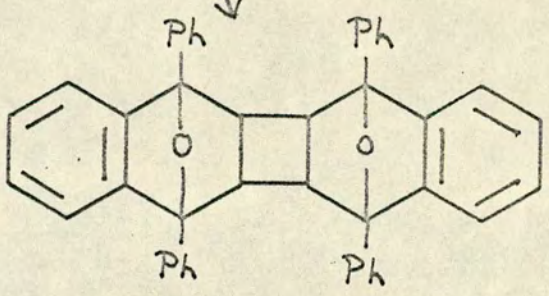
XLIII

Li/Hg + XXXIX



XLII

+ XXXIX

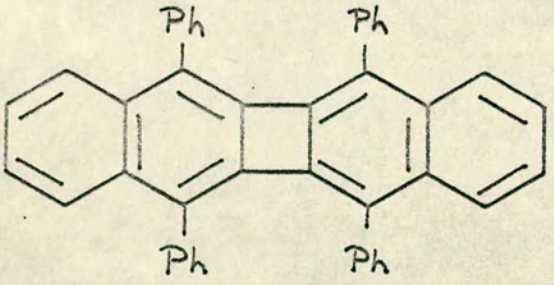


XLIV

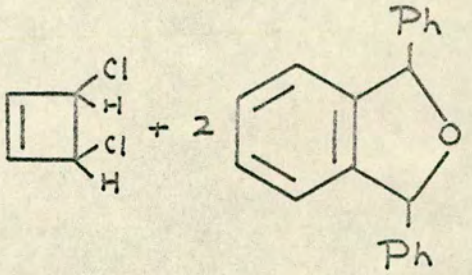
$H^{\oplus}$ / $-H_2O$

$H^{\oplus}$ / $-H_2O$

Li/Hg



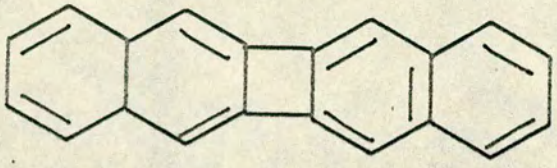
XL



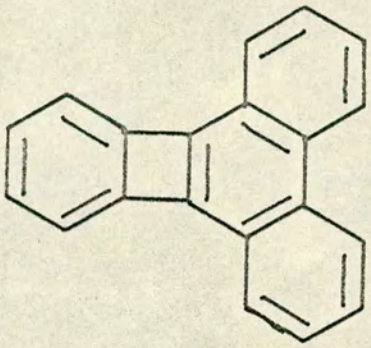
XLV XXXIX

refluxed for fifteen minutes with 5% methanolic potassium hydroxide to yield 70% 5, 6, 11, 12 - tetraphenyl - 5, 12 - epoxy - 5, 5a, 11b, 12 - tetrahydrodibenzo[b, h] biphenylene. (XLII).

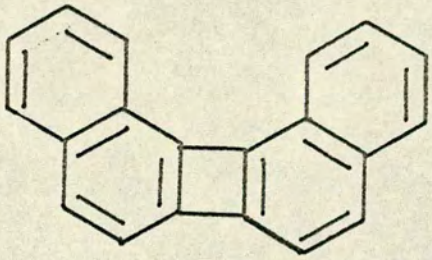
2, 5 - Diphenyl - 3, 4 - benzofuran (XXXIX) and 3, 8 - diphenyl - 3, 8 - epoxy - 2a, 3, 8, 8a, - tetrahydrocyclobuta[b] naphthalene (XLIII) fused together at 120° gave a 68% yield of 5, 6, 11, 12 - tetraphenyl - 5: 12, 6: 11 - diepoxy - 5, 5a, 5b, 6, 11, 11a, 11b, 12 - octahydro - dibenzo[b, h]biphenylene (XLIV). The same product was obtained in 6.8% yield by the reaction of cis - 3, 4 - dichlorocyclobutene (XLV) and 2, 5 - diphenyl - 3, 4 benzofuran (XXXIX) with 5% lithium amalgam. Heating (XLII) and (XLIV) with concentrated hydrochloric acid and acetic anhydride led to the formation of 5, 6, 11, 12 - tetraphenyldibenzo [b, h] biphenylene (XL).



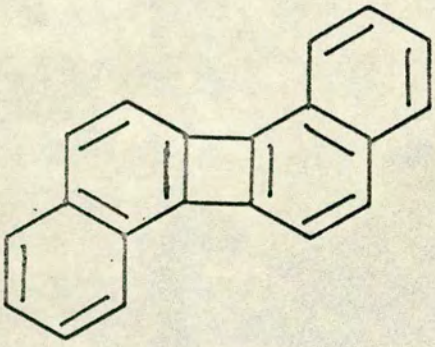
I



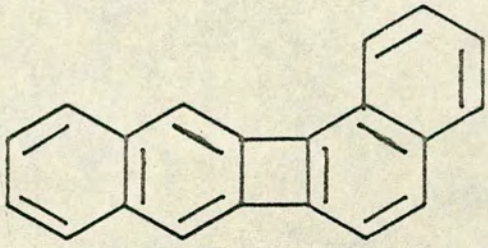
II



III



IV

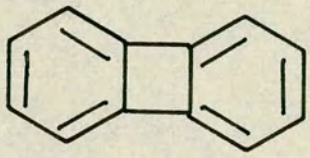


V

STABILITY AND STRUCTURE

The stability of the known dibenzobiphenylenes is in the order I > II > III ~ IV.

(I) is a pale yellow compound and remarkably stable, subliming with only slight decomposition at 375°. Its ultraviolet spectrum is complex and exhibits nine major and four minor maxima, similar to those of (III) and, although showing the expected bathochromic shift, similar in general form to that of biphenylene (XVIII)



XVIII

There is also a fair agreement with the theoretical values calculated by Crawford. (22).

In compound (II), the 8b, 12b, bond corresponds to a phenanthrene 9, 10 bond and thus the four numbered ring might be expected to possess considerable cyclobutadienoid character. In fact, the hydrocarbon is orange red but is much more stable than (III) or (IV). It appears that the double bond character of bond 8b, 12b is offset by bond fixation in the benzene ring, so that structure (II) represents the main contributor to the resonance hydrid. The ultraviolet spectrum of the hydrocarbon exhibits ten maxima and shows a general similarity to spectra of the other angularly annellated dibenzobiphenylenes.

The proton magnetic resonance spectrum at 60 mc./sec. shows three multiplets centred at 390, 450, and 505 c/sec. from tetramethylsilane due to protons at positions 9 - 12 (4 protons), 1 - 3 and 6 - 8 (6 protons) and 4 - 5 (2 protons) respectively.

Compound (III) forms dark red needles melting at 137 - 139° and is converted to a dark brown gum on heating at 160°/3.5mm. for a short time.

Extensive decomposition takes place even on boiling an ethanolic solution in the dark for one hour. The orange solution of the compound is quite stable in the cold when protected from light, but exposure to light, particularly in the ultraviolet range, causes rapid decomposition.

The benzenoid annellation is the same in both (III) and (IV) but the latter is more symmetrical in that bonds 6a - 6b and 12a - 12b must be of equal length and bond order. The hydrocarbon (IV) forms orange red plates which decompose at their melting point to become almost colourless. Solutions in hexane or methanol decompose slowly at room temperature and more rapidly on heating or on exposure to ultraviolet light, with the formation of yellow amorphous material. Thus, hydrocarbon (IV) appears to be similar in stability to isomer (III). Its ultraviolet spectrum shows a marked resemblance to that of benzo [a] biphenylene except that there is the expected overall shift of the curve to longer wavelengths.

The dibenzobiphenylenes are derived from biphenylene by benzenoid annellation but they may equally be regarded as derived from the hypothetical cyclobutadiene by annellations of naphthalene

nuclei in the 1: 2 and 2: 3 positions or in the case of dibenzo[a, c] biphenylene (II), by annellation of a benzene and phenanthrene nucleus.

Since it is impossible to determine the molecular weight of (I), Curtis (23) argued that the large difference in properties between it and (III) might be attributed to a structure of higher molecular weight than that appropriate for (I), especially as only a low yield of 2, 2' - binaphthyl was obtained on reduction.

To test this hypothesis, he determined the mass spectrum of (I) which clearly showed a molecular weight of 252 ($C_{20}H_{12}$) and a breakdown pattern indicative of a biphenylene nucleus.

The greater stability of (I) with respect to (III) must be related to the electron distribution in the region of this cyclobutadiene - like ring. Cyclobutadiene is not stable in a totally aromatic ie. square configuration but tends to distort in such a way as to favour a rectangular Kekule structure such as :-

It would follow from this that if the naphthalene fragments in (I) and (III) took up the predominant Erlenmeyer bond diagrams as shown, then in (III) there would be a situation in which the bonds 6a: 6b and 12a: 12b would inevitably be weak. (III) might therefore be

expected to have a lower stability than (I) where none of the π-electron influences responsible for the instability of cyclobutadiene would arise.

It might be argued in the terminology introduced by Craig (24) that (III) had a pseudo aromatic structure and would therefore be expected to be unstable and unconjugated by analogy.

Recently, Baker et al. (25) have shown that the chemical reactivity of biphenylene can be well understood in conjunction with simple Molecular Orbital theory, if it is assumed that the most important contributing structure is that shown in (XVIII)

By calculation of the bond orders in (I) and (III), it should be possible to see whether the above explanation of the difference between the molecules is correct.

Simple Molecular Orbital calculations of the π - electron energies and bond orders cf. (XLVII) in (I) and (III) carried out by several workers (22), (26), (29), (30) are sufficient to show that the resonance energy of (I) exceeds that of (III) by 4.3 kcal/mole.

Similar conclusions follow from the bond orders in the central cyclobutadiene - like ring. The degree of double bond fixation increases in the sequence (I) < (XVIII< (III) which corresponds to the stability order of these molecules. The greater the degree of bond fixation, the less the extent of conjugation and the lower the stability.

That the resonance energy of (I) is greater than that of (III) is a curious phenomenon, since it is observed that in a series of purely polybenzenoid hydrocarbons, the phenes have a resonance

energy greater than that of their acenic isomers. The resonance energy difference alone is not great enough however to account for the experimentally observed difference.

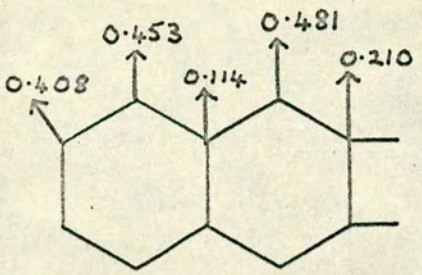
The other factors (26) which may be responsible for the instability of (III) are :-

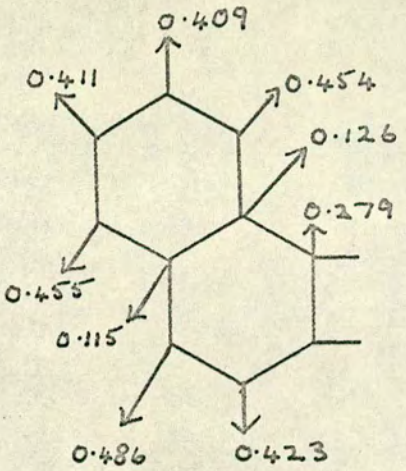
1) The asymmetric deformation of the square ring.
2) The steric interactions between positions 1 and 12 analogous to but less pronounced than that experimentally observed in 3, 4 - benzophenanthrene, and finally
3) the proximity of a triplet state which will be taken into further consideration.

The energy of the transition between the bonding and the antibonding orbitals N - V1, larger in (I) than in (III) gives a good account of the colour difference of the two isomers, the difference again being the inverse of that observed in the polybenzenoid compounds where the acenes absorb at a longer wavelength than the phenes and rather analagous to that observed for the naphthofulvenes (27).

The weak energy separation in (III) between the highest occupied orbital and the lowest empty orbital, leads one to envisage the existence of a triplet state, situated exceptionally near to the fundamental singlet and being responsible for the thermal instability of this isomer.

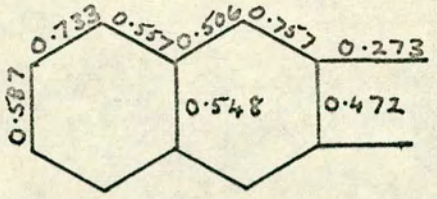
Concerning chemical reactivity, it can be forecast (26) that the dibenzobiphenylenes should be more reactive with respect to substitutions than biphenylene and that the most reactive positions

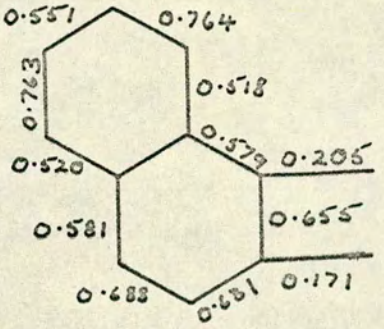




XLVI

FREE VALENCY VALUES (26)





XLVII

π-BOND ORDERS (29)

with respect to substitutions should be carbon atom 12 in (I) and 5 in (III). This prediction is based on the values of the corresponding free valencies (XLVI) but there is some danger (as in the difference found to occur in biphenylene by Baker et al. (28) that it will be modified by the corresponding values of the polarisation energies. As for addition reactions, these should take place particularly easily in (III) on the 1: 2, and 3: 4, bonds and not on bond 5: 6 as might be envisaged by analogy with the behaviour of the phenes.

OBJECT OF RESEARCH

The dibenzobiphenylenes are mainly of interest since they and biphenylene are the only known cases of incorporation of a four membered ring into simple aromatic systems.

Although, as mentioned in the Introduction, a large volume of theoretical work has been done in the elucidation of the structure of these compounds, no chemical evidence concerning the nature of bond fixation in the nuclei, comparable to that amassed for compounds such as naphthalene and biphenylene itself, has yet appeared in the literature. This is presumably largely due to the experimental difficulties in obtaining these compounds in reasonable amounts.

It was therefore hoped that if suitably substituted dibenzobiphenylenes could be synthesised by the already known routes or by novel methods, then the extent of bond fixation could be determined by methods similar to those discussed by Badger (67).

D I S C U S S I O N

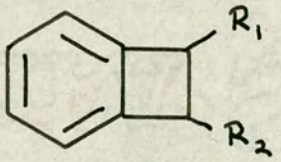
SECTION I

Formation of Bicyclo [4.2.0] octa -1, 3, 5 -trienes.

Part I. By intramolecular malonic ester condensation.

Part II. By elimination-addition reactions involving benzyne intermediates.

The formation of bicyclo [4.2.0] octa -1, 3, 5 -trienes (XLVIII)



XLVIII

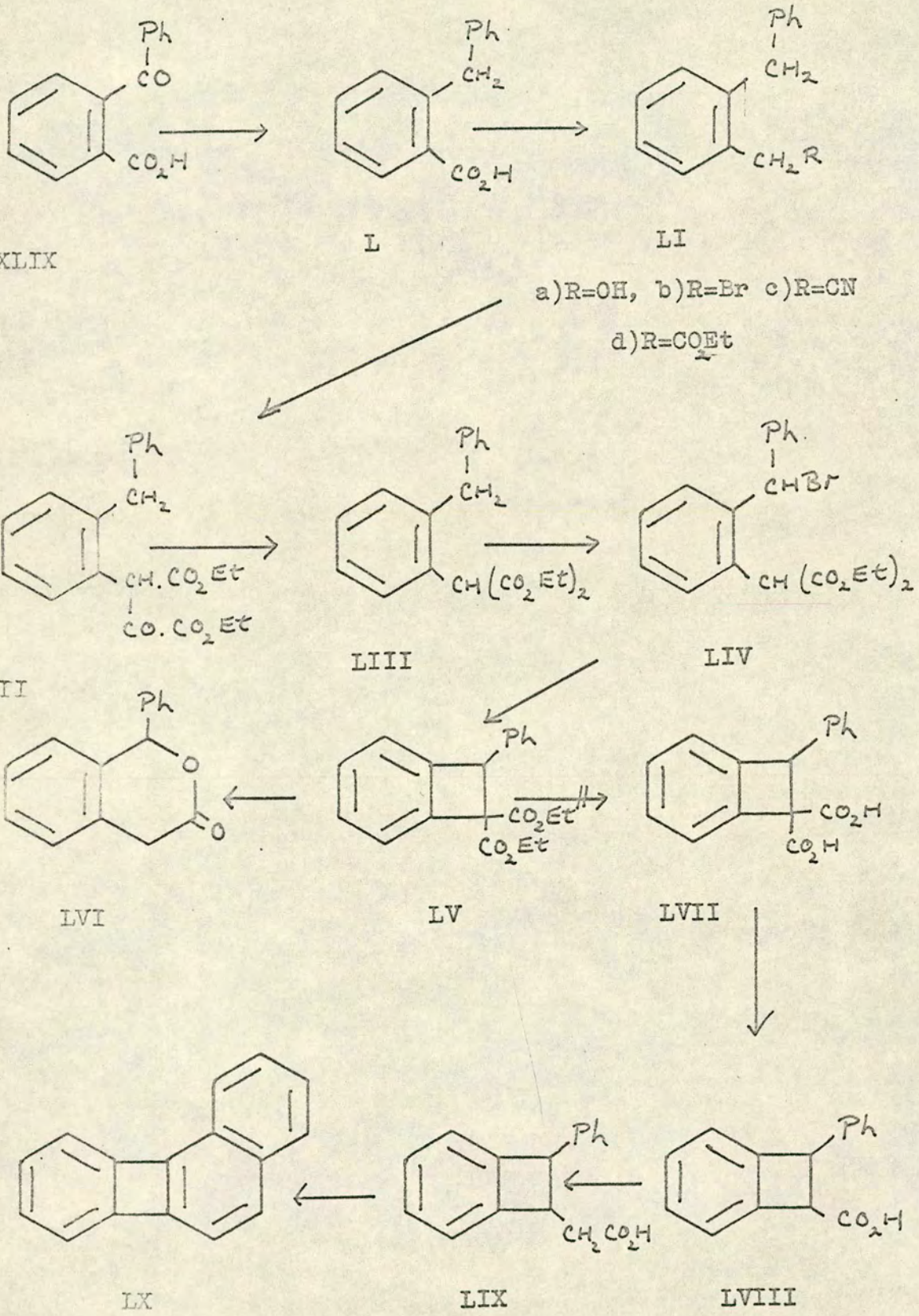
with substituents on carbon atoms 7 and 8 was attempted so that further elaboration of the substituents might give rise to benzobiphenylenes. For example cyclisation of (XLVIII) (R_1 = $-CH_2$ Ph, R_2 = $-CO_2H$), followed by aromatisation would give 2, 3 -benzobiphenylene and with (XLVIII) (R_1 = $-CH_2CO_2H$, R_2 = -Ph), the same sequence of reactions would give 1, 2 - benzobiphenylene.

SECTION 1

PART 1

Attempted preparation of 7-PHENYLBICYCLO [4.2.0] OCTA-1,3,5 -TRIENE-8-CARBOXYLIC ACID and resulting formation of 1-PHENYLISOCHROMAN-3-ONE.

SCHEME A



XLIX L LI

a)R=OH, b)R=Br c)R=CN d)R=CO2Et

LII LIII LIV

LVI LV LVII

LX LIX LVIII

Intramolecular ring closure by malonic ester condensation is a well known and widely used method in the synthesis of small rings.

It was therefore hoped that if 2- (α-bromobenzyl) phenylmalonic ester (LIV) could be synthesised as shown in Scheme A, then subsequent intramolecular malonic ester condensation would give 7 - phenyl bicyclo [4.2.0] octa -1, 3, 5 - triene - 8, 8 - diethyl carboxylate (LV.) Hydrolysis and monodecarboxylation of this compound would give 7 - phenylbicyclo [4.2.0] octa -1, 3, 5 - triene - 8 - carboxylic acid (LVIII). Formation of the higher homologous acid (LIX) by the Arndt Eistert synthesis followed by ring closure would give a ketone which could be aromatised to 1, 2 - benzobiphenylene (LX.).

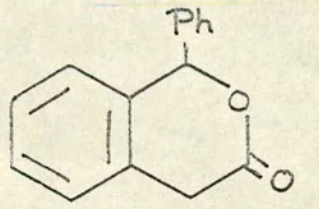
The synthesis began with reduction of the carbonyl group in 2-benzoylbenzoic acid (XLIX) with zinc in ammonia to give 2-benzylbenzoic acid (L) Following the general route to formation of homologous acids via reduction of the ester of the acid (L) with lithium aluminium hydride, bromination of the alcohol (LIa) with phosphorus tribromide, cyanation of the bromide (LIb) with potassium cyanide in aqueous ethanol, and hydrolysis of nitrile (LIc) gave ethyl 2-benzylphenyl acetate (LId).

Claisen condensation of (LId) with diethyl oxalate gave the keto-ester (LII) which lost carbon monoxide on heating to yield 2-benzylphenylmalonic ester (LIII). A peak in the N.M.R. spectrum of this substance at 6.0 τ was assigned to the $-CH_2-$ protons between the phenyl groups. Bromination of (LIII) with N - bromosuccinimide gave an oil whose N.M.R. spectrum showed no absorption at 6.0 τ but a singlet appeared at 3.55 τ corresponding to 1 proton. The singlet appearing at 5.3 τ in the spectrum of (LIII) and attributed to the unsubstituted proton of the malonic ester was also present in the spectrum of the brominated product at 5.15 τ. From this evidence, it was assumed that the brominated product was 2-(α-bromobenzyl) phenylmalonic ester (LIV). This compound was then condensed intramolecularly to give 7-phenylbicyclo[4.2.0] octa -1, 3, 5 - triene -8, 8 - diethyl carboxylate (LV).

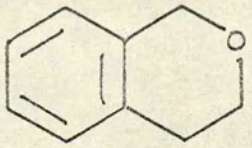
At this point, the synthesis took an unexpected turn when hydrolysis of the dicarboxylic ester (LV) in both basic and acidic conditions gave instead of the expected acids (LVII) and (LVIII), a lactone which was shown to be 1 - phenylisochroman -3- one (LVI).

Proof of the formation of 1-phenylisochroman -3- one (LVI) was obtained as indicated in Scheme B and also by interpretation of the N.M.R. spectra of the compounds shown in it. The spectrum of (LVI) had a singlet at 3.7 τ (1 proton), a split singlet at 6.5 τ

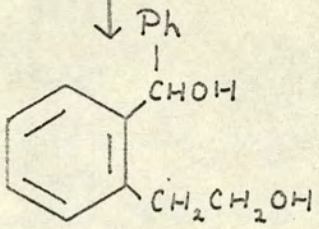
SCHEME B



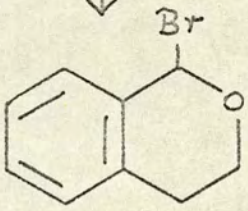
LVI



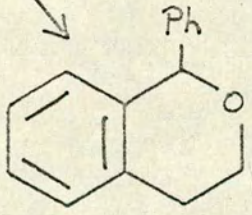
LXIV



LXII



LXV



LXIII

(2 protons) and two aromatic multiplets at 2.7 - 3τ and 3 - 3.3 τ (9 protons). This information plus the information that the compound was non-acidic and had a single carbonyl absorption in the infrared spectrum at 1700cm.$^{-1}$, limited the possibilities for the structure of (LVI) to 1-phenylindan -2- one and 1- phenylisochroman -3- one. However, the former compound is known (38) to melt at 53° and (LVI) melted at 83°. Elementary analysis indicated an empirical formula of $C_{15}H_{12}O_2$ and a molecular weight determination showed that this must also be the molecular formula. This corresponds to the lactone (LVI).

Reduction of (LVI) with lithium aluminium hydride gave an alcohol whose N.M.R. spectrum and elementary analysis showed it to be the diol (LXII). Cyclodehydration of (LXII) in strong acid gave the known (39) 1-phenyl isochroman (LXIII) whose nature was confirmed by an independent synthesis when 1- bromoisochroman (LXV), formed by free radical bromination of isochroman (LXIV), gave (LXIII) in a "coupling" reaction with phenylmagnesium bromide.

Formation of the lactone (LVI) must result from the fission of the 7, 8 bond and this is supported by the observation of Blomquist and Bottomley (44) that trans-7- phenyl bicyclo[4.2.0]octa -1, 3, 5 -

triene -8- carboxylic acid (LVIII) ring opens by cleavage of the 7, 8 bond in 5% KOH at 100° to give 1- phenylisochroman -3- one (LVI) m.p. 75°.

It is of interest to compare these cleavages of the 7, 8 -bond with the findings of Horner, Schmelzer and Thomson (46) on the cleavage of substituted bicyclo [4.2.0] octa -1, 3, 5 -trienes. They found :

1) that cleavage was always unsymmetrical with the result that the aliphatic C -C bond of the four membered ring was left intact.

2) that protonation of the aromatic nucleus always occurred and

3) that the bond in the four membered ring with the highest electron density was always cleaved.

From these observations, they put forward the hypothesis that cleavage was due to the action of the anion or cation in the transition state causing the shift of the bonding electrons between carbon atoms 6, 7 or 1, 8 in the direction of the aromatic ring.

The reaction pathway leading to the formation of the lactone (LVI) from the diester (LV) probably varies depending on whether acidic or basic hydrolysis is used. This conclusion was reached on considering the following observations :-

a) The report by Blomquist and Bottomley (44)mentioned above about the formation of the lactone (LVI) from trans -7- phenylbicyclo [4.2.0] octa -1, 3, 5 - triene -8- carboxylic acid (LVIII) in basic conditions.

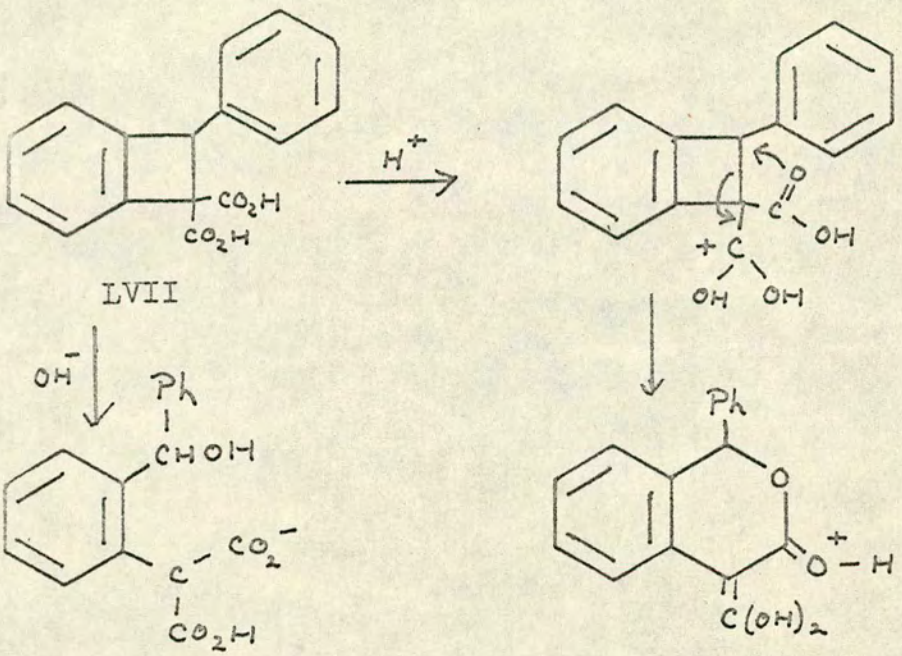
b) The report by the same authors that the acid (LVIII) decomposes in concentrated sulphuric acid at 40°.

c) The experimental observation that the lactone (LVI) could be formed from the diester (LV) in boiling hydrobromic acid.

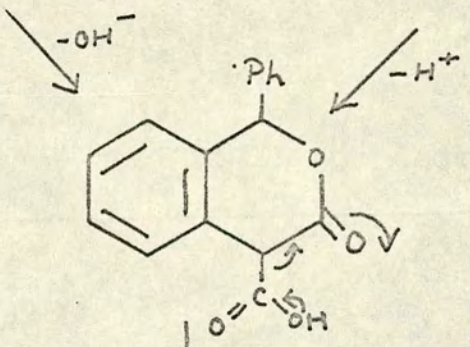
d) Bus et al. (36) showed that decarboxylation of cyclopropane -1, 1 - dicarboxylic acids in water, dilute sodium hydroxide or aqueous sulphuric acid did not occur directly like most gem - dicarboxylic acids, but that the primary process was an isomerisation to γ - lactone carboxylic acids, which subsequently decarboxylated. They were able to detect by N.M.R. spectra and in some cases to isolate the intermediate lactone carboxylic acids: by carrying out the reactions in D_2O, D_2SO_4 and in NaOD they were able to show that formation of olefinic acids with subsequent ring closure to lactones (37) could be ruled out.

e) No report of isomerisation of a lactone followed by decarboxylation appears in the literature for cyclobutane -1, I, - dicarboxylic acids.

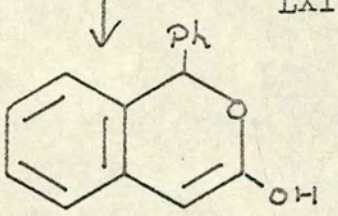
SCHEME C

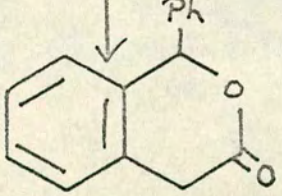


LVII



LXI





LVI

Concerning observations (d) and (e), it is likely that the annellated benzene ring in the diacid (LVII) increases the ring strain beyond that normally observed in the cyclobutanes to a value approaching that found in the cyclopropanes.

From observations (b) and (c) it seems probable that the reaction pathway leading to the lactone (LVI) in hydrobromic acid is that outlined in Scheme C. This is analogous to the mechanism in acidic media for cyclopropane -1, 1 - dicarboxylic acids' decarboxylations demonstrated by Bus et al. (36).

However, in basic media, the reaction pathway could occur possibly in two different ways. The first, by monodecarboxylation of the diacid (LVII) to the mono - acid (LVIII) which then isomerises to the lactone as shown by Blomquist et al. cf. (a). The second pathway is shown in Scheme C where isomerisation occurs first to give the lactone carboxylic acid (LXI) which then decarboxylates normally to give the lactone (LVI).

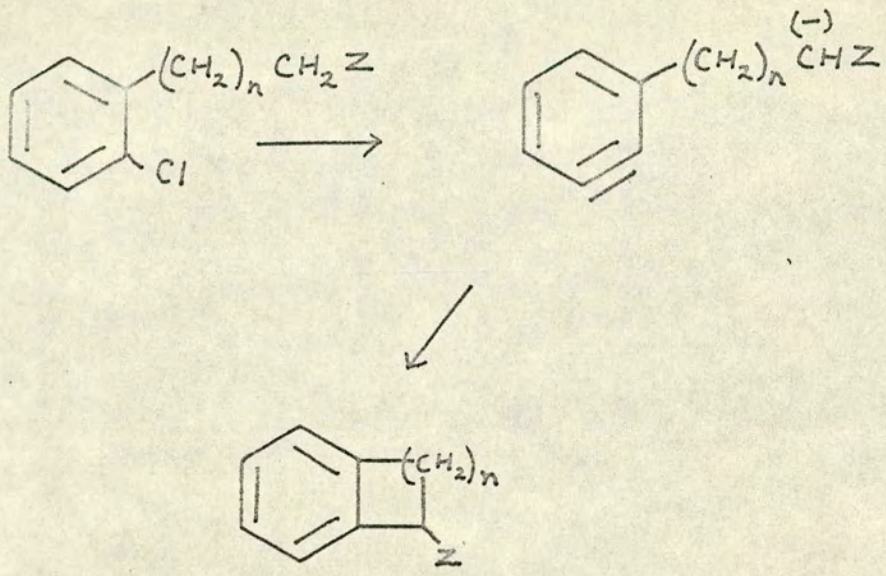
The substitution in the four membered ring of the diacid (LVII) renders the possibility of formation of an olefinic acid followed by lactone formation (37) most unlikely.

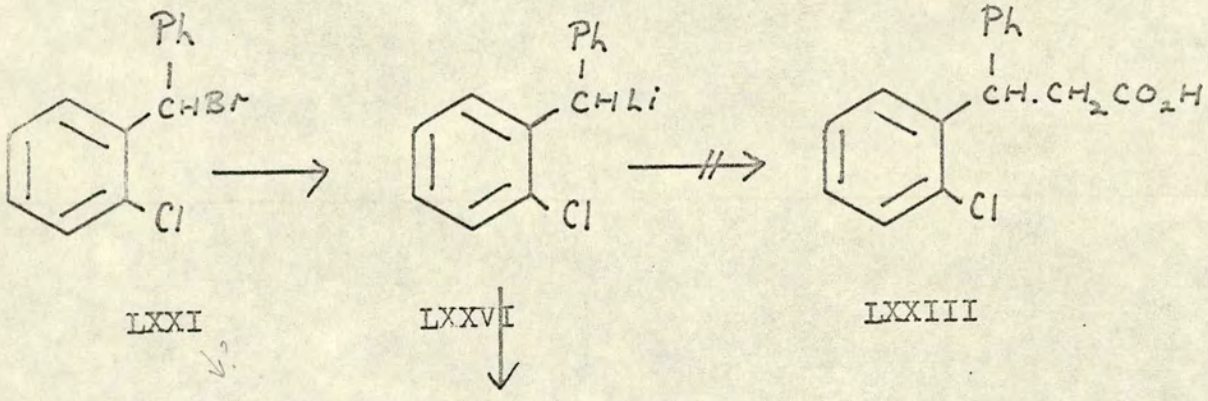
SECTION I

PART II

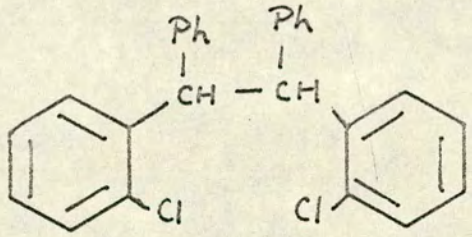
FORMATION OF BICYCLO [4.2.0] OCTA -1, 3, 5 -TRIENES BY ELIMINATION - ADDITION REACTIONS INVOLVING ARYNE INTERMEDIATES.

SCHEME D





LXXI LXXVI LXXIII



LXXVII

Strong nucleophiles add readily to arynes and if the nucleophile is situated on the side arm of the aryne, intramolecular addition forms a new ring fused to the original aromatic nucleus. In 1962, Bunnett and Skorcz (40) reported the formation of homocyclic rings fused to benzene rings by the reaction of aliphatic nitriles, esters, sulphones and ketones bearing an ω - (2-chlorophenyl) group with potassamide in liquid ammonia. These reactions gave good yields of cyclised products.

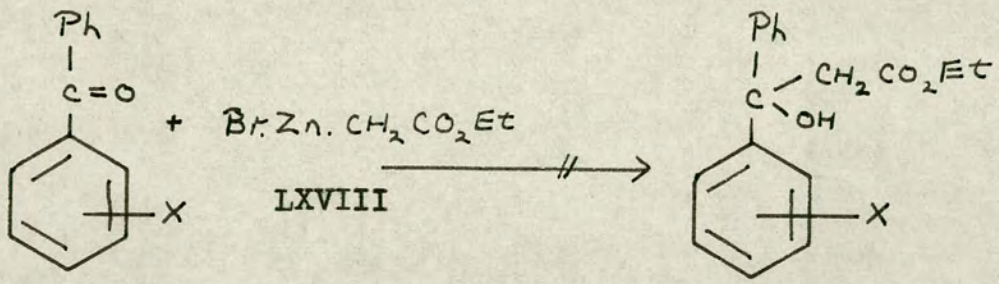
These reactions and their presumed mechanism are symbolised in a general way in Scheme D where (z) is a cyano, sulphonyl, carbethoxy or acyl group. Proof of the intermediate benzyne was obtained when it was shown that 2 and 3-chloro precursors gave the same cyclised product through the same intermediate benzyne. The authors explored the effects of different chain lengths i.e. of varying n, and also the different activating groups (z) on the yield of ring closed product. In the case of four membered ring formation, it was found that the cyano group was the best activating group with a yield of 61%, phenylsulphonyl next with 47% and then carbethoxy with 10%.

Both in yield and availability of precursors, these ring closures compare favourably with other methods of synthesis of bicyclo [4.2.0] octa -1, 3, 5 - trienes (XLVIII). Furthermore,

it seemed probable that these syntheses could be generalised so as to yield directly in the ring closure step, bicyclooctatrienes substituted in the benzene and/or four membered ring. Also the ring closure products would provide active sites for further structural elaboration.

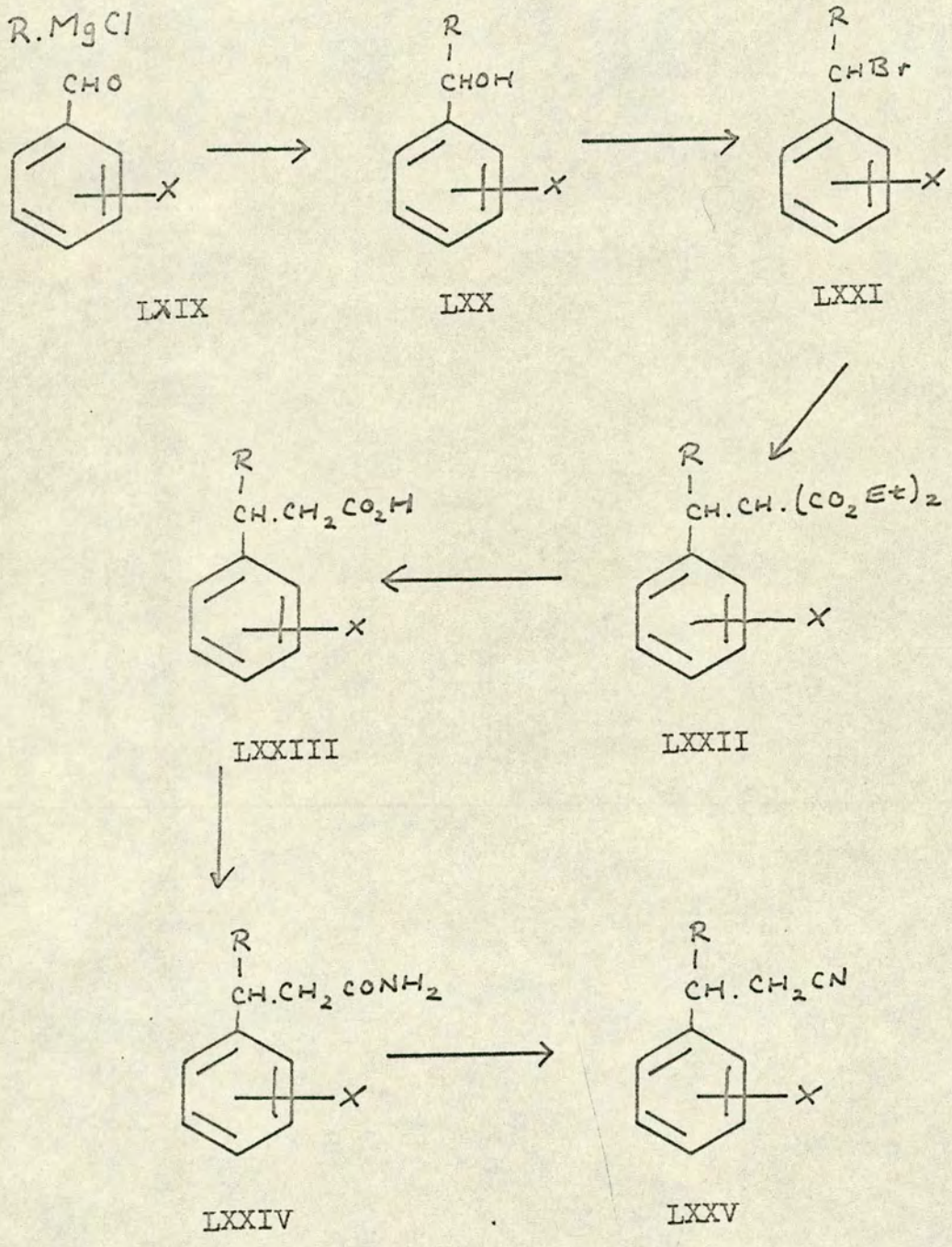
We therefore attempted a synthesis of bicyclo [4.2.0] octa - 1, 3, 5 - trienes with substituents in the 7 and 8 positions which in further reactions could lead to the formation of benzobiphenylenes as indicated on page 26.

Several precursors for the ring closure stage were synthesised by the same general pathway outlined in Scheme E. Prior to the discovery of this route, attempts were made to form esters of the type (LXVI) by Reformatskii reactions of substituted benzophenones (LXVII) with ethyl bromoacetate. Although in all cases, the formation of the organozinc halide (LXVIII) was observed to have taken place, only unchanged ketones were isolated from the reaction mixture.



LXVII LXVI

SCHEME E

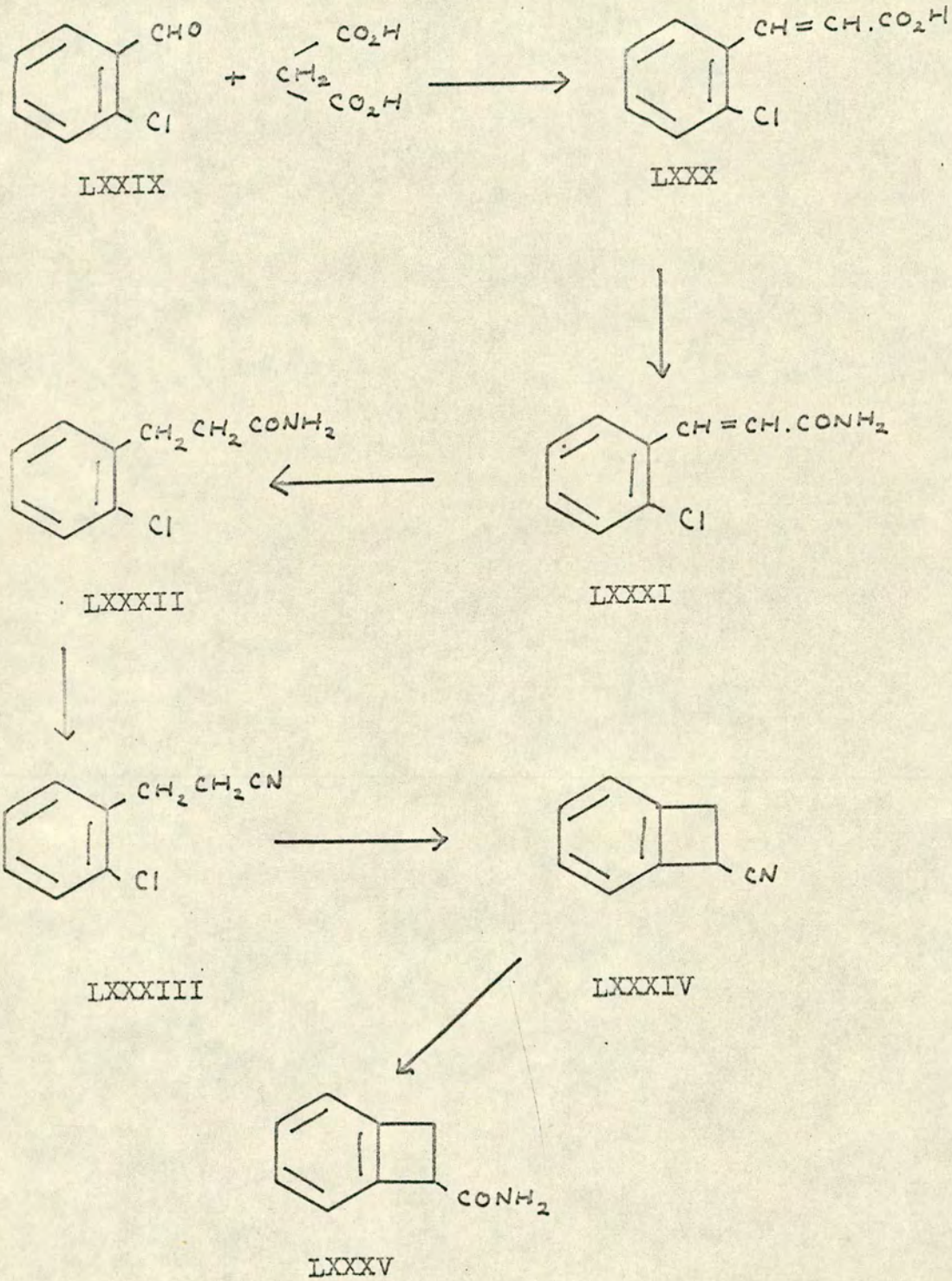

R.MgCl
CHO
X
LXIX
R
CHOH
X
LXX
R
CHBr
X
LXXI
R
CH.CH.(CO2Et)2
X
LXXII
R
CH.CH2CO2H
X
LXXIII
R
CH.CH2CONH2
X
LXXIV
R
CH.CH2CN
X
LXXV

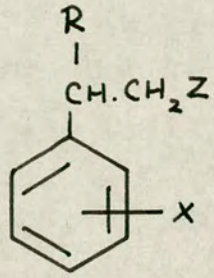
An attempt was made to form 2-phenyl 2- (2chlorophenyl) priopionic acid (LXXIII) (R =Ph) by reaction of the lithio compound (LXXVI) from phenyl - 2- chlorophenyl - bromomethane (LXXI) (R = Ph) with chloroacetic acid but a halogen metal exchange probably occurred between the chloroacetic acid and the lithium compound (LXXVI) with the reformation of (LXXI) which then coupled with the unchanged LITHIO COMPOUND to form the dimer, 1, 2 -diphenyl -1, 2 -di-2-chlorophenylethane (LXXVII) which was identified by elementary analysis and comparison of its melting point with that recorded in the literature (41).

The eventual successful synthesis outlined in Scheme E gave good yields of fairly pure products in all the stages. Grignard reaction of the alkyl, aralkyl or aryl magnesium halide with either 2- or 3-chlorobenzaldehyde yielded the corresponding substituted methanols (LXX) which on reaction with phosphorus tribromide gave the bromides (LXXI). Malonic ester synthesis led to the substituted malonic esters (LXXII) which on hydrolysis and monodecarboxylation gave the propionic acids (LXXIII). Dehydration of the amides (LXXIV) of these acids with thionyl chloride gave the required nitrile precursors. In the cases where esters were used as precursors, they were prepared by esterification of the corresponding acids (LXXIII).

In this way the following precursors (LXXVIII) were obtained :

SCHEME F


CHO
Cl
+
CO2H
CH2
CO2H
CH=CH.CO2H
Cl
LXXIX
LXXX
CH2CH2CONH2
Cl
CH=CH.CONH2
Cl
LXXXII
LXXXI
CH2CH2CN
Cl
CN
LXXXIII
LXXXIV
CONH2
LXXXV



LXXVIII

	R	X	Z
a)	PHENYL	2-CHLORO	CYANO
b)	PHENYL	3-CHLORO	CYANO
c)	PHENYL	2-CHLORO	CARBETHOXY
d)	PHENYL	3-CHLORO	CARBETHOXY
e)	BENZYL	2-CHLORO	CYANO
f)	METHYL	2-CHLORO	CYANO

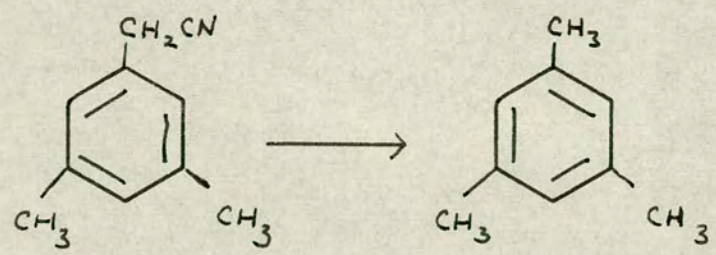
In order to ensure that the proper experimental conditions could be attained, it was decided to synthesise and carry out the ring closure step on 2-(2-chlorophenyl) propionitrile (LXXXIII) which had been used by Bunnett & Skorcz (40) to form 7-cyanobicyclo [4.2.0] octa -1, 3, 5 - triene (LXXXIV). Compound (LXXXIII) was synthesised by the procedure outlined in Scheme F which is a different route from that used by Bunnett & Skorcz (40).

2- chlorobenzaldehyde (LXXXIX) was condensed with malonic acid and spontaneous decarboxylation occurred to give 2-chlorocinnamic acid (LXXX) whose amide (LXXXI) was reduced over platinum catalyst to give 2- (2-chlorophenyl) propionamide (LXXXII) which was then dehydrated to give 2-(2-chlorophenyl) propionitrile (LXXXIII). When this compound was reacted under the ring fusion (elimination addition)

conditions, a nitrile (LXXXIV) was obtained which on hydrolysis in hydrogen peroxide solution gave an amide whose melting point and elementary analysis were in accord with the values for the known (40) compound bicylo [4.2.0] octa -1, 3, 5 - triene -7- carboxamide (LXXXV).

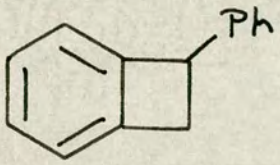
This indicated that we were able to achieve the proper conditions to effect the elimination-addition reactions. The results of these reactions are given below.

2-Phenyl -2- (2-chlorophenyl) propionitrile (LXXVIIIa) yielded an oil which chromatographed on alumina as a single band as the product. Its infrared spectrum exhibited no band in the region 2,260 -2, 240 $cm.^{-1}$ indicating that the nitrile group was no longer present. Also, no bands attributable to either C = N -H or $\rangle C - NH_2$, the reduction products of a nitrile, were found indicating that the nitrile had probably been cleaved from the molecule. This was confirmed when it was shown by elementary analysis that the product contained no nitrogen. An example of this reductive cleavage has been reported (42) in which mesitylene (CLXXXIII) was obtained from the reaction of 3, 5 - dimethylbenzyl cyanide (CLXXXIV) with sodamide in liquid ammonia.



CLXXXIV CLXXXIII

However, the elementary analysis also showed that chlorine was present to the extent of 3.4% and that the ratio of carbon to hydrogen was ca. 7: 10 indicating since 7-phenylbicyclo [4.2.0] octa -1, 3, 5 -triene (LXXXI) requires a carbon: hydrogen ratio of 14: 12, that reduction of the phenyl groups had also probably occurred.



LXXXI

Attempted nitration with concentrated nitric/acetic acids mixture and oxidation with aqueous potassium permanganate failed to give any solid identifiable products. The infrared spectrum shows no absorptions characteristic of cycloalkane derivatives (47) and thus there is no evidence for formation of a four membered ring although ring fusion followed by ring fission may have occurred by analogy with the findings of Blomquist & Bottomley (44) on the effect of base on the 7-phenylbicyclo [4.2.0] octa -1, 3, 5 - triene -8- carboxylic acid as mentioned on page 32 .

Thus it appears that the reaction product from (LXXVIIIa) is a mixture in which ring closure may or may not have occurred, but cleavage of the nitrile group and also extensive reduction of probably both phenyl groups have occurred.

With 2-phenyl -2- (3-chlorophenyl) propionitrile as precursor an oil which again chromatographed as one band on alumina was obtained. Its infrared spectrum exibited two nitrile peaks and also a very small doublet at 3400 $cm.^{-1}$ due to the absorption of an amino group. The elementary analysis of the product indicated an empirical formula of ca. $C_{19}H_{18}N_3$, the high proportion of nitrogen being due to the amino groups. These amino groups are probably aromatic rather than just being reaction products of the nitrile since aromatic amines are expected as products of the electrophilic attack on ammonia by the benzyne intermediate. The infrared spectrum also showed that a peak present in the spectrum of the precursor (LXXVIIIb) at 890 $cm.^{-1}$ attributed to the C-H absorption of the C - atom between the substituent in 1: 3 - disubstituted benzene, was missing in the product and that a pattern very similar to that obtained in the 690 - 770 $cm.^{-1}$ region for the ring closed product from (LXXVIIIe) was present which indicates that ring closure to give the four membered ring has probably occurred. A peak appears in the I.R. spectrum at 1000$cm.^{-1}$ but this cannot be attributed to the cycloalkane ring as a similar peak appears in the I.R. spectrum of the precursor.

Hydrolysis of the product with sodium hydroxide and hydrogen peroxide gave an amide and further hydrolysis of the amide gave an acid but both of these hydrolysis products were uncrystallisable oils. An attempt to cyclise the acid in hydrogen fluoride in the hope that a solid ketone might be obtained gave only unchanged starting material. Later examination of models indicated that it would be impossible to cyclise trans-7-phenylbicyclo [4.2.0] octa -1, 3, 5 - triene 8-carboxylic acid XLVIII R_1 = phenyl and R_2 = CO_2H and that cyclisation of the cis isomer, if it did occur, would give a highly strained product. Similarly unsuccessful were the attempts to form the hydrochloride of the imino ether from the nitrile by the method of Hager et al. (43) and to oxidise the nitrile in aqueous potassium permanganate to an identifiable solid product.

Thus it appears that if the cyclised product has been formed, it is a component of a complex mixture containing ring opened nitrile (cf. results of ring closure of LXXVIIIa) and other artefacts such as aromatic amines.

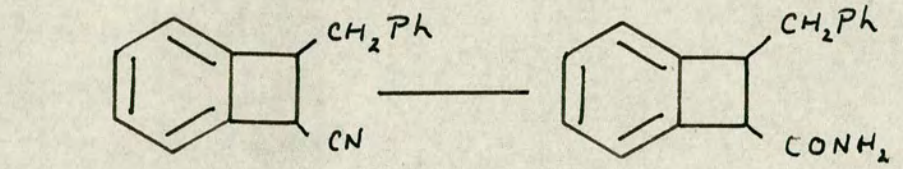
With a normal reaction time of fifteen minutes and also with a time of one hour only unchanged starting material was obtained when ethyl 2-phenyl -2-(2-chlorophenyl) propionate LXXVIIIc was used as precursor. This was confirmed by hydrolysis of the ester to the acid and comparison of its melting point and mixed melting point with an authentic sample.

With ethyl 2-phenyl -2- (3-chlorophenyl) propionate LXXVIIId as precursor, a product was obtained which was separable by chromatography on alumina into two fractions. The first fraction was unchanged starting material confirmed when on hydrolysis it gave an acid whose m.p. and mixed m.p. with 2-phenyl -2- (3-chlorophenyl) propionic acid was 96°. The second fraction was an oil which was shown to be an aromatic amine by its infrared spectrum and by the production of an orange dye on coupling its diazonium salt with β -naphthol. It is probably ethyl 2- (3-aminophenyl) -2-phenyl propionate since its infrared spectrum has a medium intensity band at 875cm.$^{-1}$ characteristic of 1: 3 disubstituted benzenes.

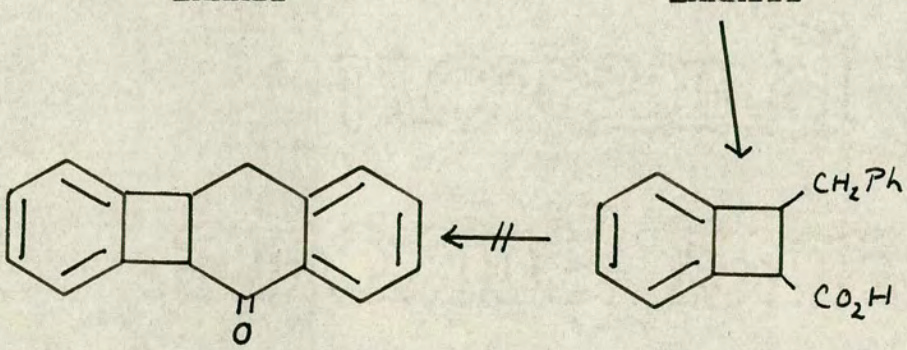
The results of these reactions involving the isomeric esters LXXVIII (c) and (d) bear out the observation of Bunnett & Skorcz (40) that in the case of four membered ring formation, the ester group is only weakly activating.

2-(2-Chlorophenyl) -3- phenylbutyronitrile LXXVIIIe yielded 7-benzyl -3- cyanobicyclo [4.2.0] octa -1, 3, 5 -triene as an

oil with a single nitrile absorption at 2290cm.$^{-1}$. Hydrolysis of the nitrile LXXXII with a sodium hydroxide and hydrogen peroxide solution gave an amide whose elementary analysis agreed closely with that required for LXXXIII, 7-benzyl - bicyclo [4.2.0] octa -1, 3, 5 -triene -8- carboxamide. Hydrolysis of the amide LXXXIII gave the acid LXXXIV.



LXXXII LXXXIII

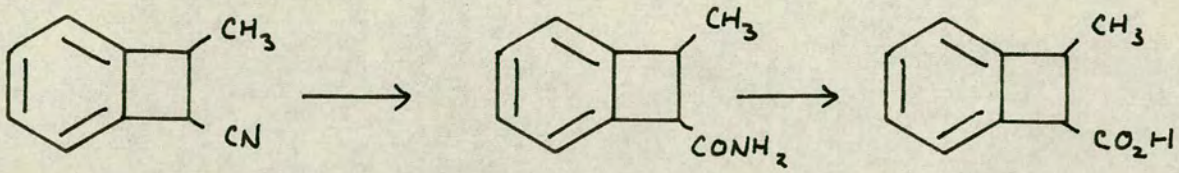


LXXXIV

The nitrile, amide and acid each had a small peak at 1000-1008cm.$^{-1}$ in the infrared spectrum, indicative of a cyclobutane ring, which

was not present in the precursors. Attempts to cyclise the acid LXXXIV in hydrofluoric acid, polyphosphoric acid and with aluminium trichloride in dichloromethane gave oils whose infrared spectra indicated that they were lactones. These were probably formed due to ring opening of the four membered ring with the formation of olefinic acids cf. Horner et al. (46) which then underwent ring closure cf. Ansell & Palmer (37), to give lactones. Later examination of models indicated that although acid LXXXIV could cyclise intramolecularly to give a stable product if the benzyl and carboxyl groups were in a cis configuration about the 7, 8-bond, the trans isomer would give rise to a highly strained product in the unlikely event of cyclisation occurring.

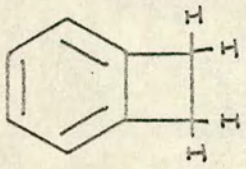
In a model experiment with 2- (2-chlorophenyl) butyronitrile LXXVIIIf. as precursor, an oil with a nitrile absorption in the infrared spectrum at 2280cm.$^{-1}$ was obtained. Hydrolysis of this nitrile LXXXVI gave the amide LXXXVII m.p. 108-110° whose elementary analysis was in agreement with that required for 7-methylbicyclo [4.2.0] octa -1, 3, 5 - triene -8- carboxamide. From the same hydrolysis, some of the corresponding acid LXXXVIII was obtained m.p. 144-146°.



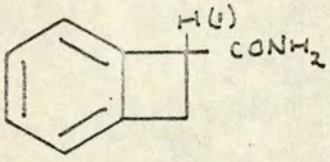
LXXXVI LXXXVII LXXXVIII

SCHEME G

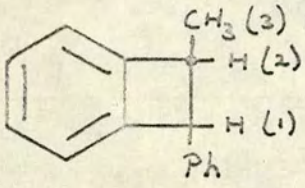
N.M.R. PARAMETERS OF BICYCLO[4.2.0.]OCTA-I.3.5-TRIENES.

	τ_1	τ_2	τ_3
	6.86	–	–

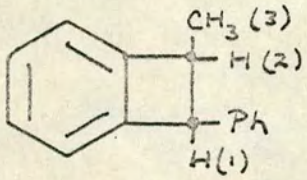
7-CARBOXAMIDE.

	5.83	–	–

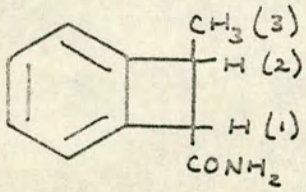
TRANS-7-METHYL-8-PHENYL.

	5.63 (doublet)	6.43 (octet)	8.44 (doublet)

CIS-7-METHYL-8-PHENYL.

	4.89 (doublet)	5.93 (quintet)	9.07 (doublet)

TRANS(?)-7-METHYL-8-CARBOXAMIDE.

	5.7 (doublet)	6.3 (multiplet)	8.5 (doublet)

The N.M.R. data for the amide LXXXVII is given along with that for several known bicyclo [4.2.0] octa -1, 3, 5 - trienes in Scheme G. Consideration of the values given leads one to the conclusion that the amide LXXXVII probably has a trans configuration, a not unexpected situation when the steric interaction that would occur between cis substituents is considered. The N.M.R. spectrum obtained for the benzyl-amide LXXXIII was too weak for any readings to be taken from it but by analogy with LXXXVIII, it does not seem unreasonable to assume that it too has a trans configuration about the 7, 8 bond.

In conclusion, although the methods used are fairly successful in the synthesis of substituted bicyclo [4.2.0] octa 1, 3, 5 - trienes, it appears that the susceptibility of the four membered ring to ring opening under a variety of conditions renders them unsuitable for further reaction leading to benzobiphenylenes.

SECTION II

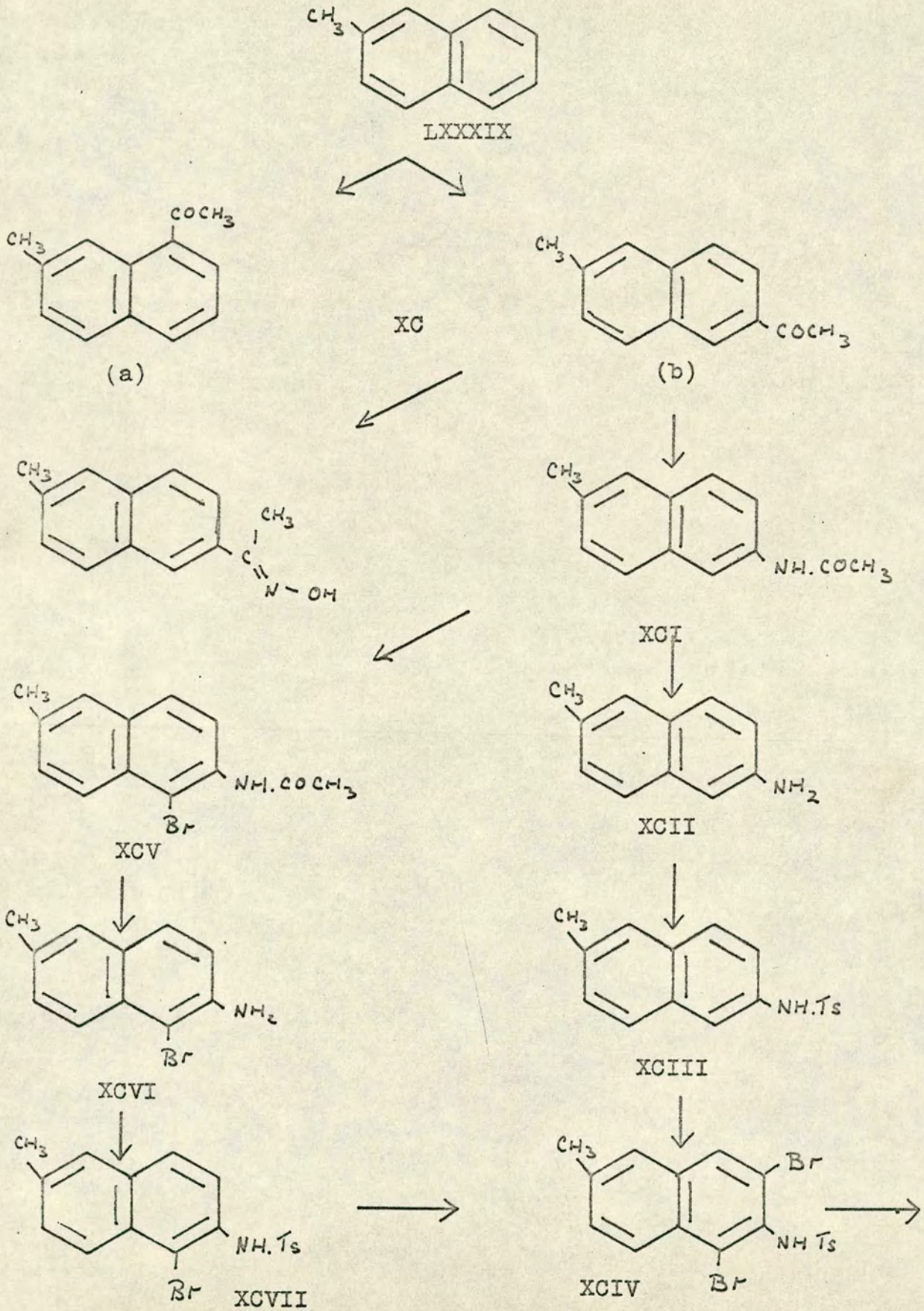
MISCELLANEOUS ATTEMPTED SYNTHESES.

SECTION II

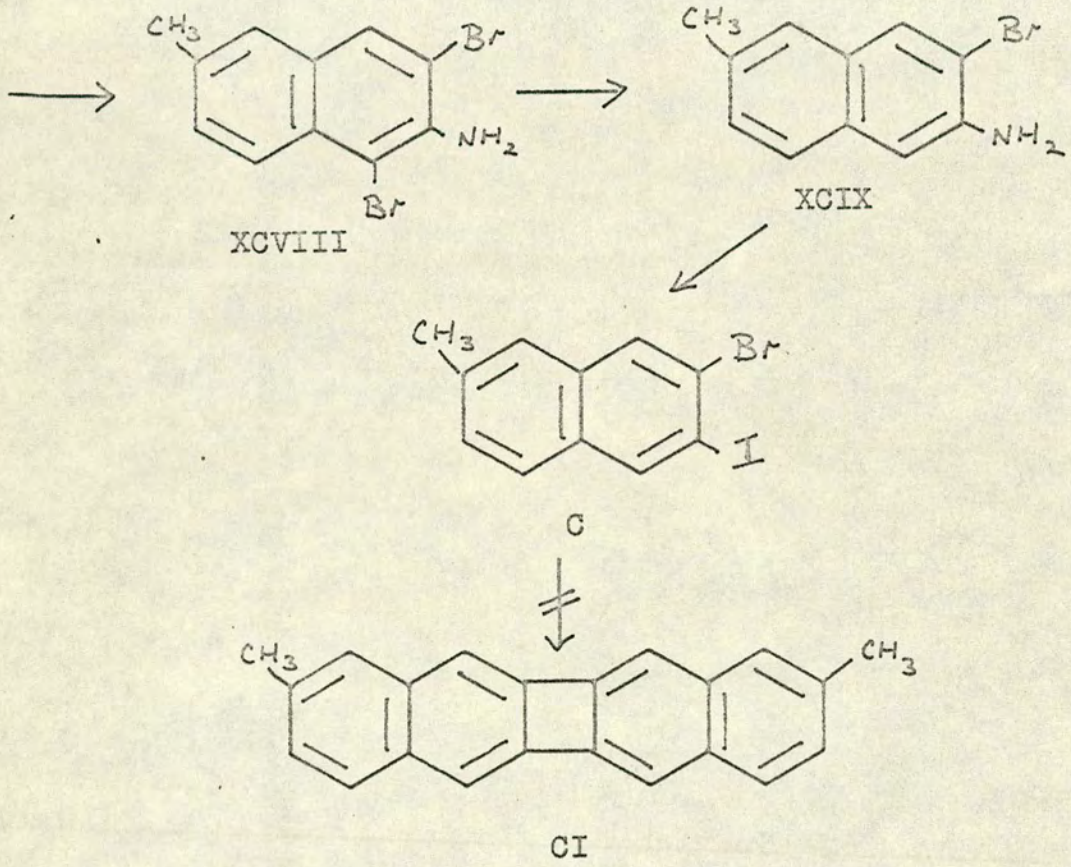
PART I

ATTEMPTED SYNTHESIS OF 2, 9-DIMETHYLDIBENZO [b, h] BIPHENYLENE.

SCHEME H



SCHEME H (contd.)



Pearson (6) reported the reaction of 2-bromo- 3 - iodonaphthalene with copper bronze in dimethyl formamide as giving a low yield of dibenzo [b, h] biphenylene and although no chemical evidence could otherwise be obtained, the reaction was considered to have involved the dimerisation of a β -naphthalyne intermediate (see page 6) by analogy with a reaction carried out by Wittig and Pohmer (7). 2-Bromo -3- iodo -7- methylnaphthalene C was synthesised in the hope that under Pearson's reaction conditions, it would give rise to 2, 9-dimethyldibenzo [b, h] biphenylene CI.

The synthesis leading to the formation of compound C is outlined in Scheme H.

Friedel-Crafts acetylation of 2-methylnaphthalene LXXXIX gave a mixture of 1-acetyl -7- methylnaphthalene XCa. and 2-acetyl -6- methylnaphthalene XCb. The predominating isomer XCb. is presumably formed due to acetylation by a complex of the acetyl chloride and nitrobenzene which finds easier steric accomodation in the less hindered β -position. The other isomer is thus formed by a reagent of lower steric requirements in an independent synthesis. The mixture was separated by virtue of the lesser solubility of the semicarbazone of isomer XCb in hot methanol. Conversion of this isomer to 2-acetamido -6- methylnaphthalene XCI was accomplished with similar overall yields via either the Schmidt reaction of the ketone or by its conversion to an oxime followed by a Beckmann Rearrangement. Judging from the yield of pure amide obtained

from the Beckmann Rearrangement and the fact that no other amide seemed to be contaminating it, the oxime formed from the ketone XCb must be the anti - (6-methyl -2- naphthyl) - methyl ketoxime. This is probably due to steric interaction, which would result in the syn form, between the naphthalene nucleus and the hydroxyl group. Hydrolysis of the amide with 25% methanolic potassium hydroxide gave 2-amino -6-methylnaphthalene XCII which was converted into its p-toluenesulphonyl derivative XCIII. Bromination of XCIII with bromine in pyridine gave 1, 3-dibromo -2- p-toluenesulphonamido -6- methylnaphthalene XCIV. Bromination in position 3 is considered by Bell (32) to be due to the enhanced reactivity of the sulphonamido group by salt formation in pyridine. This enhanced activity is due to the production of a negative pole on the nitrogen :-

$$Ar.NH.SO_2R \longrightarrow Ar.\overset{(-)}{N}SO_2R, \overset{(+)}{HN}C_6H_5$$

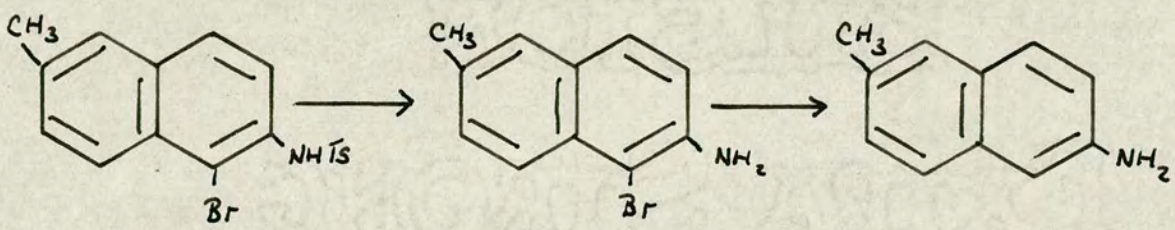
The effectiveness of the attack is also probably in part due (32)to the positive bromine derived from the additive compound $C_5H_5NBr_2$ reported by Hofmann (33).

Compound XCIV was alternatively arrived at by bromination of 2-acetamido -6- methylnaphthalene XCI in acetic acid to give 1-bromo -2- acetamido -6- methylnaphthalene XCV.

Due to the anomalous analyses (cf. page116) obtained for compound XCV, some doubt arose as to whether a mono or dibromo compound had been obtained. Since not enough 2-acetamido -1- bromo -6-

methylnaphthalene XCV was available, it was decided to investigate the nature of the substitution in 1-bromo -2- sulphonamido -6- methylnaphthalene XCVII which had been obtained by acid hydrolysis and subsequent tosylation of XCV.

If XCV is a monobromo compound, with bromine in position 1, then the sequence of reactions outlined below should give rise to the known 2-amino -6- methylnaphthalene XCII m.p. 129°.



XCVII XCVI XCII

When this reaction sequence was carried out, a compound melting at 129° and giving a mixed melting point of 129° with XCII, prepared as in Scheme H, was obtained, thus confirming the structure of XCV.

Attempted bromination of 2-methyl -6- aminonaphthalene XCII and further bromination of XCV were unsuccessful. The acetamido compound XCV was therefore hydrolysed in 1:1:1 mixture of concentrated

sulphuric acid: acetic acid: water to give 1-bromo -2- amino -6- methylnaphthalene XCVI which was then converted into its p-toluenesulphonyl derivative XCVII which in turn gave 1, 3 - dibromo -2- p-toluenesulphonamido -6-methylnaphthalene XCIV on bromination in pyridine. Hydrolysis of XCIV in concentrated sulphuric acid gave 1, 3-dibromo -6- methyl -2- naphthylamine XCVIII. Boiling of this compound with a tin/ethanol/conc. hydrochloric acid mixture led to the removal of the bromine from position 1 with the formation of 3-bromo -2- amino -6- methylnaphthalene XCIX. This preferential removal of bromine from the 1 position in naphthalene with an amino group in the 2-position was first observed by Franzen and Stauble (35) who attributed it to the effect of the amino group being greater in the 1 than the 3-position due to the greater double bond character of the 1-2 bond with respect to the 2-3 bond. Diazotisation of XCIX followed by decomposition with iodine and potassium iodide gave red crystals of 2-iodo -3- bromo -6- methylnaphthalene C.

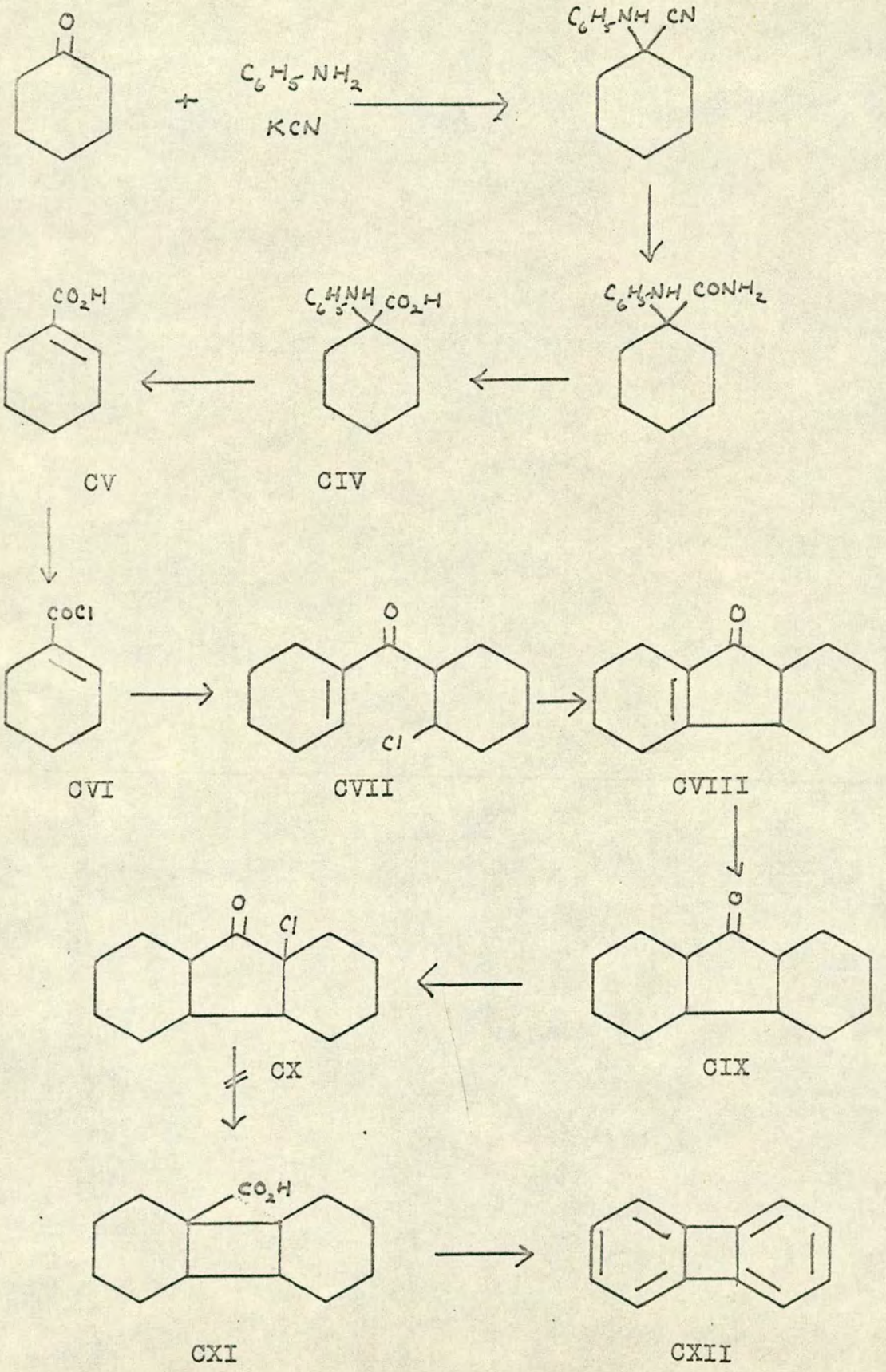
Reaction of this compound under conditions similar to those of Pearson (6) gave no isolable 2, 9 - dimethyldibenzo [b, h] biphenylene. The only product obtained was an off white amorphous solid m.p. 119 - 120^{o} whose analysis showed it to be a mixture and whose ultraviolet spectrum showed only naphthalene type absorption. In view of the variety of possible reactions promoted by the copper bronze catalyst cf. Bacon and Hill (48), it seems pointless to speculate on the nature of the mixture of products obtained.

SECTION II

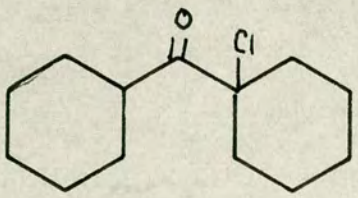
PART II

ATTEMPTED SYNTHESIS OF BIPHENYLENE INVOLVING RING CONTRACTION BY FAVORSKII REARRANGEMENT.

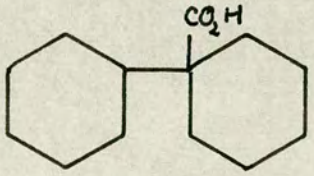
SCHEME I


C6H5NH2
KCN
C6H5NH CN
C6H5NH CONH2
C6H5NH CO2H
CO2H
COCl
Cl
CV
CIV
CVI
CVII
CVIII
CIX
CX
CXI
CXII

The ring contraction of α-halogenocyclanones to carboxylic acid derivatives of the next lower cycle is an important application of the Favorskii reaction. The reaction is reasonably general for α-halocyclanones in rings of from six to ten carbon atoms but no report of the reaction of an α-halocyclopentanone appears in the literature although 2-bromocyclobutanone gives cyclopropane carboxylic acid in good yield (49). It has also been reported (50) that α-chlorodicyclohexyl ketone CII gives 1-carboxyperhydrodiphenyl CIII.



CII



CIII

Thus it appeared feasible that if α-chloroperhydrofluorenone CX could be synthesised, it stood a good chance of yielding 4a--carboxyperhydrobiphenylene CXI in a Favorskii rearrangement which, on decarboxylation and dehydrogenation, would give biphenylene CXII.

1-Anilinocyclohexanecarboxylic acid CIV obtained from cyclohexanone as described by Walther and Hubner (51) and Betts, Muspratt, and Plant (52) provided a mixture of aniline and cyclohex -1- enecarboxylic acid CV on distillation. The acid chloride of the latter was then reacted under Friedel-Crafts conditions with aluminium trichloride and

cyclohexane to give a product CVII which on heating with a mixture of formic and phosphoric acids gave 1, 2, 3, 4, 4b, 5, 6, 7, 8, 8a -decahydrofluorenone CVIII. This interesting cyclisation was reported by Baddeley et al. (53).

The reduction of the decahydrofluorenone CVIII over platinic oxide in methanol has been reported by Braude and Coles (54) but our product failed to react under these conditions, reduction to the perhydrofluorenone CIX being accomplished over 10% palladised charcoal in ethanol containing a small volume of dilute hydrochloric acid. The perhydrofluorenone was then chlorinated with N-chlorosuccinimide.

In the chlorination of aliphatic ketones under free radical conditions, the hydrogen atoms α to the keto group are substituted first and the rate of substitution probably follows the usual sequence, tertiary > secondary > primary.

Thus, in the free radical chlorination of perhydrofluorenone, the α-chloro perhydrofluorenone CX is expected to be the major product. However, reaction of the unpurified chloroperhydrofluorenone under Favorskii rearrangement conditions gave neither 4a - carboxyperhydrobiphenylene CXI nor any other identifiable product.

From the failure of this reaction, it might be inferred that little or none of the supposed α-chloroperhydrofluorenone CX has been formed in the chlorination stage but this seems unlikely when the theroetical considerations above are reviewed. Elementary analysis of CX showed that dehydrochlorination had not occurred.

Two examples (55) (56) of the rearrangement of 2-halo -2- alkylcyclohexanones, which have in certain aspects, an analogous structure to CX, have been reported as failing although 2-chloro -2- methylcycloheptanone gives the expected 1-methylcyclohexane carboxylic acid (55).

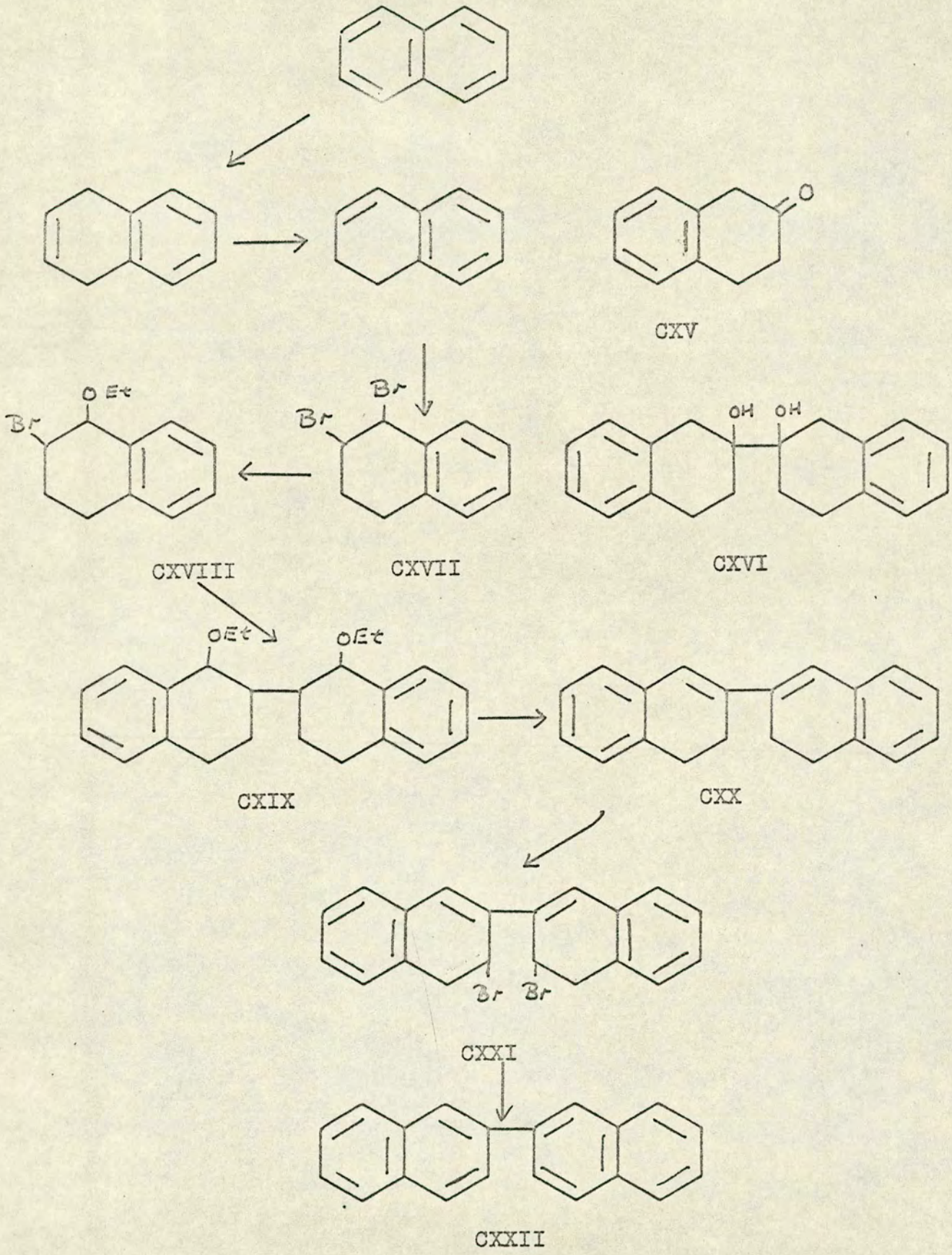
Other possibilities are that the competing side reactions cf. Kende (57) are more favoured or that the product or its intermediates are susceptible to decomposition under the reaction conditions.

SECTION II

PART III

ATTEMPTED FORMATION OF DIBENZO [b, h] BIPHENYLENE.

SCHEME J



CXV

CXVIII

CXVII

CXVI

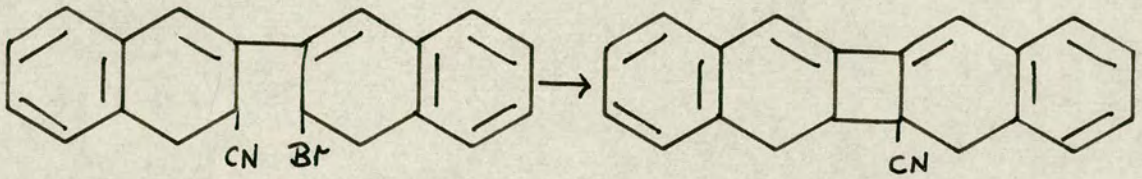
CXIX

CXX

CXXI

CXXII

An attempt was made to form 3-cyano -3- bromo - 3, 3' 4, 4' - tetrahydro -2, 2' -binaphthyl CXIII in the hope that it might dehydrobrominate in such a way as to yield 5a -cyano -5, 5a, 5b, 6 - tetrahydrodibenzo [b, h] biphenylene CXIV.



CXIII CXIV

Hydrolysis of the nitrile followed by decarboxylation and dehydrogenation would then give dibenzo [b, h] biphenylene (I). The synthetic approaches are outlined in Scheme J. Rather surprisingly, we were unable to form the pinacol CXVI from 2- tetralone CXV, although 1-tetralone gave a pinacol under the same conditions. A more successful approach was that used by von Braun and Kirshbaum (58) to synthesise 3, 3' , 4, 4' - tetrahydro -2, 2' -binaphthyl CXX. Partial reduction of naphthalene to 1, 4 - dihydronaphthalene followed by isomerisation gave 1, 2 - dihydronaphthalene, whose double bond was easily brominated to give 1, 2- dibromo -1, 2, 3, 4 - tetrahydronaphthalene CXVII. Boiling of this compound in ethanol gave 1-ethoxy -2- bromo

-1, 2, 3, 4 -tetrahydronaphthalene CXVIII. A Wurtz type reaction of this compound with magnesium gave 1, 1' -diethoxy -1, 1', 2, 2', 3, 3', 4, 4' -octahydro - 2, 2' - binaphthyl CXIX. which lost two molecules of ethanol on boiling in a 1:1 mixture of ethanol and concentrated sulphuric acid, to yield 3, 3', 4, 4' -tetrahydro -2, 2' -binaphthyl CXX.

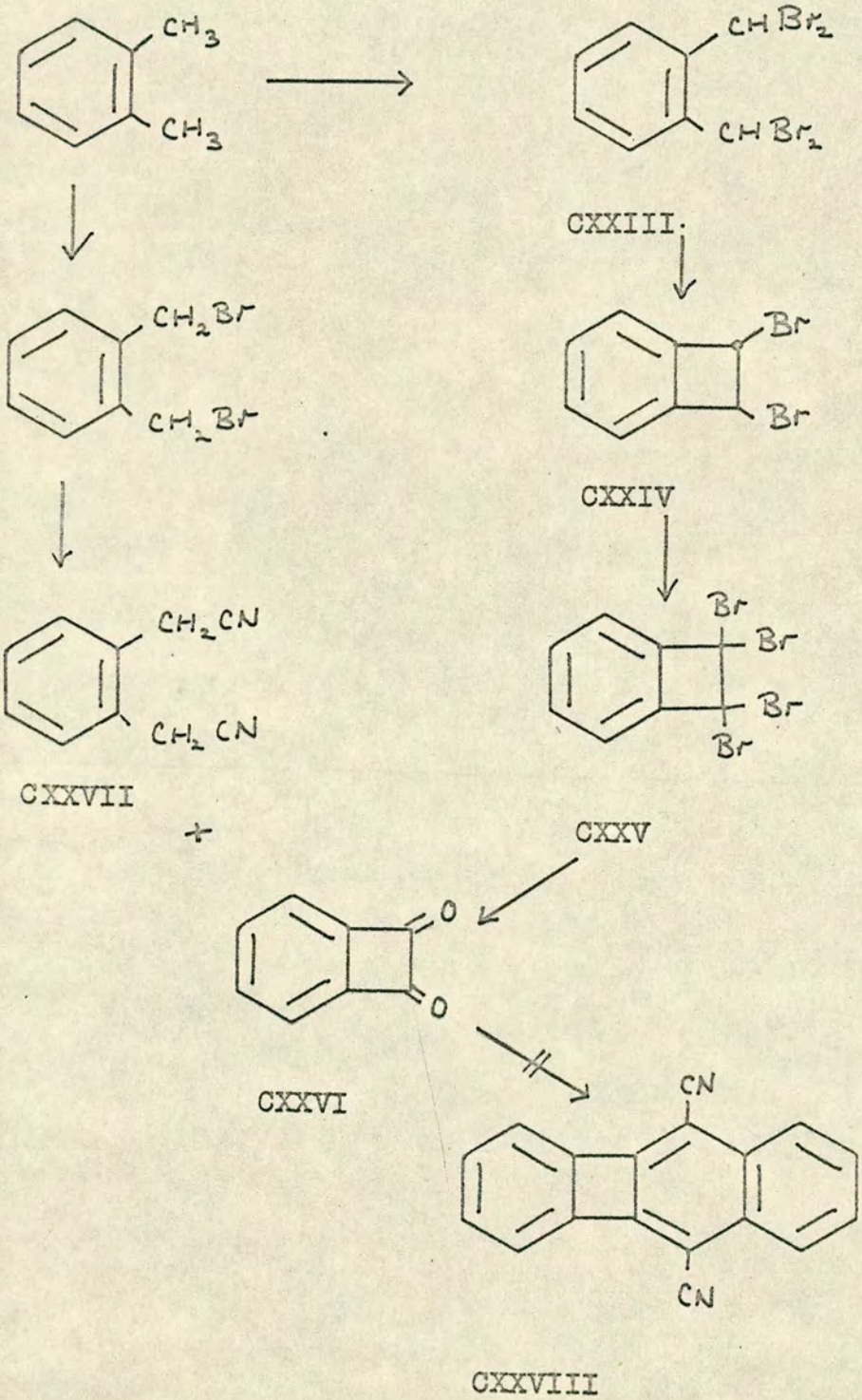
However, bromination of this compound with N-bromosuccinimide in the two allylic positions gave 3, 3' - dibromo - 3, 3' 4, 4' - tetrahydro -2, 2'- binaphthyl CXXI which could not be isolated even when the bromination was carried out at room temperature, as it dehydrobrominated spontaneously to give 2, 2' -binaphthyl CXXII.

SECTION II

PART IV

ATTEMPTED CONDENSATION OF BICYCLO [4.2.0] OCTA -1, 3, 5 -TRIENE -7, 8 -DIONE (CXXVI)

SCHEME K


CH3
CH3
CHBr2
CHBr2
CXXIII.
CH2Br
CH2Br
Br
Br
CXXIV
Br
Br
Br
Br
CH2CN
CH2CN
CXXVII
+
CXXV
O
O
CXXVI
CN
CN
CXXVIII

In 1910, Hinsberg (59) reported the condensation of diethyl oxalate with the reactive methylene groups of α, α' -dicyano -o- xylene in sodium methoxide solution to yield 1, 4 - dicyano -2, 3-dihydroxynaphthalene. This condensation of an α -dicarbonyl compound with α, α' -dicyano -o- xylene was shown to be a fairly general type of reaction by Moureu et al. (60) who also demonstrated that piperidine was the prefered condensing reagent.

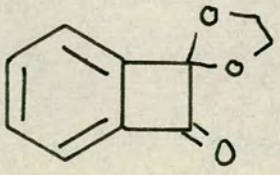
Since the preparation of bicyclo [4.2.0] octa -1, 3, 5 -triene -7, 8 - dione CXXVI had been reported (61) (62) (63) it looked as though its condensation with α, α' -dicyano -o- xylene CXXVII might provide an easy synthesis of 5, 10 -dicyanobenzo [b] biphenylene CXXVIII.

Cava, Napier and Pohl's synthesis of the dione CXXVI is outlined in Scheme K. The reaction of $\alpha, \alpha, \alpha', \alpha'$ -tetrabromo -o- xylene CXXIII with sodium iodide in aqueous ethanol first reported by Finkelstein (64) gave trans 7, 8-dibromobicyclo [4.2.0] octa - 1, 3, 5 - triene CXXIV which on further bromination with N-bromosuccinimide gave the tetr bromide CXXV. Treatment of this compound with silver trifluoroacetate, followed by water gave the dione CXXVI.

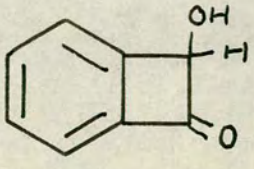
However, attempted condensations under a variety of both basic and acidic conditions failed to give any of the hoped for 5, 10 -dicyanobenzo[b] biphenylene CXXVIII. The failures in the basic

media are probably due to the susceptibility of the α -diketone to rupture between the carbonyl groups in basic conditions to give o-phthalaldehydic acid, a result observed by Cava, Napier and Pohl (63). This was confirmed when the condensation was carried out in piperidine, an oil being obtained which was characterised as o-phthalaldehydic acid by its red 2, 4 - dinitrophenylhydrazone. Other products were isolated from the reactions in basic media whose infrared spectra and analyses indicated that they were probably products of the interaction of phthalaldehydic acid and the particular base used. No reaction occurred under the acidic conditions.

Attempts to prepare 7-ethylenedioxybicyclo [4.2.0] octa -1, 3, 5 -triene -8- one CXXIX and to reduce the diketone CXXVI to 7-hydroxybicyclo [4.2.0] octa -1, 3, 5 - triene -8- one CXXX were unsuccessful.

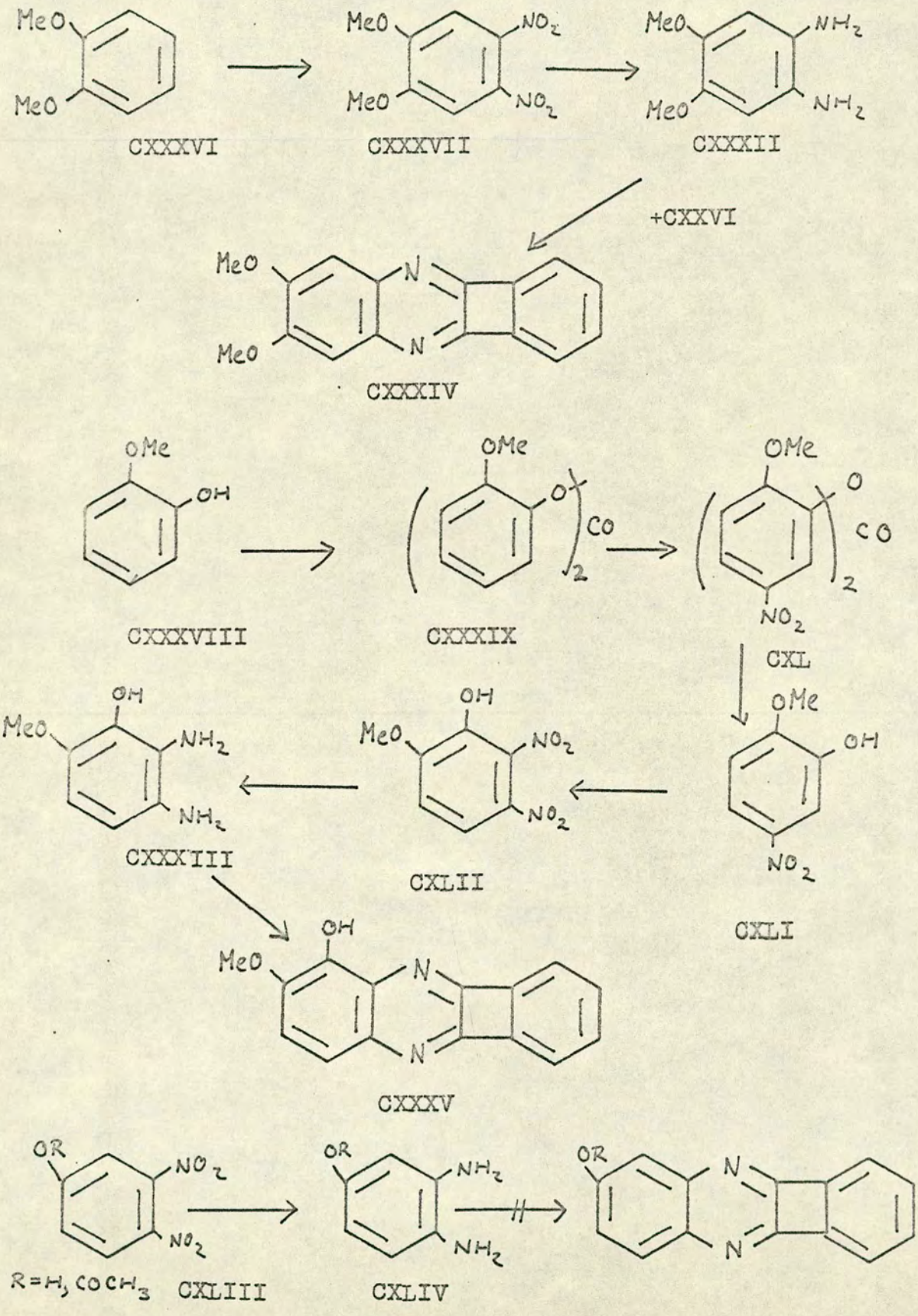


CXXIX

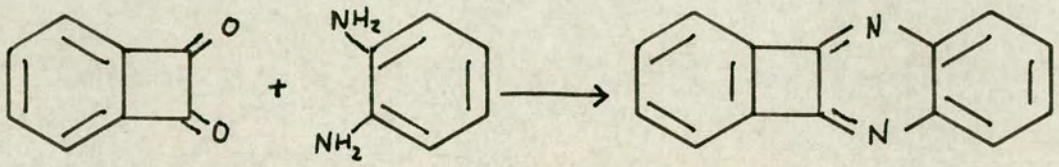


CXXX

SCHEME L


MeO
MeO
CXXXVI
NO2
NO2
CXXXVII
NH2
NH2
CXXXII
+CXXVI
N
N
CXXXIV
OMe
OH
CXXXVIII
CO
2
CXXXIX
O
NO2
CXL
CXLI
CXLII
CXXXIII
CXXXV
OR
R=H, COCH3
CXLIII
CXLIV

Cava, Napier, and Pohl (63) formed the new type of compound, benzo [3, 4] cyclobuta [1, 2-b] quinoxaline CXXXI by reaction of the diketone CXXVI with o-phenylenediamine.



CXXVI CXXXI

It was thought that if similar condensations could be effected with 4, 5 - dimethoxy -o-phenylenediamine CXXXII and 3-hydroxy -4- methoxy -o-phenylenediamine CXXXIII, then demethylation of the corresponding products CXXXIV and CXXXV would give phenolic compounds in which the extent of bond fixation in the nucleus, due to incorporation of the four membered ring, could be determined by coupling reactions with diazonium salts.

Dinitration of o-dimethoxybenzene CXXXVI by the method of Ehrlich and Bogert (65) gave 4, 5-dinitro -o- dimethoxybenzene CXXXVII. Reduction of the nitro groups over Raney nickel give 4, 5 - dimethoxy -o-phenylenediamine CXXXII as shown in Scheme L Guaiacol (2-methoxyphenol) CXXXVIII was converted into the carbonate CXXXIX which when nitrated following the method of Pollecoff and Robinson (66) gave 2-methoxy -5-nitrophenol carbonate CXL.

Hydrolysis of this compound gave 2-methoxy -5- nitrophenol CXLI converted by further nitration to 3-hydroxy -4- methoxy -o- dinitrobenzene CXLII. Reduction of the two nitro groups over Raney nickel gave 3-hydroxy -4-methoxy -o- phenylenediamine CXXXIII.

However, although the o-diamines CXXXII and CXXXIII reacted readily with the diketone CXXVI to give the respective quinoxalines CXXXIV and CXXXV, neither of the condensed products could be demethylated under a variety of conditions.

It was therefore decided to try to react a phenolic compound with the diketone. 3, 4-Dinitrophenol CXLIII was prepared by nitration of 3-nitrophenol. Reduction of CXLIII over Raney nickel gave 4-hydroxy -o-phenylenediamine CXLIV which failed to give a quinoxaline with the diketone CXXVI. The acetyl derivative of CXLIV also failed to react with the diketone.

The reason for the failure of the two latter reactions is not clear since p-aminophenol is known to undergo condensation reactions of the amino group.

At this point, the inquiry into the structure of the benzo [3, 4] cyclobuta [1, 2 -b] quinoxaline nucleus was discontinued.

SECTION III

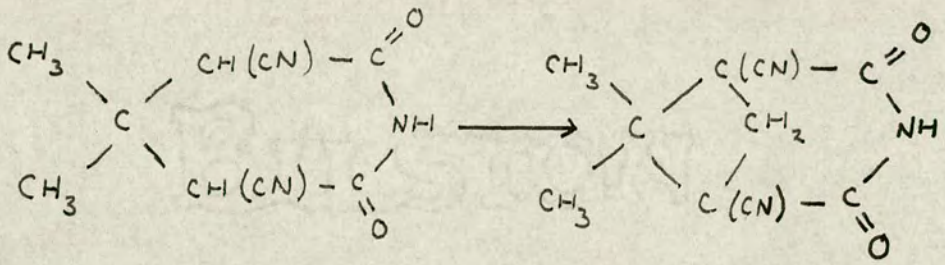
ATTEMPTED FORMATION OF DIBENZOBIPHENYLENES FROM CYCLOBUTANE DERIVATIVES.

SECTION III

PART I

ATTEMPTED SYNTHESIS OF BICYCLIC IMIDES LEADING TO CYCLOBUTANE DERIVATIVES.

In 1929, Kerr (68) reported that the sodium derivative of Guareschi's imide, α ,α' -dicyano - β ,β - dimethyl glutarimide CXLV reacted with methylene iodide to give a 70% yield of the dicyclic imide CXLVI.

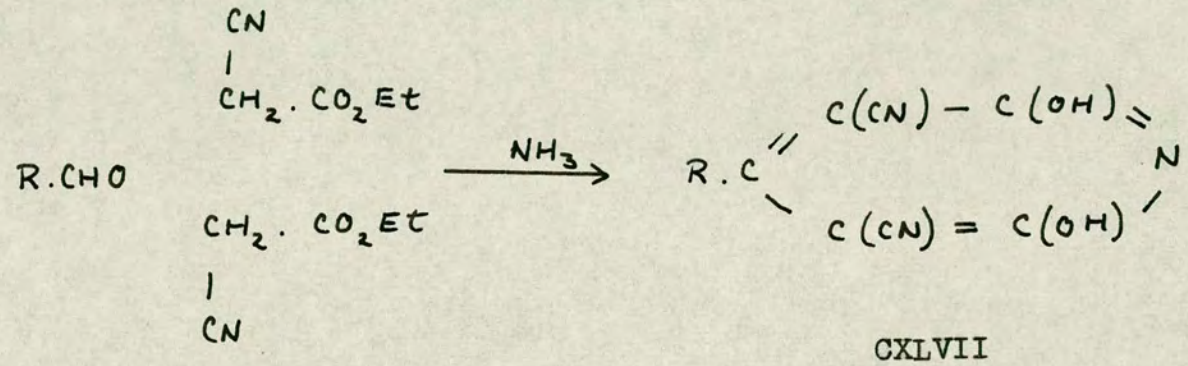


CXLV CXLVI

Since previous attempts by himself and other workers to form four membered rings from open chain compounds had been discouraging, Kerr thought that if an easily ruptured six membered ring were first formed then the spacial configuration of the atoms might be more prone to the formation of four membered rings. It is interesting to note that in spite of the number of ways in which sodium derivatives of the imide might react with methylene iodide, cyclobutane ring formation took preference.

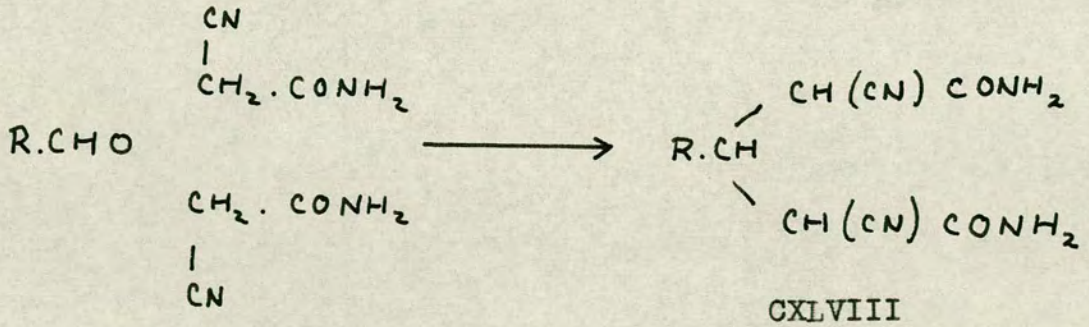
The imide CXLV was prepared by Guareschi (69) by the interaction of 1 mole acetone, 2 moles ethyl cyanoacetate and ammonia and was shown by him to be a general method of preparation of β ,β - disubstituted glutaric imides. However, Guareschi also showed

that by this method, aldehydes gave stable pyridine derivatives CXLVII which could not be hydrolysed to the nitrogen free acid.



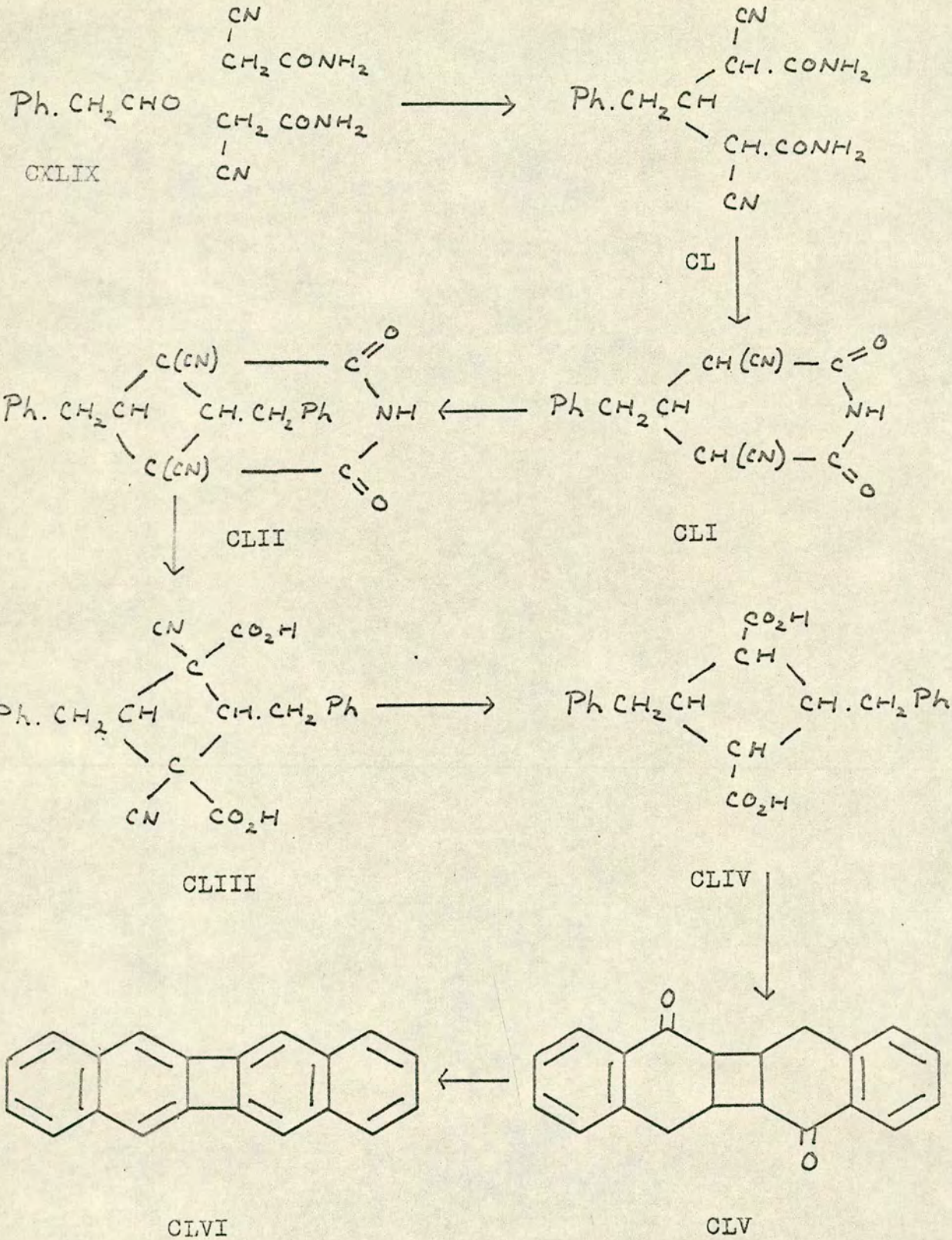
CXLVII

but Day and Thorpe (70) showed that aliphatic aldehydes condensed smoothly in the presence of a trace of alkali hydroxide with 2 moles of cyanoacetamide to give yields of 90% or more of open chain cyanoacetamides CXLVIII



CXLVIII

SCHEME M


Ph.CH2CHO
CXLIX
CN
CH2CONH2
CH2CONH2
CN
CN
CH.CONH2
Ph.CH2CH
CH.CONH2
CN
CL
CH(CN)—C=O
Ph CH2CH
NH
CH(CN)—C=O
C(CN)—C=O
Ph.CH2CH
CH.CH2Ph
NH
C(CN)—C=O
CLII
CLI
CN
CO2H
C
Ph.CH2CH
CH.CH2Ph
C
CN
CO2H
CO2H
CH
Ph CH2CH
CH.CH2Ph
CH
CO2H
CLIII
CLIV
O
O
CLVI
CLV

It was thought that if phenylacetaldehyde CXLIX could be made to react with two moles of cyanoacetamide under the conditions used by Day and Thorpe (70), then the cyanoacetamide CL would be formed. Formation of the cyclic imide CLI from this followed by the reaction of its sodium derivative with 2, 2 - diiodo - 1- phenylethane would give the bicyclic imide CLII with a cyclobutane ring. Hydrolysis of the imide CLII would give the dibasic acid CLIII and hydrolysis of the nitrile groups followed by decarboxylation would give the dibasic acid CLIV which could be cyclised to give the ketone CLV. Aromatisation of the ketone would then give dibenzo [b, h] biphenylene.

A reaction of phenylacetaldehyde with two moles of cyanoacetamide following the method of Day and Thorpe (70) gave a very small yield of a solid product with two nitrile peaks in its infrared spectrum. As this was obviously not the required product, a further condensation of phenylacetaldehyde with two moles of cyanoacetic ester was attempted, following the method of Gutzheit and Jahn (71) in which diethylamine was the condensing agent. The product obtained was an oil which, when the ester groups were hydrolysed, gave a further uncrystallisable oil whose infrared spectrum was substantially different from that of an authentic sample of β -benzyl - α , α' -dicyanoglutaric acid prepared by the method of Haworth et al (72) .

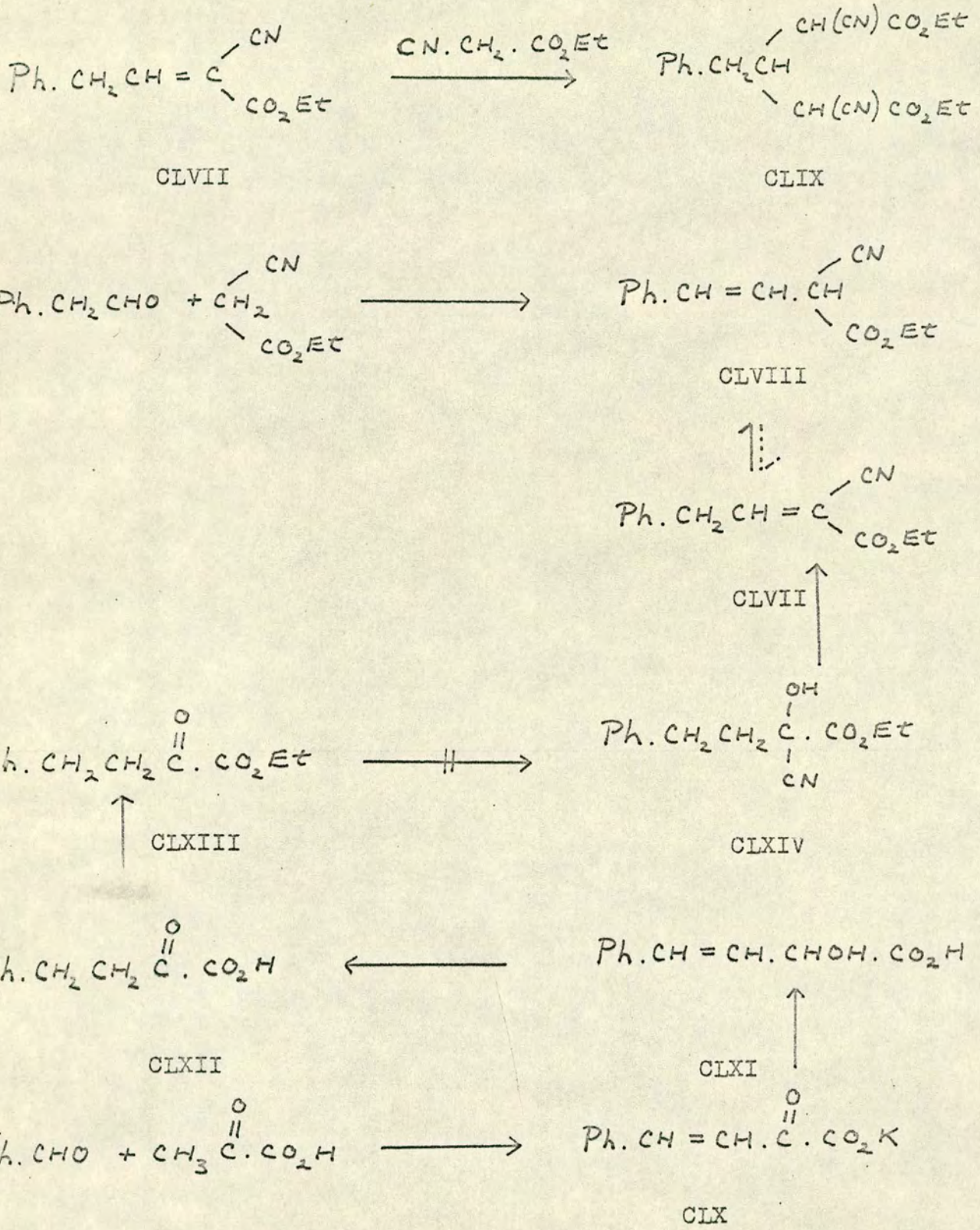
This method of Haworth et al. (72) however, gives the required β-benzyl - α , α' -dicyanoglutaric acid only as a by product, and is valueless in the fairly large scale synthesis required at this stage.

It thus appears that in the two condensations carried out, the competing reactions, largely bimolecular condensations, predominated and that if the desired reaction of the aldehyde with two moles of nitrile occurred, it did so to only a very small extent.

The diethyl ester of α , α' -dicyano -β- benzylglutaric acid CLIX could also be formed by Michael addition of cyano acetic ester to ethyl 1-cyano -3- phenyl but -1- enoate CLVII as shown in Scheme N. The preparation of CLVII is not reported in the literature, a synthesis by Haworth et al. (72) in which phenylacetaldehyde was condensed with an equivalent of cyanoacetic ester in basic conditions, giving, instead of CLVII, the tautomeric ethyl 1-cyano -3- phenyl but -3- enoate CLVIII which is presumably the thermodynamically more stable tautomer.

It was hoped that by carrying out this reaction in an acidic medium cf. Hauser (73) that the equilibrium mixture of the tautomers might contain more of the form CLVII but the product obtained had an ultraviolet spectrum with an absorption maximum at 215 mμ. characteristic of a styrene group and also on ozonolysis it gave benzaldehyde, characterised by its D.N.P. derivative with no trace of phenylacetaldehyde.

SCHEME N


Ph.CH2CH=C(CN)CO2Et
CN.CH2.CO2Et
Ph.CH2CH(CH(CN)CO2Et)CH(CN)CO2Et
CLVII
CLIX
Ph.CH2CHO + CH2(CN)CO2Et
Ph.CH=CH.CH(CN)CO2Et
CLVIII
Ph.CH2CH=C(CN)CO2Et
CLVII
Ph.CH2CH2C(OH)(CN)CO2Et
Ph.CH2CH2C(=O).CO2Et
CLXIII
CLXIV
Ph.CH2CH2C(=O).CO2H
Ph.CH=CH.CHOH.CO2H
CLXII
CLXI
Ph.CHO + CH3C(=O).CO2H
Ph.CH=CH.C(=O).CO2K
CLX

A final attempt to form ethyl 1 - cyano -3- phenyl but- -1- enoate CLVII by dehydration of ethyl 1-cyano -2- benzyllactate CLXIV failed when it was found that the cyanohydrin could not be formed from ethyl benzylpyruvate CLXIII by the method of Ültée (74) who formed the cyanohydrins of ethyl pyruvate and cyclohexanone. However, when the experiments described by Ültée were repeated on these two compounds, only the latter formed a cyanohydrin.

The ethyl benzylpyruvate CLXIII was formed by esterification of benzylpyruvic acid prepared as shown in Scheme N by the route of Bougault and Cordier (75). Benzaldehyde condensed with pyruvic acid to give the potassium salt of benzylidene pyruvic acid CLX which on reduction with potassium borohydride gave 2-benzallactic acid CLXI. Rearrangement of this acid in dilute alkali gave benzylpyruvic acid CLXII.

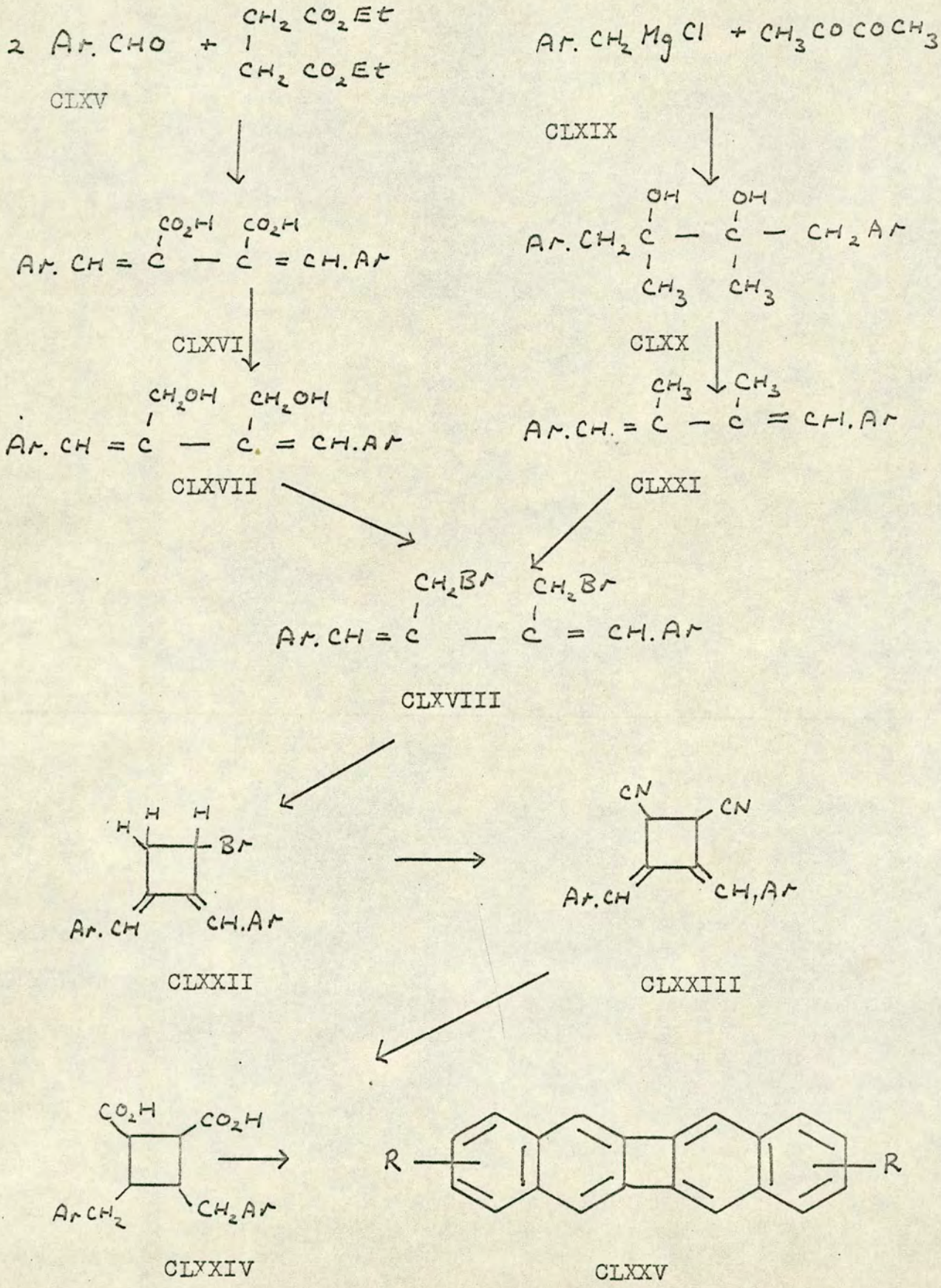
The equilibrium between CLVII and CLVIII is probably such that the β , γ - isomeride is the exclusive form since the researches of Kon and Linstead (76) indicate that the equilibrium between the α,β and β,γ -unsaturated forms of a three carbon system is not particularly sensitive to the nature of the activating group, in this case the ester and nitrile groups combined, but is highly sensitive to substitution, the γ phenyl group shifting the balanced reaction towards the side of the β,γ -unsaturated isomer, till it becomes the exclusive form in equilibrium.

SECTION III

PART II

ATTEMPTED SYNTHESIS OF CYCLOBUTANE DERIVATIVES.

SCHEME O


2 Ar.CHO + CH2CO2Et / CH2CO2Et
CLXV
Ar.CH2MgCl + CH3COCOCH3
CLXIX
CO2H CO2H
Ar.CH = C — C = CH.Ar
CLXVI
CH2OH CH2OH
Ar.CH = C — C = CH.Ar
CLXVII
OH OH
Ar.CH2 C — C — CH2Ar
CH3 CH3
CLXX
CH3 CH3
Ar.CH = C — C = CH.Ar
CLXXI
CH2Br CH2Br
Ar.CH = C — C = CH.Ar
CLXVIII
H H H Br
Ar.CH CH.Ar
CLXXII
CN CN
Ar.CH CH.Ar
CLXXIII
CO2H CO2H
ArCH2 CH2Ar
CLXXIV
R R
CLXXV

It was thought that if compounds such as CLXVIII in Scheme O could be synthesised, then they might bedehydrobrominated in such a way as to yield a compound containing a cyclobutane ring CLXXII. Further bromination with N - bromosuccinimide would then yield the dibromo-compound which after conversion to the dinitrile CLXXIII could be hydrolysed to the dibasic acid which on reduction of the two double bonds would give the acid CLXXIV. Cyclisation of the acid to give a diketone followed by aromatisation would then give the substituted dibenzobiphenylenes CLXXV.

However, none of several approaches tried, led to the formation of the compound CLXVIII, the precursor for the dehydrobromination stage.

The first approach was by a synthesis carried out by Freudenberg et al. (77) in which two moles of 3, 4-methylenedioxy benzaldehyde CLXV (Ar = 3, 4-methylenedioxyphenyl) were condensed with one mole of diethyl succinate to give 1, 4 - (3, 4-methylenedioxyphenyl) buta -1, 3 - diene - 2, 3 - dicarboxylic acid CLXVI. Esterification with diazomethane followed by reduction of the ester groups with lithium aluminium hydride gave the diol CLXVII. However, in our hands, the overall yield for these three stages was ca. 2% and in view of the number of stages that would have to follow, it was decided that this was not a practicable route.

The second approach was the attempted addition of two moles of Grignard reagent from 3, 4-methylenedioxy - benzyl chloride CLXIX (Ar = 3, 4-methylenedioxyphenyl) and 4-methoxybenzyl chloride CLXIX (Ar = 4 -methoxyphenyl) with one mole of diacetyl to give the corresponding diol CLXX. However this reaction gave in both cases only the product of dimerisation of the aralkyl groups although a similar reaction carried out using benzyl magnesium chloride CLXIX (Ar = phenyl) and diacetyl gave the corresponding diol CLXX (Ar = phenyl) which dehydrated in an acetyl chloride/acetic anhydride mixture to give 1, 4 - diphenyl -2, 3 - dimethylbuta - 1, 3 - diene as reported by Langer and Wessely (78).

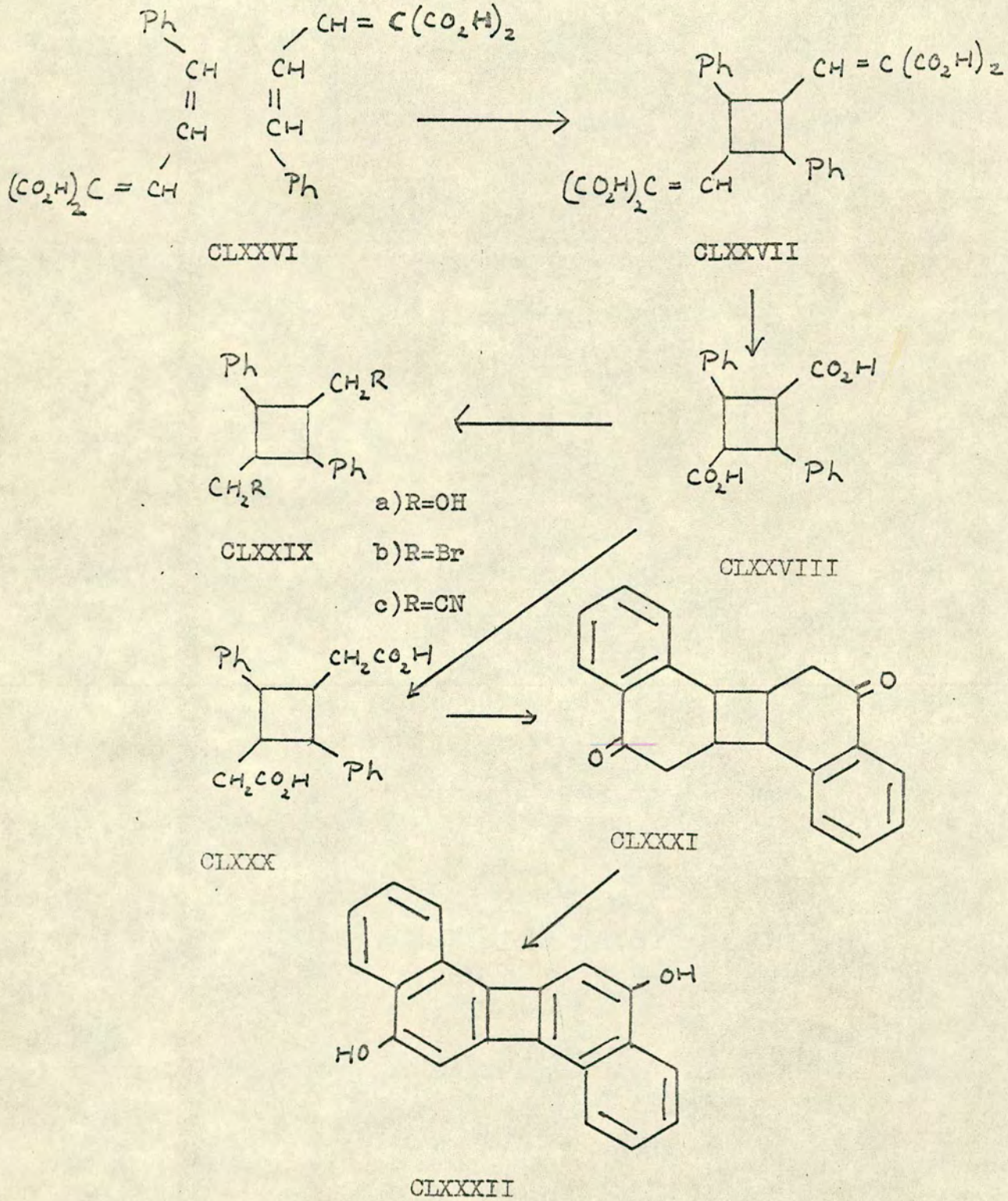
Although arylated methyl halides commonly yield products in Grignard reactions attributable to dimerisation of the free radical derived from the organic halide, it seems strange that the benzyl magnesium halide should react with the diacetyl to give the required product whereas the 4 - methoxybenzyl and the 3, 4 - methylenedioxybenzyl magnesium halides gave dimers since there is little difference in stability between the benzyl, 4-methoxybenzyl and the 3, 4 - methylenedioxybenzyl radicals.

SECTION III

PART III

ATTEMPTED SYNTHESIS OF 5, 11-DIHYDROXYDIBENZO [a, g] BIPHENYLENE FROM α -TRUXILLIC ACID.

SCHEME P


Ph
CH = C(CO2H)2
CH
CH
CH
CH
(CO2H)2C = CH
Ph
CLXXVI
Ph
CH = C(CO2H)2
(CO2H)2C = CH
Ph
CLXXVII
Ph
CO2H
CO2H
Ph
CLXXVIII
Ph
CH2R
CH2R
Ph
a)R=OH
b)R=Br
c)R=CN
CLXXIX
Ph
CH2CO2H
CH2CO2H
Ph
CLXXX
O
O
CLXXXI
OH
HO
CLXXXII

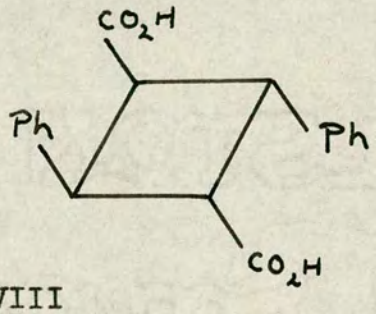
In this synthesis, the cyclobutane ring was formed by the photodimerisation of CINNAMylidene malonic acid CLXXVI as shown in Scheme F following the method of preparation of α -truxillic acid CLXXVIII of Criegee et al. (79).

Ozonolysis of the dimer CLXXVII of CINNAMylidene malonic acid followed by oxidation of the resulting di-aldehyde with hydrogen peroxide gave α -truxillic acid, 1, 3 - diphenylcyclobutane - 2, 4 - dicarboxylic acid CLXXVIII.

It was hoped that the higher homologous diacid, 1, 3 - diphenylcyclobutane -2, 4 - diacetic acid CLXXX might be formed by the common route to higher homologous acids ie. acid CLXXVIII → ester → alcohol CLXXIXa → bromide CLXXIXb → nitrile CLXXIXc → homologous acid CLXXX. However, this procedure failed when it was found that attempted bromination of the diol CLXXIXa with phosphorus tribromide gave a phosphorus containing compound, probably the diphosphate ester of the diol. A further attempted bromination in boiling hydrobromic acid gave a viscous oil which afforded a nitrile on reaction with potassium cyanide. This nitrile could not be chromatographed on alumina and did not yield an acid on hydrolysis. It seems likely that the bromination in hydrobromic acid has led to rupture of the cyclobutane ring since such rings are susceptible to ring opening in strong acid. cf. Kerr (68), Jones (87).

The diacetic acid CLXXX was eventually arrived at by an Arndt-Eistert synthesis with the α-truxillic acid CLXXVIII.

The configuration of α-truxillic acid CLXXVIII is such that one phenyl and one carboxyl group lie on each side of the plane of the four membered ring.



CLXXVIII

Thus, it can be shown on models that intramolecular cyclisation of the diacetic acid CLXXX to give the diketone CLXXXI should occur readily to give a not particularly highly strained ring closed product.

When this cyclisation step was carried out in hydrofluoric acid a ketone was obtained whose analysis agreed with that required for the diketone CLXXXI. Dibromination of this diketone with N- bromosuccinimide gave an oil which is presumably the diketone brominated in the two α positions to the keto groups. It was hoped that dehydrobromination of this product in basic conditions would give a product which would isomerise to give the dihydricphenol CLXXXII. However attempts at dehydrobromination and aromatisation with ethanolic pyridine and potassium acetate failed to give any

phenolic products. It seems probable that the dibenzobiphenylene nucleus can be formed from the diketone, either by this method providing a suitable base can be found, or by reduction of the diketone and dehydrogenation.

There was, unfortunately, no more time for experimenting.

EXPERIMENTAL

INTRODUCTION TO EXPERIMENTAL SECTION

1. Melting points were determined on a Kofler micromelting - point apparatus with a calibrated thermometer, and fitted with a polariser.

2. Infrared (I.R.) spectra were recorded on a Unicam S.P.200 Spectrophotometer. The intensity of absorption maxima are indicated by strong (s), medium (m) and weak (w). The group corresponding to the particular absorption maximum is written after the absorption wave number.

3. Ultraviolet (U.V.) spectra were obtained on a Perkin-Elmer 137 U.V. Spectrophotometer. Spectroscopic ethanol was used as solvent unless otherwise stated.

4. Nuclear magnetic resonance (N.M.R.) spectra were recorded on a Perkin Elmer R 10 (60 m/c) instrument. In the N.M.R. data given, the numbers of protons assigned to particular signals, were the integral ratios for that spectrum.

5. Alumina was of Type -H as supplied by Peter Spence and Son, Widnes.

6. Analyses were carried out by Drs. Weiler and Strauss, Oxford; or A. H. Baird Ltd., Edinburgh.

EXPERIMENTAL SECTION I

PART I

ATTEMPTED PREPARATION OF 7-PHENYLBICYCLO [4.2.0] OCTA -1, 3, 5 - TRIENE -8- CARBOXYLIC ACID (LVIII) AND RESULTING FORMATION OF 1-PHENYLISOCHROMAN -3- ONE (LVI)

PREPARATION OF 2-BENZYLBENZOIC ACID (L)

Barnett, Cook, and Nixon, J., 1927, 508.

The reduction of 2- benzoylbenzoic acid (XLIX) with zinc in aqueous ammonia gave an 80% yield of 2-benzylbenzoic acid (L).

m.p. 117 -118°. Lit. m.p. 118°

PREPARATION OF 2- BENZYLBENZYL ALCOHOL (LIa)

Barnett, Cook, and Nixon, J., 1927, 508.

Reduction with lithium aluminium hydride of the ethyl ester of o-benzylbenzoic acid gave a 90% yield of the alcohol. This compound has hitherto been characterised by its boiling point in the literature, no melting point being recorded but it was obtained as colourless prisms from 40/60° petrol-ether.

m.p. 40°.

ANALYSIS : calc. for $C_{14}H_{14}O$. C: 84.9% H: 7.1%

found. C:85.2% H: 7.2%

PREPARATION OF 2-BENZYLBENZYL BROMIDE (LIb)

Barnett, Cook, and Nixon, J., 1927, 508.

Reaction of the alcohol (LIa) with 48% aqueous hydrobromic acid gave a 95% yield of the bromide.

m.p. 44-45°. Lit. m.p. 45 - 45.5°.

PREPARATION OF 2-BENZYLBENZYL CYANIDE (LIc)

Barnett, Cook and Nixon, J., 1927, 508.

Reaction of the bromide (LIb) with potassium cyanide in aqueous ethanol gave the nitrile as an oil in 95% yield.

2-BENZYL-α-TOLUIC ACID.

Barnett, Cook, and Nixon, J., 1927, 508.

Hydrolysis of the nitrile in a 1/1/1 mixture of acetic acid, water and conc. sulphuric acid gave the acid in 90% yield.

m.p. 94-95°. Lit. m.p. 95 - 95.5°.

CLAISEN CONDENSATION OF THE ETHYL ESTER OF 2-BENZYL - α -TOLUIC ACID WITH DIETHYL OXALATE.

The ester (LId) of 2-benzyl-α-toluic acid was prepared by refluxing a solution of the acid in absolute ethanol containing 3% sulphuric acid for four hours.

b.p. 150 - 160°. / 0.7mm.

0.91 g. (0.04m.) sodium was added to 20ml. dry ethanol in a flat bottomed 100 ml. flask equipped with stirrer and reflux condenser. When all the sodium had reacted, the temperature of the solution was adjusted to 60° and then 5.8g. (0.04m.) oxalic ester was run in followed by 10g. (0.04m.) of ethyl 2-benzyl-α - toluate (LId). The solution was then heated to its boiling point and allowed to cool. A precipitate of the sodium salt of the keto-ester formed and was filtered off and washed well with ether. The salt was then added to dilute sulphuric acid to liberate the keto-ester (LII) which was extracted with ether and after drying of the ether layer and removal of the ether, an oil was obtained which solidified on

standing and was recrystallised from methanol.

Yield. 10g. (71.5%) m.p. 53°.

ANALYSIS : $C_{21}H_{22}O_5$ requs. C: 71.2% H: 6.2%

found. C: 69.4% H: 5.8%

I. R. SPECTRUM. 1650 $cm.^{-1}$ (s) (ketonic carbonyl abs.)

1740 $cm.^{-1}$ (s) (ester carbonyl abs.)

2-BENZYLPHENYL DIETHYL MALONATE (LIII)

The keto-ester (LII) was heated at 170 - 180° for 1 hour in an admixture with powdered glass while carbon monoxide was evolved. The product was an oil which solidified on standing and was recrystallised from ethanol.

m.p. 71°.

Yield. 96%

ANALYSIS. $C_{20}H_{22}O_4$ requs. C: 73.7% H: 6.75%

C: 74.4% H: 7.1%

I. R. SPECTRUM. 1740 $cm.^{-1}$ (s) (C = O doublet)

2- (α-BROMOBENZYL) -PHENYL DIETHYLMALONATE (LIV)

2- benzylphenyl diethyl malonate (LIII) was refluxed in dry carbon tetrachloride with a molar equivalent of N-bromosuccinimide and 10mg. dibenzoyl peroxide for 45 minutes. On cooling, the succinimide was filtered off and the solvent was removed to give an oil.

Yield. quantitative.

The position of bromination in this compound was determined by the use of N.M.R. spectra in carbon bisulphide solution. 2-Benzylphenyl

diethyl malonate (LIII) has a singlet at 5.3τ corresponding to - CH$<$ (1 proton) of the malonate group and another singlet at 6.0 τ (2 protons) corresponding to the $-CH_2-$ of the benzyl group.

The product (LIV) of the above reaction has a singlet at 5.13τ (1 proton) corresponding to the -CH$<$ of the malonate group and a singlet at 3.53τ (1 proton) corresponding to the -CHBr - in the benzyl group.

INTRAMOLECULAR MALONIC ESTER SYNTHESIS OF 2- (α-BROMOBENZYL) PHENYL DIETHYL MALONATE (LIV)

The 2 - (α- bromobenzyl)phenyl diethyl malonate (LIV) prepared from 10g. 2-benzylphenyl diethyl malonate (0.31m.) (LIII) was added dropwise with shaking to a solution of 0.72g. sodium (0.031m.) in 100ml. dry ethanol.

The solution was refluxed for three hours during which the formation of a precipitate of sodium bromide was observed. The crude product isolated from the reaction was hydrolysed in a solution of 20g. sodium hydroxide in 200 ml. of a 1/1 mixture of ethanol and water for 12 hrs. After dilution of this mixture with water and ether extraction, the ether extract was washed with sodium carbonate solution. Acidification of the sodium carbonate layer with dilute hydrochloric acid gave an oil which solidified on standing or triturating with benzene. This product proved to be uncrystallisable from the more common solvents and melted at ca. 160°.

Heating it at 200°C. for 1 hour resulted in the evolution of carbon dioxide with the formation of an acid (0.5g.) whose m.p. and mixed m.p. was 94° with a sample of 2-benzyl -α-toluic acid. This product, m.p. ca. 160°, presumably results from unchanged starting material in the bromination stage.

The sodium carbonate washed ether layer on drying and removal of the ether gave an oil which solidified on standing. It recrystallised from ether.

m.p. 83°.

Yield. 5.7g. (82%)

ANALYSIS: $C_{15}H_{12}O_2$ requs. C: 80.5% H:5.35% M.W. 224

found. C: 81.1% H:5.35% M.W. 218

I. R. SPECTRUM. 1700 cm.$^{-1}$ (C = O abs. of δ-lactone)

N. M. R. SPECTRUM. 2.60 - 3.30 τ (multiplet, 9 aromatic protons.)

(CS_2 soln.) 3.76 τ (singlet, 1 alicyclic proton.)

6.47 τ (split singlet, 2 alicyclic protons.)

From the above information it was deduced that the compound m.p. 83° was 1-phenylisochroman -3- one (LVI).

Hydrolysis of the product of the malonic ester synthesis with 48% hydrobromic acid gave similar experimental results to the basic hydrolysis followed by monodecarboxylation.

REDUCTION OF 1-PHENYLISOCHROMAN -3- ONE TO 2- PHENYL -2- (2-HYDROXYMETHYL PHENYL) ETHANOL - (LXII)

The 1-phenyl isochroman -3-one 1.5g.- (0.067m.) was dissolved in 10ml. dry ether and added dropwise to a mixture of 0.14g. (0.037m.) lithium aluminium hydride in 10 ml. dry ether. After the addition, stirring was continued for 1 hour and then the excess lithium aluminium hydride was decomposed with 10% aqueous sulphuric acid. The product was isolated in the usual way as an oil which solidified on trituration with benzene to give white solid.

m.p. 97°.

Yield . 1.45g. (95%)

ANALYSIS : $C_{15}H_{16}O_2$ requs. C:78.9% H:7.0%

found. C:78.35% H:7.0%

I. R. SPECTRUM 3380 cm.$^{-1}$ (-OH)

N.M.R. SPECTRUM (CDCl$_3$ soln.) 2.60 - 2.87 τ (complex, 9 aromatic protons)

4.04 τ (singlet, 1 aliphatic proton)

6.32 τ, J = 6c.p.s. (triplet, 2 aliphatic protons)

7.20 τ, J = 6c.p.s. (triplet (split), 2 aliphatic protons)

PREPARATION OF 1-PHENYLISOCHROMAN (LXIII)

1g. of the diol (LXII) prepared in the previous experiment was dissolved in 25 ml. acetic acid and 1 ml. conc. sulphuric acid was added dropwise with stirring at room temperature. Stirring was continued for 10 minutes and then ice was added. A white solid separated out and was recrystallised from 40/60° petrol-ether.

m.p. 90. 5°. Lit. m.p. 89° (39)

Yield. 0.8g. (87%)

ANALYSIS: calc. for $C_{15}H_{14}O$. C:85.7% H:6.7%

found. C:85.6% H:6.8%

N.M.R. SPECTRUM 2.80 - 3.50 τ (complex, 9 aromatic protons)

4.60 τ (singlet, 1 aliphatic proton)

5.82 - 6.52 τ (complex, 2 alicyclic protons)

7.00 - 7.60 τ (complex, 2 alicyclic protons)

1- BROMOISOCHROMAN (LXV)

Rieche and Schmitz, Ber., 89, 1254. (1956).

Bromination of isochroman (LXIV) under the influence of ultraviolet radiation in benzene gave a quantitative yield of the bromocompound.

1- PHENYLISOCHROMAN (LXIII)

Rieche and Schmitz, Ber, 89, 1254. (1956).

A coupling reaction of 1-bromoisochroman (LXV) with the Grignard reagent, phenylmagnesium bromide, gave the 1-phenylisochroman.

m.p. 90°. Lit. m.p. 89°.

Yield. 20%.

EXPERIMENTAL SECTION I

PART II

FORMATION OF 7, 8-DISUBSTITUTED BICYCLO [4.2.0] OCTA -1, 3, 5-TRIENES BY ELIMINATION-ADDITION REACTIONS INVOLVING ARYNE INTERMEDIATES.

2-CHLOROCINNAMIC ACID (LXXX)

Pandya and Pandya J. Chem. Ed., 28, 46. (1951).

2-chlorobenzaldehyde (LXXIX) 13.5g. (0.096m.) was mixed with 10g. (0.096m.) malonic acid and 1.3 ml. freshly distilled pyridine. This mixture was heated on a water bath for 4 hours. The resulting solid was dissolved in hot aqueous sodium hydroxide solution and the o-chlorocinnamic acid was obtained on acidification with conc. hydrochloric acid and was recrystallised from ethanol.

m.p. 210°. Lit. m.p. 211°.

Yield. 14.7g. (84%)

2-CHLOROCINNAMIC ACID AMIDE (LXXXI)

2-chlorocinnamic acid (LXXX) was heated for 1 hour on a water bath with excess thionyl chloride and then the excess thionyl chloride was distilled off under reduced pressure. The residual oil was dissolved in dry benzene and conc. ammonia was added dropwise with stirring. The required amide separated out of solution and was recrystallised from aqueous ethanol.

m.p. 166°. Lit. m.p. 168°. (80).

Yield. 90%.

2-CHLOROHYDROCINNAMIC ACID AMIDE 3-(2-chlorophenyl)-propionamide (LXXXII)

Reduction of 2-chlorocinnamic acid amide (LXXXI) over platinum in ethanol gave the required amide.

m.p. 119°. Lit. m.p. 119°. (80).

Yield. 95%.

3-(2-CHLOROPHENYL) PROPIONITRILE (LXXXIII).

3-(2-Chlorophenyl) propionamide (LXXXII) was refluxed with excess thionyl chloride for 90 minutes and the excess was evaporated off under reduced pressure. The residual oil was taken up in ether and the ethereal solution was washed successively with water, dilute sodium hydroxide solution, and water, before drying over anhydrous sodium sulphate. On removal of the ether, the nitrile was obtained as an oil which was purified by chromatography on alumina with a 1/1 mixture of benzene and 60/80° petrol-ether. Yield. 80%.

I. R. SPECTRUM 2250 $cm.^{-1}$ (m) (CN).

7 - CYANOBICYCLO [4.2.0] OCTA -1, 3, 5 -TRIENE (LXXXIV)

Bunnett and Skorcz, J. Org. Chem., 27, 3836. (1962).

The experimental procedure described by these authors gave a 50% yield of the nitrile.

I. R. SPECTRUM 2240 $cm.^{-1}$ (m) (CN), 1000$cm.^{-1}$ (w) (cyclobutene CH).

BICYCLO [4.2.0] OCTA -1, 3, 5 - TRIENE - 7 - CARBOXAMIDE (LXXXV)

0.5g. of 7-cyanobicyclo [4.2.0] octa -1, 3, 5 - triene (LXXXIV) was hydrolysed in 10 ml. of a 3/1 mixture of 10% hydrogen peroxide and 6N. sodium hydroxide solution. Enough ethanol was added to dissolve the nitrile and the solution was heated at 55° for 3 hours. On neutralisation of the solution with hydrochloric acid, and removal of most of the ethanol, an oil was obtained which was extracted

into ether. The ether extract was washed with aqueous sodium carbonate solution before drying over anhydrous sodium sulphate. On removal of the ether, a solid was obtained which was recrystallised from chloroform/40-60°-petrol-ether.

m.p. 155°. Lit. m.p. 155°. (40).

Yield. 0.44g. (78%).

ANALYSIS: calc. for C_9H_8NO N: 9.5%

found. N: 9.3%

I. R. SPECTRUM 1630cm.$^{-1}$ (s) (C = O), 3400cm.$^{-1}$ (m) (NH_2 doublet).

ATTEMPTED REFORMATSKII REACTION WITH HALOGENOBENZOPHENONES (LXVII)

The following compounds o-bromobenzophenone, o-chlorobenzophenone, and p- bromobenzophenone were added to the product of the reaction of 2 molar equivalents of bromocacetic ester and zinc in a mixture of anhydrous benzene and toluene but only starting materials were isolated after refluxing for 1 hour and working up in the usual way.

REACTION OF THE LITHIUM COMPOUND OF PHENYL-2-CHLOROPHENYL BROMOMETHANE (LXXVI) AND CHLOROACETIC ACID.

A solution of 0.0358m. phenyl lithium in dry ether was prepared under nitrogen and then added dropwise with stirring to a solution of 10g. (0.0358m.)bromo compound (LXXI). The solution turned brown and refluxed gently. On completion of the addition, a solution of 3.5g. (0.037m.) chloroacetic acid was added dropwise with stirring. A vigorous reaction ensued with the formation of a white precipitate,

loss of colour and boiling of the solution. The precipitate was filtered off and shown to be largely inorganic. The solution was extracted with a solution of sodium carbonate which on acidification showed no visible precipitate. The ethereal layer was washed with water and dried over anhydrous sodium sulphate. On removal of the ether, an off white solid (8.5g.) was obtained which gave clear prisms m.p. 185°. on recrystallisation from benzene. This product has no carbonyl absorption in its I.R. spectrum and is probably 1, 2 -bis (2-chlorophenyl) -1, 2 - diphenylethane (LXXVII).

Lit. m.p. 179 - 181°. (41).

ANALYSIS: $C_{26}H_{20}Cl_2$ requs. C:77.5% H:5.0% Cl:17.6%

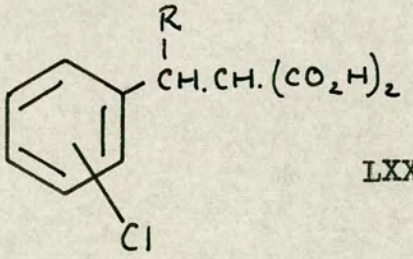
found. C:77.5% H:4.9% Cl:17.6%

PREPARATION OF SUBSTITUTED MALONIC ACIDS (LXXII) (GENERAL METHOD)

Several substituted malonic acids were prepared by the same general method described below.

The substituted bromomethanes (LXXI) were prepared by the reaction of the Grignard reagents RMgX where R = phenyl, benzyl, and methyl with 2 - and 3 - chlorobenzaldehyde (LXIX) to give the corresponding alcohols (LXX) which were converted to the bromomethanes (LXXI) on reaction with excess phosphorus tribromide. 1g. (0.0435m.) Sodium in small pieces was added to 35 ml. dry ethanol and after all the sodium had disappeared and the solution had cooled to 50.°C, 7g. (0.0435m.) ethyl malonate in a little dry ethanol was added with

occasional shaking. To the resulting clear solution was added (0.0435m.) of the substituted bromomethane (LXXI) in a little dry methanol. The solution was then heated for 5 hours on a boiling water bath and then most of the ethanol was distilled off. 100 ml. Water was added and the mixture was extracted with ether. After drying and removal of the ether, an oil was obtained. This was refluxed for 5 hours with 100 ml. 10% sodium hydroxide solution in a 1/1 mixture of water and ethanol. Most of the ethanol was then distilled off and on cooling, the solution was extracted with ether. The basic aqueous layer was then acidified with dilute hydrochloric acid and the dibasic acid was precipitated, often as an oil which solidified on standing. By this method the following substituted malonic acids (LXXII) were synthesised.



LXXII

R = PHENYL AND Cl IN POSN. 2.

m.p. 168 - 170°. (colourless prisms from aqu. ethanol)

Yield. 10.6g. (80%)

ANALYSIS: $C_{16}H_{13}ClO_4$ requs. C: 63.1% H: 4.3% C: 11.7%

found. C: 63.8% H: 4.2% Cl: 11.7%

R = PHENYL, AND Cl IN POSN. 3.

m.p. 152-155°. (water)

Yield. 7.9g. (60%)

ANALYSIS : $C_{16}H_{13}ClO_4$ requs. C: 63.1% H: 4.3% Cl: 11.7%

found. C: 65.0% H: 4.5% Cl: 8.3%

Product is probably hydrated.

R = BENZYL, AND Cl IN POSN. 2.

m.p. 172°. (water)

Yield 6.9g. (50%)

ANALYSIS: $C_{17}H_{15}ClO_4$ requs. C: 60.7% H: 5.1% Cl: 10.6%

found. C: 61.3% H: 5.3% Cl: 10.6%

R = METHYL, AND Cl IN POSN. 2.

m.p. 152°. (water)

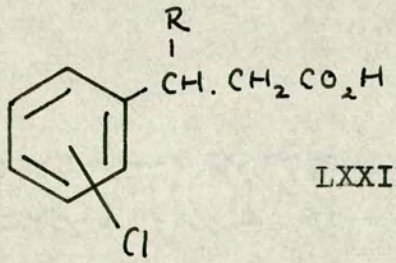
Yield. 6.8g. (64%)

ANALYSIS: $C_{11}H_{10}ClO_4$ requs. C: 54.4% H: 4.5%

found. C: 54.3% H: 4.9%

PREPARATION OF SUBSTITUTED PROPIONIC ACIDS. (LXXIII) (GENERAL METHOD)

The corresponding substituted propionic acids were prepared by the general method now described from the substituted malonic acids (LXXII). The malonic acid was heated at 200° for 1 hour in a metal bath. There was a strong effervescence initially due to the evolution of carbon dioxide but this soon died away. The resulting oil solidified on standing and was recrystallised. In this way the following substituted propionic acids (LXXIII) were prepared:-



LXXIII

R = PHENYL, AND Cl IN POSN. 2.

m.p. 108-111°. (aqu. methanol)

Yield. quantitative.

ANALYSIS : $C_{15}H_{13}ClO_2$ requs. C: 69.1% H: 5.0% Cl: 13.6%

found. C: 69.8% H: 4.9% Cl: 13.35%

R = PHENYL, AND Cl IN POSN. 3.

m.p. 96°. (60/80° petrol-ether)

Yield. quantitative.

ANALYSIS: $C_{15}H_{13}ClO_2$ requs. C:69.1% H:5.0% Cl:13.6%

found. C:69.8% H:5.0% Cl:13.0%

R = BENZYL, AND Cl IN POSN. 2.

m.p. 85°. (40/60° petrol-ether)

Yield. quantitative.

ANALYSIS: $C_{16}H_{15}ClO_2$ requs. C:69.9% H:5.5% Cl:12.9%

found. C:69.7% H5.9% Cl:13.3%

R = METHYL, AND Cl IN POSN. 2.

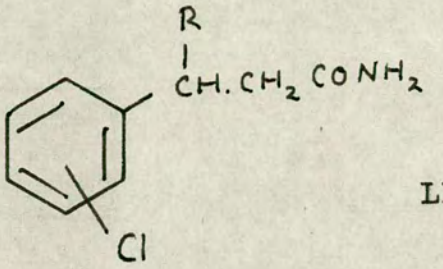
m.p. 60°. Lit. m.p. 60°. (81).

Yield. quantitative.

PREPARATION OF SUBSTITUTED PROPIONAMIDES. (LXXIV) (GENERAL METHOD)

The substituted propionic acid (LXXIII) 1g. was heated on a water bath for ½ hour with excess thionyl chloride and then the excess thionyl chloride was distilled off under reduced pressure. The residual acid chloride was dissolved in twice its volume of dry benzene and concentrated ammonia was added dropwise with shaking of the flask. A vigorous reaction ensued and on standing for ½ hour, a crystalline precipitate separated out from the benzene layer.

In this way the following substituted propionamides (LXXIV) were prepared :-



LXXIV

R = PHENYL, AND Cl IN POSN. 2.

m.p. 121 - 122°. (aqu. ethanol)

Yield. 70%.

ANALYSIS: $C_{15}H_{14}ClNO$ requs. N: 5.5% Cl: 13.7%

found. N: 5.5% Cl: 13.7%

R = PHENYL, AND Cl IN POSN. 3.

Product was an uncrystallisable oil.

Yield. 87%.

ANALYSIS: $C_{15}H_{14}ClNO$ requs. C:69.5% H:5.5% N:5.5% Cl:13.7%

found. C:69.9% H:6.2% N:4.2% Cl:10.3%

R = BENZYL, AND Cl IN POSN. 2.

m.p. 94°. (benzene/petrol-ether)

Yield. 72%.

ANALYSIS: $C_{15}H_{16}ClNO$ requs. C:70.3% H:5.9% N:5.1%

found. C:70.0% H:6.0% N:4.6%

R = METHYL, AND Cl IN POSN. 2.

m.p. 119°. (aqu. methanol).

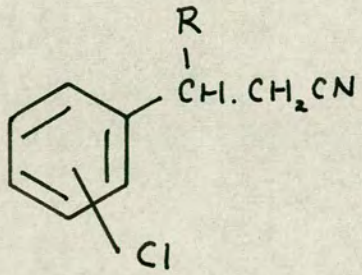
Yield. 85%.

ANALYSIS: $C_{10}H_{12}ClNO$ requs. C:60.8% H:6.1% N:7.1%

found. C:60.8% H:6.4% N:5.9%

PREPARATION OF SUBSTITUTED PROPIONITRILES. (LXXV) (GENERAL METHOD)

The substituted propionamide (LXXIV) was refluxed with excess thionyl chloride for 1.5 hrs. and then the excess thionyl chloride was distilled off under reduced pressure. The product, which in all cases was an oil, was dissolved in a little ether and the ethereal solution was washed successively with water, dilute alkali, and water. After drying the ethereal layer and removal of the ether, the residual oil was chromatographed on alumina with benzene as eluant. In this way the following substituted propionitriles (LXXV) were obtained.



LXXV

R = PHENYL, AND Cl IN POSN. 2.

Yield. 87%.

ANALYSIS: $C_{15}H_{12}ClN$ requs. N:5.8% Cl:14.7%

found. N:5.5% Cl:14.5%

R = PHENYL, AND Cl IN POSN. 3.

Yield. 72%.

ANALYSIS: $C_{15}H_{12}ClN$ requs. C:74.5% H:5.0% Cl:14.7% N:5.8%

found. C:75.3% H:5.8% Cl:9.5% N:1.0%

R = BENZYL, AND Cl IN POSN. 2.

Yield. 84%.

ANALYSIS: $C_{16}H_{14}ClN$ requs. C:75.2% H:5.9% N:5.5%

found. C:75.7% H:5.9% N:6.9%

R = METHYL, AND Cl IN POSN. 2.

Yield. 90%.

ANALYSIS: $C_{10}H_{10}ClN$ requs. C:66.8% H:5.6% N:7.8%

found. C:67.7% H:5.7% N:6.0%

REACTION OF 2-PHENYL -2- (2-CHLOROPHENYL) PROPIONITRILE (LXXVIIIa) WITH POTASSAMIDE IN LIQUID AMMONIA.

The proceedure of Bunnett and Skorcz (40), which was demonstrated above to give an elimination addition reaction with 2- (2-chlorophenyl) propionitrile (LXXXIII) yielding the ring closed product, 7-cyanocyclobuta[4.2.0] octa - 1, 3, 5 - triene, (LXXXIV) was used in this and the subsequent reactions involving potassamide and

liquid ammonia.

The product from the reaction with 2-phenyl -2- (2-chlorophenyl) propionitrile (LXXVIIIa) was a viscous oil which proved uncrystallisable from the commoner solvents.

Yield. 1.7g.

ANALYSIS: found. C:85.4% H:10.4% Cl:3.4% N: NIL

EXPERIMENTS CARRIED OUT ON THE PRODUCT OF THE PRECEEDING REACTION.

1) NITRATION

0.2g. of the product was refluxed in a 1/1 mixture (5 ml.) of concentrated nitric acid and acetic acid for 15 minutes. On cooling and dilution by addition to 20 ml. water, an oil was obtained after the usual procedure of ether extraction etc.

Yield. 0.1g.

I.R. SPECTRUM

1540cm.$^{-1}$ (s), 1355cm.$^{-1}$ (s) - (NO_2).

2) ATTEMPTED OXIDATION

Oxidation with aqueous potassium permanganate gave no isolable acid product.

REACTION OF 2-PHENYL -2- (3-CHLOROPHENYL) PROPIONITRILE (LXXVIIIb) WITH POTASSAMIDE IN LIQUID AMMONIA.

The product chromatographed as a single band on alumina with benzene as eluant.

Yield. 1.8g.

I. R. SPECTRUM. 2190cm.$^{-1}$(m), 2220cm.$^{-1}$(m) (CN), 3400cm.$^{-1}$(w) (NH_2 doublet), 1000cm.$^{-1}$ (m)

ANALYSIS: found C:75.8% H:6.0% N:18.1%

EXPERIMENTS CARRIED OUT ON THE PRODUCT OF THE PRECEDING REACTION

1) HYDROLYSIS a) FORMATION OF THE AMIDE

The nitrile product (0.5g.) was added to a solution of 10ml. 10% hydrogen peroxide and 2ml. 6N. sodium hydroxide solution and enough ethanol was added to effect solution. This solution was heated at 55°C. for 3 hours and then the ethanol was evaporated off. The solution was neutralised with dilute hydrochloric acid and extracted with ether. The ether extract was washed with dilute sodium hydroxide solution and with water. After drying of the ethereal layer and removal of the ether, the amide was obtained as a viscous oil.

Yield. 0.41g. (75%)

I. R. SPECTRUM 1700cm.$^{-1}$(s), 1760cm.$^{-1}$(m), 1680cm.$^{-1}$(s) (C =O), 3400cm.$^{-1}$(m) ($-NH_2$).

b) FORMATION OF THE ACID

The amide 0.2g. was shaken with 1g. concentrated sulphuric acid and gently heated until it dissolved. The solution was then cooled with iced water and 0.2g. sodium nitrite in 1 ml. water was added very slowly. The solution was then gently warmed until the evolution of nitrogen ceased. The solution was then diluted with iced water, extracted with ether and then the ether extract washed

with dilute alkali. The alkaline extract was acidified with dilute hydrochloric acid. The acid was obtained as a very viscous oil.

Yield. 1.75g. (81%)

I. R. SPECTRUM 1660 $cm.^{-1}$(s) (acid C = O).

c) ATTEMPTED INTRAMOLECULAR CYCLISATION OF THE ACID FROM THE PREVIOUS REACTION.

The acid was allowed to stand overnight in excess hydrogen fluoride and then the hydrogen fluoride was allowed to evaporate off but only unchanged starting material was obtained.

2) OXIDATION

An attempt to oxidise the nitrile in aqueous potassium permanganate gave no acid product.

3) ATTEMPTED FORMATION OF AN IMINO ETHER

An attempt to form the imino ether of the nitrile by the method of Hager et al. (43) failed when no precipitate formed on bubbling through the dry hydrogen chloride and allowing to stand.

REACTION OF 2- (2-CHLOROPHENYL) - 3 - PHENYLBUTYRONITRILE (LXXVIIIe) WITH POTASSAMIDE IN LIQUID AMMONIA.

The product was an oil which chromatographed as a single band on alumina on elution with benzene.

Yield. 2.1g.

I. R. SPECTRUM. 2580 cm.$^{-1}$(m) (CN), 1008cm.$^{-1}$ (cyclobutene CH)
699 cm.$^{-1}$, 708 cm.$^{-1}$, 770 cm.$^{-1}$(s) (aromatic CH)

FORMATION OF 7-BENZYLBICYCLO [4.2.0] OCTA -1, 3, 5 - TRIENE - 8-CARBOXAMIDE (LXXXIII) AND 7-BENZYLBICYCLO [4.2.0] OCTA -1, 3, 5 - TRIENE - 8 - CARBOXYLIC ACID (LXXXIV)

The nitrile (LXXXII) (0.5g.) was added to a solution of 10 ml. 10% hydrogen peroxide and 2 ml. 6N. sodium hydroxide and enough ethanol was added to effect solution. The mixture was heated at 50-55°C. with stirring for 3 hours and then most of the ethanol was distilled off. The solution was neutralised with dilute hydrochloric acid and was then extracted with ether. The ethereal solution was extracted with dilute alkali which on acidification gave an oil which solidified on standing and was recrystallised from aqueous ethanol.

m.p. 142 - 144°.

Yield. 0.18g. (34%)

I. R. SPECTRUM.

1700 cm.$^{-1}$ (s) (C = O), 1000 cm.$^{-1}$ (w) (cyclobutene - CH),
700 cm.$^{-1}$ 750 cm.$^{-1}$ (s) (aromatic CH).

The ethereal layer was washed with water, dried and then the ether was distilled off to leave an oil which solidified on standing to give the amide.

m.p. 107-108°. (benzene/petrol-ether)

Yield. 0.3g. (56%)

ANALYSIS: $C_{16}H_{15}NO$ requs. C:81.0% H:6.3% N:5.9%

found. C:81.1% H6.3% N:5.7%

I. R. SPECTRUM 1650cm.$^{-1}$(s) (C = O), 3300cm.$^{-1}$(m) (NH_2 doublet), 1000cm.$^{-1}$(w) (cyclobutene CH).

ATTEMPTED INTRAMOLECULAR CYCLISATIONS OF 7-BENZYLBICYCLO [4.2.0] OCTA -1, 3, 5 - TRIENE -8- CARBOXYLIC ACID (LXXIV)

1) IN HYDROGEN FLUORIDE

The acid (LXXIV) (0.5g.) was allowed to stand in hydrogen fluoride solution for 18 hours before the hydrogen fluoride was allowed to evaporate off.

The residue was taken up in ether and the ethereal solution was washed with dilute sodium hydroxide to remove unreacted acid. On drying of the ethereal solution and removal of the ether, an oil (5mg.) was obtained with three carbonyl absorptions in the I.R. spectrum. This oil was chromatographed on alumina with benzene and gave a fluorescent oil (3mg.) which had a strong carbonyl absorption at 1770cm.$^{-1}$ with two other carbonyl absorptions at lower wavenumbers.

The experiment was repeated, allowing the acid to stand in hydrogen fluoride for 72 hours. After working the products up as above, it was found that chromatography on alumina gave two non acidic products. The first product off the column on elution with benzene was a yellow oil (10mg.)

I. R. SPECTRUM 1805 cm.$^{-1}$ (s). (C = O).

The second product off the column was a fluorescent oil (5mg.)

I. R. SPECTRUM 1805cm.$^{-1}$(s), 1720cm.$^{-1}$(s), 1690cm.$^{-1}$(s), (various C = O).

It is obvious that none of these products is the required cyclic ketone but they are probably lactones judging from their I.R. spectra.

2) IN POLYPHOSPHORIC ACID

An attempt to cyclise the acid (LXXXIV) by heating it with polyphosphoric acid at 95° for 2 hours failed to give any non acidic products on working up.

3) WITH ALUMINIUM TRICHLORIDE IN DICHLOROMETHANE.

An attempt was made to cyclise the acid, by refluxing its acid chloride with 1.5 molar equivalents of aluminium trichloride in dichloromethane. After the working up, the non acidic product obtained on chromatography on alumina with benzene was an oil 50mg. (from 0.5g. acid) which again appeared to be a lactone.

I. R. SPECTRUM 1780cm.$^{-1}$(s) (lactone C = O).

REACTION OF 2- (2-CHLOROPHENYL) BUTYRONITRILE (LXXVIIIf) WITH POTASSAMIDE IN LIQUID AMMONIA

The product was an oil which chromatographed as a single band on alumina on elution with benzene.

Yield. 1.83g.

ANALYSIS: $C_{10}H_9H$ requs. C:84.0% H:6.3% N:9.8%

found. C:83.05% H:7.0% N:8.1%

I. R. SPECTRUM. 2580cm.$^{-1}$(m) (CN).

This product is probably 7-methyl -8- cyanobicyclo [4.2.0] octa -1, 3, 5 - triene (LXXXVI).

PREPARATION OF 7-METHYLBICYCLO [4.2.0] OCTA -1, 3, 5 -TRIENE -8- CARBOXYLIC ACID (LXXXVIII)

0.5g. nitrile (LXXXVI) was added to a mixture of 10 ml. 10% hydrogen peroxide solution and 2 ml. 6N. sodium hydroxide solution and enough ethanol was added to effect solution of the nitrile. This solution was heated at 50-55°C. with stirring for 2 hours. The ethanol was then distilled off, more aqueous sodium hydroxide was added and the solution was extracted with ether. The ethereal layer was then washed with water and dried over anhydrous sodium sulphate. On removal of the ether, a solid was obtained which was recrystallised from benzene/40/60° petrol-ether to give the amide.

m.p. 108-110°.

Yield. 0.2g. (36%)

ANALYSIS: $C_{10}H_{11}NO$ requs. C:74.5% H:6.8% N:8.7%

found. C:74.6% H:6.9% N :8.75%

I. R. SPECTRUM. 1660cm.$^{-1}$(s) (C = O), 3600cm.$^{-1}$(m) (NH_2doublet), 750cm.$^{-1}$(s) 680cm.$^{-1}$(m) (aromatic CH)

N. M. R. SPECTRUM. 2.60 - 2.98 τ (complex, 4 aromatic protons).

5.70 τ, J = 6c.p.s. (doublet, 1 cycloalkyl proton).

6.30 τ (multiplet, 1 cycloalkyl proton).

8.50 τ, J = 6c.p.s (doublet, 3 methyl protons).

The aqueous basic layer was then acidified with dilute hydrochloric acid and extracted with ether. The ethereal layer, after drying and removal of the ether gave an oil which solidified on standing and was recrystallised from benzene/petrol-ether, to give the acid.

m.p. 144-146°.

Yield. 0.1g. (18%)

I. R. SPECTRUM. 1690cm.$^{-1}$(s) (C = O)

1010cm.$^{-1}$(w) (cyclobutene CH)

670cm.$^{-1}$ 708cm.$^{-1}$ 760cm.$^{-1}$(m) (aromatic CH)

REACTION OF ETHYL 2-PHENYL -2- (2-CHLOROPHENYL) PROPIONATE (LXXVIIIc) WITH POTASSAMIDE IN LIQUID AMMONIA

With contact times in liquid ammonia of 15 minutes and 60 minutes, only starting material was obtained in each case. This was demonstrated by hydrolysis of the resulting ester in a 20% sodium hydroxide solution 1/1 mixture of water and ethanol and by observation of the mixed m.p. value of the resulting acid with anauthentic sample of 2-phenyl -2- (2-chlorophenyl) propionic acid.

REACTION OF ETHYL 2-PHENYL -2- (3-CHLOROPHENYL) PROPIONATE (LXXVIIId) WITH POTASSAMIDE IN LIQUID AMMONIA

The product of this reaction when chromatographed on alumina gave two distinct bands on elution with benzene. The first band off the column 3g. (from 5g. starting material) was shown to be unchanged starting material by hydrolysis to 2-phenyl -2- (3-chlorophenyl) propionic acid in a 20% sodium hydroxide solution in a 1/1 mixture of

water and ethanol.

The second band was an orange oil and its I.R. spectrum indicated that it was an amine, and further evidence was obtained that it was an aromatic amine when an orange precipitate was obtained when the diazo salt formed from it, coupled with alkaline β-naphthol.

Yield. 0.05g.

I. R. SPECTRUM 3400cm.$^{-1}$(w) (NH_2 doublet)

875cm.$^{-1}$(m) (aromatic CH)

EXPERIMENTAL SECTION II

PART I

ATTEMPTED SYNTHESIS OF 2, 9-DIMETHYLDIBENZO [b, h] BIPHENYLENE

PREPARATION OF 2-METHYL -6- ACETONAPHTHALENE (XCb)

Kon & Weller, J., 1939, 793.

The acetylation of 2-methylnaphthalene (LXXXIX) with acetyl chloride in carbon disulphide gives a mixture of the 2, 6 and 2, 8 derivatives which are separated by virtue of the latter's semicarbazone's greater solubility in hot methanol.

Yield. 18.5%. This could be slightly improved by the substitution of a molar equivalent of acetic anhydride for the acetyl chloride.

m.p. 70°. Lit. m.p. 70-71°.

PREPARATION OF 2-METHYL -6- ACETAMIDONAPHTHALENE (XCI) (SCHMIDT REACTION)

To a solution of 5g. (0.027m.) 2-methyl -6- acetylnaphthalene (XCb) in 35g. trichloroacetic acid at ca. 60° were added 2.7g. (0.042m.) sodium azide all at once. The solution was maintained at ca.60° for 7 hours. A further 1g. (0.015m.) of sodium azide was added after 4 hours. The mixture was poured onto 100g. crushed ice and the precipitated material was washed with water, dried, and recrystallised from aqueous ethanol.

Yield. 3.3g. (60%)

m.p. 155°. Lit. m.p. 155-156°. (83)

PREPARATION OF THE OXIME OF 2-METHYL -6- ACETONAPHTHALENE

To a solution of 25g. sodium hydroxide in 160ml. water and 140g. crushed ice, 20g. (0.29m.) hydroxylamine hydrochloride were added. After dissolution, 20g. (0.1m.) 2-methyl -6- acetonaphthalene (XCb) were added followed by sufficient ethanol (ca. 250 ml.) to give

a clear solution. After two days, the mixture was neutralised to phenolphthalein with dilute hydrochloric acid and diluted with water to 2 litres. The precipitate was collected, dried, and recrystallised from aqueous ethanol.

Yield. quantitative.

m.p. 180°. Lit. m.p. 180°. (84)

BECKMANN REARRANGEMENT OF OXIME

15g. of powdered phosphorus pentachloride were added to a suspension of 10g. oxime in 125 ml. benzene in small amounts. After 3 hours, water was added and the mixture was allowed to stand a further 3 hours. The benzene was evaporated in a current of air and the amide (XCI) was collected by filtration, washed, dried and recrystallised from aqueous ethanol.

Yield. 6g. (60%)

m.p. 156°. Lit. m.p. 155-156°. (83)

2-METHYL -6- AMINONAPHTHALENE (XCII)

5g. (0.025m.) 2-methyl -6- acetamidonaphthalene (XCI) were boiled for 2 hours with 50 ml. 25% methanolic potassium hydroxide. The methanol was then distilled off.

Distilled water and benzene (50 ml. each) were added to the residue and the mixture was warmed until two clear layers resulted. The aqueous layer was extracted a further two times with 25 ml. benzene and the extracts were combined. After drying, the benzene

was distilled off and the product was recrystallised from aqueous ethanol.

Yield. 3.5g. (89%)

m.p. 129°. Lit m.p. 129 - 130°. (83)

TOLUENE -p- SULPHONYL DERIVATIVE OF 2-METHYL -6- AMINONAPHTHALENE(XCIII)

20g. (0.128m.) 2-methyl -6- aminonaphthalene (XCII) were dissolved in 60 ml. dry pyridine and 25g. (0.13m.) toluene -p- sulphonyl chloride were added. The solution was boiled gently for an hour under reflux and then added to excess dilute hydrochloric acid. An oil separated and was crystallised from a methanol water mixture or acetic acid.

Yield. 34g. (85%)

m.p. 117°.

ANALYSIS: $C_{18}H_{17}NO_2S$ requs. S:10.3%

found. S:10.7%

1, 3 - DIBROMO -2- p - TOLUENE SULPHONAMIDO -6- METHYLNAPHTHALENE(XCIV)

Andrews et al., J., 1962, 3440.

Bromination by the method of the above authors of the toluene -p- sulphonyl derivative (XCIII) of 2-methyl - 6-aminonaphthalene gave the required dibromo product in 60% yield.

m.p. 201 - 202°. Lit. m.p. 203°

1, 3 - DIBROMO -6- METHYL -2- NAPHTHYLAMINE (XCVIII)

Andrews et al., J., 1962, 3440

Hydrolysis of the tosyl derivative (XCIV) in concentrated sulphuric acid gave an 80% yield of the amine.

m.p. 130°. Lit. m.p. 131°.

PREPARATION OF 3-BROMO -6- METHYL -2- NAPHTHYLAMINE(XCIX).

A mixture of 5g. (0.015m.) 1, 3-dibromo -6- methyl -2- naphthylamine (XCVIII), 40 ml. ethanol, 40 ml. concentrated hydrochloric acid and 5g. granulated tin was boiled for 2 hours. The filtered cold solution deposited 6-methyl -3- bromo -2- naphthylamine hydrochloride, which was decomposed with alcoholic sodium hydroxide to yield the free amine which was recrystallised from ethanol.

Yield. 1.6g. (43%)

m.p. 178°.

ANALYSIS: $C_{11}H_{10}BrN$ requs. Br:33.9% N:5.9%

found. Br:36.3% N:6.2%

2-IODO -3- BROMO -6- METHYLNAPHTHALENE (C)

6-Methyl- 3-bromo -2- naphthylamine (XCIX) 3g. (0.013m.) was dissolved in a solution of 1.2g. (0.017m.) sodium nitrite in 12 ml. concentrated sulphuric acid and the mixture was stirred into 24 ml. acetic acid below 30°. After 1 hour, the diazonium solution was decomposed by adding to a solution of iodine 1.8g. (0.014m.) and potassium iodide 5.5g. (0.033m.) in 3.6 ml. water with stirring. After 1 hour, the solids were collected by filtration and shaken with 10% w/v aqueous sodium thiosulphate, collected again, washed with water, dried and dissolved in benzene. The solution in benzene

was filtered through alumina, reduced to small volume and the product crystallised out as red prisms.

Yield. 1.77g. (40%)

m.p. 102°.

ANALYSIS: $C_{11}H_8BrI$ requs. Br:23.0% I:36.6%

found. Br:20.8% I:31.8%

ATTEMPTED PREPARATION OF 2, 9 - DIMETHYLDIBENZO [b , h] BIPHENYLENE (CI).

12.5g. (0.036m.) 2-methyl -6- iodo -7-bromonaphthalene (C), 120 ml. dimethylformamide, and 20g. copper bronze were boiled for three hours and the solution was filtered while still hot. The hot filtrate was added to 1.5l. water with stirring and allowed to stand overnight. The resulting solid precipitate was filtered off, washed with water and dried at room temperature. This precipitate was dissolved in benzene and chromatographed on alumina using benzene as eluant. A whit ish fluorescent band on the column, gave, on evaporation of the solvent, a greenish yellow solid (3g.) which on recrystallisation from acetic acid followed by recrystallisation from ethanol gave a pale yellow amorphous solid.

m.p. 119 - 120°.

ANALYSIS: found. C:43.8% H:2.93% Br:42.2% I:9.6% M.W. 381

U. V. SPECTRUM. MAX. 234mμ.

I. R. SPECTRUM. 810, 890, 900, 918(s), 1575cm.$^{-1}$(m)

No other products were isolated.

1-BROMO -2- ACETAMIDO -6- METHYLNAPHTHALENE (XCV)

5g. (0.025m.) 2-methyl -6- acetamidonaphthalene (XCI) were dissolved in 20 ml. acetic acid and 1.5ml. (0.029m.) bromine were added dropwise with shaking. On standing for a few minutes, a crystalline precipitate formed. This was filtered off and recrystallised from aqueous acetic acid to give fine clear needles.

Yield. 4.7g. (67%)

m.p. 211°.

ANALYSIS: $C_{13}H_{12}BrNO$ requs. Br:28.7% N:5.0%

found. Br:42.6% N:3.7%

Br:41.8% N:5.2%

I. R. SPECTRUM. 1660cm.$^{-1}$(s) (C = O), 3260cm.$^{-1}$(m) (NH).

N.M.R. SPECTRUM. 7.8 τ (singlet, 3 methyl protons)

7.37 τ (singlet, 3 methyl protons)

2-METHYL -5- BROMO -6- NAPHTHYLAMINE (XCVI)

0.5g. (0.0018m.) 1-Bromo- 2-acetamido -6- methylnaphthalene (XCV) was added to a 1/1/1 mixture of water, concentrated sulphuric acid and glacial acetic acid, (10 ml. of each). This mixture was boiled for an hour and on cooling, the product settled out of solution and was recrystallised from acetic acid.

Yield: 0.38g. (90%).

m.p. 118°.

I. R. SPECTRUM. 3350cm.$^{-1}$(w) (NH_2 doublet).

0.5g. of the above product was added to 20 ml. of a 1:1 mixture

of ethanol and concentrated hydrochloric acid and boiled for 1 hour. On cooling, the hydrochloride of the amine crystallised out as fine yellowish needles.

Yield. 0.52g. (90%)

m.p. 216°. Lit m.p. 219° (85)

1-BROMO -2- p-TOLUENESULPHONAMIDO -6- METHYLNAPHTHALENE (XCVII).

2-methyl - 5-bromo -6- naphthylamine hydrochloride 7.5g. (0.028m.) was dissolved in 50 ml. pyridine and toluene -p- sulphonyl chloride 5g. (0.028m.) was added. The solution was boiled gently for an hour and allowed to cool. Excess dilute hydrochloric acid was added and an oil separated. This was extracted with chloroform and after drying and removal of the chloroform, the resulting oil solidified on rubbing with ethanol and was recrystallised from ethanol.

Yield. 6.1g. (57%)

m.p. 125°.

ANALYSIS: $C_{18}H_{16}BrNO_2S$ requs. Br:20.5% N:3.6% S:8.2%

found. Br:21.5% N:3.7% S:7.7%

I. R. SPECTRUM. 3250cm.$^{-1}$ (m) (NH)

1, 3 - DIBROMO -2- p- TOLUENESULPHONAMIDO -6- METHYLNAPHTHALENE(XCIV)

5g. (0.013m.) 1-bromo -2-p- toluenesulphonamido -6- methyl-naphthalene (XCVII) were dissolved in excess pyridine (ca. 20ml.) and bromine 2.2g. (0.013m.) was added dropwise with stirring. The solution was allowed to stand overnight and then excess dilute

hydrochloric acid was added. The solid which separated was filtered off and washed with water and then triturated with a little methanol. The sandy coloured solid was then filtered off and recrystallised from acetic acid.

Yield. 3.4g. (65%)

m.p. 200°, Lit. m.p. 203° (85).

ANALYSIS: $C_{18}H_{15}Br_2NO_2S$ requs. N:3.0% Br:34.1% S:6.8%

found. N:3.1% Br:33.1% S:7.2%

5g. (0.013m.) 1-Bromo -2-p-toluenesulphonamido -6-methylnaphthalene (XCVII) were dissolved in 20 ml. pyridine and 2.5g. (0.014m.) N-bromosuccinimide were added. The solution was allowed to stand overnight and cold dilute hydrochloric acid was added. An oil separated which on standing solidified to a sandy solid which was separated and purified by washing with methanol and recrystallisation from acetic acid.

Yield. 3.65g. (70%)

m.p. 201°, Lit. m.p. 203° (85).

1-BROMO -6- METHYL -2- NAPHTHYLAMINE XCVI

5g. (0.013m.) 1-Bromo -2-p- toluenesulphonamido -6- methylnaphthalene (XCVII) were dissolved in 50 ml. concentrated sulphuric acid with shaking and kept at room temperature for 45 minutes. The solution was then poured onto crushed ice and the solid was filtered off, washed with water, suspended twice in N. sodium hydroxide solution, and washed free of alkali with water. The product was recrystallised

from acetic acid.

Yield. 2.03g. (68%)

m.p. 118°. Lit. m.p. 118° (cf. page 116)

2-AMINO -6-METHYLNAPHTHALENE (XCII)

A mixture of 5g. (0.021m.) 1-bromo -6- methyl -2- naphthylamine (XCIV), 40 ml. ethanol, 40 ml. concentrated hydrochloric acid and 5g. granulated tin was boiled for 2 hours. The mixture was then filtered hot, and on cooling, a precipitate of 2-amino -6-methylnaphthalene hydrochloride formed. This was filtered off and treated with alcoholic potassium hydroxide to yield the free base which was recrystallised from aqueous ethanol.

Yield. 2g. (60%)

m.p. 129° Lit. m.p. 129-130° (83)

m.m.p. 129° with sample of alternatively synthesised product (cf. page112)

ATTEMPTED BROMINATION OF 6-METHYL -2-NAPHTHYLAMINE (XCII)

cf. Andrews et al., J., 1962, 3440.

5g. (0.026m.) 6-methyl -2-naphthylamine hydrochloride were dissolved in 200 ml. acetic acid and the solution was cooled to incipient crystallisation. A stream of air was passed through a bubbler containing bromine and into the amine solution which was stirred. When an excess of bromine appeared to be present, the ppt. formed was filtered off and purified by dissolution in aqueous ethanol and precipitation by adding concentrated hydrochloric acid. The product was shown to the hydrochloride of 6-methyl

-2- naphthylamine by formation of the free amine, 6-methyl -2- naphthylamine (XCII).

m.p. 129°. Lit. m.p. 129 - 130° (83) on treatment with base.

ATTEMPTED BROMINATION OF 1-BROMO -2- ACETAMIDO -6-METHYLNAPHTHALENE (XCV)

5g. (0.018m.) of the bromo-compound were dissolved in 30 ml. pyridine and bromine 3.2g. (0.02m.) was added dropwise with stirring. The solution was allowed to stand overnight and then excess dilute hydrochloric acid was added. The solid which separated was filtered off and washed with water. Crystallisation from aqueous acetic acid give fine clear needles.

m.p. and m.m.p. with starting material 211°.

EXPERIMENTAL SECTION II.

PART II.

ATTEMPTED SYNTHESIS OF BIPHENYLENE INVOLVING RING CONTRACTION BY FAVORSKII REARRANGEMENT.

1-ANILINO -1-CYANOCYCLOHEXANE

Walther and Hubner, J. Prakt. Chem., 93, 124. (1916).

The preparation described by these authors was carried out in 52% yield.

m.p. 76°. Lit. m.p. 76°.

1-ANILINOCYCLOHEXANE -1- CARBOXAMIDE

Betts, Muspratt and Plant, J., 1927, 1312.

Treatment of 1-anilino -1- cyanocyclohexane with concentrated sulphuric acid give the amide in quantitative yield.

m.p. 148°. Lit. m.p. 148°.

1-ANILINOCYCLOHEXANE -1- CARBOXYLIC ACID (CIV)

Betts, Muspratt and Plant, J., 1927, 1312.

Hydrolysis of the amide with concentrated hydrochloric acid gave the acid in 92% yield.

m.p. 142°. Lit. m.p. 142°.

CYCLOHEX -1- ENE CARBOXYLIC ACID (CV)

Betts, Muspratt and Plant, J., 1927, 1312.

Distillation at atmospheric pressure of the 1-anilinocyclohexane -1- carboxylic acid (CIV) gave a mixture of aniline and cyclohex-1-ene carboxylic acid (CV). The acid was isolated in 71% yield and converted by the action of thionyl chloride to the acid chloride (CVI).

b.p. of acid 34° /0.7mm.

b.p. of acid chloride 58-62° /0.9mm.

1, 2, 3, 4, 4b, 5, 6, 7, 8, 8a, - DECAHYDROFLUORENONE (CVIII)

Baddeley et al., J., 1953, 124.

Reaction of 9g. (0.063m.) cyclohex -1-ene carboxylic acid chloride (CVI), on heating with phosphoric and formic acids gave the decahydrofluorenone (CVIII).

Yield. 2.0g. (17%).

b.p. 130 - 140°/1mm.

m.p. of D.N.P. derivative 64-65°. (red needles). Lit. m.p. 68-69°.

PERHYDROFLUORENONE (CIX)

3g. (0.02m.) decahydrofluorenone (CVIII) were dissolved in 50 ml. absolute ethanol and 3 ml. 3N. hydrochloric acid and 0.3g. 10% Pd/charcoal were added and the mixture was hydrogenated until the theoretical amount of hydrogen had been absorbed at atmospheric pressure.

Yield. 2.9g. (95%)

I. R. SPECTRUM. 1715cm.$^{-1}$(s) (C = O).

X -CHLOROPERHYDROFLUORENONE (CX)

3g. (0.02m.) perhydrofluorenone (CIX) were dissolved in 30 ml. carbon tetrachloride and 2.75g. (0.02m.) N-chlorosuccinimide were added. The mixture was boiled for 24 hours, the succinimide filtered off after cooling of the mixture, and then the carbon tetrachloride was evaporated off.

Yield. Quantitative.

ANALYSIS: (crude oil) $C_{13}H_{19}C10$ requs. C:68.8% H:8.4% C1:15.7%

found. C:64.5% H:8.0% C1:15.8%

I. R. SPECTRUM 1703cm.$^{-1}$(s) (C = O).

FAVORSKII REACTION WITH α -CHLOROPERHYDROFLUORENONE (CX)

Potassium 3g. was added to 30 ml. anhydrous dioxane and the mixture was heated until the potassium melted. The flask was then stoppered and shaken vigorously to form small granules of potassium. The mixture was then cooled and 3g. α -chloroperhydrofluorenone (CX) were added and the solution was refluxed overnight. On cooling, the excess potassium was filtered off and the solution was added to 200 ml. water. A few pellets of potassium hydroxide were added and the solution was extracted with ether and the aqueous layer was acidified with 10% sulphuric acid but no organic acid was precipitated.

EXPERIMENTAL SECTION II

PART III

ATTEMPTED FORMATION OF DIBENZO [b, h] BIPHENYLENE.

ETHYL -2- NAPHTHYL ETHER

Davis, J., 1900, 33.

The product was obtained quantitatively on refluxion of a mixture of 2-naphthol, ethanol and concentrated sulphuric acid.
m.p. 37°. Lit. m.p. 37.5°.

2-NAPHTHYL KETONE (β-TETRALONE) (CXV)

Soffer et al., Org. Synth., 32, 97.

This preparation was carried out exactly as described in the reference and a similar yield was obtained.

1, 1'-DIHYDROXY - 1, 1', 2, 2', 3, 3', 4, 4' - OCTAHYDRO -1, 1'-BINAPHTHYL

Bergmann et al., J. Org. Chem., 8, 185. (1943)

Pinacol formation was carried out in 30% yield as described in the reference from α-tetralone with aluminium and mercuric chloride as catalysts.
m.p. 189°. Lit. m.p. 191°.

3, 3', 4, 4' - TETRAHYDRO -1, 1' - BINAPHTHYL

Bergmann et al., J. Org. Chem., 8, 185. (1943)

Dehydration of the pinacol in a 1:1 mixture of acetic acid and acetic anhydride gave an 80% yield of the product.
m.p. 138°. Lit. m.p. 141°.

ATTEMPTED FORMATION OF 2,2'-DIHYDROXY - 1, 1', 2, 2', 3, 3', 4, 4' - OCTAHYDRO -2, 2'-BINAPHTHYL (CXVI)

cf. Bergmann et al., J. Org. Chem., 8, 185. (1943)

The procedure described in the reference for α-tetralone was carried out with β-tetralone (CXV) but no pinacol was isolated. Instead, on addition of the ether extract to the decanted benzene solution, a white precipitate was formed which proved insoluble in the common organic solvents. The precipitate was extracted in a Soxhlet extractor with a 1:1 mixture of butyl acetate and acetic acid. An insoluble residue was left in the thimble and on evaporation of the extract, an uncrystallisable oil was obtained.

An attempt was made to dehydrate the residue left in the thimble by refluxing with 20 ml. of a mixture of acetic acid and acetic anhydride for three hours when a solid was obtained. m.p. $> 360^{\circ}$.

Another attempt was made to form the pinacol using the method of Gomberg and Bachmann, J. Amer. Chem. Soc., 49, 244. (1927) with MgI_2 and magnesium as catalysts but only unchanged starting materials were isolated.

1, 2 - DIHYDRONAPHTHALENE

Strauss and Lemmel, Ber., 46, 232. (1913)

This was prepared in 83% yield by reduction of naphthalene to 1, 4 - dihydronaphthalene followed by isomerisation to the 1, 2 - dihydronaphthalene.

b.p. $96\text{-}100^{\circ}$ /25 mm.

1, 2 - DIBROMO - 1, 2, 3, 4 - TETRAHYDRONAPHTHALENE (CXVII)

Fujita, J. Amer Chem. Soc., 79, 2492. (1957)

Bromination of the double bond in 1, 2 - dihydronaphthalene gave a 70% yield of the product.

1-ETHOXY -2-BROMO -1, 2, 3, 4 - TETRAHYDRONAPHTHALENE (CXVIII)

von Braun and Kirshbaum, Ber., 54B, 597. (1921)

Boiling of the dibromo compound (CXXVII) in dry ethanol gave a 90% yield of the product.

b.p. 170 - 172°./20 mm.

3, 3' 4, 4' - TETRAHYDRO - 2, 2' - BINAPHTHYL (CXX)

von Braun and Kirshbaum, Ber., 54B, 597. (1921)

Preparation of this product in 21% yield was achieved by a coupling reaction of the bromo compound with magnesium followed by loss of ethanol by refluxion in ethanolic sulphuric acid.

m.p. 156°. Lit. m.p. 156°.

BROMINATION OF 3, 3', 4, 4' -TETRAHYDRO -2, 2' -BINAPHTHYL (CXX)

3.5g. (0.0179m.) N - bromosuccinimide were added to a solution of 25g. (0.0096m.) (CXX) in 70 ml. carbon tetrachloride and the solution was refluxed for ½ hour. Hydrogen bromide was observed to be evolved. The precipitate of succinimide was filtered off on cooling the solution before removal of the solvent. A solid product was obtained whose m.p. 186°. and U.V. spectrum. max 214 mμ. $\log_{10}\epsilon$ 4.6, 255mμ. $\log_{10}\epsilon$ 5.0 showed it to be 2, 2' - binaphthyl.

The experiment was repeated at room temperature and also at $-30^{\circ}C$ with methylene chloride as solvent but in both cases 2, 2' - binaphthyl (CXXII) was formed.

EXPERIMENTAL SECTION II

PART IV

ATTEMPTED CONDENSATIONS OF BICYCLO [4.2.0] OCTA - 1, 3, 5 - TRIENE - 7, 8 - DIONE.

$\alpha, \alpha, \alpha', \alpha'$ -TETRABROMO -o- XYLENE

Bill & Tarbell, Org. Synth., 34, 82.

Bromination of o-xylene with 4 moles bromine in U.V. light gave a 70% yield of the tetrabromide.

m.p. 114° Lit. m.p. 115-116°.

α, α' -DIBROMO -o- XYLENE

Perkin, J., 1888, 5.

Bromination of o-xylene with 2 moles of bromine at boiling temperature gave a 70% yield of the dibromide.

m.p. 92°. Lit. m.p. 93°.

α, α' -DICYANO -o-XYLENE (CXXVII)

Moore and Thorpe, J., 1908, 175.

Cyanation of the dibromide with potassium cyanide in ethanol containing enough water to dissolve the potassium cyanide gave the dinitrile in 57% yield.

m.p. 59°. Lit. m.p. 60°.

7. 8 - DIBROMOBICYCLO [4.2.0] OCTA -1, 3, 5 -TRIENE (CXXIV)

Finkelstein et al., Ber., 92, XXXVII. (1959)

Refluxion of the tetrabromide (CXXIII) 100g. (0.24m.) in 500ml. absolute ethanol with 122g. (0.74m.) potassium iodide gave 30g. of crude product. This product contained iodine which would inhibit the next stage in the synthesis which is a free radial reaction. To remove the iodine, the product was kept in contact with bromine in carbon tetrachloride at room temperature. The solution was then washed with sodium bisulphite solution to remove precipitated iodine and excess bromine. After washing again with dilute sodium hydroxide solution, the carbon tetrachloride layer was dried and then distilled to give the purified product. This procedure was carried out thrice, 1x16 hr. and 2 x 2 hrs. in contact with bromine in carbon tetrachloride solution.

Yield. 26.5g. (43%)

m.p. 52°. Lit. m.p. 52.4°.

b.p. 110-115° /5 mm.

7, 7, 8, 8 - TETRABROMOBICYCLO [4.2.0] OCTA -1, 3, 5 - TRIENE (CXXV)

Cava and Muth, J. Org. Chem., 27, 757, (1962)

Further bromination with N - bromosuccinimide of the dibromide (CXXIV) gave the tetrabromide in 55% yield.

m.p. 117°. Lit. m.p. 116 - 117°.

BICYCLO [4.2.0] OCTA -1, 3, 5 - TRIENE - 7, 8 - DIONE. (CXXVI)

Cava, Napier and Pohl, J. Amer. Chem. Soc. 85, 2079 (1963)

Reaction of the tetrabromide (CXXV) with silver trifluoroacetate in aqueous acetonitrile gave a 43% yield of the diketone.

m.p. 128°. Lit. m.p. 130-131°.

ATTEMPTED CONDENSATIONS OF BICYCLO [4.2.0] OCTA -1, 3, 5 - TRIENE -7, 8 -DIONE (CXXVI) WITH α, α' -DICYANO -o-XYLENE (CXXVII)

cf. Moureu et al. (60).

0.5g. (0.0038m.) diketone (CXXVI) and 0.58g. (0.0038m.) dinitrile (CXXVII) were dissolved in 5 ml. piperidine with the evolution of heat. A sample was immediately removed from the solution and acidified with dilute hydrochloric acid. The acidified solution was extracted with methylene chloride and after drying the organic layer, the solvent was removed. An oil was obtained I.R. SPECTRUM 1705cm.$^{-1}$(s) (C = O) which was dissolved in a little ethanol and treated with Brady's solution. The dinitrophenylydrazone thus formed was recrystallised from acetic acid, giving red needles m.p. 257 - 259°. Lit m.p. of o-phthalaldehydic acid 263°.

The piperidine solution was allowed to stand 24 hours and a small amount of white crystals was formed m.p. 170°.

I. R. SPECTRUM 1620cm.$^{-1}$ (C = O), no (CN) absorption.

ANALYSIS: found C:74.6% H:9.8% N:11.8%

The experiment was repeated using :

a) Pyridine as base.

b) Aluminium chloride in methylene chloride.

c) Pyridine and 1 drop piperidine.

d) 1/1 Triethylamine/Pyridine.

e) Benzyl Trimethyl Ammonium hydroxide.

f) 1/1 Triethylamine/ethanol.

g) 1/1 Triethylamine/benzene.

(a) and (b) yielded only starting materials on standing at room temperature for 1 day (c), (d), (e) and (f) gave no solid recognisable products and (g) gave 10mg. needles m.p. 240° with a carbonyl absorption in its I.R. SPECTRUM at 1780cm.$^{-1}$(s).

ATTEMPTED FORMATION OF 7-ETHYLENEDIOXYBICYCLO [4.2.0] OCTA - 1, 3, 5 - TRIENE -8-ONE (CXXIX)

cf. Ringold, J. Amer. Chem. Soc., 1362 (1954)

Reaction of the diketone (CXXVI) under the conditions described by Ringold for 4-androstene -3, 17-dione gave a few crystals.

m.p. 270°.

I. R. SPECTRUM 3500cm.$^{-1}$(s) (-OH), 1760cm.$^{-1}$(s) (-C = O).

ATTEMPTED MEERWEIN-PONDORFF REDUCTION OF BICYCLO [4.2.0] OCTA -1, 3, 5 - TRIENE -7, 8 - DIONE (CXXVI) TO BICYCLO [4.2.0] -1, 3, 5 -TRIENE -7 - ONE - 8 - OL. (CXXX)

A small amount of aluminium isopropoxide was prepared from 1g. aluminium. 0.05g. mercuric chloride, 20 ml. dry isopropanol and 0.2ml. carbon tetrachloride as described in Org. Reactions Vol. II The reduction was also carried out by the method described in this reference. The product obtained was an oil. (5mg. from 0.5g. diketone) which solidified on contact with ethanol.

m.p. ~ 328°.

I. R. SPECTRUM. 3450cm.$^{-1}$(m) (OH).

1710-1770cm.$^{-1}$ (s) (C = O).

4, 5 -DINITRO -o- DIMETHOXYBENZENE (CXXXVII)

Ehrlich and Bogert (65)

Dinitration of o-methoxybenzene (CXXXVI) with nitric acid and fuming nitric acid in acetic acid gave the product in 83% yield.

m.p. 128-130°. Lit. m.p. 125. -130.5°

7, 8 - DIMETHOXYBENZO [3, 4] CYCLOBUTA [1, 2 -b] QUINOXALINE (CXXXIV)

1g. (0.0044m.) 4, 5 - dinitro -o- dimethoxybenzene (CXXXVII) was dissolved in 20 ml. ethanol and 5 ml. acetic acid and the nitro groups were reduced at atmospheric pressure over Raney nickel. After the theoretical amount of hydrogen had been absorbed, the nickel was filtered off and 0.5g. (0.0038m) bicyclo [4.2.0]

octa -1, 3, 5 - triene - 7, 8 - dione (CXXVI) was added with 0.5g. sodium acetate. The solution was refluxed for 4 hours and on cooling yellow needles precipitated out. These were recrystallised from ethanol.

Yield. 0.5g. (50% w.r.t. diketone)

m.p. 230°.

ANALYSIS: $C_{16}H_{12}N_2O_2$ requs. C:72.8% H:4.6% N:10.6%

found. C:73.4% H:4.3% N:10.5%

GUAIACOL CARBONATE (CXXXIX)

Behal and Choay, Bull. Soc. Chim. France., [3]11, 704. (1894)

By passing phosgene into a basic solution of guaiacol (CXXXVIII), the carbonate was obtained in 63% yield.

m.p. 86° Lit. m.p. 86°.

2-METHOXY -5- NITROPHENOL (CXLI)

Pollecoff and Robinson, J., 1918, 648.

Nitration of guaiacol carbonate with concentrated nitric acid gave 2- methoxy -5- nitrophenol carbonate (CXL) which gave the 3-methoxy -5- nitrophenol (CXLI) in 20% yield on hydrolysis in basic solution.

m.p. 98-102°. Lit. m.p. 103-104°.

3-HYDROXY -4- METHOXY -o- DINITROBENZENE (CXLII)

Pollecoff & Robinson, J., 1918, 648.

Nitration of 2-methoxy -5- nitrophenol (CXLI) with nitric acid in acetic acid gave a 27% yield of the dinitro product.

m.p. 204°. Lit. m.p. 205°

6-HYDROXY, 7 -METHOXYBENZO [3, 4] CYCLOBUTA [1, 2 -b] QUINOXALINE (CXXXV)

1g. (0.0047m.) 3-Hydroxy -4- methoxy -o- dinitrobenzene (CXLII) was dissolved in 20 ml. ethanol and 5 ml. acetic acid and the nitro groups were reduced at atmospheric pressure over Raney nickel. After the theoretical amount of hydrogen had been absorbed, 0.6g. (0.0045m.) bicyclo [4.2.0] octa -1, 3, 5 -triene -7, 8 -dione (CXXVI) was added with 0.5g. sodium acetate. The solution was refluxed for 4 hours and on cooling green fibrous needles were deposited.

m.p. > 360°.

Treatment of this product with dilute hydrochloric acid in the cold and washing the resulting yellow product with water gave the hydroxy product (CXXXV).

m.p. 274°.

Yield. 0.74g. (65% w.r.t. diketone)

ANALYSIS: $C_{15}H_{10}N_2O_2$ requs. C:72.0% H:4.0% N:11.2%

found. C:70.2% H:4.8% N:11.5%

ATTEMPTED DEMETHYLATIONS OF THE METHOXY QUINOXALINES.

1) IN 48% HYDROBROMIC ACID.

200 mg. of methoxy compound (CXXXIV) or (CXXXV) were added to 5 ml. 48% hydrobromic acid and the mixture was refluxed for 12 hours. In both cases, an almost quantitative retrieval of starting material was achieved.

2) IN HYDRIODIC ACID

A solution of 200 mg. methoxy compound (CXXXIV) or (CXXXV) in 5 ml. hydriodic acid (D1.96) was gradually heated to boiling. No methyl iodide was observed to evolve and after refluxing for 2 hours, only starting materials were obtained.

3) WITH ALUMINIUM CHLORIDE

To 200 mg. methoxy compound (CXXXIV) or (CXXXV) in 5 ml. dry benzene, was added anhydrous aluminium chloride (0.5g.). After three hours on the steam bath the mixture was diluted with 5 ml. benzene and poured onto ice. In both cases only starting materials were obtained.

3-NITROPHENOL

Vogel, Elementary Practical Org. Chem. Part I. p.260.

Treatment of the diazonium salt solution of 3-nitroaniline with aqueous sulphuric acid gave a 47% yield of 3-nitrophenol.
m.p. 46°. Lit. m.p. 46°.

3, 4 -DINITROPHENOL (CXLIII, R = H)

Holleman and Wilhemy Rec. Trav. Chim., 21, 434. (1902)

Further nitration of 3- nitrophenol with nitric acid ($D = 1.2$) gave a mixture of dinitrophenols from which the 3, 4 - dinitrophenol was isolated in 22% yield.
m.p. 135°. Lit. m.p. 134.7°

ATTEMPTED CONDENSATION OF 3, 4-DIAMINOPHENOL (CXLIV, R = H) WITH BICYCLO - [4.2.0] OCTA -1, 3, 5 - TRIENE -7, 8 - DIONE (CXXVI)

0.65g. (0.0035m.) 3, 4 -dinitrophenol was dissolved in a little ethanol and reduced at 20°C. and atmospheric pressure. When the theoretical amount of hydrogen required to reduce the two nitro groups had been absorbed, the nickel was filtered off and added to a solution of 10 ml. ethanol and 10 ml. acetic acid containing 0.5g. (0.0038m.) dione and 0.5g. sodium acetate. This solution was refluxed for four hours and on cooling, yellow crystals of the diketone settled out. No other recognisable product could be isolated from the reaction.

The acetyl derivative (CXLIII R = CH_3 CO) of 3, 4-dinitrophenol was prepared by the usual method of preparation of acetyl derivatives. m.p. 47°

ANALYSIS: $C_8H_6N_2O_6$ requs. C:42.5% H:2.7% N:12.4%

found. C:42.8% H:2.9% N:12.8%

Reduction of the two nitro groups of (CXLIII, R = CH_3 CO) as described above for the phenol and attempted condensation with the diketone (CXXVI) gave no identifiable product.

EXPERIMENTAL SECTION III

PART I

ATTEMPTED SYNTHESIS OF BICYCLIC IMIDES LEADING TO CYCLOBUTANE DERIVATIVES.

PREPARATION OF PHENYLACETALDEHYDE (CXLIX)

Shumeiko, Chem. Abs., 36, 436. (1942)

Oxidation of phenylethyl alcohol gave the aldehyde in 5% yield.

ATTEMPTED PREPARATION OF β -BENZYL -α,α' -DICYANOGLUTARIC DIAMIDE. (CL)

cf. Day & Thorpe, J., 1920, 1465.

Phenylacetaldehyde (CXLIX) 0.5g. (0.0042m.) and cyanoacetamide 0.72g. (0.0084m.) were dissolved in water, the minimum amount of alcohol being added to effect the solution of the phenylacetaldehyde. A drop of 50% aqueous potassium hydroxide was added and the solution was allowed to stand overnight. A precipitate (0.2g.) formed and was filtered off and washed first with dilute hydrochloric acid and then with hot ethanol.

m.p. 230 - 235°.

I. R. SPECTRUM 2200, 2250cm.$^{-1}$ (w) (CN)

ATTEMPTED PREPARATION OF β -BENZYL -α,α' -DICYANOGLUTARIC ACID DIETHYL ESTER

cf. Gutzheit & Jahn, J. prakt. Chem., [2] 66, 1. (1902)

Phenylacetaldehyde (CXLIX) 2.5g. (0.021m.) was mixed with cyano acetic ester 4.7g. (0.042m.) and 2 drops of diethylamine were added with cooling in ice. The mixture was allowed to stand overnight and finally was heated for 2 hours on a boiling water bath.

Distillation of the products under reduced pressure gave a mixture of phenylacetaldehyde and the cyanoacetic ester boiling below 100°/7mm. and a fraction b.p. 170 - 180°/7mm. (0.8g.)

I.R. SPECTRUM 2270cm.$^{-1}$(w) (CN), 1748cm.$^{-1}$(s) (C =O) .

This product was an uncrystallisable oil.

PREPARATION OF β-BENZYL -α, α'-DICYANO GLUTARIC ACID.

Haworth et al., J., 95, 848. (1909)

Condensation of two moles of the sodium derivative of cyanoacetic ester with phenylacetaldehyde (CXLIX) gave the glutaric acid in 24% yield.

m.p. 173°. Lit. m.p. 173°.

I. R. SPECTRUM 2280cm.$^{-1}$(s) (CN)

1730cm.$^{-1}$(s) (C = O)

ACID CATALYSED CONDENSATION OF PHENYLACETALDEHYDE (CXLIX) WITH CYANOACETIC ESTER

cf. Hauser et al., J. Amer, Chem. Soc, 62, 2387. (1940)

To a solution of 10g. (0.084m.) phenylacetaldehyde, (CXLIX) 9.5g. (0.084m.) cyanoacetic ester and 75 ml. 40/60° petrol-ether were added with stirring, 40g. (0.03m.) of finely ground aluminium trichloride. The mixture refluxed gently during the addition and after the addition the mixture was refluxed for an additional five hours. The reaction mixture was then cooled and added to crushed ice and a little concentrated hydrochloric acid. The mixture was then extracted with ether and the ethereal layer was washed with

dilute potassium carbonate solution until the washings were alkaline. The ether extract was then dried before removal of the ether. The residual oil was distilled and gave a fraction (1.5g.) b.p. 182 - 186° /5 mm.

I. R. SPECTRUM 2250cm.$^{-1}$(w) (CN), 1690cm.$^{-1}$(s) (C = O), 1608cm.$^{-1}$(m) (C = O).

U. V. SPECTRUM max. 215 mμ. $\log_{10}\epsilon$ 4.44, 250 mμ. $\log_{10}\epsilon$ 4.14, 300mμ $\log_{10}\epsilon$ 4.19.

OZONOLYSIS OF THE PRODUCT OF THE PREVIOUS REACTION

The product of the previous reaction 0.3g. was dissolved in 10 ml. methylene chloride and subjected to a stream of ozonised oxygen until excess ozone was clearly present. The ozonide was decomposed by shaking the methylene chloride solution with water. After removal of the methylene chloride, the residue was steam distilled and gave 0.10g. (68%) benzaldehyde.
m.p. of D.N.P. derivative 237°. Lit. m.p. 237°.

BENZYLIDENE PYRUVIC ACID(CLX)

Bougault et Cordier, Comptes Rend., 238, 2004. (1954).

Condensation of pyruvic acid and benzaldehyde in the presence of dilute alcoholic potassium hydroxide gave the potassium salt of the acid in 60% yield.

BENZALLACTIC ACID (CLXI)

Bougault et Cordier, Comptes Rend., 238, 2004. (1954).

Reduction of the keto acid (CLX) with potassium borohydride in water gave a quantitative yield of the lactic acid.
m.p. 137°. Lit. m.p. 137°.

BENZYLPYRUVIC ACID (CLXII)

Bougault et Cordier, Comptes Rend., 238, 2004. (1954).

Rearrangement of the lactic acid (CLXI) in 5% aqueous sodium hydroxide solution gave the pyruvic acid in 60% yield.

m.p. 45°. Lit. m.p. 45°.

ETHYL BENZYLPYRUVATE (CLXIII)

Equimolecular amounts of absolute ethanol and benzylpyruvic acid (CLXII) were refluxed overnight and on distillation, the pure ester was obtained.

Yield. 95%.

b.p. 164 - 166° /10mm.

ANALYSIS : $C_{12}H_{14}O_3$ requs. C:69.9% H:6.8%

found. C:70.2% H:7.3%

ATTEMPTED PREPARATION OF α-CYANOBENZYLLACTIC ACID ESTER (CLXIV)

cf. Ultée, Rec. Trav. Chim., 28, 7. (1909)

2.3 ml. Liquid hydrogen cyanide were added to 8g. ethyl benzylpyruvate (CLXIII) and 2 drops of concentrated potassium hydroxide solution were added. No reaction was observed and the solution was heated slightly for 10 minutes and then cooled. 5 drops of concentrated sulphuric acid were added to destroy the hydroxide which catalyses the reverse reaction on heating. The solution was then heated at 100°C. to remove excess hydrogen cyanide. The solution was then ether extracted, the ethereal layer washed with water and dried. Removal of the ether gave an oil whose I. R. spectrum was identical with that of the starting material.

The experiment was repeated using ethyl pyruvate and cyclohexanone, both of which were reported by Ultée to react with hydrogen cyanide but only the latter was observed to react.

EXPERIMENTAL SECTION III

PART II.

ATTEMPTED SYNTHESES OF CYCLOBUTANE DERIVATIVES.

1, 4 -(3, 4 -METHYLENEDIOXPHENYL) BUTA -1, 3 - DIENE - 2, 3 - DICARBOXYLIC ACID (CLXVI).

Haworth & Woodcock, J., 1938, 1985.

2 moles of 3, 4 -methylenedioxy benzaldehyde (CLXV) were condensed with one mole of diethyl succinate to give the required acid in 21% yield.

m.p. 207 - 208°. Lit. m.p. 207 - 208°.

DIMETHYL ESTER OF 1, 4 - (3, 4 - METHYLENEDIOXYPHENYL) BUTA - 1, 3 - DIENE - 2, 3 - DICARBOXYLIC ACID

Freudenberg et al., Annalen, 602, 184. (1957)

Esterification of the diacid with diazomethane gave the diester in 54% yield m.p. 183°. Lit. m.p. 183.5 - 184.5°.

1, 4 - (3, 4 - METHYLENEDIOXYPHENYL) BUTA -1, 4 -DIENE -2, 3 DIMETHANOL (CLXVII)

Freudenberg et al., Annalen, 602, 184. (1957)

Reduction of the diester with lithium aluminium hydride under nitrogen gave the diol in 20% yield m.p. 145°. Lit. m.p. 147°.

p-METHOXYBENZYL ALCOHOL

Davidson & Bogert, J. Amer. Chem Soc., 57, 915 (1935)

A crossed Cannizzaro reaction with anisaldehyde and formalin gave a 50% yield of the alcohol.

b.p. 100 - 105° /1mm.

p-METHOXYBENZYL CHLORIDE

Lee et al., Chem. Abs., 41, 6253. (1947)

p-methoxybenzyl alcohol (10g.) was dissolved in 100 ml. dry benzene and the solution was cooled to -10° and dry hydrogen chloride was passed through it for 1 hour. The water formed during the reaction was separated from the benzene solution which was then dried over calcium chloride for an hour. The benzene was then distilled off under reduced pressure in an atmosphere of nitrogen and the residual oil was distilled under the same conditions.

Yield. 60%.

b.p. 80-85° /0.5mm.

1, 4 - DI - (p-METHOXYPHENYL) -2, 3 - DIMETHYL -2, 3 - BUTANDIOL (CLXX)

cf. Langer & Wessely, Monatsh., 86, 887. (1955).

Elderfield & Meyer, J. Amer Chem. Soc., 76, 1883. (1954)

A solution p-methoxybenzylmagnesium chloride in ether prepared from 18g. (0.1 2m.) p-methoxybenzyl chloride by the method of Elderfield & Meyer was filtered through a sintered glass filter. At this point, a precipitate started to form in the solution of Grignard reagent which was added dropwise with stirring for 1 hour to 3.5g. (0.041m.) diacetyl in 40 ml. ether. After standing overnight at room temperature and working up in the usual fashion, an oil was obtained which solidified on standing and was recrystallised from methanol.

Yield, 50%,

m.p. 125°. Lit. m.p. of 4, 4' -dimethoxybibenzyl 125°. (86)

ANALYSIS : $C_{16}H_{18}O_2$ requs. C:78.6% H:6.55%

found. C:79.6% H:7.3%

2, 3 - BIBENZYL -2, 3 - BUTANDIOL (CLXX)

Langer & Wessely, Monatsh., 86, 887. (1955)

Reaction of benzyl magnesium chloride (CLXIX) with diacetyl gave the diol in 60% yield.

m.p. 94-95°. Lit. m.p. 100-101°.

2, 3 - BIBENZYL -1, 4 - BUTADIENE (CLXXI)

Langer & Wessely, Monatsh. 86, 887. (1955)

Dehydration of the diol with acetic anhydride and acetyl chloride gave a 93% yield of the diene.

m.p. 135°. Lit. m.p. 135°.

3, 4 - METHYLENEDIOXYBENZYL ALCOHOL

Davidson & Bogert, J. Amer. Chem. Soc., 57, 905, (1935)

A crossed Cannizzaro reaction with 3, 4 -methylenedioxybenzaldehyde and formalin gave the alcohol in 83% yield.

m.p. 50°. Lit. m.p. 50°.

3, 4 -METHYLENEDIOXYBENZYL CHLORIDE

3, 4-Methylenedioxyphenylbenzylalcohol (6g.) was dissolved in 1 litre 60/80° petrol-ether and hydrogen chloride was bubbled through the solution until saturation point was reached. The solution was decanted from the water which had formed during the

reaction and dried over calcium chloride. The solvent was distilled off under reduced pressure and in an atmosphere of nitrogen and the chloride was distilled under similar conditions.

Yield. 5.2g. (78%)

b.p. 132 - 134°/10mm.

ATTEMPTED FORMATION OF 1, 4 - (3, 4-METHYLENEDIOXYPHENYL) - 2, 3 - DIMETHYL - 2, 3 - BUTANDIOL (CLXX)

cf. Langer and Wessely, Monatsh., 86, 887. (1955)

A solution of 3, 4 -methlenedioxybenzylmagnesium chloride prepared from 10g. (0.059m.) 3, 4-methylenedioxybenzyl chloride in 100 ml dry ether was added dropwise with stirring over a period of 1 hour to a solution of 2.15g. (0.025m.) diacetyl in 30 ml dry ether. A precipitate formed and after working up in the usual manner, the only product isolated was a solid.

Yield. 5g. (64%)

m.p. 141° Lit. m.p. of 3, 4: 3', 4' -dimethylenedioxydibenzyl 138°. (86)

EXPERIMENTAL SECTION III

PART III

ATTEMPTED SYNTHESIS OF 5, 11-DIHYDROXYDIBENZO [a, g] BIPHENYLENE FROM α-TRUXILLIC ACID.

1-PHENYLBUTADIENE -4, 4-DICARBOXYLIC ACID. (CLXXVI)

(CINNAMYLIDENAMALONIC ACID)

Liebermann, Ber., 28, 1439, (1895).

A mixture of equal parts of malonic acid, cinnamaldehyde and acetic acid gave a 25% yield of the diacid.

m.p. 208°. Lit. m.p. 208°.

PHOTODIMER OF 1-PHENYLBUTADIENE -4, 4-DICARBOXYLIC ACID. (CLXXVII).

Criegee et al., Ber., 93, 2521. (1960).

Irradiation of cinnamylidene malonic acid (CLXXVI) in U.V. light while suspended in a weakly acidified aqueous solution gave a quantitative yield of the dimer.

m.p. 192-194°. Lit. m.p. 195°.

2, 4 - DIPHENYLCYCLOBUTANE -1, 3 - DICARBOXYLIC ACID. (α -TRUXILLIC ACID) (CLXXVIII)

Criegee et al., Ber., 93, 2521. (1960)

Ozonolysis of the dimer of 1-phenylbutadiene -4, 4-dicarboxylic acid followed by oxidation of the resulting dialdehyde with hydrogen peroxide gave the diacid in 40% yield.

m.p. 274°. Lit. m.p. 274°.

DIMETHYL ESTER OF α -TRUXILLIC ACID

Boiling α -truxillic acid (CLXXVIII) in excess absolute methanol containing 3% by weight of conc. sulphuric acid for 4 hours gave on cooling an almost quantitative yield of diester.

m.p. 174° Lit. m.p. 174°.

2, 4-DIPHENYLCYCLOBUTANE -1, 3-DIMETHANOL. (CLXXIX, R = OH)

The diester of α-truxillic acid 0.5g. (0.0017m.) was dissolved in 15ml. dry tetrahydrofuran and added dropwise with stirring to 0.08g. (0.0021m.) lithium aluminium hydride in 15 ml. tetrahydrofuran. After the addition was completed, the mixture was refluxed for an hour, cooled and the excess lithium aluminium hydride was decomposed by the careful addition of 10% aqueous sulphuric acid. The resulting mixture was extracted with ether and the extract, after drying and removal of the ether gave the diol as an oil which solidified on standing. The product was recrystallised from benzene.

m.p. 106°.

Yield. 0.3g. (66%)

ANALYSIS: $C_{18}H_{20}O_2$ requs. C:80.5% H:7.5%

found. C:80.1% H:7.35%

ATTEMPTED PREPARATION OF 1, 3 - BROMOMETHYL -2,4-DIPHENYLCYCLOBUTANE (CLXXIX, R = Br)

a) WITH PHOSPHORUS TRIBROMIDE

The diol (CLXXIX, R = OH) 0.5g. was treated with excess phosphorus tribromide (10 ml) in the cold and then heated on a boiling water bath for 30 minutes. After cooling and decomposition of excess phosphorus tribromide with ice, a solid product was obtained which could not be extracted into ether or benzene and which recrystallised from water as small nodules.

Yield. 0.4g.

m.p. 143-146°.

ANALYSIS: found. C:54.1% H:6.45% Br:2.1% P:15.95%.

b) WITH HYDROBROMIC ACID.

The diol (CLXXIX, R = OH) (0.5g.) was heated under reflux for 3 hours with 20ml, 48% hydrobromic acid. On cooling and dilution with water, an oil was obtained which was extracted into ether. After washing the ether extract with water, drying it and removal of the ether, a dark brown viscous oil (0.55g.) was obtained whose infrared spectrum exhibited no hydroxyl peak. However an attempted cyanation of this supposedly dibromo compound with potassium cyanide (2.5 molar equivalents) in aqueous ethanol gave a product with a small nitrile peak in its infrared spectrum. This product could not be chromatographed on alumina and an attempted hydrolysis of crude nitrile to acid in a 1/1/1 acetic acid/conc. sulphuric acid/water mixture failed to yield any acid.

THE ARNDT-EISTERT SYNTHESIS.

5.2g. (0.0175m.) α-truxillic acid (CLXXVIII) were refluxed in 50 ml. thionyl chloride containing 1 drop of dimethylaniline for $1\frac{1}{2}$ hours. Excess thionyl chloride was then distilled off under reduced pressure. The last traces of thionyl chloride were removed by distillation with benzene (3 x 50 ml.), under the same conditions.

A solution of the acid chloride in dry ether (100 ml.) was added dropwise to a solution of diazomethane 3.4g. (0.08m.) in 120 ml. dry ether and the reaction mixture was allowed to stand overnight. Evaporation of the ether under reduced pressure gave the diazoketone as a semi-solid yellow oil.

I. R. SPECTRUM. 2100cm.$^{-1}$(s) (-CHN_2) 1620, 1710cm.$^{-1}$(s) (C = O)

A solution of this yellow solid in absolute methanol (80 ml.) was added to a mixture of absolute methanol (60 ml.) and silver oxide (750mg.) which had been previously boiled until a silver mirror formed. The mixture was refluxed for 30 minutes, another portion of silver oxide (750 mg.) added, and heating continued for a total of $2\frac{1}{2}$ hours. Upon cooling, the reaction mixture was filtered through celite and the methanol evaporated under reduced pressure to yield an oil which was chromatographed on a short column of alumina to give the diacetic acid ester as an oil which solidified on standing and was recrystallised from methanol.

m.p. 100-105°.

Yield. 3g. (52%)

ANALYSIS: $C_{22}H_{24}O_4$ requs. C:75.0% H:6.8%

found. C:74.0% H:6.65%

Hydrolysis of this diester in a 20% sodium hydroxide solution in a 1/1 ethanol/water mixture gave a quantitative yield of the diacetic acid .

m.p. 188-190° (benzene/petrol-ether)

CYCLISATION OF 1, 3-DIPHENYLCYCLOBUTANE- 2, 4-DIACETIC ACID. (CLXXX)

The diacetic acid (CLXXX) 1g. (0.0031m.) was allowed to stand in excess (15ml.) hydrogen fluoride for 24 hours and then the excess was allowed to evaporate off. The residue was extracted into benzene (50 ml.) and washed with dilute alkali. The benzene extract was dried and reduced to small volume before chromatography on a short column of alumina with ether as eluant. A solid was obtained which was recrystallised from ethanol in small prisms.

m.p. 184°.

Yield. 0.42g. (47%)

I. R. SPECTRUM. 1678cm.$^{-1}$(s) (C = O)

ANALYSIS: $C_{20}H_{16}O_2$ requs. C:83.3% H:5.55%

found. C:83.4% H:6.0%

ATTEMPTED PREPARATION OF 5, 11 - DIHDROXYDIBENZO [a,g] BIPHENYLENE (CLXXXII)

N-Bromosuccinimide 0.62g. (0.0035m.) and dibenzoylperoxide 10mg. were refluxed in 20 ml. carbontetrachloride containing 0.5g. (0.00175m.) diketone CLXXXI. After three hours, the resulting succinimide was filtered off and the solvent was removed under reduced pressure. The residual brown oil was taken up in 15 ml. ethanol containing two drops of pyridine and the solution was boiled for three hours. Most of ethanol was then distilled off and water was added. The mixture was extracted with ether and the ethereal solution was itself extracted with sodium carbonate solution. Acidification of the basic solution gave no organic material.

The experiment was repeated using potassium acetate in place of pyridine, and allowing the mixture to stand at room temperature for 4 days. On working up as above, an oil was obtained on acidification of the basic layer.

I. R. SPECTRUM. 1670cm.$^{-1}$(s) (C = O)

No hydroxyl absorption.

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Bob Morris